SHIPMAN & GOODWIN LLP®

COUNSELORS AT LAW

31901

Joan W. Feldman
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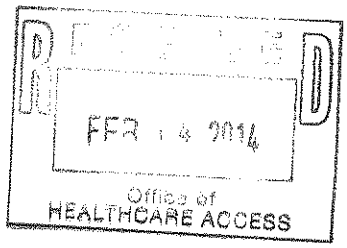
Jfeldman@goodwin.com

February 14, 2014



Kimberly Martone
Director of Operations
Department of Public Health
Office of Health Care Access
410 Capital Avenue, MS#13 HCA
P.O. Box 340308
Hartford, Connecticut 06134-0308

Re: Certificate of Need Application: Acquisition of 3T MRI

Dear Ms. Martone:

On behalf of Hartford Hospital, enclosed please find a Certificate of Need Application for the acquisition of a 3T MRI. As requested, I have included 1 original and 4 hard copies of the Application in 3-ring binders along with a CD with the electronic version of the enclosed documents and materials. Also attached to this letter is a check in the amount of $500.00 for the filing fee.

Please do not hesitate to contact me at 860-251-5104 if you have any questions.

Sincerely,

Joan W. Feldman

Enclosures

3253442v1

Application Checklist

Instructions:

1. **Please check each box below, as appropriate; and**
2. **The completed checklist *must* be submitted as the first page of the CON application.**

☒ **Attached is the CON application filing fee in the form of a certified, cashier or business check made out to the "Treasurer State of Connecticut" in the amount of $500.**

For OHCA Use Only:

Docket No.: 14-31901 **Check No.:** 489185

OHCA Verified by: KR **Date:** 2/18

☒ **Attached is evidence demonstrating that public notice has been published in a suitable newspaper that relates to the location of the proposal, 3 days in a row, at least 20 days prior to the submission of the CON application to OHCA. (*OHCA requests that the Applicant fax a courtesy copy to OHCA (860) 418-7053, at the time of the publication)***

☒ **Attached is a paginated hard copy of the CON application including a completed affidavit, signed and notarized by the appropriate individuals.**

☒ **Attached are completed Financial Attachments I and II.**

☒ **Submission includes one (1) original and four (4) hard copies with each set placed in 3-ring binders.**

Note: A CON application may be filed with OHCA electronically through email, if the total number of pages submitted is 50 pages or less. In this case, the CON Application must be emailed to ohca@ct.gov.

Important: For CON applications(less than 50 pages) filed electronically through email, the singed affidavit and the check in the amount of $500 must be delivered to OHCA in hardcopy.

☒ **The following have been submitted on a CD**

1. **A scanned copy of each submission in its entirety, including all attachments in Adobe (.pdf) format.**
2. **An electronic copy of the documents in MS Word and MS Excel as appropriate.**

AFFIDAVIT

Applicant: **Hartford Hospital, Olin Center for Neuropsychiatry Research**

Project Title: **Acquisition of a Siemens Skyra 3T MRI**

I, **Stuart Markowitz, Chief Executive Officer**

of **Hartford Hospital**, being duly sworn, depose and state that
(Hospital or Facility Name)

Hartford Hospital's information submitted in this Certificate of
(Hospital or Facility Name)

Need Application is accurate and correct to the best of my knowledge.

Stuart Markowitz
Signature

1-28-14
Date

Subscribed and sworn to before me on 1-28-14

Florence M. Leishman

Notary Public/Commissioner of Superior Court

My commission expires: 5-31-18

HARTFORD HOSPITAL
ATTN: ACCOUNTS PAYABLE
PO BOX 5037
HARTFORD, CT 06102-5037

51-57
119

Check Number
489185
Bank of America

THE FACE OF THIS DOCUMENT HAS A COLORED BACKGROUND ON WHITE PAPER

Five hundred and 00/100 Dollars

Pay to the order of

TREASURER STATE OF CONNECTICUT
DEPT OF PUBLIC HEALTH
DIV. OF HEALTH SYSTEMS REGULATIONS
PO BOX 1080
HARTFORD, CT 06143-1080

Date	Payment Amount
02/07/2014	******$500.00

VOID AFTER 90 DAYS

THE BACK OF THIS DOCUMENT CONTAINS LAID LINES AND AN ARTIFICIAL WATERMARK. HOLD AT AN ANGLE TO VIEW.

TREASURER STATE OF CONNECTICUT
DEPT OF PUBLIC HEALTH
DIV. OF HEALTH SYSTEMS REGULATIONS
PO BOX 1080
HARTFORD, CT 06143-1080

Entity	Vendor ID / Location	Check Number
PNK	08112 010	489185

HARTFORD HOSPITAL

Invoice Number	Invoice Date	Gross Amount	Discount Amount	Withholding Amount	Net Amount
FILING FEE CON APPL BARBARA DURDY HHC PLANNING X24231	01/20/2014	500.00			500.00

0003 (02/14/14)

HH571485 1/03

TOTALS	$500.00	0.00	0.00	$500.00

The Hartford Courant.

A TRIBUNE PUBLISHING COMPANY

Affidavit of Publication

State of Connecticut

Thursday, November 21, 2013

County of Hartford

I, Claire Blissett, do solemnly swear that I am Sales Assistant of the Hartford Courant, printed and published daily, in the state of Connecticut and that from my own personal knowledge and reference to the files of said publication the advertisement of Public Notice was inserted in the regular edition.

On date as follows: 11/19/2013 11/20/2013 11/21/2013

In the amount of $146.18

Mintz & Hoke

ZONE 6

Claire Blissett

Sales Assistant
Claire Blissett

Subscribed and sworn to before me November 21, 2013

Renee N Janes

Notary Public

RENEE N. JANES
NOTARY PUBLIC
MY COMMISSION EXPIRES MAR. 31, 2018

2565614

HARTFORD COURANT PROOF

Customer: MINTZ & HOKE
Contact: KELLIE TRALLI Phone: 8606799737

Ad Number: **2565614**
Insert Dates: 11/19/2013 11/20/2013 11/21/2013

Price: 146.18
Section: ROP Class: 8584; TM6 ZONED LEGALSSize: 1 x 2.00
Printed By: CBLISSETT Date: 11/21/2013

Signature of Approval:_____ Date:_____

Public Notice
Filing for Hartford Hospital
Institute of Living
Olin Center 3T MRI

Statutory Reference: Connecticut General Statutes §19a-638

Applicant: Hartford Hospital Institute of Living

Project Address: Located at the Hartford Hospital Olin Neuropsychiatry Research Center, 400 Washington Street, Hartford, CT 06114

Proposal: The Applicant intends to file a Certificate of Need application with the State of Connecticut Office of Health Care Access for the purchase of a 3T MRI.

Capital Expenditure: $3,000,000

PUBLIC NOTICES

Public Notice
Filing for Hartford Hospital Institute of Living Olin Center 3T MRI

Statutory Reference: Connecticut General Statutes §19a-638

Applicant: Hartford Hospital Institute of Living

Project Address: Located at the Hartford Hospital Olin Neuropsychiatry Research Center, 400 Washington Street, Hartford, CT 06114

Proposal: The Applicant intends to file a Certificate of Need application with the State of Connecticut Office of Health Care Access for the purchase of a 3T MRI.

Capital Expenditure: $3,000,000

NOTICE TO CREDITORS

ESTATE OF Beryl Duncan, Deceased, Late of Wethersfield, Connecticut (13-0667)

The Hon. Robert A. Randich, Judge of the Court of Probate, Newington Probate District, by decree dated November 8, 2013, ordered that all claims must be presented to the fiduciary at the address below. Failure to promptly present any such claim may result in the loss of rights to recover on such claim.

Linda Stevens-Nadeau, Clerk

The fiduciary is:
Linda Avery, 39 Ox Yoke Drive, Wethersfield, CT 06109

NOTICE TO CREDITORS

ESTATE OF Jay B. Roberts, Jr., Late of West Hartford, AKA Jay B. Roberts (13-0688)

The Hon. Sydney W. Elkin, Judge of the Court of Probate, West Hartford Probate District, by decree dated November 19, 2013, ordered that all claims must be presented to the fiduciary at the address below. Failure to promptly present any such claim may result in the loss of rights to recover on such claim.

James Felice, Clerk

The fiduciary is:
Judith G. Roberts
c/o Jeffrey W. Stein, Esq., 28 North Main Street, Suite G-01, West Hartford, CT 06107-1928

NOTICE

A public sale of the contents of the storage units listed below will take place on December 5th, 2013 at 2:30PM. This sale will take place at CubeSmart, 522 Cottage Grove Rd, Bloomfield, CT 06002. Each space will be sold as one lot. All items in storage units contain household items unless otherwise mentioned.

337 Robin C Johnson
535 Jackie D Wilson
306 Kellee Ann Turnipseed
9 Wright Consulting Service LLC

NOTICE TO CREDITORS

ESTATE OF Julia Ann Johnson, Late of Newingotn, CT., deceased, AKA Julia Anna Johnson (13-0688)

The Hon. Robert A. Randich, Judge of the Court of Probate, Newington Probate District, by decree dated November 18, 2013, ordered that all claims must be presented to the fiduciary at the address below. Failure to promptly present any such claim may result in the loss of rights to recover on such claim.

Pamela B. Friedeberg, Clerk

The fiduciary is:
Carl J. Johnson, 108 Spring Street, Hopkinton, MA 01748-1516

NOTICE TO CREDITORS

ESTATE OF Mildred F. Skinner, Late of West Hartford (13-0683)

The Hon. Sydney W. Elkin, Judge of the Court of Probate, West Hartford Probate District, by decree dated November 19, 2013, ordered that all claims must be presented to the fiduciary at the address below. Failure to promptly present any such claim may result in the loss of rights to recover on such claim.

James Felice, Clerk

The fiduciary is:
Barbara S. Bourn
c/o Jo-Ellen Z. Jagos, Esquire, BBA&D, 664 Farmington Avenue, Hartford, CT 06105

LEGAL NOTICE
TOWN OF BLOOMFIELD
INLAND WETLANDS & WATERCOURSES COMMISSION

Notice is hereby given that the Inland Wetlands and Watercourses Commission, at a meeting held on November 18, 2013, rendered the following decisions:

1.Approved Calendar of Meetings for 2014.

2.Approval minutes of September 16, 2013 meeting.

5.Wetlands Agent permits: 219 Terry Plains Road & 1000 Mountain Road.

Dated at Bloomfield, Connecticut this 19th day of November, 2013.

INLAND WETLANDS & WATERCOURSES COMMISSION

Nicholas Panke, Chairman

NOTICE TO CREDITORS

ESTATE OF Martin C. Maznio, Late of Rocky Hill, CT., deceased, AKA Martin Casmir Maznio (13-0725)

The Hon. Robert A. Randich, Judge of the Court of Probate, Newington Probate District, by decree dated November 18, 2013, ordered that all claims must be presented to the fiduciary at the address below. Failure to promptly present any such claim may result in the loss of rights to recover on such claim.

Pamela B. Friedeberg, Clerk

The fiduciary is:
M. Michael Maznio, 33 Dogwood Court, Rocky Hill, CT 06067

NOTICE TO CREDITORS

ESTATE OF Nataliya Molchanov, late of West Hartford (13-0658)

The Hon. Sydney W. Elkin, Judge of the Court of Probate, West Hartford Probate District, by decree dated November 19, 2013, ordered that all claims must be presented to the fiduciary at the address below. Failure to promptly present any such claim may result in the loss of rights to recover on such claim.

James Felice, Clerk

The fiduciary is:
Dmitriy Molchanov, 342 East 55th Street, Apt 5C, New York, NY 10022

NOTICE TO CREDITORS

ESTATE OF Zigford J. Kriss, late of West Hartford (13-0570)

The Hon. Sydney W. Elkin, Judge of the Court of Probate, West Hartford Probate District, by decree dated November 18, 2013, ordered that all claims must be presented to the fiduciary at the address below. Failure to promptly present any such claim may result in the loss of rights to recover on such claim.

James Felice, Clerk

The fiduciary is:
Lorraine L. Powers, 14 Emily Way, West Hartford, CT 06107

PUBLIC HEARING LEGAL NOTICE
TOWN OF EAST GRANBY
CONSERVATION COMMISSION
INLAND/WETLANDS & WATER COURSE AGENCY

The East Granby Conservation Commission and Inland/Wetland Watercourse Agency will hold a public hearing on Wednesday December 4, 2013 at 7:30 p.m. in the Senior/Community Center at 20 Center Street concerning the following: Application #CC-13-05 by Craig Timpson/Galasso Materials LLC to perform a significant activity within a wetland and/or watercourse for property at 60 South Main Street to allow for a southerly extension of the quarry. At this hearing, interested persons may appear and be heard and written communications will be received. This application is on file in its entirety and may be seen in the office of the Building Department. Dated in East Granby, Connecticut, this 15th day of November, 2013.

George Cornelius, Chairman

0006 (02/14/14)

State of Connecticut
Office of Health Care Access
Certificate of Need Application

Instructions: Please complete all sections of the Certificate of Need ("CON") application. If any section or question is not relevant to your project, a response of "Not Applicable" may be deemed an acceptable answer. If there is more than one applicant, identify the name and all contact information for each applicant. OHCA will assign a Docket Number to the CON application once the application is received by OHCA.

Docket Number:

Applicant:	Hartford Hospital, Olin Center for Neuropsychiatry Research
Contact Person:	Barbara A. Durdy
Contact Person's Title:	Director, Strategic Planning Hartford HealthCare
Contact Person's Address:	181 Patricia M. Genova Blvd, Newington, CT 06111
Contact Person's Phone Number:	860-972-4231
Contact Person's Fax Number:	860-972-9025
Contact Person's Email Address:	barbara.durdy@hhchealth.org
Project Town:	Hartford
Project Name:	Acquisition of 3T MRI
Statute Reference:	Section 19a-638, C.G.S.
Estimated Total Capital Expenditure:	$3,342,905

1. Project Description: Acquisition of Equipment

a. Please provide a narrative detailing the proposal.

The Institute of Living (the "IOL") was one of the first mental health centers in the United States, and the first hospital of any kind in Connecticut. Today, as a Division of Hartford Hospital (the "Hospital"), it is one of America's leading not-for-profit centers for comprehensive patient care, research and education in the fields of behavioral, psychiatric, and addiction disorders. The Olin Center for Neuropsychiatry Research (the "Olin Center") is an integral component of the IOL and is foundational to the application of translational research into clinical practice.

The Olin Center was founded in 2002. The mission of the Olin Center is to be at the forefront of research in brain disorders. Techniques employed by Olin Center faculty include functional, structural, and spectroscopic magnetic resonance imaging ("MRI"), electrophysiology ("EEG", "ERP"s), and transcranial magnetic stimulation ("TMS").

The Olin Center is directed by Dr. Godfrey Pearlson, Founding Director of the Olin Center. The Olin Center currently has ongoing research studies in the areas of cognitive function including normal aging, working and long term memory, error monitoring, language and attention. In addition, the Olin Center is also currently involved in research on multiple neuropsychiatric diseases including depression, schizophrenia, Alzheimer's disease, manic-depressive illness, and alcohol/drug abuse, further details of which are provided later.

The Olin Center is supported by a number of grants from the National Institute of Health, National Institute of Mental Health, National Institute of Neurologic Disorders and Stroke, National Institute on Aging, and National Institute on Drug Abuse. The Olin Center faculty provides education, mentorship and training for undergraduate, graduate, and postdoctoral fellows with interests in neurosciences and behavioral health.

The Olin Center has received over approximately Thirty Five Million Dollars ($35,000,000) in federal and private foundation research grants and has grown from a five person enterprise at its inception in 2002 to a research center with greater than fifty-five employees. Due to the increasing volume of funded research and limitations of the current imaging equipment in use at the Olin Center, the Hospital purchased an additional 3T MRI scanner on September 27, 2012 to be used for research purposes at the Olin Center.

Until most recently, the Olin Center had only used a Siemens Allegra 3T MRI scanner (the "Allegra 3T") to conduct research studies on a broad array of research projects including those funded by the National Institute of Health, Brain and Behavior Research Foundation (formerly National Alliance for Research on Schizophrenia and Depression, NARSAD), the Donaghue Foundation, Autism Speaks and several other well-known organizations.

However, over the past several years, the scale and type of research conducted by the Olin Center has grown substantially creating a need for enhanced technological capacity and cutting edge imaging. Unfortunately, we have learned that the Allegra 3T will not undergo any further development by Siemens and thus, no parallel imaging coil is or will be available for this equipment. Thus, because the head coil will not be updated, the coil will lag technologically and scan times will be prolonged in comparison to state-of-the-art MRI imaging. Prolonged image acquisition times are a problem for restless children/teenagers, claustrophobic patients, research subjects with ADHD and anxiety disorders, anxious/paranoid patients with major mental illnesses, and patients with drug-induced restlessness, who collectively constitute the majority of the research subject population. These patients either move excessively in the scanner creating artifacts, want to get out of the scanner as quickly as possible, or both. Accordingly, prolonged times in the scanner can interfere with the quality of the information and data obtained. In addition, the Hospital has been notified by the manufacturer of the Allegra 3T that maintenance is only guaranteed until December 31, 2016.

In furtherance of its clinical research purposes and in order to maintain state of the art imaging at the Olin Center, the Hospital purchased a Siemens Skyra 3T MRI scanner (the "Skyra 3T") equipped with the technological capacity required for advanced research studies as a replacement for the Allegra 3T. This new platform provides access to additional neuroimaging techniques (e.g. MRS, DTI, ASL) that facilitate existing studies and enables scanning new types of subjects.

The new Skyra 3T will be used for structural and functional magnetic resonance imaging ("fMRI") research and is equipped with parallel-coil imaging, which produces excellent quality images with significantly shortened acquisition time without compromising the ability to acquire meaningful data (e.g, whole brain BOLD sampling at a faster effective rate to preserve ability to resolve signal-to-noise in shorter modeled fMRI time series). The fMRI technology uses a combination of a magnet and radio frequencies to study oxygen flow and metabolism in areas of the brain. More specifically, fMRI shows the researcher where the blood is rich in oxygen and where it is not, resulting in images which help in the diagnosis and understanding of disorders related to speech, hearing, vision and motor skills.[1]

> Conventional MRI uses a powerful magnet and radio waves to safely and noninvasively produce images of the brain or other structures inside your body. In the early 1990s, researchers thought up a new way to use this imaging technology: as a research tool rather than a diagnostic method. Putting the "f" in fMRI, these researchers focus on function. Using an MRI scanner, they monitor the flow of blood to different regions of the brain as their research subjects respond to a specific stimulus—a sound, an image, even a touch. While conventional MRI results in snapshots of what's inside the body, fMRI produces movies starring the brain.[2]

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[1] See http://www.technologyreview.com/article/401111/functional-mri/.
[2] See http://www.apa.org/research/tools/fmri-adult.pdf.

As represented in the Determination letter dated August 19, 2013, the Hospital originally intended that this new Skyra 3T scanner would replace the existing Allegra 3T scanner as gradually and overtime all on-going research studies would be transitioned to the Skyra 3T. As the transition period for on-going research would extend through May 2016, because a number of the Olin Center's ongoing studies are longitudinal in nature and must be conducted over time on exactly the same scanner as used originally. This is because the slight differences in brain function due for example to progression of the disease would be overwhelmed by the differences in signal if the patient were imaged on different scanners at different times. Thus, the Office of Health Care Access requested that the Hospital file a Certificate of Need Application for the acquisition of the Skyra 3T.

Since filing the Determination letter with OHCA, the volume of anticipated and applied for funded research at the Olin Center has increased by over 60%. Please see Table A below for the Olin Center's current and pending research studies. Thus, it has become apparent to the Olin Center that two (2) MRI scanners are required to handle the ongoing research volume at the Olin Center. Accordingly, the Hospital would like not to take the existing Allegra 3T off-line as originally planned.

b. Provide letters that have been received in support of the proposal.

Please see Exhibit 1 for letters of support from Dr. Godfrey Pearlson, Founding Director Olin Center for Neuropsychiatry Research and from Dr. Harold Schwartz, Vice President, Behavioral Health, Hartford HealthCare.

c. Provide the Manufacturer, Model, Number of slices/tesla strength of the proposed scanner (as appropriate to each piece of equipment).

The Hospital purchased a Siemens Skyra 3T MRI for use at the Olin Center. A copy of the vendor invoice is attached as Exhibit 2.

d. List each of the Applicant's sites and the imaging modalities and other services currently offered by location.

Neuropsychiatry research at the Hospital is conducted at the Olin Center located at the IOL, 400 Washington Street, Hartford, CT. There are two MRI scanners at the Olin Center; the Allegra 3T and the newly purchased Skyra 3T MRI scanner.

2. Clear Public Need

a. Explain why there is a clear public need for the proposed equipment. Provide evidence that demonstrates this need.

The need for a second MRI at the Olin Center is based on the following factors:

1. Increase in the number of funded research studies and the inability to accommodate all on-going studies with one MRI.

2. Obsolescence of the existing Allegra 3T scanner.

Increase in the Number of Funded Research Studies

In the last several years, the number of scientific research projects at the Olin Center has grown substantially. For example, research studies have included a 2000-person study of alcoholism in college students, a 700-person study of psychosis endophenotypes, and a 325-person study of imaging endophenotypes of bipolar disorder. Due to the Olin Center's success in these endeavors and due to the need for additional technical capability, the Olin Center is in need of a second scanner equipped with cutting-edge imaging technology to support the ongoing growth and scientific productivity.

The number of MRI research subject slots available per week on one scanner is twenty-five (25). Typical slots are 1.5 to 3 hours. As set forth in Table A below, the Olin Center is currently operating at levels beyond capacity for one machine.

Table A

Hartford Hospital, Olin Center for Neuropsychiatry Research
Table of Current and Pending Research Studies
MRI Utilization

	MRI Utilization Number of slots/Week	ALLEGRA	SKYRA
Current Research Study			
UCONN Steffens	2		2
Tolin Hoarding	1		1
College Alcohol	2	2	
Pearlson PARDIP Bipolar Study	2	2	
HH Obesity	3		3
Assaf Autism/Schizophrenia	2		2
Yale CTNA	4	4	
Glahn Bipolar	1		1
Pearlson Psychosis NIMH MERIT Award	2	2	
Pearlson COG Rehab	1	1	
HH Neurosurgery	0.5		0.5
HH Cardiology/Lipid	1	1	
UCONN MJ	1		1
UCONN HIV Exercise	1	1	
Karen Blank Alzheimer	2		2
HH Cardiology Alzheimer	0.5		0.5
QC Studies	4	2	2
TOTAL CURRENT	**30**	**15**	**15**
Pending NIH Grants			
PearlsonAlcohol/Driving #2	3		3
Stevens Emotion Adolescence	2	2	
Pearlson BSNIP-2	3		3
Oncology/Chemo-Memory	2	2	
Pearlson/Stevens Driving MJ	1.5		1.5
Stevens/Pearlson ADHD	1	1	
Pearlson/Stevens Affective	1		1
Skudlarski	0.5	0.5	
Dager K Award (Spectro)	1		1
Glahn UO1	3		3
Stevens/Pearlson- Driving Alcohol	1		1
TOTAL PENDING	19	5.5	13.5
TOTAL SLOTS, CURRENT PLUS PENDING GRANTS	**49**	**20.5**	**28.5**

Table A portrays current and projected future MRI scanner utilization. As noted above, one scanner running five (5) days a week provides capacity for twenty-five (25) total subject slots per/week. Currently, the Olin Center is running above capacity for one machine with an average demand of thirty (30) subject slots per week. With multiple new grants pending, the need for the second MRI scanner is essential to the research being conducted by the Olin Center.

The Olin Center currently supports multiple NIH-funded research projects (including sub-contracted studies from other institutions and the Hospital) and funded research sponsored by NARSAD, the Donaghue Foundation, Autism Speaks and other local funders, including Hartford Hospital open competition grants. There are several proposals currently submitted to NIH from Olin Center investigators awaiting funding decisions. Current funding from primary projects and from collaborator subcontracts represents a broad array of research ranging from schizophrenia, bipolar disorder, alcohol, cannabis and cocaine abuse, autism spectrum disorders, Alzheimer's disease, multiple disease endophenotypes, normal adolescent brain development, ADHD, pathological hoarding, OCD, conduct disorder, exercise, and other topics. Without additional MRI scanner capacity, the Olin Center will not able to conduct additional large-scale projects, or to support further planned research studies. With only one scanner operating at full capacity, attracting additional faculty to the Olin Center would be impossible because there is insufficient capacity for research with one scanner.

Obsolescence of the existing Allegra 3T scanner

As previously stated, the Hospital has been notified by the vendor that maintenance on the existing Allegra 3T scanner is only available until December 31, 2016. The Allegra 3T will not undergo any further development by Siemens and no parallel imaging coil will be developed for this equipment. Consequently, the Allegra 3T is rapidly becoming obsolete and substandard for the Olin Center's clinical research purposes and mission. Imaging times are substantially longer with the current Allegra 3T scanner due to the substandard head coil system. This is a problem for children and teenagers, claustrophobic patients, subjects with ADHD and anxiety disorders and anxious/paranoid patients with major mental illnesses and patients with drug-induced restlessness, who collectively constitute the majority of the subject population at the Olin Center. These patients either move excessively in the scanner creating artifacts, want to get out of the scanner as quickly as possible, or both. An effective solution to greatly mitigate these problems was the acquisition of a second scanner with parallel-coil imaging, which produces excellent quality images with significantly shortened imaging time without compromising the ability to acquire meaningful data (e.g, whole brain BOLD sampling at a faster effective rate to preserve ability to resolve signal-to-noise in shorter modeled fMRI time series).

The proposed MRI will be used for functional magnetic resonance imaging ("fMRI") research. Newer systems like the Skyra 3T offer software options for online movement visualization or correction, and/or methods for real-time fMRI modeling to ensure data quality for research participant groups who are hard to recruit, or who refuse to be re-scanned in an additional session should they provide poor data because of movement.

Relatively few researchers use the Allegra 3T worldwide, and Siemens research development group does not focus on pulse sequence development for this platform. Therefore, many new developments in functional neuroimaging are difficult, if not technologically impossible to implement on the Allegra 3T. Due to the technological limitations of the Allegra 3T, the Allegra 3T will increasingly become "out-of-step" with techniques used by other neuroimaging researchers. This will decrease the likelihood of Olin Center investigators participating in future multi-site projects, which have become a valuable tool to increase the pace and impact of NIH-sponsored neuropsychiatric research.

The new Skyra 3T platform (i) provides access to additional neuroimaging techniques (e.g., MRS, DTI, ASL) that facilitates existing projects, (ii) enables scanning of new types of subjects and new body areas not possible with the original Allega 3T scanner (whole body scans, obese subjects), allowing us to be more competitive for NIH federal research grants, and (c) to stay at the cutting-edge of the neuroscience field.

Over the past several years, the scale and type of research conducted by the Olin Center has grown substantially. For example, recently the Olin Center was funded by the Hartford Healthcare Corporation in a collaboration with the Hospital's Bariatric Surgical Group, to scan one hundred (100) extremely obese patients (e.g. some weighing between 300 and 450 pounds), prior to and twelve months post bariatric surgical procedures, along with thirty (30) patients of healthy weight, to assess brain changes in order to predict surgical success and brain adaptations to food and reward stimuli following surgery. These patients can only be accommodated in a special whole-body large-bore scanner such as the Skyra 3T, as the Allegra 3T scanner is a brain-only narrow bore MRI scanner; the maximum weight of subjects it can accommodate is approximately 250 pounds.

Current research protocol requires a variety of MR techniques, including structural MRI, DTI, BOLD fMRI, ASL, proton spectroscopy and angiography. The new Skyra 3T platform allows the Olin Center to accommodate the various MR techniques required under current protocols. Many of the proposals integrate numerous other scientific techniques, including PET scanning, pharmacologic challenges, genotyping, EEG/ERP, oculomotor assessments, and sensorimotor gating. The MRI resources at the Olin Center are frequently used synergistically with other neuroscience research techniques, building on the faculty of the Olin Center's expertise in multimodal data integration. The addition of the new Skyra 3T permits expansion of research capabilities and furthers the Olin Center's development plan allowing for the recruitment of an additional one to three new scientists over the next 3 years. Without the new Skyra 3T scanner, such expansion plans would be constrained due to capacity limitations.

b. Provide the utilization of existing health care facilities and health care services in the Applicant's service area.

The Olin Center is the only neuropsychiatry research facility within the Hospitals' service area.

c. Complete Table 1 for each piece of equipment of the type proposed currently operated by the Applicant at each of the Applicant's sites.

Table 1: Existing Equipment Operated by the Applicant

Provider Name Street Address Town, Zip Code	Description of Service *	Hours/Days of Operation **	Utilization *** FY 2013
The Olin Center for Neuropsychiatry Research 400 Washington Street Hartford, CT 06110	Closed Allegra 3T MRI	Monday through Friday 9am -7pm	583
The Olin Center for Neuropsychiatry Research 400 Washington Street Hartford, CT 06110	Closed Skyra 3T MRI	Monday through Friday 9am -7pm	183

* Include equipment strength (e.g. slices, tesla strength), whether the unit is open or closed (for MRI)
** Days of the week unit is operational, and start and end time for each day; and
*** Number of scans/exams performed on each unit for the most recent 12-month period (identify period).

d. Provide the following regarding the proposal's location:

i. The rationale for locating the proposed equipment at the proposed site;

The Skyra 3T is located at the Olin Center on the IOL's campus because the studies relate to mental disorders.

ii. The population to be served, including specific evidence such as incidence, prevalence, or other demographic data that demonstrates need;

The Skyra 3T will be used for neuroscience research activities. As such, the patient population is comprised of research study participants as described in detail above. To the extent that there is any available capacity, the Skyra 3T may be used for clinical patients who require a wide-bore scanner; provided, however, such use is expected to be limited to no more than ten (10%) percent of capacity.

iii. How and where the proposed patient population is currently being served;

Neuropsychiatry research is currently conducted at the Olin Center using an Allegra 3T scanner and the new Skyra 3T scanner.

iv. All existing providers (name, address) of the proposed service in the towns listed above and in nearby towns;

N/A.

v. The effect of the proposal on existing providers; and

N/A.

vi. If the proposal involves a new site of service, identify the service area towns and the basis for their selection.

N/A.

e. Explain why the proposal will not result in an unnecessary duplication of existing or approved health care services.

The Skyra 3T will be used primarily for neuroscience research activities as described in the narrative above.

3. Actual and Projected Volume

a. Complete the following tables for the past three fiscal years ("FY"), current fiscal year ("CFY"), and first three projected FYs of the proposal, for each of the Applicant's existing and proposed pieces of equipment (of the type proposed, at the proposed location only). In Table 2a, report the units of service by piece of equipment, and in Table 2b, report the units of service by type of exam (e.g. if specializing in orthopedic, neurosurgery, or if there are scans that can be performed on the proposed scanner that the Applicant is unable to perform on its existing scanners).

Table 2a: Historical, Current, and Projected Volume, by Equipment Unit

	Actual Volume (Last 3 Completed FYs)			**CFY Volume***	**Projected Volume (First 3 Full Operational FYs)****		
	FY 2011	FY 2012	FY 2013	FY2014 (3 months) FYTD December 2013	FY 2015	FY 2016	FY 2017
Allegra 3T MRI	914	698	583	72	TBD- pending Grant approval (please see response to 3.e. below)		
Skyra 3T MRI	N/A	N/A	183	108	TBD- pending Grant approval (please see response to 3.e. below)		
Total	**914**	**698**	**766**	**180**			

* For periods greater than 6 months, report annualized volume, identifying the number of actual months covered and the method of annualizing. For periods less than six months, report actual volume and identify the period covered.
** If the first year of the proposal is only a partial year, provide the first partial year and then the first three full FYs. Add columns as necessary.
*** Identify each scanner separately and add lines as necessary. Also break out inpatient/outpatient/ED volumes if applicable.
**** Fill in years. In a footnote, identify the period covered by the Applicant's FY (e.g. July 1-June 30, calendar year, etc.). **Please note that the period covered by the Applicant's FY is Oct. 1 - Sept. 30).**

Table 2b: Historical, Current, and Projected Volume, by Type of Scan/Exam

	Actual Volume (Last 3 Completed FYs)			CFY Volume*	Projected Volume (First 3 Full Operational FYs)**		
	FY2011	FY 2012	FY 2013	FY2014 (3 months) FYTD December 2013.	FY 2015	FY 2016	FY 2017
Allegra pre-surgical brain mapping	14	25	17	4	TBD- pending Grant approval (please see response to 3.e. below)		
Allegra Functional brain scans	900	673	566	68	TBD- pending Grant approval (please see response to 3.e. below)		
Skyra Functional brain scans	N/A	N/A	183	108	TBD- pending Grant approval (please see response to 3.e. below)		
Total	**914**	**698**	**766**	**180**			

* For periods greater than 6 months, report annualized volume, identifying the number of actual months covered and the method of annualizing. For periods less than six months, report actual volume and identify the period covered.
** If the first year of the proposal is only a partial year, provide the first partial year and then the first three full FYs. Add columns as necessary.
*** Identify each type of scan/exam (e.g. orthopedic, neurosurgery or if there are scans/exams that can be performed on the proposed piece of equipment that the Applicant is unable to perform on its existing equipment) and add lines as necessary.
**** Fill in years. In a footnote, identify the period covered by the Applicant's FY (e.g. July 1-June 30, calendar year, etc.). **Please note that the period covered by the Applicant's FY is Oct. 1 - Sept. 30).**

b. Provide a breakdown, by town, of the volumes provided in Table 2a for the most recently completed full FY.

Patient town of origin for research subjects is not available. Patient subject demographic information is not collected for reporting purposes.

c. Describe existing referral patterns in the area to be served by the proposal.

N/A.

d. Explain how the existing referral patterns will be affected by the proposal.

N/A.

e. Explain any increases and/or decreases in volume seen in the tables above.

First, projected volume for FYs 2015, 2016, and 2017 cannot be accurately provided for Tables 2a and 2b above as such volumes are dependent upon the approval of the Olin Center's pending research grant applications. Nevertheless, and as reflected in this Application, the (2) MRI scanners will be required to handle the ongoing and future research volume at the Olin Center. The Olin Center will maximize the usage of both MRI scanners and will continuously apply for research study grants until both MRI scanners are at capacity.

Second, any increases or decreases are based on the completion of research studies and the grant approval and commencement of new research studies.

f. Provide a detailed explanation of all assumptions used in the derivation/ calculation of the projected volume by scanner and scan type.

N/A

g. Provide a copy of any articles, studies, or reports that support the need to acquire the proposed scanner, along with a brief explanation regarding the relevance of the selected articles.

Please see Exhibit 3 for the following studies supporting the Skyra 3T platform for neuropsychiatric research:

1) Toward Discovery Science of Human Brain Function, Proceedings of the National Academy of Sciences, March 9, 2010

   This article discusses the types of MRI scanners required for running state-of-the-art Connectome research sequences for neurosciences in particular the need for fMRI scanning which is possible using the Skyra 3T platform. Connectome is the flagship MRI brain anatomy project. The lead site for these studies is based in Minneapolis and uses a Skyra 3T scanner for these studies.

2) The Human Connectome Project: A data acquisition perspective, National Institute of Health, Neuroimage, October 2012.

   This article discusses the need for fMRI scanning and illustrates the types of brain/gene Connectome projects that the Olin Center runs using the Skyra 3T platform.

4. Quality Measures

a. Submit a list of all key professional, administrative, clinical, and direct service personnel related to the proposal. Attach a copy of their Curriculum Vitae.

Please see Exhibit 4 for copies of curriculum vitae for the key administrative and clinical personnel related to this proposal.

b. Explain how the proposal contributes to the quality of health care delivery in the region.

The proposal contributes to the quality of health care delivery in the region by facilitating the advancement of neuropsychiatry research and clinical practice significantly improving the treatment for behavioral health diagnoses and patient outcomes.

5. Organizational and Financial Information

a. Identify the Applicant's ownership type(s) (e.g. Corporation, PC, LLC, etc.).

Hartford Hospital is a non-profit corporation.

b. Does the Applicant have non-profit status?

☒ Yes (Provide documentation) ☐ No

Please see Exhibit 5 for a copy of the IRS Determination letter for Hartford Hospital

c. Provide a copy of the State of Connecticut, Department of Public Health license(s) currently held by the Applicant and indicate any additional licensure categories being sought in relation to the proposal.

Please see Exhibit 6 attached hereto for a copy of the Hartford Hospital license issued by the Connecticut Department of Public Health. This proposal does not involve any change to licensure.

d. Financial Statements

i. **If the Applicant is a Connecticut hospital: Pursuant to Section 19a-644, C.G.S., each hospital licensed by the Department of Public Health is required to file with OHCA copies of the hospital's audited financial statements. If the hospital has filed its most recently completed fiscal year audited financial statements, the hospital may reference that filing for this proposal.**

Hartford Hospital's most recent audited financial statements are on file with OHCA.

ii. **<u>If the Applicant is not a Connecticut hospital (other health care facilities):</u> Audited financial statements for the most recently completed fiscal year. If audited financial statements do not exist, in lieu of audited financial statements, provide other financial documentation (e.g. unaudited balance sheet, statement of operations, tax return, or other set of books.)**

N/A.

e. Submit a final version of all capital expenditures/costs as follows:

Table 3: Proposed Capital Expenditures/Costs

Medical Equipment Purchase	$
Imaging Equipment Purchase	**$2,116,837**
Non-Medical Equipment Purchase	
Land/Building Purchase *	
Construction/Renovation **	**$1,226,068**
Other Non-Construction (Specify)	
Total Capital Expenditure (TCE)	**$3,342,905**
Medical Equipment Lease (Fair Market Value) ***	$
Imaging Equipment Lease (Fair Market Value) ***	
Non-Medical Equipment Lease (Fair Market Value) ***	
Fair Market Value of Space ***	
Total Capital Cost (TCC)	**$3,342,905**
Total Project Cost (TCE + TCC)	**$3,342,905**
Capitalized Financing Costs (Informational Purpose Only)	
Total Capital Expenditure with Cap. Fin. Costs	**$3,342,905**

** If the proposal involves a land/building purchase, attach a real estate property appraisal including the amount; the useful life of the building; and a schedule of depreciation.*
*** If the proposal involves construction/renovations, attach a description of the proposed building work, including the gross square feet; existing and proposed floor plans; commencement date for the construction/ renovation; completion date of the construction/renovation; and commencement of operations date.*
**** If the proposal involves a capital or operating equipment lease and/or purchase, attach a vendor quote or invoice; schedule of depreciation; useful life of the equipment; and anticipated residual value at the end of the lease or loan term.*

Please see <u>Exhibit 7</u> for a copy of the Olin Building 3T MRI scanner architectural narrative. Please also see <u>Exhibit 2</u> attached hereto for a copy of the invoice.

f. List all funding or financing sources for the proposal and the dollar amount of each. Provide applicable details such as interest rate; term; monthly payment; pledges and funds received to date; letter of interest or approval from a lending institution.

The project has been funded from Applicant's operating capital.

g. Demonstrate how this proposal will affect the financial strength of the state's health care system.

N/A. The Skyra 3T will be used for research purposes.

6. Patient Population Mix: Current and Projected

a. Provide the current and projected patient population mix (based on the number of patients, not based on revenue) with the CON proposal for the proposed program.

N/A. The Skyra 3T MRI will be used for research purposes.

Table 4: Patient Population Mix

	Current** FY ***	Year 1 FY ***	Year 2 FY ***	Year 3 FY ***
Medicare*				
Medicaid*				
CHAMPUS & TriCare				
Total Government				
Commercial Insurers*				
Uninsured				
Workers Compensation				
Total Non-Government				
Total Payer Mix				

* Includes managed care activity.
** New programs may leave the "current" column blank.
*** Fill in years. Ensure the period covered by this table corresponds to the period covered in the projections provided.

b. Provide the basis for/assumptions used to project the patient population mix.

N/A. The Skyra 3T MRI will be used for research purposes.

7. Financial Attachments I & II

a. Provide a summary of revenue, expense, and volume statistics, without the CON project, incremental to the CON project, and with the CON project. Complete Financial Attachment I. (Note that the actual results for the fiscal year reported in the first column must agree with the Applicant's audited financial statements.) The projections must include the first three full fiscal years of the project.

Please see Exhibit 8 for Financial Attachment I.

b. Provide a three year projection of incremental revenue, expense, and volume statistics attributable to the proposal by payer. Complete Financial Attachment II. The projections must include the first three full fiscal years of the project.

Please see Exhibit 9 for Financial Attachment I.

c. Provide the assumptions utilized in developing both Financial Attachments I and II (e.g., full-time equivalents, volume statistics, other expenses, revenue and expense % increases, project commencement of operation date, etc.).

Useful life for depreciation expense has been determined based on a 5 year life for the MRI and 10 year life for the renovation costs. Other expenses have been trended forward based on expected inflationary increases.

	2014	2015	2016	2017
	Total	Total	Total	Total
	FTE	**FTE**	**FTE**	**FTE**
Research Technologist	0.81	0.84	0.87	0.91
Research Assistant II	0.20	0.21	0.21	0.22
MRI Tech	0.47	0.49	0.50	0.53
	1.48	1.53	1.58	1.66

d. Provide documentation or the basis to support the proposed rates for each of the FYs as reported in Financial Attachment II. Provide a copy of the rate schedule for the proposed service(s).

N/A. The Skyra 3T MRI will be used for research purposes.

e. Provide the minimum number of units required to show an incremental gain from operations for each fiscal year.

N/A. The Skyra 3T MRI will be used for research purposes.

f. Explain any projected incremental losses from operations contained in the financial projections that result from the implementation and operation of the CON proposal.

Incremental losses are related to increased depreciation expense.

g. Describe how this proposal is cost effective.

This proposal supports the advancement of science and applied research which leads to greater clinical efficacy and improved outcomes for patients.

EXHIBIT 1

Institute of Living
Hartford Hospital

Yale University

SCHOOL OF MEDICINE
Department of Psychiatry

February 3, 2014

To whom it may concern:

The Olin Neuropsychiatry Research Center at the Institute of Living, (ONRC) part of Hartford Healthcare Corp (HHC), is in the process of replacing its current 11-year old Siemens Allegra MRI scanner with a new 3-Tesla advanced, wide-bore, parallel-coil imaging equipped, Siemens Skyra MRI scanner, installed at the ONRC in a new NIH NCRR-funded building extension.

Acquiring this new instrument helps resolve a cross-institutional need for a suitable research scanner for multidisciplinary, translational research that significantly helps with the Olin Center's growing research needs and HHC's wish to "jump-start" successful funded research across the institution. The ONRC has rapidly evolved over the past 11 years from a small, four-person operation to a productive 55-person research Center scanning in excess of 1200 neuropsychiatric and healthy control subjects per year for numerous NIH- and private research foundation-funded studies.
Collectively, the 5 faculty-level investigators currently have numerous R01 awards (equivalent to several million annual direct costs), publish ~ 50 peer-reviewed papers in top-tier academic journals annually, and direct the training of multiple postdoctoral fellows for research careers of their own. There are many research collaborations within Hartford Hospital / The Institute of Living, but also numerous active projects performed in conjunction with collaborators at nearby institutions (Trinity, Yale, UCHC, CCSU, UConn Storrs & Wesleyan). In addition to collaborative projects within the department of Psychiatry at the Institute of Living, the Olin Center has numerous collaborations with other departments at Hartford Hospital, including NIH funded investigators in Neurology, Cardiology, Neurosurgery, Bariatric Medicine, etc. A particular advantage of the proposed new scanner is that it can image the entire body, not just the brain, as is the case with our current MRI.

In the last several years, the scale of scientific projects at the Olin Center has grown substantially. For example, our funded research studies include a 2000-person study of alcoholism in college students, a 700-person study of psychosis endophenotypes and a 325-person study of imaging endophenotypes of bipolar disorder. Because of our success in these endeavors and due to the need for additional technical capability, we have outgrown our current MRI scanner and are seeking funds to purchase a new one equipped with cutting-edge imaging technology to foster ongoing growth and scientific productivity.

Current funding from primary projects and from collaborator subcontracts represents a broad array of research ranging from pre-surgical mapping in patients with epilepsy and brain tumors, balance disorders in the elderly, schizophrenia, bipolar disorder, alcohol, cannabis and cocaine abuse, autism/autism spectrum disorders, Alzheimer's disease, multiple disease endophenotypes, normal adolescent brain development, ADHD, pathological hoarding, OCD, conduct disorder, exercise, to statin drug effects and other areas. The total requested scan time on the new machine (not counting time on the existing Siemens Allegra) will initially amount to ~ 30 hrs/week. However, the addition of the new MRI will permit us to upgrade our current long-term Olin Center development plan to attract at least 1, up to 3 new mid-career or early career scientists over the next 3 years. Currently, such expansion plans are stifled by the fact that our existing MRI machine is near capacity.

Major limitations of our current instrument, (a Siemens Allegra 3T scanner) are that it runs from 9 AM to 7 PM during the week and most weekend days. An average of >20,000 separate MRI sequences for >1200 research subjects annually are currently collected using our Allegra scanner. Thus, there is little time available for new projects, despite ongoing new funded studies by Olin Research Center principal investigators. In the event of funding for the majority of pending projects over the next year, we will completely outstrip our feasible capacity on the

Institute of Living, Olin Neuropsychiatry Research Center, 200 Retreat Avenue, Hartford, CT 06106
Email: godfrey.pearlson@yale.edu Phone: 860.545.7800 Fax: 860.545.7797

Allegra 3T, and no new projects will be possible. However merely replacing the current scanner with a newer one is not a solution- we have already outstripped the capacity of a single scanner. New studies or non-NIH funded projects (which is true of most pilot projects) are already forced to run in the late evenings when suitable subjects are often hard to schedule or staff are not typically available to support data acquisition. This stifles the ability to rapidly develop new lines of research and keep pace with emerging scientific findings in various fields.

Because many of our MR protocols can be lengthy (typically 1 - 1.5 hrs), more participants can be run in a shorter scan session should we obtain the technological upgrades in speed offered by parallel imaging on the new MR platform. Thus, there will be greater availability of available scan time.

There are limits on types of research participants: The Allegra magnet bore is small. Many of our seriously mentally ill patients take second-generation antipsychotic medications and are obese. We currently need to exclude up to 25 to 30% of otherwise qualifying subjects due to high BMI – up to 150 such otherwise ideal and hard-to-recruit research participants annually. This limitation also excludes the Bariatric Medicine subjects in our funded collaboration with Drs. Tischler and Papasavas from the HHC Surgical Weight Loss Ctr. In addition, the small magnet bore encourages claustrophobia. Not only does this have a general effect on willingness to participate in research, it represents a particular problem in our anxiety disorder patients.

Resolution on the existing MRI magnet is adequate, but no longer state-of-the-art. The new capabilities of the Siemens Skyra 3T scanner such as improved spectroscopy and the ability to scan cardiac and peripheral muscle will result in submission of new research grants during the first budgetary year, both from Olin Center investigators and from collaborators in cardiology, neurology and neurosurgery. Several grants and the Olin Center are due for competitive renewal over the next year or two; having the new scanner in place will position us at a competitive advantage with regard to placement of virtual reality equipment in the scanner, the ability to look at large numbers of subjects in larger scale planned studies and to image new populations. The limited accessibility lengthens set-up time and is not optimal for highly accurate structural measures. There is the continual risk of possible poor data quality as participants shift position within or between scans. The Allegra is a brain-only scanner. We would like to expand our types of MRI-based collaborations, but our scanner limits this. For example, our actively-funded collaborators within Hartford Hospital
would like to examine peripheral and cardiac muscle, for which a full-body scanner is required. Our center has the only research-dedicated MR facility in the local clinical/academic community, making it logical to begin such studies as collaborative ventures at the Olin Research Center without interfering with hospital clinical operations.
Much of the virtual reality equipment that we use for many functional neuroimaging studies (an area in which the Olin Research Center specializes) is ideally accommodated within a large-bore rather than small-bore scanner.

Obsolescence: The 3T Allegra will not undergo further development by Siemens. No parallel imaging coil is or ever will be available for this instrument, so it is slipping behind technologically and scan time is relatively prolonged in comparison to state-of-the-art. Thus, with the current single-coli head coil system imaging times are longer than standard. This is a problem for children/teenagers, claustrophobic patients, subjects with ADHD and anxiety disorders and anxious/paranoid patients with major mental illnesses and patients with drug-induced restlessness, who collectively constitute the majority of our subject population. These patients either move excessively in the scanner creating artifacts, want to get out of scanner as quickly as possible, or both. An effective solution to greatly mitigate these problems is to acquire scanner with parallel-coil imaging, which produces excellent quality images with significantly shortened acquisition time without compromising the ability to acquire meaningful data (e.g, whole brain BOLD sampling at a faster effective rate to preserve ability to resolve signal-to-noise in shorter modeled fMRI time series).

The Skyra has 32 channels, compared to 1 in the existing Allegra. It can therefore acquire images significantly faster, so subjects stay in the scanner for shorter times

Only a handful of investigators now use the Allegra worldwide, and Siemens research development group
does not focus on pulse sequence development for this platform. Therefore, many new developments in functional neuroimaging are difficult, if not technologically impossible to implement on the Allegra. Because of its technological limitations and discontinued development, the Allegra will increasingly become 'out-of-step' with techniques used by other neuroimaging researchers. This will decrease the likelihood of Olin investigators participating in future multi-site projects, which have become a valuable tool to increase the pace and impact of NIH-

sponsored neuropsychiatric research. For all of the above reasons, we need to obtain a new scanner to replace our existing Allegra.

The proposed new instrument will allow our growth trajectory to proceed on track at IOL and continue with job creation. One of the strengths of research at the Olin Center is our ability to perform very large-scale neuroimaging studies where all subjects are genotyped.

Another advantage is that outside collaborators, such as Dr. Victor Hesselbrock at the University of Connecticut would like to collaborate with us on large-scale imaging projects such as the second wave of the Consortium on the Genetics of Alcoholism (COGA). This project is conceptually very much in line with the type of genetics/neuroimaging/endophenotype approach currently ongoing at the Olin Center, with subjects numbering in the hundreds (400). Although we believe that our neuroimaging strengths will complement the depth of expertise of the University of Connecticut in alcoholism genetics research, our current lack of ability to schedule additional large-scale imaging projects currently precludes our participation in this type of venture. It is clear to us that obtaining the new instrument will open the door to this and many future important scientific collaborations. Participation in the UCONN CTSA will also aid in this category. If even a proportion of the pending grants listed above are funded, this will have significant impact on our ability to hire new staff at all levels.

Locally, over a dozen projects are conducted in collaboration with our colleagues at Trinity, Yale, UCHC, CCSU, UConn Storrs & Wesleyan and others. **National** active collaborations include projects with Harvard University, the University of New Mexico, University of Texas Southwestern in Dallas, Wayne State University, University of Pittsburgh, Johns Hopkins University, The Kennedy Krieger Institute in Baltimore MD, University of Maryland, University of Illinois at Chicago (UIC), University of Chicago, University of Texas Health Science Center at San Antonio, the Southwest Foundation for Biomedical Research, San Antonio, Texas, University of California at Los Angeles, Wright State University Boonshoft School of Medicine, Dayton, Ohio), State University of New York, Upstate, Columbia University NY, and UC Davis.
International collaborations include: Bergen Norway, San Jose Costa Rica, Institute of Psychiatry, London UK, Oxford UK and Tel Aviv Israel.

In summary, the replacement 3-T Skyra MRI scanner will continue to serve our research needs, but in a way that provides higher-quality, faster, more efficient and more comfortable imaging. Because several research projects at ONRC are longitudinal, these will need to be completed before we completely stop using the current Allegra, so that that there will be a transitional time when both scanners will be in use at the same time, as outlined in the supporting documents.

Please feel free to contact me if you have any further questions regarding the above.

Yours sincerely,

Godfrey Pearlson MD
Director, Olin Neuropsychiatry Research Center, Institute of Living.
Professor of Psychiatry and Neurobiology, Yale University School of Medicine,

Institute of Living
A Division of Hartford Hospital

January 27, 2014

Deputy Commissioner Lisa Davis, MBA, BSN, RN
Department of Public Health
Office of Health Care Access (OHCA)
410 Capital Avenue, MS#13 HCA
P.O. Box 340308
Hartford, Connecticut 06134

Re: Hartford Hospital's Application to Acquire a Siemens Skyra MRI scanner

Dear Deputy Commissioner Davis:

I am writing in my role as Psychiatrist-in-Chief of the Institute of Living/Hartford Hospital to request that the State of Connecticut Office of Healthcare Access approve Hartford Hospital's request for a Siemens Skyra MRI scanner.

As stated in our Application, the Institute of Living established the Olin Neuropsychiatry Research Center in 2002 for the purpose of creating a state of the art fMRI brain imaging and genetics research center focused entirely on translational research relating to severe mental illness. Historically, behavioral health has been a medical discipline that has all too often received the short end of the stick when it comes to research funding. With the creation of the Olin Neuropsychiatry Research Center, which operates under the direction of Dr. Godfrey Pearlson, a highly regarded clinical researcher in the psychiatric field, the Olin Neuropsychiatry Research Center has been able to attract significant funding and underwriting to conduct translational research relating to severe mental illness. The volume of our studies and the need to maintain consistency by conducting studies on one fMRI scanner necessitates that we have at least two scanners to keep pace with the number of studies that we have undertaken. It is especially important that as one scanner reaches the end of its useable life ("ages out"), another scanner be in place so that our research enterprise continues without interruption.

The Institute of Living is very committed to conducting this important research and our funders expect that we conduct our studies with the very best technology, and for these reasons, I respectfully request that you approve this application for the Siemens Skyra MRI scanner.

Sincerely,

Harold I. Schwartz, M.D.
Psychiatrist-in-Chief

00026 (02/14/14)

3174185v1

EXHIBIT 2

SIEMENS

Siemens Medical Solutions USA Inc.
51 Valley Stream Parkway, Malvern PA 19355

FINAL INVOICE

INVOICE NUMBER	90293275
INVOICE DATE	09/27/2012
CUSTOMER NO.	6646
SALES ORDER NO.	30144139
DISTRICT	11
DIVISION	02

BILL TO:

HARTFORD HOSPITAL
PO Box 5037
HARTFORD CT 06102-5037

SHIP TO:

SHIPPED ON:
HARTFORD HOSPITAL
80 SEYMOUR ST
HARTFORD CT 06106

YOUR PURCHASE ORDER:
NUMBER: C830058 DATE: 09/29/2010

FOB POINT	CARRIER'S NAME, FREIGHT REMARKS	SHIPPED VIA
FOB - Destination		
TERMS OF PAYMENT	TAX STATE	
00/80/20	CT	

DESCRIPTION/SERIAL NO.	TOTAL PRICE
Equipment Contract Total	2,116,837.00
EQUIPMENT TYPE: MAGNETOM Skyra YMAT	
Portion Billed Previously	1,693,470.00-
20.00 % Final Amount Due	423,367.00
Taxes for Equipment Contract Total	
AMOUNT DUE NOW:	423,367.00

PLEASE DIRECT ANY INQUIRIES REGARDING THIS BILLING TO:
csgsibillinginquirycentral.healthcare@siemens.com

PLEASE REMIT TO:
Siemens Medical Solutions USA, Inc. PO Box 120001 - Dept. 0733, DALLAS, TX 75312-0733

The customer is hereby informed that section 1128B(b) of the Social Security Act requires that discounts and other reductions in price or the existence of discount programs be properly disclosed and reflected in the costs claimed or charges made by a provider under Medicare or a State Health Program.

EXHIBIT 3

Toward discovery science of human brain function

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Although it is being successfully implemented for exploration of the genome, discovery science has eluded the functional neuroimaging community. The core challenge remains the development of common paradigms for interrogating the myriad functional systems in the brain without the constraints of a priori hypotheses. Resting-state functional MRI (R-fMRI) constitutes a candidate approach capable of addressing this challenge. Imaging the brain during rest reveals large-amplitude spontaneous low-frequency (<0.1 Hz) fluctuations in the fMRI signal that are temporally correlated across functionally related areas. Referred to as functional connectivity, these correlations yield detailed maps of complex neural systems, collectively constituting an individual's "functional connectome." Reproducibility across datasets and individuals suggests the functional connectome has a common architecture, yet each individual's functional connectome exhibits unique features, with stable, meaningful interindividual differences in connectivity patterns and strengths. Comprehensive mapping of the functional connectome, and its subsequent exploitation to discern genetic influences and brain–behavior relationships, will require multicenter collaborative datasets. Here we initiate this endeavor by gathering R-fMRI data from 1,414 volunteers collected independently at 35 international centers. We demonstrate a universal architecture of positive and negative functional connections, as well as consistent loci of inter-individual variability. Age and sex emerged as significant determinants. These results demonstrate that independent R-fMRI datasets can be aggregated and shared. High-throughput R-fMRI can provide quantitative phenotypes for molecular genetic studies and biomarkers of developmental and pathological processes in the brain. To initiate discovery science of brain function, the 1000 Functional Connectomes Project dataset is freely accessible at www.nitrc.org/projects/fcon_1000/.

database | neuroimaging | open access | reproducibility | resting state

Much like the challenge of decoding the human genome, the complexities of mapping human brain function pose a challenge to the functional neuroimaging community. As dem-

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onstrated by the 1000 Genomes Project (1), the accumulation and sharing of large-scale datasets for data mining is necessary for the first phase of discovery science.

Although the neuroimaging community has traditionally focused on hypothesis-driven task-based approaches, resting-state functional MRI (R-fMRI) has recently emerged as a powerful tool for discovery science. Imaging the brain during rest reveals large-amplitude spontaneous low-frequency (<0.1 Hz) fluctuations in the fMRI signal that are temporally correlated across functionally related areas (2–5). A single R-fMRI scan (as brief as 5 min) can be used to interrogate a multitude of functional circuits simultaneously, without the requirement of selecting a priori hypotheses (6). Building on the term "connectome," coined to describe the comprehensive map of structural connections in the human brain (7), we use "functional connectome" to describe the collective set of functional connections in the human brain.

Buttressed by moderate to high test–retest reliability (8–10) and replicability (11, 12), as well as widespread access, R-fMRI has overcome initial skepticism (13) regarding the validity of examining such an apparently unconstrained state (5, 8, 14). Recent R-fMRI studies have identified putative biomarkers of neuropsychiatric illness (12, 15–18), provided insight into the development of functional networks in the maturing and aging brain (19–22), demonstrated a shared intrinsic functional architecture (23) between humans and nonhuman primates (24, 25), and delineated the effects of sleep (26), anesthesia (27), and pharmacologic agents on R-fMRI measures (28, 29). Given the many sources of variability inherent in fMRI, the remaining challenge is to demonstrate the feasibility and utility of adopting a high-throughput model for R-fMRI, commensurate with the scale used by human genetics studies to have the power to detect both single gene and combinatorial genetic and environmental effects on complex phenotypes.

Accordingly, the 1000 Functional Connectomes Project was formed to aggregate existing R-fMRI data from collaborating centers throughout the world and to provide an initial demonstration of the ability to pool functional data across centers. As of December 11, 2009, the repository includes data from 1,414 healthy adult participants contributed by 35 laboratories (Table S1). The intent is to expand this open resource as additional data are made available.

Here we provide an initial demonstration of the feasibility of pooling R-fMRI datasets across centers. Specifically, we (i) establish the presence of a universal functional architecture in the brain, consistently detectable across centers; (ii) investigate the influence of center on R-fMRI measures; (iii) explore the potential impact of demographic variables (e.g., age, sex) on R-fMRI measures; and (iv) demonstrate the use of an intersubject variance–based method for identifying putative boundaries between functional networks.

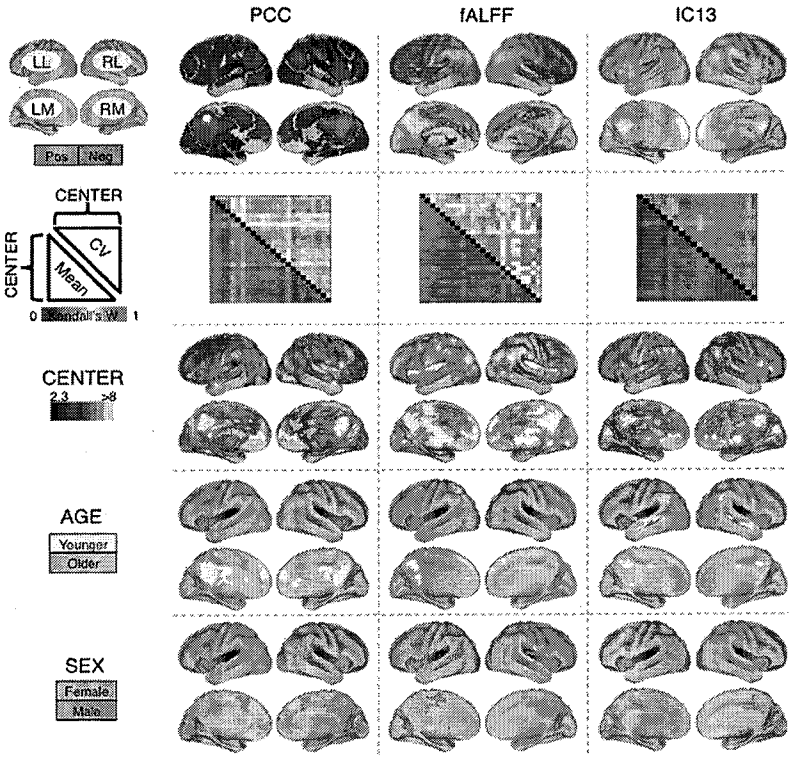

Fig. 1. Independent center-, age-, and sex-related variations detected in R-fMRI measures of functional connectivity and amplitude fluctuation. The first row depicts group-level maps for representative seed-based (column 1) and ICA-based (column 3) functional connectivity analyses (*SI Results*), as well as fALFF (column 2). Group-level maps were derived from one-way ANOVA across 1,093 participants from 24 centers (factor: center; covariates: age and sex). All group-level maps depicted were corrected for multiple comparisons at the cluster level using Gaussian random-field theory ($Z > 2.3$; $P < 0.05$, corrected). For each measure, the second row shows robust between-center concordances (Kendall's W), with the voxelwise coefficients of variation above the diagonal and the voxelwise means below the diagonal. Kendall's W concordance between any two centers was calculated across all voxels in the brain mask for the mean (or coefficient of variation) connectivity map across all participants included in each center. Rows 3, 4, and 5 depict voxels exhibiting significant effects of center, age, and sex, respectively, as detected by one-way ANOVA. "Male" refers to significantly greater connectivity (or amplitude, i.e., fALFF) in males; similarly, "female" refers to significantly greater connectivity (or amplitude) in females. "Older" refers to significantly increasing connectivity (or amplitude) with increasing age, whereas "younger" refers to significantly increasing connectivity (or amplitude) with decreasing age. "Pos" refers to positive functional connectivity, and "neg" refers to negative functional connectivity. The PCC seed region is indicated by a white dot. (*Top Left*) Surface map legend: LL, left lateral; RL, right lateral; LM, left medial; RM, right medial. All surface maps are rendered on the PALS-B12 atlas in CARET (http://brainvis.wustl.edu).

Results

We applied three distinct analytic methods commonly used in the R-fMRI literature: seed-based functional connectivity, independent component analysis (ICA), and frequency-domain analyses. Across the three approaches, we found evidence of (i) a universal intrinsic functional architecture in the human brain, (ii) center-related variation in R-fMRI measures, and (iii) consistent effects of age and sex on R-fMRI measures, detectable across centers despite the presence of center-related variability (Fig. 1). Specifically, seed-based correlational analyses revealed highly consistent patterns of functional connectivity across centers for both the "default mode" (30) and "task-positive" networks (31), supporting a universal functional architecture (Fig. S1). Similarly, a data-driven, temporal concatenation ICA approach, combined with dual regression (32–34), revealed consistent patterns of functional connectivity across centers for 20 spatially independent functional networks (Fig. 1 and Figs. S2 and S3). In addition, for each of the functional connectivity measures, within-center coefficient of variation maps showed a high degree of concordance across centers (Fig. S4). This suggests that common loci of variation exist: centers demonstrated a high degree of agreement on which connections are characterized by relative variance or invariance. Despite the high degree of concordance between centers, there were appreciable center-related variations in the strength of functional connectivity throughout the brain (8). The effect of center was especially prominent in regions exhibiting greater interregional connection strength, because these have the least within-center variability (See *SI Results* and Fig. S5 for further discussion of center-related variability.) However, even when taking this center-related variability into account, robustly reliable effects of age and sex remained appreciable (Fig. 2 and Figs. S1 and S2). (See *SI Results* and Fig. S6 for an examination of the impact of sample size on effects of age and sex.)

The detection of sex differences was particularly noteworthy, because these differences are rarely appreciated in the R-fMRI literature (35). Sexual dimorphism in human genomic expression (36) is known to affect numerous physiological variables that can influence the fMRI signal (37, 38). For example, males and females differ in terms of hemoglobin concentrations and hematocrit (39). However, global variables such as these do not explain the regionally specific sex-related phenomenon noted in the present work. Hormonal effects (e.g., estrogen), operating both during brain development (40) and acutely (41), are known to have regional specificity (42), making them potential contributors to the differences observed. Given the discovery nature of the present work and the lack of prior coordination among centers, the specific sex differences that we observed should be interpreted with caution until replicated in an independent sample.

Along with examining patterns of functional connectivity, we measured the amplitude of low-frequency fluctuations at each voxel using two common periodogram-based measures: amplitude of low frequency fluctuation (ALFF; total power <0.1 Hz) (2, 17, 43) and fractional ALFF (fALFF; total power <0.1 Hz/total power in the measured spectrum) (44). Concordant with previous work, the dominance of low-frequency fluctuations was consistently noted within gray matter regions, but not white matter (44). As with our analyses of functional connectivity, despite clear evidence of center-related effects, we were again able to demonstrate age- and sex-related differences in the magnitude of low-frequency fluctuations in various regions, particularly medial wall structures (Fig. 2 and Fig. S7).

Beyond data pooling for statistical analyses, we demonstrate the potential to use high-throughput datasets to develop normative maps of functional systems in the brain, which is a prerequisite for clinical applications. Specifically, we exploit a key property of functional connectivity maps, the presence of well-differentiated borders between functionally distinct regions (45). The voxelwise measures of coefficients of variation for each type of functional connectivity map delineate putative functional boundaries based on the presence of marked variability in func-

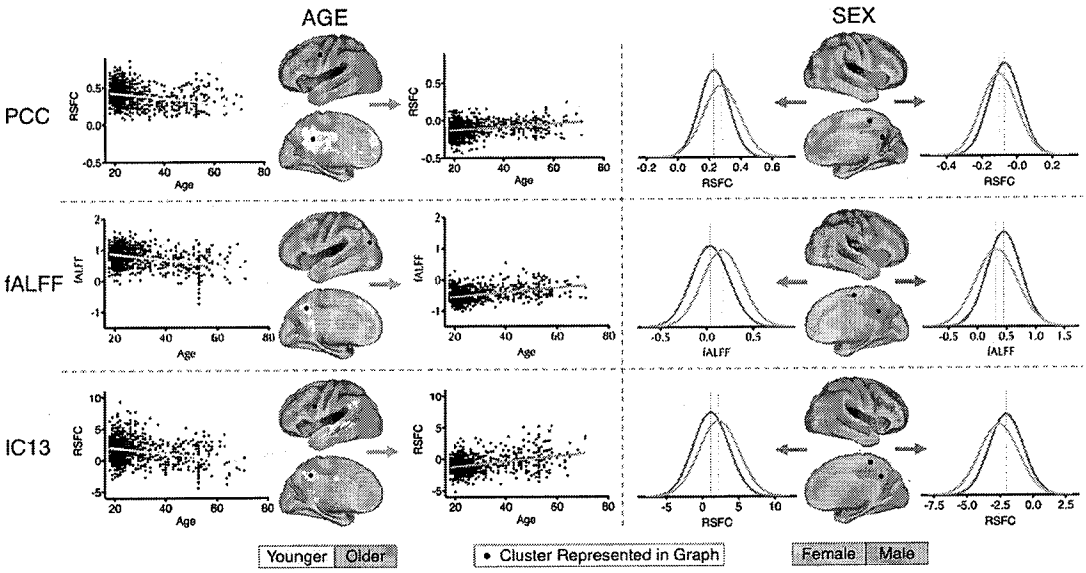

Fig. 2. Illustrative areas exhibiting age- and sex-related variation in R-fMRI properties. Significant group-level variance in functional connectivity maps was explained by age and sex (cluster-based Gaussian random-field corrected: $Z > 2.3$; $P < 0.05$). For each of three methods (seed-based, fALFF, and ICA), variance in connectivity strength explained by age (*Left*) and sex (*Right*) is illustrated both anatomically and graphically. Age-related differences are represented as scatterplots. Sex-related differences are represented as histograms depicting the distributions of resting-state functional connectivity (RSFC) values for males and females separately. Vertical lines indicate peak values. Corresponding topographical brain areas are indicated with dots. "Male" refers to significantly greater connectivity (or amplitude, i.e., fALFF) in males; similarly, "female" refers to significantly greater connectivity (or amplitude) in females. "Older" refers to significantly increasing connectivity (or amplitude) with increasing age, whereas "younger" refers to significantly increasing connectivity (or amplitude) with decreasing age.

tional connectivity across participants. The variation observed at these boundaries stands in contrast to the low degree of variability observed in regions exhibiting consistently positive or negative connectivity (Fig. 3). In addition, examination of the coefficients of variation for fALFF measures revealed sharp boundary zones between white matter and gray matter. It also identified areas of variability in the amplitude of spontaneous fluctuations that coincided with anatomic areas of notable sulcal variability (e.g., cingulate and frontal opercular regions).

Discussion

The present work represents a watershed event in functional imaging: demonstration of the feasibility of sharing and pooling functional data across multiple centers, alongside the establishment of an open-access data repository. We have demonstrated (i) the presence of a universal functional architecture, with remarkable stability in the functional connectome and its loci of variation across participants and centers; (ii) evidence of systematic sex differences in R-fMRI measures, as well as age-related gradients even in middle adulthood; and (iii) a method for highlighting the complex array of putative functional boundaries between networks from which normative maps can be developed. Future work should focus on using the functional connectome to catalog phenotypic diversity in brain–behavior relationships.

Functional connectivity is both related to and distinct from anatomic connectivity. Specifically, a recent study reported that a structural core appears to play "a central role in integrating information across functionally segregated brain regions" (23). As such, our finding of a universal functional architecture was not unexpected. But structure and function are not completely coupled, as illustrated by the robust homotopic (i.e., contralateral) functional connectivity for such regions as the primary visual cortex or the amygdala, both of which lack direct callosal projections (24, 46). Such findings imply that functional connectivity is subserved by polysynaptic as well as monosynaptic anatomic circuits. In addition, functional connectivity exhibits dynamic properties that are absent in structural connectivity. For instance, functional connectivity is modulated by cognitive (47) and emotional state (48), arousal, and sleep (26), whereas structural connectivity is grossly unaffected by such factors. In short, the presence of a demonstrable structural connection does not necessitate that of a functional connection, nor does the demonstration of a functional connection imply the presence of a direct structural connection.

Task-based fMRI and R-fMRI approaches have complementary roles in the study of human brain function. Task-based approaches require sufficient a priori knowledge to articulate specific hypotheses, and they are invaluable in refining such hypotheses. But when the knowledge base is insufficient, task-based approaches may be compared to candidate gene studies, which have had limited success when applied to complex genetic disorders. In contrast, genome-wide association studies are increasingly providing initial findings for complex traits (49) and diseases that are subsequently validated through replication, extension, and deep sequencing (50). Our demonstration that R-fMRI data can be aggregated and pooled, and that variability among individuals can be explained in terms of specific subject variables (e.g., sex, age), suggests that this approach can provide quantitative phenotypes to be integrated into molecular studies.

Our results must be considered in light of several limitations of the present study. First, we used a convenience sample comprising previously collected data from an array of centers, without prior coordination of acquisition parameters or scanning conditions. Although the robustness of our results attests to the consistency of intrinsic brain activity, it still represents a potential underestimate of the true across-center consistency. Our demographic data warrant caution, because centers were heterogeneous with respect to male:female ratio, mean age, and age range. Our findings should motivate more systematic exploration of these variables, because future high-throughput imaging studies will need to take such factors into account.

Despite the promise of R-fMRI, some theoretical and pragmatic issues need to be addressed. Examples include the determination of

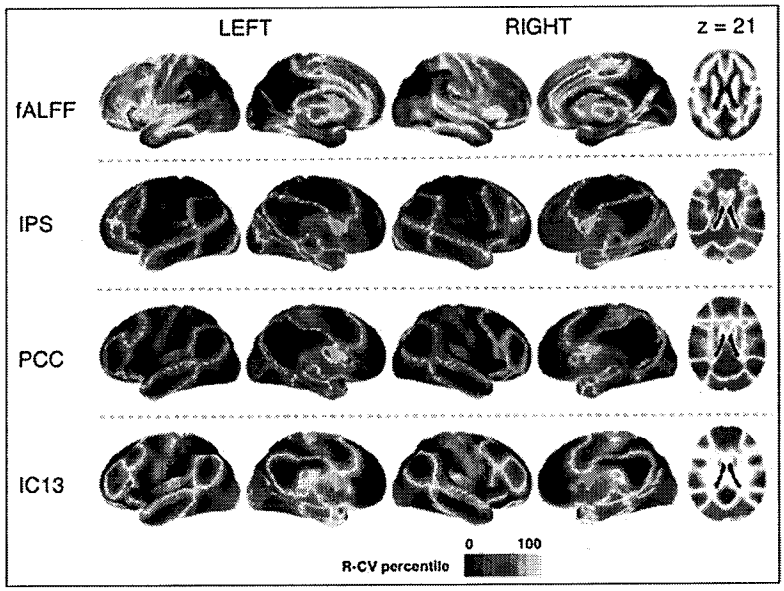

Fig. 3. Variation across individuals reveals functional boundaries. Previous work has noted that functionally segregated regions are frequently characterized by well-demarcated boundaries for an individual (45). As such, variability in boundary areas is detectable across participants. Here we detect functional boundaries via examination of voxelwise coefficients of variation (absolute value) for fALFF and selected seed-based [intraparietal sulcus (IPS), posterior cingulate/precuneus (PCC)] and ICA-based (IC13) functional connectivity maps. For the purpose of visualization, coefficients of variation were rank-ordered, whereby the relative degree of variation across participants at a given voxel, rather than the actual value, was plotted to better contrast brain regions. Ranking coefficients of variation efficiently identified regions of greatest interindividual variability, thus delineating putative functional boundaries.

the origins and biological significance of spontaneous low-frequency fluctuations of neuronal and hemodynamic activity, the impact of intrinsic activity on evoked responses (and vice versa), and the ideal means of acquiring, processing, and analyzing R-fMRI data. Nevertheless, the potential of discovery science is vast, from the development of objective measures of brain functional integrity to help guide clinical diagnoses and decision-making, to tracking treatment response and assessing the efficacy of treatment interventions. Finally, whereas the present work examines functional connectivity alone, future studies may combine R-fMRI with other modalities (e.g., EEG, magnetoencephalography, diffusion-tensor imaging, volumetrics) and genetics to achieve a more complete understanding of the human brain.

All data and analytic tools used in the present work will be made available at www.nitrc.org/projects/fcon_1000/. We anticipate that the open availability of the 1000 Functional Connectomes dataset will recruit the broad participation and collaboration among the scientific community necessary for successful implementation of discovery-based science of human brain function. In addition, we hope that it will further advance the ethos of data sharing and collaboration initiated by such efforts as fMRIDC (www.fmridc.org), FBIRN (www.birncommunity.org), OASIS (www.oasis-brains.org), BrainScape (www.brainscape.org), and BrainMap (www.brainmap.org).

Methods

Resting-state fMRI scans were aggregated from 35 community-based datasets (n = 1,414). The present analysis was restricted to 24 centers (n = 1,093; 21 published, 3 unpublished; mean age <60 years; only participants over age 18; one scan per participant; duration: 2.2–20 min; n = 970 at 3 T, n = 123 at 1.5 T; voxel size, 1.5–5mm within plane; slice thickness, 3–8 mm). Each contributor's respective ethics committee approved submission of deidentified data. The institutional review boards of NYU Langone Medical Center and New Jersey Medical School approved the receipt and dissemination of the data.

For functional connectivity, we used seed-based correlation analysis, based on six previously identified seed regions (31), and model-free ICA, using temporal concatenation to generate group-level components and dual regression to generate individual participant maps. For amplitude measures at each voxel, we used the FFT-based ALFF (2, 17, 43) and its normalized variant, fALFF (44).

Standard image preprocessing was performed (i.e., motion correction, spatial filtering with FWHM = 6 mm, 12-dof affine transformation to MNI152 stereotactic space). For seed-based correlation approaches and dual regression following ICA analysis, nuisance signals (e.g., global signal, WM, CSF, motion parameters) were regressed out. Temporal filtering was tailored for each analytic approach (29, 31, 32, 44).

ICA components for dual regression analyses were determined by (i) low-dimensional (20 components) temporal concatenation ICA carried out 25 times (each with 18 participants randomly selected from each of 17 centers with minimum of 165 time points) and (ii) low-dimensional (20 components) meta-ICA, a second concatenation-based ICA using the component sets produced by the 25 runs (see *SI Results* for a description of an alternative method). For each participant, dual regression (32–34) was performed using the 20 components identified by the meta-ICA (Fig. S3), yielding a connectivity map for each component.

Aggregate statistical analyses of center, sex, and age effects were based on a generalized linear model implementation of one-way ANOVA (factor: center; covariates: age and sex). To identify functional boundaries, we calculated voxelwise coefficients of variation across all 1,093 participants, and ranked each voxel based on the absolute value of its coefficient of variation.

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1. Wise J (2008) Consortium hopes to sequence genome of 1000 volunteers. *BMJ* 336: 237.
2. Biswal B, Yetkin FZ, Haughton VM, Hyde JS (1995) Functional connectivity in the motor cortex of resting human brain using echo-planar MRI. *Magn Reson Med* 34: 537–541.
3. Fox MD, Raichle ME (2007) Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging. *Nat Rev Neurosci* 8:700–711.
4. Margulies DS, et al. (2007) Mapping the functional connectivity of anterior cingulate cortex. *Neuroimage* 37:579–588.
5. Smith SM, et al. (2009) Correspondence of the brain's functional architecture during activation and rest. *Proc Natl Acad Sci USA* 106:13040–13045.
6. Van Dijk KR, et al. (2010) Intrinsic functional connectivity as a tool for human connectomics: Theory, properties, and optimization. *J Neurophysiol* 103:297–321.
7. Sporns O, Tononi G, Kötter R (2005) The human connectome: A structural description of the human brain. *PLOS Comput Biol* 1:e42.
8. Shehzad Z, et al. (2009) The resting brain: Unconstrained yet reliable. *Cereb Cortex* 19: 2209–2229.
9. Zuo XN, et al. (2010) Reliable intrinsic connectivity networks: test-restest evaluation using ICA and dual regression approach. *Neuroimage* 49:2163–2177.
10. Zuo XN, et al. (2010) The oscillating brain: Complex and reliable. *Neuroimage* 49: 1432–1445.
11. He Y, et al. (2009) Uncovering intrinsic modular organization of spontaneous brain activity in humans. *PLoS One* 4:e5226.
12. Buckner RL, et al. (2009) Cortical hubs revealed by intrinsic functional connectivity: Mapping, assessment of stability, and relation to Alzheimer's disease. *J Neurosci* 29: 1860–1873.
13. Morcom AM, Fletcher PC (2007) Does the brain have a baseline? Why we should be resisting a rest. *Neuroimage* 37:1073–1082.
14. Damoiseaux JS, et al. (2006) Consistent resting-state networks across healthy subjects. *Proc Natl Acad Sci USA* 103:13848–13853.
15. Castellanos FX, et al. (2008) Cingulate precuneus interactions: A new locus of dysfunction in adult attention-deficit/hyperactivity disorder. *Biol Psychiatry* 63: 332–337.
16. Church JA, et al. (2009) Control networks in paediatric Tourette syndrome show immature and anomalous patterns of functional connectivity. *Brain* 132:225–238.
17. Zang YF, et al. (2007) Altered baseline brain activity in children with ADHD revealed by resting-state functional MRI. *Brain Dev* 29:83–91.
18. Rombouts SA, et al. (2009) Model-free group analysis shows altered BOLD FMRI networks in dementia. *Hum Brain Mapp* 30:256–266.
19. Kelly AMC, et al. (2009) Development of anterior cingulate functional connectivity from late childhood to early adulthood. *Cereb Cortex* 19:640–657.
20. Supekar K, Musen M, Menon V (2009) Development of large-scale functional brain networks in children. *PLoS Biol* 7:e1000157.
21. Fair DA, et al. (2009) Functional brain networks develop from a "local to distributed" organization. *PLoS Comput Biol* 5:e1000381.
22. Andrews-Hanna JR, et al. (2007) Disruption of large-scale brain systems in advanced aging. *Neuron* 56:924–935.
23. Hagmann P, et al. (2008) Mapping the structural core of human cerebral cortex. *PLoS Biol* 6:e159.
24. Vincent JL, et al. (2007) Intrinsic functional architecture in the anaesthetized monkey brain. *Nature* 447:83–86.
25. Margulies DS, et al. (2009) Precuneus shares intrinsic functional architecture in humans and monkeys. *Proc Natl Acad Sci USA* 106:20069–20074.
26. Fukunaga M, et al. (2006) Large-amplitude, spatially correlated fluctuations in BOLD fMRI signals during extended rest and early sleep stages. *Magn Reson Imaging* 24: 979–992.
27. Greicius MD, et al. (2008) Persistent default-mode network connectivity during light sedation. *Hum Brain Mapp* 29:839–847.
28. Achard S, Bullmore E (2007) Efficiency and cost of economical brain functional networks. *PLoS Comput Biol* 3:e17.
29. Kelly C, et al. (2009) L-dopa modulates functional connectivity in striatal cognitive and motor networks: A double-blind, placebo-controlled study. *J Neurosci* 29:7364–7378.
30. Gusnard DA, Raichle ME, Raichle ME (2001) Searching for a baseline: Functional imaging and the resting human brain. *Nat Rev Neurosci* 2:685–694.
31. Fox MD, et al. (2005) The human brain is intrinsically organized into dynamic, anticorrelated functional networks. *Proc Natl Acad Sci USA* 102:9673–9678.
32. Beckmann CF, DeLuca M, Devlin JT, Smith SM (2005) Investigations into resting-state connectivity using independent component analysis. *Philos Trans R Soc Lond B Biol Sci* 360:1001–1013.
33. Filippini N, et al. (2009) Distinct patterns of brain activity in young carriers of the APOE-epsilon4 allele. *Proc Natl Acad Sci USA* 106:7209–7214.
34. Calhoun VD, Pekar JJ, Pearlson GD (2004) Alcohol intoxication effects on simulated driving: Exploring alcohol-dose effects on brain activation using functional MRI. *Neuropsychopharmacology* 29:2097–3017.
35. Liu H, Stufflebeam SM, Sepulcre J, Hedden T, Buckner RL (2009) Evidence from intrinsic activity that asymmetry of the human brain is controlled by multiple factors. *Proc Natl Acad Sci USA* 106:20499–20503.
36. Ellegren H, Parsch J (2007) The evolution of sex-biased genes and sex-biased gene expression. *Nat Rev Genet* 8:689–698.

37. Goldstein JM, et al. (2001) Normal sexual dimorphism of the adult human brain assessed by in vivo magnetic resonance imaging. *Cereb Cortex* 11:490–497.
38. Gur RC, et al. (1995) Sex differences in regional cerebral glucose metabolism during a resting state. *Science* 267:528–531.
39. Zeng SM, Yankowitz J, Widness JA, Strauss RG (2001) Etiology of differences in hematocrit between males and females: Sequence-based polymorphisms in erythropoietin and its receptor. *J Gend Specif Med* 4:35–40.
40. Lenroot RK, et al. (2007) Sexual dimorphism of brain developmental trajectories during childhood and adolescence. *Neuroimage* 36:1065–1073.
41. Protopopescu X, et al. (2008) Hippocampal structural changes across the menstrual cycle. *Hippocampus* 18:985–988.
42. McEwen BS (1999) Permanence of brain sex differences and structural plasticity of the adult brain. *Proc Natl Acad Sci USA* 96:7128–7130.
43. Cordes D, et al. (2001) Frequencies contributing to functional connectivity in the cerebral cortex in "resting-state" data. *AJNR Am J Neuroradiol* 22:1326–1333.
44. Zou QH, et al. (2008) An improved approach to detection of amplitude of low-frequency fluctuation (ALFF) for resting-state fMRI: Fractional ALFF. *J Neurosci Methods* 172:137–141.
45. Cohen AL, et al. (2008) Defining functional areas in individual human brains using resting functional connectivity MRI. *Neuroimage* 41:45–57.
46. Roy AK, et al. (2009) Functional connectivity of the human amygdala using resting-state fMRI. *Neuroimage* 45:614–626.
47. Albert NB, Robertson EM, Miall RC (2009) The resting human brain and motor learning. *Curr Biol* 19:1023–1027.
48. Harrison BJ, et al. (2008) Modulation of brain resting-state networks by sad mood induction. *PLoS ONE* 3:e1794.
49. Lettre G (2009) Genetic regulation of adult stature. *Curr Opin Pediatr* 21:515–522.
50. Manolio TA, et al. (2009) Finding the missing heritability of complex diseases. *Nature* 461:747–753.

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The Human Connectome Project: A data acquisition perspective

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Abstract

The Human Connectome Project (HCP) is an ambitious 5-year effort to characterize brain connectivity and function and their variability in healthy adults. This review summarizes the data acquisition plans being implemented by a consortium of HCP investigators who will study a population of 1200 subjects (twins and their non-twin siblings) using multiple imaging modalities along with extensive behavioral and genetic data. The imaging modalities will include diffusion imaging (dMRI), resting-state fMRI (R-fMRI), task-evoked fMRI (T-fMRI), T1- and T2-weighted MRI for structural and myelin mapping, plus combined magnetoencephalography and electroencephalography (MEG/EEG). Given the importance of obtaining the best possible data quality, we discuss the efforts underway during the first two years of the grant (Phase I) to refine and optimize many aspects of HCP data acquisition, including a new 7T scanner, a customized 3T scanner, and improved MR pulse sequences.

Keywords

Connectivity; fMRI; Diffusion imaging; MEG/EEG; Twins; Behavior

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Appendix A. Supplementary data

Supplementary data to this article can be found online at doi:10.1016/j.neuroimage.2012.02.018.

Introduction

Recent advances in neuroimaging, including many that are discussed in this special issue, have made it feasible to examine human brain connectivity systematically and across the whole brain in large numbers of individual subjects. Progress in the nascent field of connectomics led NIH in 2009 to announce a Request for Applications for the Human Connectome Project (HCP), with an overarching objective of studying human brain connectivity and its variability in healthy adults. In September, 2010, grants were awarded to two consortia (http://www.neuroscienceblueprint.nih.gov/connectome/). One is a 5-year grant to a consortium of ten institutions in the United States and Europe, led by Washington University and the University of Minnesota (the 'WU-Minn HCP Consortium'). This consortium aims to study brain connectivity and function with a genetically-informative design in 1200 individuals using four MR-based modalities plus MEG and EEG. Behavioral and genetic data will also be acquired from these subjects. The second is a 3-year grant to a consortium led by Harvard/MGH and UCLA to develop an advanced MR scanner for diffusion imaging.

A deeper understanding of human brain connectivity and its variability will provide valuable insights into what makes us uniquely human and what accounts for the great diversity of behavioral capacities and repertoires in healthy adults. It will provide a critical baseline of knowledge for future studies of brain connectivity during development and aging and in myriad neurodevelopmental, neuropsychiatric and neurological disorders. Also, the data acquisition strategies and analysis methods developed under the auspices of the HCP will be freely shared and will benefit many other projects. Increasing both the commonality and the sensitivity of methods used to characterize human brain connectivity across different studies will enhance our ability to detect subtle links between genetics, human brain connectivity patterns, and behavioral variation.

Despite their great promise, all of the modalities that can be applied to *in vivo* human connectomics currently have serious limitations in their sensitivity, accuracy, and resolution (Van Essen and Ugurbil, 2012). Hence, during Phase I of the grant (until the summer of 2012) the WU-Minn HCP consortium is making a major effort to improve the methods of data acquisition and analysis. This includes a new 3T MRI scanner designed to improve the quality and resolution of connectivity data, as well as a new 7T scanner, both of which will capitalize on major improvement in MR pulse sequences. This initial phase will be followed by a 3-year period of data acquisition from the main cohort (Phase II). The combination of methods refinement followed by extensive data acquisition makes the HCP a unique enterprise compared to several other large-scale imaging efforts that are also underway (see Discussion).

This review focuses on the data acquisition aspects of the HCP, given their critical importance for the endeavor. After a brief overview of the HCP objectives, we describe the subject cohort and behavioral measures, followed by the hardware configuration and data acquisition strategies for each of the main imaging modalities. Already there have been significant methodological advances that provide grounds for optimism about the data quality that will be attainable. Approaching near-optimal solutions will be very challenging given the large number of factors and parameters needing evaluation. We provide examples of our general approach to this problem.

Overview of the HCP

Fig. 1 provides a high-level view of our plans for data acquisition in Phase II of the project. Data will be acquired from 1200 subjects, comprising young adult sibships of average size 3–4, including twins and their non-twin siblings. Each subject will spend 2 days at WashU

for behavioral assessment, blood draw for eventual genotyping, and multiple MR scanning sessions (4 sessions, with 3 lasting 1 h). The WashU scans will be carried out using a customized 3T Connectome Scanner adapted from a Siemens Skyra (Siemens AG, Erlanger, Germany); a subset of 200 subjects will also be scanned at UMinn using a new 7T scanner (MR hardware section). On both the 3T and 7T systems, the MR scans will use advanced pulse sequences to acquire dMRI, R-fMRI, and T-fMRI, plus T1w and T2w anatomical scans. T-fMRI scans will include a range of tasks aimed at providing broad coverage of the brain and identifying as many functionally distinct domains and cortical parcels as possible.

A subset of 100 subjects will also be studied with combined MEG/EEG at St. Louis University (SLU); if possible, some of these will be in the group also scanned at 7T. MEG and EEG provide much better temporal resolution (milliseconds instead of seconds) but lower spatial resolution than MR (MEG/EEG section).

The behavioral measures will span a broad range in the domains of cognition, emotion, perception, and motor function (Behavioral measures section). They will be drawn mainly from the NIH Toolbox but will be supplemented by a number of complementary additional measures. Blood samples from all subjects will be used for genotyping in year 5, at which time full-genome sequencing may be affordable (Genetics section).

Extensive efforts to refine many aspects of data analysis are underway for each modality, as will be discussed in future publications. Another major thrust is to implement a robust and user-friendly informatics platform to support data management and data mining (Marcus et al., 2011).

In principle, it would be valuable to collect data from additional noninvasive0020imaging modalities (*e.g.*, PET and NIRS). However, given overall budget constraints this would require reducing the total number of subjects studied. The strategy we adopted reflects a trade-off and balance between (i) acquiring as much information as is feasible using multiple modalities related to brain connectivity and function, and (ii) having a subject population sufficiently large to systematically explore the neurobiological and genetic bases of individual variability in brain circuitry and behavioral phenotype.

Study subjects

A key objective is to understand inter-individual variability of brain circuits, including its genetic bases and its relation to behavior, rather than merely aiming to determine the average, or typical connectivity in healthy adults. This will be achieved by sampling 300–400 young adult sibships of average size 3–4, with most of these sibships including a MZ or DZ twin pair. All subjects will be between 22 and 35 years old, an age range chosen to represent healthy adults beyond the age of major neurodevelopmental changes and before the onset of neurodegenerative changes. While the HCP will be cross-sectional, many participants will be drawn from ongoing longitudinal studies (Sartor et al., 2011; Edens et al., 2010); they will have extensive previous assessments, particularly with respect to history of the presence or absence of emotional and behavioral problems. This will allow us to recruit a sample of relatively healthy individuals free of a prior history of significant psychiatric or neurological illnesses. Our goal is to capture a broad range of variability in healthy individuals with respect to behavioral, ethnic, and socioeconomic diversity. We will define 'healthy' broadly, to avoid having an unduly narrow 'supernormal' case series that might not be representative of the population at large. We will exclude sibships with individuals having severe neurodevelopmental disorders (*e.g.* autism), documented neuropsychiatric disorders (*e.g.* schizophrenia or severe recurrent depression) or neurologic disorders (*e.g.* Parkinson's disease), but will include individuals who are smokers, are overweight, or have a history of heavy drinking or recreational drug use without having

experienced severe symptoms (Supplemental Table S1 lists the full set of inclusion and exclusion criteria under consideration). This strategy will enable future connectivity studies on psychiatric patients, many of whom smoke, are overweight, or have subclinical substance use behaviors, to be compared to connectivity data on HCP 'healthy individuals' having similar profiles. Twins born prior to 34 weeks gestation and non-twins born prior to 37 weeks gestation will be excluded. This acknowledges the higher incidence of prematurity in twins and focuses on exclusion of individuals born very prematurely. Our initial screening will include a detailed questionnaire developed explicitly for the HCP to determine presence or absence of the inclusion/exclusion criteria. This will be followed by an additional extensive, reliable, and valid psychiatric interview, the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA, Bucholz et al., 1994), to confirm the absence of significant psychiatric illness. This will also allow us to include information about subthreshold psychiatric symptoms in the database, as analyses of such data may be of interest to many researchers.

The utility of twin pairs in furthering our understanding of the causes of human variation extends beyond estimating the contribution of genetic differences to individual variation (for classic early studies, see Eaves, 1982 and Martin et al., 1997; for a discussion of statistical analysis approaches, see Neale and Cardon, 1992). MZ twinning occurs randomly, so MZ twin pairs should capture the full range of genetic variability in a population. These twin pairs are genetically nearly identical; while they may share many aspects of rearing history and socioeconomic background, they also have within-pair variance due to differences in environmental exposures, stochastic processes and measurement error. Accordingly, assessment of MZ twin pairs on its own is valuable in three distinct respects. (i) It provides a within-pair contrast for effects of environmental exposure or physical or physiologic state (*e.g.* in pairs discordant for smoking, overweight/obesity, or diabetes). (ii) It provides a lower-bound estimate of the test–retest reliability of various HCP measures. (It is a lower bound because it reflects only genetic effects plus environmental effects shared by the twin pairs; however, it is especially valuable in experiments that for technical reasons are non-repeatable.) (iii) It provides an estimate of the covariance structure of multiple measures that is uncontaminated by individual-specific stochastic and measurement error effects.

Dizygotic twin pairs are as genetically related as ordinary full siblings, but they share their childhood environment to a much greater extent than do siblings of different ages. When added to MZ twin data, DZ twin data thus allow estimation of the extent to which genotype, shared environment, and non-shared influences each contribute to variation in traits. In multivariate analysis, this extends to understanding why traits A and B co-vary. The inclusion of additional siblings along with twins provides a further increase in statistical power for resolving genetic and environmental influences (Posthuma and Boomsma, 2000). These basic applications may be elaborated to test for genotype × environment interaction effects, where genetic influences are modified as a function of environmental exposure or experimental manipulation; conditional effects (*e.g.* how smoking status may affect connectivity patterns); and to test for certain strong directional models (event A leads to event B, rather than *vice versa*) (Neale and Cardon, 1992).

Genetics

Participants will provide blood samples that will be used to create cell-lines and for DNA extraction, with these resources available to other qualified investigators. In the final year of the project, we will genotype samples from all study participants. The genotyping method will be chosen from those available at that time, with the goal of obtaining the maximum amount of data given budgetary constraints; this may include full-genome sequencing. HCP genetic data will allow investigators to look for the effects of specific genetic variants (as identified in powerful large-scale genome-wide association studies of clinical or behavioral

phenotypes) on brain connectivity patterns in healthy adults. As one example, it will be interesting to see whether differences in brain connectivity patterns are associated with genetic variants that contribute to the risk of developing Alzheimer's disease later in life (*e.g.* ApoE e4). The HCP data may also enable direct discovery of gene variants that affect brain connectivity patterns, especially if the HCP core protocol is replicated across multiple studies worldwide. Overall, our use of a twin-family study paradigm to analyze individual variation in brain connectivity will facilitate progress in understanding the genetic bases of individual differences in connectivity, and their covariation with normal behavior.

Behavioral measures

HCP's behavioral measures will provide important phenotypic data to compare with brain imaging and genetics. Our goal is to cover as many domains of behavior as feasible within 2–3 h of testing outside of the scanner. Our base set of assessment tools will be the NIH Toolbox, which is being developed as a brief, well-validated assessment of the domains of cognition, emotion, motor function and sensation that can be used with healthy individuals from childhood through older age (see http://www.nihtoolbox.org). This will include domains of cognition (verbal IQ, working memory, executive function, attention, language, and processing speed), emotion (negative affect, positive affect, stress and coping, and social relationships), motor function (locomotion, dexterity, strength, and endurance), and sensation (hearing, taste, touch and smell). To facilitate cross-project comparisons, we plan to incorporate additional measures similar or identical to those used by other large-scale data acquisition projects measuring brain function, structure, and connectivity that are non-overlapping with the NIH-Toolbox measures. These include measures of attention, episodic memory, visual spatial processing, and emotional face processing as used by Gur et al. (2010); the Achenbach Adult Self Report (Achenbach et al., 2005), as used in the NKI-Rockland project (http://fcon_1000.projects.nitrc.org/indi/pro/nki.html); and a variant of matrix reasoning as a measure of fluid intelligence and the NEO-FFI-60 measure of personality (McCrae and Costa, 2004), as used in a study on cognitive aging (R. Buckner, personal communication). Finally, we plan to include the Farnsworth test of color vision, the Mars test of visual contrast sensitivity, the EVA test of visual acuity, and a measure of impulsivity (delay discounting) (Estle et al., 2006). Supplemental Table S2 lists all measures we plan to acquire (Toolbox and non-Toolbox).

The broad spectrum of behavioral information acquired from all HCP subjects will enable many types of comparison and correlation between behavior and brain connectivity (functional, structural, and electrophysiological). For example, behavioral measures can be used to identify factors or eigenvectors of common variability across subjects, which are then correlated with measures of connectivity. This can be done within a cognitive domain, as in working memory (*e.g.* Hampson et al., 2006), or across domains and connectivity patterns, as in comparing motor behavior to measures of connectivity across networks such as motor and attention (Carter et al., 2010). An alternative strategy is to test whether specific patterns of brain connectivity co-vary in a meaningful way with behavioral measures. For example, some studies have emphasized a correlation with global measures of connectivity (Chiang et al., 2009; van den Heuvel et al., 2009). It will be important to explore how behavioral performance relates to a variety of connectivity measures, including: 'dense connectome' representations at the level of voxels and surface vertices; 'parcellated connectome' representations of connectivity between cortical and subcortical parcels defined anatomically and/or functionally; different approaches for estimating the connectivities themselves (*e.g.*, "functional" *vs.* "effective" connectivity measures (Friston et al., 2003)); and graph-theoretical representations at the level of brain networks and subnetworks (Bullmore and Sporns, 2009). Accordingly, it is important that the HCP

informatics platform provides access to connectivity data at each major level of analysis, including voxelwise time-course data (Marcus et al., 2011).

MR hardware

To obtain the best possible MR data quality while scanning many subjects for the HCP, we decided to pursue a dual path involving customized 3T and 7T scanners. 3T systems are the more mature and robust platforms, compatible with the need to scan a large number of subjects. 7T systems offer advantages, especially for the resting and task-based fMRI studies, but also for diffusion-based techniques if sufficiently short echo times can be achieved for diffusion weighting. However, 7T platforms are less mature and more challenging to work with, and are thus incompatible with an ambitious data collection strategy. Accordingly, our plan is to scan all 1200 subjects at 3T, and 200 of them also at 7T. Both scanners will be modified to improve performance compared to what is available on a standard platform. There is also a possibility of imaging some HCP subjects using a new 10.5T whole body scanner that the CMRR at UMinn is building through support from a separate NIH grant. However, whether the HCP is able to scan at this ultrahigh field will depend on when the system becomes operational and key scanning protocols implemented.

New Connectome 3T scanner

Our design for the Connectome 3T MRI scanner took into consideration issues of reliability, subject comfort, and potential risks inherent in new hardware development. Unique features of the Connectome 3T involve the gradients and the RF-receive hardware. Diffusion imaging (dMRI) benefits from high gradient amplitudes that can shorten the diffusion encoding period and thus increase SNR. Multichannel receive capability is critical to parallel imaging techniques that are being developed in this project to significantly reduce whole brain data acquisition times both for fMRI and for dMRI (see below).

We considered several options for achieving gradient amplitudes higher than the 40 mT/m available on standard Siemens 3T scanners. Over the range from 40 mT/m to 300 mT/m the SNR gains depend nonlinearly on the b-value as well as the gradient strength. Fig. 2 demonstrates simulated SNR values achievable with a Stejskal–Tanner pulsed gradient diffusion sequence modeled assuming infinite slew gradients. Due to the sequence's $G^2 T_p^3$ non-linear dependence of b-value, stronger gradients (G) do not proportionately reduce pulse width (T_p) or the minimum possible echo time (TE) on which SNR is dependent.[1] The relative SNR (normalized to 100% for 300 mT/m) depends on the b-value. However, even for very ambitious b values (10^4 s/mm^2), 100 mT/m maximum gradient strength provides ~70% of the SNR achievable relative to a 300 mT/m maximum.

Based on these considerations, we chose a gradient configuration that can achieve a maximum gradient strength of 100 mT/m using existing and tested hardware components. Specifically, we are using a Siemens 3T Skyra scanner modified to include a Siemens SC72 gradient coil that has been used extensively in 7T scanners, where its maximum gradient strength is 70 mT/m. This will be further increased to ~ 100 mT/m using gradient amplifiers

[1] Calculations were performed using 3T T2 for white matter, relative to b = 0 for the minimum achievable TE in a Stejskal and Tanner spin echo sequence with one refocusing pulse. Ramp times were ignored for these calculations. The minimum δ (see diagram) was calculated for a given b, G and d (note: $\Delta = \delta + d$) by solving $0 = b - (2\pi \cdot 42.58 \times 10^{-3} \cdot G \cdot \delta) \cdot 10^{-3} \cdot (2\delta/3 + d)$ where b is s/mm^2, δ and d in ms and G in mT/m. The minimum TE = 2δ + MinTE, where MinTE = minimum TE achievable with δ = 0, d = 0, which was taken to be 15 ms based on existing sequences with partial Fourier acquisition. SNR is calculated using the biexponential diffusion approximation and SNR_μ $(0.75e^{-bD_F} + 0.25e^{-bD_S})\, e^{-(2\delta+MinTE)/T2}$ where D_F and D_S are fast and slow apparent diffusion constants, respectively, (assumed to be 0.8×10^{-3} and 1×10^{-4} mm^2/s) with corresponding fractional pool sizes of 0.75 and 0.25 (taken from Ronen et al., 2005), with d = 6 ms. White matter 3T T2 was assumed to be 70 ms (Stanisz et al., 2005).

with higher current output, adapted from the Siemens 1.5T Aera scanner. This design entails only low technical risk and is well suited to our HCP objectives.

Alternative available *de novo* designs that theoretically could approach 300 mT/m are technically demanding and at risk of not meeting key performance characteristics (*e.g.* eddy currents, nonlinearities, stability, duty cycle, safety *etc.*). The SC72 has excellent eddy current performance in its standard configuration in an 82 cm bore magnet and should perform even better in the 90 cm bore 3T magnet. The Skyra scanner has 64 receiver channels, for use with a commercial 32-channel head coil and with customized arrays having larger number of coils that will be designed at CMRR and explored for improved SNR and acceleration.

7T scanner

The (new) UMinn 7T is also equipped with SC72 gradients and will have 32 channels initially, but will be upgraded to 64 channels before 7T scanning on the main cohort commences. The system will have third-order shims, which will improve EPI quality. RF coils will consist of multichannel receive and transmit arrays to be built at CMRR.

MR data acquisition

Important advances in pulse sequences will benefit three MR modalities (dMRI, R-fMRI, and T-fMRI) and are described in Pulse sequence improvements section. This description is followed by subsections on modality-specific aspects of MR data acquisition.

Pulse sequence improvements

The primary approach to fMRI and diffusion imaging for connectivity studies involves single shot imaging using EPI. Since its initial application, EPI scan times for whole brain coverage have not substantially decreased. Progress in shortening the EPI acquisition time for spatial encoding (Pruessmann et al., 1999; Sodickson et al., 1999; Griswold et al., 2002; Liang et al., 2003) only modestly reduces acquisition time for whole brain coverage. This modest reduction is because each slice incorporates a physiological contrast preparation period that can equal or exceed the time employed for collecting the EPI echo train. A major objective of the HCP is to achieve rapid whole-brain image acquisition with high spatial resolution for both diffusion imaging and fMRI.

Our approach to reducing scan time capitalizes on the simultaneous excitation of multiple brain slices and sharing diffusion or BOLD preparation among all slices excited. This is accomplished with multiple receivers and multiband excitations (Larkman et al., 2001), as developed for fMRI by the UMinn group (Moeller et al., 2010), and with SIR, involving acquisitions of multiple slices adjacent in time but in the same echo train (Feinberg et al., 2002). These can be combined into Multiplexed EPI (Feinberg et al., 2010). Acquiring many slices in the time of a single EPI echo train (or marginally longer echo train when SIR is employed) and a single contrast preparation period, permits sub-second whole brain coverage at 2 or 3 mm isotropic resolution (Fig. 3), yielding improved resting state fMRI results (see R-fMRI acquisition strategies section), and substantially reduced acquisition times for dMRI. These advances will benefit both diffusion and fMRI data directly through higher data acquisition rates, without serious losses in SNR, and indirectly, by reducing the total number of diffusion gradient pulses per whole brain scan, allowing more time for gradient coil cooling when very high b-values are used.

Another important technical consideration involves various distortions that can plague subsequent analyses if not adequately corrected. Field map scans will be acquired and used to correct fMRI images for distortions arising from magnetic field inhomogeneities. For

dMRI, pulse sequences that traverse k space in opposite phase encoding directions will be acquired and used to calculate and eliminate the image distortions (Andersson et al., 2003).

dMRI strategies

The MR hardware and pulse sequence developments described above have significant implications for the diffusion imaging strategies to be used by the HCP. Accelerated imaging will enable collection of many hundreds or even thousands of diffusion-encoded data points per voxel. The customized gradient coils on the Connectome 3T will enable acquisition of high b-value data while reducing the usual SNR trade-off. Because such data have not previously been acquired in human subjects, Phase I of the HCP will entail extensive piloting and testing by the diffusion imaging team on both 3T and 7T datasets.

We aim to identify a diffusion imaging acquisition and reconstruction protocol that will (a) provide veridical reconstructions of fiber orientations in a physical phantom; (b) provide high multi-orientation sensitivity and low uncertainty in regions of crossing fibers *in vivo*; (c) provide high test–retest reliability over the whole brain; and (d) provide accurate connectivity data when compared to expectations from macaque tracer studies and from same-subject functional connectivity derived from R-fMRI (R-fMRI acquisition strategies section). Among the many decisions that must be made, the most significant are the choice of diffusion-encoding scheme, for maximizing orientation sensitivity, and the choice of spatial resolution, which involves a trade-off between the accuracy of orientation peaks and the sensitivity to crossing fibers and minor pathways. We will evaluate and compare diffusion encoding schemes that sample k-space using single or multiple spherical shells, with the parameters of each scheme pre-optimized. Testing on the customized 3T Skyra, which commenced in the fall of 2011, will aim to efficiently narrow down the primary choices using multiple criteria as described above. This will be followed by fine-tuning of acquisition parameters.

In conjunction with data acquisition improvements, we are performing extensive evaluation and optimization of diffusion imaging reconstruction methods. The availability of high resolution and high SNR data will open up new possibilities. For example, we are extending multi-fiber fitting algorithms to account for (i) more complex fiber architectures, such as fanning and bending fibers and (ii) more complex data types, such as multi-q-shell or Cartesian acquisitions (Aganj et al., 2010). These new techniques will be evaluated against established techniques such as compartment modeling (Behrens et al., 2007), spherical deconvolution (Tournier et al., 2004), and Diffusion Spectrum Imaging reconstructions (Wedeen et al., 2008).

R-fMRI acquisition strategies

As illustrated already (Pulse sequence improvements section), important advances in pulse sequences have emerged from early HCP efforts. This includes combining two EPI accelerations that in combination markedly reduce TR (Feinberg et al., 2010). The reduction in TR (to less than a half second, *i.e.*, much less than T_1) decreases the SNR in each individual fMRI image, but with respect to final time series statistics, the increased number of timepoints more than compensates for this. The expected overall SNR change is a gain of 10–15%. However, for high-dimensional multiple regressions (such as that implicit in a high-dimensional functional parcellation using independent component analysis), we found an increase in effective SNR of 60% when reducing TR from 2.5 s to 0.4 s, because of the importance of the temporal degrees of freedom in such analysis. A similar gain (and for similar reasons) may occur in some network modeling analyses, such as those involving partial correlation (Smith et al., 2011) to estimate 'direct' network connections.

Additional increases in acceleration factors are anticipated, but they are likely to yield diminishing returns, because distortions and reconstruction artifacts may increase, while the temporal sampling becomes much faster than useful temporal information available in the (hemodynamically blurred) fMRI timeseries. On the other hand, there may be additional valuable gains, including an improved ability to model and remove physiological artifacts (Glover et al., 2000) including head motion (Power et al., 2012); improved ability to model nonstationarities (temporal variation) in the network structure (Chang and Glover, 2010); improvement in estimating higher-order statistics for network modeling (Shimizu et al., 2006); and richer modeling of the temporal dynamics of R-fMRI fluctuations and in the interactions between different functional areas (Smith et al., 2012).

As with dMRI, the effort to optimize R-fMRI acquisition parameters for Phase II data acquisition will require choices among many competing factors that will differ for 3T and 7T scanners. It will entail careful choice of pulse sequence parameters along with 'standard' parameters such as spatial and temporal resolution, echo-time (TE), bandwidth, MB and SIR slice acceleration factors, and within-slice parallel acceleration factor (which have different effects on g-factors and the use of partial-k-space). The interdependencies can be complex, and the choices for single parameters can involve tradeoffs. For example, one TE might give better overall SNR, whereas a different value might show better signal localization in tissue *vs.* local larger veins. A key objective will be to achieve sub-second TR while minimizing EPI distortion and dropout, and maximizing SNR and spatial resolution. Endpoints by which the results will be judged will include maximization of the number of functional parcels that can be reproducibly distinguished from one another, as well as the reproducibility of the network connections (between these parcels) that are then estimated. These R-fMRI distinctions can also be related to functional distinctions (Smith et al., 2009). Other decisions involve different kinds of tradeoffs: for example, the longer the imaging session the better, from the point of view of imaging data quality and the ability to sample dynamics of functional connectivity. However, this must be balanced against subjects' compliance and load, given the many modalities of data acquisition.

T-fMRI acquisition strategies

Our primary goals in including task-related fMRI measures (T-fMRI) are to (i) help identify as many "nodes" (functionally distinct brain parcels) as possible that can guide, validate, and interpret the results of the connectivity analyses that will be conducted on R-fMRI and dMRI data; (ii) provide task-activation data that can be combined with MEG data to better understand information flow within networks; (iii) allow comparison of network connectivity in a task context to connectivity results generated using R-fMRI; and (iv) to understand the relative utility of T-fMRI and R-fMRI in predicting individual differences in behavior and genetic influences. To accomplish these goals, we are developing a battery of tasks that can identify node locations in as wide a range of neural systems as feasible within realistic time constraints (~60 min in Phase II). In Phase I, we are piloting a larger number of tasks than we anticipate being able to use in Phase II. We will compare the sensitivity, reliability and brain coverage afforded by these tasks to arrive at a final T-fMRI battery that balances optimizing the psychometric properties of the activation measures (*i.e.*, high reliability and sensitivity are necessary for individual difference and genetic analyses) with behavioral validity and interpretability. Phase I piloting includes measures of visual-motor processes (retinotopy, motor strip mapping, biological and non-biological motion), as well as a range of cognitive (working memory, episodic memory, language, attention, stimulus category representations) and affective/social processes (emotion recognition, reward and punishment based decision making, and social cognition). When possible, we are piloting tasks that allow us to assess multiple networks simultaneously. For example, we have developed a working memory task that uses different categories of stimuli. This enables

collapsing across stimulus type to identify working memory related networks, and separately collapsing across memory loads to identify brain regions that respond differentially to different stimulus types. In choosing tasks to pilot in Phase 1, we emphasized ones with existing evidence of suitability as localizers in individual subjects, or evidence for their reliability across subjects or within subjects across time. We also emphasized paradigms suitable for optimized blocked designs to achieve maximum efficiency. Supplemental Table S3 lists the tasks currently being piloted.

Like R-fMRI, T-fMRI is likely to benefit considerably from low-TR data acquisition. For example, improved temporal resolution should aid in discerning differences in the time course of task activation/deactivation according to brain region and/or task (*e.g.*, Nelson et al., 2010). The choice of T-fMRI pulse sequence parameters along with 'standard' parameters such as spatial and temporal resolution will involve many of the same considerations as for R-fMRI (R-fMRI acquisition strategies section). We will capitalize on the improvements that are identified for R-fMRI early in Phase I by using the same acquisitions for T-fMRI (after confirming with a subset of T-fMRI tasks that the final acquisition protocol works well for task and not just rest). Measures for evaluating acquisition parameters will include assessments of the robustness, spatial extent, and reproducibility of significant task activations and deactivations.

Anatomical MRI acquisition strategies

Conventional structural MRI using T1w scans provide an essential anatomical substrate for visualizing brain structures, generating subcortical segmentations, and reconstructing cortical surfaces. We will also combine anatomical T1w and T2w scans, using the T1w/T2w ratio to map myelin content across the cortical surface and thereby distinguish many architectonic areas non-invasively (Glasser and Van Essen, 2011). This method works with standard 3T 1 mm isotropic T1w and T2w images, but we will explore whether higher resolution images improve architectonic delineations. Additionally at 7T, we will aim to use a similar strategy to map cortical myelin content at 0.6 mm isotropic resolution or higher. Myelin maps will complement other MR modalities in localizing cortical areas in individual subjects and in providing a substrate for improved intersubject registration.

MR scan duration

To obtain the highest quality imaging data feasible for each MR modality, multiple scan sessions are planned for each subject during the 2-day visit. The session structure currently being piloted includes a set of structural scans (20 min total), one diffusion imaging session (1 h), and two 1 h fMRI sessions (each 30 min resting-state followed by 30 min task-fMRI). Participants will be asked if they are willing to undergo an additional voluntary scan session of up to 1 h; this will be used to re-acquire data on any scans that failed to pass initial QC and/or to carry out additional scans using advanced acquisition protocols that might be very informative even if carried out on a modest number of individuals.

MEG/EEG

Non-invasive electrophysiological recording will be carried out in addition to MR scanning and behavioral and genetic testing on 100 subjects (some of whom may also have MR scans at 7T as well as 3T). MEG/EEG is complementary to fMRI in that it provides a window onto the neurophysiological processes underling sensory, motor, and cognitive functions at a temporal scale inaccessible to fMRI. The Blood Oxygen Level Dependent (BOLD) signal detected in fMRI reflects neuronal activity only indirectly; owing to the temporal dynamics of neurovascular coupling (the hemodynamic response function), peak sensitivity to neural activity modulations is on a time scale of seconds (Hathout et al., 1999). In contrast, MEG and EEG respectively detect external magnetic fields and scalp potentials arising from

neuronal activity within the brain with millisecond-level temporal resolution. However, the spatial specificity of non-invasive electrophysiology is worse than that of fMRI. Neural sources at the brain surface may be localized with a precision on the order of a few mm, but securely assigning responses to one of multiple simultaneously active generators requires that they be separated by several cm (Mosher et al., 1993). Moreover, MEG sensitivity is largest for parts of the brain within several cm of the sensors; the mesial and inferior cortical surfaces as well as subcortical structures including thalamus and striatum are largely inaccessible. Despite the limited spatial resolution, the richness of temporal information obtained by MEG/EEG enables assessment of how brain rhythmical activity relates to resting and task-evoked connectivity. All these characteristics influence how MEG and EEG data will be integrated with T-fMRI and R-fMRI data, as well as the methods by which cortical parcellation can be applied to these temporally dense signals.

Both R-MEG and T-MEG electrophysiology data will be acquired at SLU using the Magnes 3600 (4D Neuroimaging, San Diego, CA) equipped with 248 magnetometers, 23 MEG reference channels (5 gradiometer, and 18 magnetometer) and 64 EEG Voltage Channels (4 bipolar, 60 monopolar). The system is installed inside a magnetically shielded room that includes one layer of aluminum and two layers of high magnetic permeability material. The RMS noise of the magnetometers is ~5 fT/sqrt (Hz) on average in the white noise range (above 2 Hz). Experience gained during HCP Phase I will determine whether it will be practical to routinely record EEG during Phase II. Prior to MEG/EEG data acquisition, the positions of the EEG electrodes and shape of the subject's head will be mapped by marking fiducials on the subject's skin and using a Polhemus localization system. This will enable co-registration with anatomic MR scans performed subsequently at WashU. The MR data will be used to create anatomic models to support MEG/EEG source reconstruction and will be collected after the MEG/EEG recording session to avoid errors due to subject magnetization. Subjects will complete three resting state scans followed by a set of task runs, with all data collected in a single 2-hour session. MEG/EEG data analyses will be based on the FieldTrip platform (Oostenveld et al., 2011).

The MEG/EEG task paradigms will involve tasks that activate the lateral and dorsal surface of the brain, which are more sensitively sampled by MEG/EEG. In phase I, pilot data will be acquired for motor processes (motor strip mapping), memory (working memory, episodic memory), language, and attention tasks. To facilitate comparisons between T-MEG/EEG and T-fMRI scans, the MEG/EEG task paradigms will be identical in temporal sequence to those used for T-fMRI. Each task under consideration includes sufficient stimuli to allow presentation of different stimuli in each run, thereby avoiding priming effects that might otherwise interfere with subsequent T-fMRI protocols. While the temporal sequence of task protocols will be maintained, T-MEG/EEG protocols may be extended in duration to allow collection of enough trials to ensure adequate sensitivity. Based on the results of these pilot studies, a subset of tasks will be chosen for inclusion in phase II.

A major emphasis of the MEG/EEG component of the HCP will be on developing novel analysis strategies. Non-invasive electrophysiology historically has focused on averaging responses in phase with behaviorally salient events (Dale et al., 2000). Our behavioral protocols will support this methodology but the emphasis will be on analyses of induced oscillatory activity, *e.g.*, event-related time-frequency responses (Hoogenboom et al., 2006) and event-related changes in synchrony within and across brain regions (Siegel et al., 2008). Particular emphasis will be given to novel approaches for analyzing resting state MEG data that require analysis pipelines (Mantini et al., 2011) different from those used for T-MEG paradigms. Patterns of MEG resting connectivity can be studied through *e.g.*, correlation of band-limited power time series (de Pasquale et al., 2010) and characterizing node-pair interactions using complex coherency (Marzetti et al., 2008). Delineation of MEG resting

state networks based on beam-former techniques (Brookes et al., 2011) will also be investigated.

Quality assurance

Given the richness and complexity of the datasets to be generated in Phase II of the HCP, it is important to establish and maintain rigorous quality assurance (QA) plans and quality control (QC) processes. Although HCP is a cross-sectional study, the three-year Phase II data collection period and the importance of avoiding drift in 'healthy normal' data over time means that many QA and QC challenges faced by longitudinal studies are relevant to HCP. These issues include potential protocol changes, scanner equipment wear, and differences in behavioral interviewing techniques across research staff (Whitney et al., 1998). The HCP Phase II protocols will be fully piloted in late Phase I using adult twins/ sibships who do not meet family size criteria for participating in Phase II. We intend that the core HCP protocol, once established, will be invariant throughout Phase II. This protocol will be documented in Standard Operating Procedures made publicly available. Key advances that occur over the course of the study, *e.g.* in pulse sequences, may be evaluated in additional sessions while the subjects are on-site. To avoid data drift related to equipment performance, scanner QC will be performed daily, and the stability of primary measures associated each data type will be tracked. Many technical aspects of the quality assurance effort are described in Marcus et al. (2011). Efforts to standardize interviewing techniques will include selecting staff to minimize turnover; computerizing the majority of behavioral tests to ensure standard presentation and analysis; and careful training and occasional observation of interviews via audiotapes and two-way mirrors in our testing suite. We will establish an atmosphere in which staff and investigators understand the importance of standardization and are encouraged to discuss and address any issues that might impact this objective.

Discussion

Three issues touched upon above warrant brief discussion. These include issues of (i) limitations of *in vivo* imaging; (ii) advantages of twin–sibship families coupled with data sharing limitations; and (iii) the relationship of HCP to other large-scale neuroimaging projects.

Inherent limits of in vivo human imaging

Advances in MR scanner design and simultaneous multiplexed data acquisition described above will allow the HCP to generate an unprecedented amount of high quality data on brain connectivity and associated measures in healthy adults (see also Van Essen and Ugurbil, 2012). However, the 'macro-connectome' assessments of human brain connectivity accessible via *in vivo* imaging are on a very different scale than the 'micro-connectome' assessments of brain connectivity at the level of single neurons, axons, dendrites, and synapses (Akil et al., 2011). Macro-connectome approaches aim to estimate long-distance connectivity between gray-matter regions using isotropic voxels that are currently often 2 mm (dMRI) or 3 mm (R-fMRI) for 3T and can be 1–2 mm for 7T. The HCP anticipates reducing voxel size for both modalities and for both 3T and 7T, but the scale will remain vastly greater than that of the constituent neuronal elements: human cerebral cortex on average contains ~40,000 neurons and ~3×10^8 synapses per mm,[2] and white matter contains ~300,000 axons per mm^2 cross-sectional area.[3] Micro-connectome approaches are currently restricted to laboratory animals and aim to reconstruct circuitry at scales yet to

[2]This is based on estimates of 19 billion cortical neurons (Azevedo et al., 2009), 150 trillion cortical synapses (Pakkenberg et al., 2003), and 472 cm^3 (4.7×10^4 mm^3) cortical gray matter volume (Van Essen et al., 2011).

reach 1 mm^3 of brain tissue (Briggman and Denk, 2006; Smith, 2007; Lichtman et al., 2008). Thus, a vast gulf remains between macro- and micro-connectome scales.

Twin–sibship families and data sharing

Our decision to acquire data from twins and non-twin siblings will enable analyses of the heritability of brain circuits and will greatly increase the power of genetic analyses. However, due to the relatively small size and localized geography of the subject population, HCP faces some extra challenges with respect to subject confidentiality and privacy, especially regarding sensitive data. One likely scenario is that the publicly released HCP dataset will include all neuroimaging data and most behavioral data, along with subject sex and age range (*e.g.*, 5-year grouping). Information about family relationships, ethnic and racial identity, exact age (year), and potentially sensitive behavioral measures would be restricted to qualified investigators who agree to appropriate limits on storage and distribution of sensitive data. The publicly released data could also include a dataset consisting of only one individual per family, thereby allowing analyses not confounded by unspecified family relationships.

Relationship to other large-scale imaging projects

A growing number of projects are carrying out large-scale neuroimaging plus behavioral phenotyping on different populations. A non-exhaustive list includes the Alzheimer's Disease Neuroimaging Initiative (ADNI; http://www.adni-info.org/); the Thousand Functional Connectomes project and International Neuroimaging Data-sharing Initiative (INDI, http://fcon_1000.projects.nitrc.org/; Zuo et al., 2010); the IMAGEN study of teenagers and mental health (http://www.imagen-europe.com); the AGES Reykjavik Study of Healthy Aging (http://www.hjarta.is/english/ages); and the Rotterdam study of aging (http://www.epib.nl/research/ergo.htm). Rather than considering each project and associated database as an isolated silo of data, the neuroscience community should make such efforts synergistic to the degree that practical considerations allow. Among the obvious challenges are differences in imaging protocols and scanner hardware, differences in behavioral measures, and different database and data mining platforms. Sharing of information about plans and protocols while there is still flexibility may help to increase commonality in each of these domains and thereby enhance the ability of the community to gain information and insights from data mining that cuts across projects.

In comparison to these other endeavors, the HCP is by no means the largest in terms of the number of subjects studied or in the aggregate amount of data to be collected. However, it is surely the most complex in terms of the diversity of imaging modalities combined with the richness of the behavioral and genetic information to be collected. It also will have an informatics platform that supports an unprecedented degree of visualization and analysis capabilities customized for data mining across all of these modalities. Finally, the HCP is uniquely positioned to improve a variety of data acquisition methods and protocols for brain connectivity studies. An important part of its mission is to openly share these methods as they move from evaluation to production stages. The HCP maintains an active outreach effort to promote awareness in the neuroscience community of the data acquisition strategies outlined here and the informatics strategies described elsewhere (Marcus et al., 2011) and to facilitate coordination with other large-scale neuroimaging projects.

[3]The human corpus callosum has 2×10^8 axons (Aboitiz et al., 1992) and a cross-sectional area of 570 mm^2 (Rauch and Jinkins, 1996), yielding ~3.5×10^5 axons per mm^2. Human cerebral white matter has a volume of ~700 cm^3 (7×10^5 mm^3) (Azevedo et al., 2009; Pakkenberg et al., 2003), and ~150,000 km of aggregate axonal length (150,000–180,000 (Pakkenberg et al., 2003); 120,000 (Tang and Nyengaard, 1997)), for an average of 2.2×10^5 mm of axonal length per mm^3 of white matter.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

ADNI	Alzheimer's Disease Neuroimaging Initiative
CMRR	Center for Magnetic Resonance Research at UMinn
dMRI	diffusion imaging
DZ	dizygotic
EPI	echoplanar imaging
HCP	Human Connectome Project, WU-Minn Consortium
INDI	International Neuroimaging Data-sharing Initiative
MEG/EEG	magnetoencephalography and electroencephalography
MZ	monozygotic
NIRS	near infrared spectroscopy
PET	positron emission tomography
R-fMRI	resting state fMRI
R-MEG	resting state magnetoencephalography
RF	radio frequency
SIR	simultaneous image refocusing
SLU	St. Louis University in St. Louis, MO
SNR	signal-to-noise ratio
T-fMRI	task-evoked fMRI
T-MEG	task-evoked magnetoencephalography
T1w	T1-weighted
T2w	T2-weighted
TE	echo time
TR	repetition time
UMinn	University of Minnesota
WashU	Washington University in St. Louis, MO
WU-Minn	Washington University and University of Minnesota
3T	3 Tesla

7T 7 Tesla

References

Aboitiz F, Scheibel AB, Fisher RS, Zaidel E. Fiber composition of the human corpus callosum. Brain Res. 1992; 598:143–153. [PubMed: 1486477]

Achenbach TM, Krukowski RA, Dumenci L, Ivanova MY. Assessment of adult psychopathology: meta-analyses and implications of cross-informant correlations. Psychol. Bull. 2005; 131:361–382. [PubMed: 15869333]

Aganj I, Lenglet C, Sapiro G, Yacoub E, Ugurbil K, Harel N. Reconstruction of the orientation distribution function in single- and multiple-shell q-ball imaging within constant solid angle. Magn. Reson. Med. 2010; 64:554–566. [PubMed: 20535807]

Akil H, Martone ME, Van Essen DC. Challenges and opportunities in mining neuroscience data. Science. 2011; 331:708–712. [PubMed: 21311009]

Andersson S, Skare, Ashburner J. How to correct susceptibility distortions in spin-echo echo-planar images: application to diffusion tensor imaging. NeuroImage. 2003; 20:870–888. [PubMed: 14568458]

Azevedo FA, Carvalho LR, Grinberg LT, Farfel JM, Ferretti RE, Leite RE, Jacob Filho W, Lent R, Herculano-Houzel S. Equal numbers of neuronal and non-neuronal cells make the human brain an isometrically scaled-up primate brain. J. Comp. Neurol. 2009; 513:532–541. [PubMed: 19226510]

Behrens TE, Berg HJ, Jbabdi S, Rushworth MF, Woolrich MW. Probabilistic diffusion tractography with multiple fibre orientations: what can we gain? NeuroImage. 2007; 34:144–155. [PubMed: 17070705]

Briggman KL, Denk W. Towards neural circuit reconstruction with volume electron microscopy techniques. Curr. Opin. Neurobiol. 2006; 16:562–570. [PubMed: 16962767]

Brookes MJ, Hale JR, Zumer JM, Stevenson CM, Francis ST, Barnes GR, Owen JP, Morris PG, Nagarajan SS. Measuring functional connectivity using MEG: methodology and comparison with fcMRI. NeuroImage. 2011; 56:1082–1104. [PubMed: 21352925]

Bucholz KK, Cadoret R, Cloninger CR, Dinwiddie SH, Hesselbrock VM, Nurnberger JI Jr, Reich T, Schmidt I, Schuckit MA. A new semi-structured psychiatric interview for use in genetic linkage studies: a report on the reliability of the SSAGA. J. Stud. Alcohol. 1994; 55:149–158. [PubMed: 8189735]

Bullmore E, Sporns O. Complex brain networks: graph theoretical analysis of structural and functional systems. Nat. Rev. Neurosci. 2009; 10:186–198. [PubMed: 19190637]

Carter AR, Astafiev SV, Lang CE, Connor LT, Rengachary J, Strube MJ, Pope DL, Shulman GL, Corbetta M. Resting interhemispheric functional magnetic resonance imaging connectivity predicts performance after stroke. Ann. Neurol. 2010; 67:365–375. [PubMed: 20373348]

Chang C, Glover GH. Time-frequency dynamics of resting-state brain connectivity measured with fMRI. NeuroImage. 2010; 50:81–98. [PubMed: 20006716]

Chiang MC, Barysheva M, Shattuck DW, Lee AD, Madsen SK, Avedissian C, Klunder AD, Toga AW, McMahon KL, de Zubicaray GI, Wright MJ, Srivastava A, Balov N, Thompson PM. Genetics of brain fiber architecture and intellectual performance. J. Neurosci. 2009; 29:2212–2224. [PubMed: 19228974]

Dale AM, Liu AK, Fischl BR, Buckner RL, Belliveau JW, Lewine JD, Halgren1 E. Dynamic statistical parametric mapping: combining fMRI and MEG for high-resolution imaging of cortical activity. Neuron. 2000; 26:55–67. [PubMed: 10798392]

de Pasquale F, Della Penna S, Snyder AZ, Lewis C, Mantini D, Marzetti L, Belardinelli P, Ciancetta L, Pizzella V, Romani GL, Corbetta M. Temporal dynamics of spontaneous MEG activity in brain networks. Proc. Natl. Acad. Sci. U. S. A. 2010; 107:6040–6045. [PubMed: 20304792]

Eaves, LJ. The utility of twins. In: Anderon, V., et al., editors. Genetic Bases of the Epilepsies. New York: Raven Press; 1982.

Edens EL, Glowinski AL, Pergadia ML, Lessov-Schlaggar CN, Bucholz KK. Nicotine addiction in light smoking African American mothers. J. Addict. Med. 2010; 4:55–60. [PubMed: 20582148]

Estle SJ, Green L, Myerson J, Holt DD. Differential effects of amount on temporal and probability discounting of gains and losses. Mem. Cognit. 2006; 34:914–928.

Feinberg DA, Reese TG, Wedeen VJ. Simultaneous echo refocusing in EPI. Magn. Reson. Med. 2002; 48:1–5. [PubMed: 12111925]

Feinberg DA, Moeller S, Smith SM, Auerbach E, Ramanna S, Glasser MF, Miller KL, Ugurbil K, Yacoub E. Multiplexed echo planar imaging for sub-second whole brain FMRI and fast diffusion imaging. PLoS One. 2010; 5:e15710. [PubMed: 21187930]

Friston KJ, Harrison L, Penny W. Dynamic causal modelling. NeuroImage. 2003; 19:1273–1302. [PubMed: 12948688]

Glasser MF, Van Essen DC. Myelin content as revealed by T1- and T2-weighted MRI. J. Neurosci. 2011; 31:11597–11616. [PubMed: 21832190]

Glover GH, Li TQ, Ress D. Image-based method for retrospective correction of physiological motion effects in fMRI: RETROICOR. Magn. Reson. Med. 2000; 44:162–167. [PubMed: 10893535]

Griswold MA, Jakob PM, Heidemann RM, Nittka M, Jellus V, Wang J, Kiefer B, Haase A. Generalized autocalibrating partially parallel acquisitions (GRAPPA). Magn. Reson. Med. 2002; 47:1202–1210. [PubMed: 12111967]

Gur RC, Richard J, Hughett P, Calkins ME, Macy L, Bilker WB, Brensinger C, Gur RE. A cognitive neuroscience-based computerized battery for efficient measurement of individual differences: standardization and initial construct validation. J. Neurosci. Methods. 2010; 187:254–262. [PubMed: 19945485]

Hampson M, Driesen NR, Skudlarski P, Gore JC, Constable RT. Brain connectivity related to working memory performance. J. Neurosci. 2006; 26:13338–13343. [PubMed: 17182784]

Hathout GM, Gopi RK, Bandettini P, Gambhir SS. The lag of cerebral hemodynamics with rapidly alternating periodic stimulation: modeling for functional MRI. Magn. Reson. Imaging. 1999; 17:9–20. [PubMed: 9888394]

Hoogenboom N, Schoffelen JM, Oostenveld R, Parkes LM, Fries P. Localizing human visual gamma-band activity in frequency, time and space. NeuroImage. 2006; 29:764–773. [PubMed: 16216533]

Larkman DJ, Hajnal JV, Herlihy AH, Coutts GA, Young IR, Ehnholm G. Use of multicoil arrays for separation of signal from multiple slices simultaneously excited. J. Magn. Reson. Imaging. 2001; 13:313–317. [PubMed: 11169840]

Liang ZP, Madore B, Glover GH, Pelc NJ. Fast algorithms for GS-model-based image reconstruction in data-sharing Fourier imaging. IEEE Trans. Med. Imaging. 2003; 22:1026–1030. [PubMed: 12906256]

Lichtman JW, Livet J, Sanes JR. A technicolour approach to the connectome. Nat. Rev. Neurosci. 2008; 9:417–422. [PubMed: 18446160]

Mantini D, Della Penna S, Marzetti L, de Pasquale F, Pizzella V, Corbetta M, Romani GL. A signal-processing pipeline for magneto encephalography resting-state networks. Brain Connect. 2011; 1:49–59. [PubMed: 22432954]

Marcus D, Harwell J, Olsen T, Van Essen D. The Human Connectome Project informatics platform. Frontiers in Neuroscience. 2011; 5:4. (Electronic publication ahead of print 2011 Jun 27). [PubMed: 21326618]

Martin N, Boomsma D, Machin G. A twin-pronged attack on complex traits. Nat. Genet. 1997; 17:387–392. [PubMed: 9398838]

Marzetti L, Del Gratta C, Nolte G. Understanding brain connectivity from EEG data by identifying systems composed of interacting sources. NeuroImage. 2008; 42:87–98. [PubMed: 18539485]

McCrae RR, Costa PT Jr. A contemplated revision of the NEO Five Factor Inventory. Personal. Individ. Differ. 2004; 36:587–596.

Moeller S, Yacoub E, Olman CA, Auerbach E, Strupp J, Harel N, Ugurbil K. Multiband multislice GE-EPI at 7 Tesla, with 16-fold acceleration using partial parallel imaging with application to high spatial and temporal whole-brain fMRI. Magn. Reson. Med. 2010; 63:1144–1153. [PubMed: 20432285]

Mosher JC, Spencer ME, Leahy RM, Lewis PS. Error bounds for EEG and MEG dipole source localization. Electroencephalogr. Clin. Neurophysiol. 1993; 86:303–321. [PubMed: 7685264]

Neale, MC.; Cardon, LRE. Methodology for Genetic Studies of Twins and Families. Dordrecht: Kluwer Academic Publishers; 1992.

Nelson SM, Cohen AL, Power JD, Wig GS, Miezin FM, Wheeler ME, Velanova K, Donaldson DI, Phillips JS, Schlaggar BL, Petersen SE. A parcellation scheme for human left lateral parietal cortex. Neuron. 2010; 67:156–170. [PubMed: 20624599]

Oostenveld R, Fries P, Maris E, Schoffelen JM. FieldTrip: open source software for advanced analysis of MEG, EEG, and invasive electrophysiological data. Comput. Intell. Neurosci. 2011 156869 EPub 152010.

Pakkenberg B, Pelvig D, Marner L, Bundgaard MJ, Gundersen HJ, Nyengaard JR, Regeur L. Aging and the human neocortex. Exp. Gerontol. 2003; 38:95–99. [PubMed: 12543266]

Posthuma D, Boomsma DI. A note on the statistical power in extended twin designs. Behav. Genet. 2000; 30:147–158. [PubMed: 10979605]

Power J, Barnes K, Snyder A, Schlaggar B, Petersen S. Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. Neuroimage. 2012; 59:2142–2154. [PubMed: 22019881]

Pruessmann KP, Weiger M, Scheidegger MB, Boesiger P. SENSE: sensitivity encoding for fast MRI. Magn. Reson. Med. 1999; 42:952–962. [PubMed: 10542355]

Rauch RA, Jinkins JR. Variability of corpus callosal area measurements from midsagittal MR images: effect of subject placement within the scanner. AJNR Am. J. Neuroradiol. 1996; 17:27–28. [PubMed: 8770245]

Ronen I, Ugurbil K, Kim DS. How does DWI correlate with white matter structures? Magn. Reson. Med. 2005; 54:317–323. [PubMed: 16032693]

Sartor CE, Bucholz KK, Nelson EC, Madden PA, Lynskey MT, Heath AC. Reporting bias in the association between age at first alcohol use and heavy episodic drinking. Alcohol. Clin. Exp. Res. 2011; 35:1418–1425. [PubMed: 21438885]

Shimizu S, Chang S, Hoyer P, Hyvarinen A, Kerminen A. A linear non-Gaussian acyclic model for causal discovery. J. Mach. Learn. Res. 2006; 7:2003–2030.

Siegel M, Donner TH, Oostenveld R, Fries P, Engel AK. Neuronal synchronization along the dorsal visual pathway reflects the focus of spatial attention. Neuron. 2008; 60:709–719. [PubMed: 19038226]

Smith SJ. Circuit reconstruction tools today. Curr. Opin. Neurobiol. 2007; 17:601–608. [PubMed: 18082394]

Smith SM, Fox PT, Miller KL, Glahn DC, Fox PM, Mackay CE, Filippini N, Watkins KE, Toro R, Laird AR, Beckmann CF. Correspondence of the brain's functional architecture during activation and rest. Proc. Natl. Acad. Sci. U. S. A. 2009; 106:13040–13045. [PubMed: 19620724]

Smith SM, Miller KL, Salimi-Khorshidi G, Webster M, Beckmann CF, Nichols TE, Ramsey JD, Woolrich MW. Network modelling methods for FMRI. Neuro-Image. 2011; 54:875–891. [PubMed: 20817103]

Smith S, Miller KL, Moeller S, Xu J, Auerbach EJ, Woolrich MW, Beckmann CF, Jenkinson M, Andersson J, Glasser MF, Van Essen D, Feinberg D, Yacoub E, Ugurbil K. Temporally-independent functional modes of spontaneous brain activity. Proc. Natl. Acad. Sci. 2012; 109:3131–3136. [PubMed: 22323591]

Sodickson DK, Griswold MA, Jakob PM. SMASH imaging. Magn. Reson. Imaging Clin. N. Am. 1999; 7:237–254. vii–viii. [PubMed: 10382159]

Stanisz GJ, Odrobina EE, Pun J, Escaravage M, Graham SJ, Bronskill MJ, Henkelman RM. T1, T2 relaxation and magnetization transfer in tissue at 3T. Magn. Reson. Med. 2005; 54:507–512. [PubMed: 16086319]

Tang Y, Nyengaard JR. A stereological method for estimating the total length and size of myelin fibers in human brain white matter. J. Neurosci. Methods. 1997; 73:193–200. [PubMed: 9196291]

Tournier JD, Calamante F, Gadian DG, Connelly A. Direct estimation of the fiber orientation density function from diffusion-weighted MRI data using spherical deconvolution. NeuroImage. 2004; 23:1176–1185. [PubMed: 15528117]

van den Heuvel MP, Stam CJ, Kahn RS, Hulshoff Pol HE. Efficiency of functional brain networks and intellectual performance. J. Neurosci. 2009; 29:7619–7624. [PubMed: 19515930]

Van Essen DC, Ugurbil K. The future of the human connectome. Neuroimage. 2012 http://dx.doi.org/10.1016/j.neuroimage.2012.01.032.

Van Essen DC, Glasser MF, Dierker D, Harwell J, Coalson T. Parcellations and hemispheric asymmetries of human cerebral cortex analyzed on surface-based atlases. Cereb. Cortex. 2011

Wedeen VJ, Wang RP, Schmahmann JD, Benner T, Tseng WY, Dai G, Pandya DN, Hagmann P, D'Arceuil H, de Crespigny AJ. Diffusion spectrum magnetic resonance imaging (DSI) tractography of crossing fibers. NeuroImage. 2008; 41:1267–1277. [PubMed: 18495497]

Whitney CW, Lind BK, Wahl PW. Quality assurance and quality control in longitudinal studies. Epidemiol. Rev. 1998; 20:71–80. [PubMed: 9762510]

Zuo XN, Kelly C, Di Martino A, Mennes M, Margulies DS, Bangaru S, Grzadzinski R, Evans AC, Zang YF, Castellanos FX, Milham MP. Growing together and growing apart: regional and sex differences in the lifespan developmental trajectories of functional homotopy. J. Neurosci. 2010; 30:15034–15043. [PubMed: 21068309]

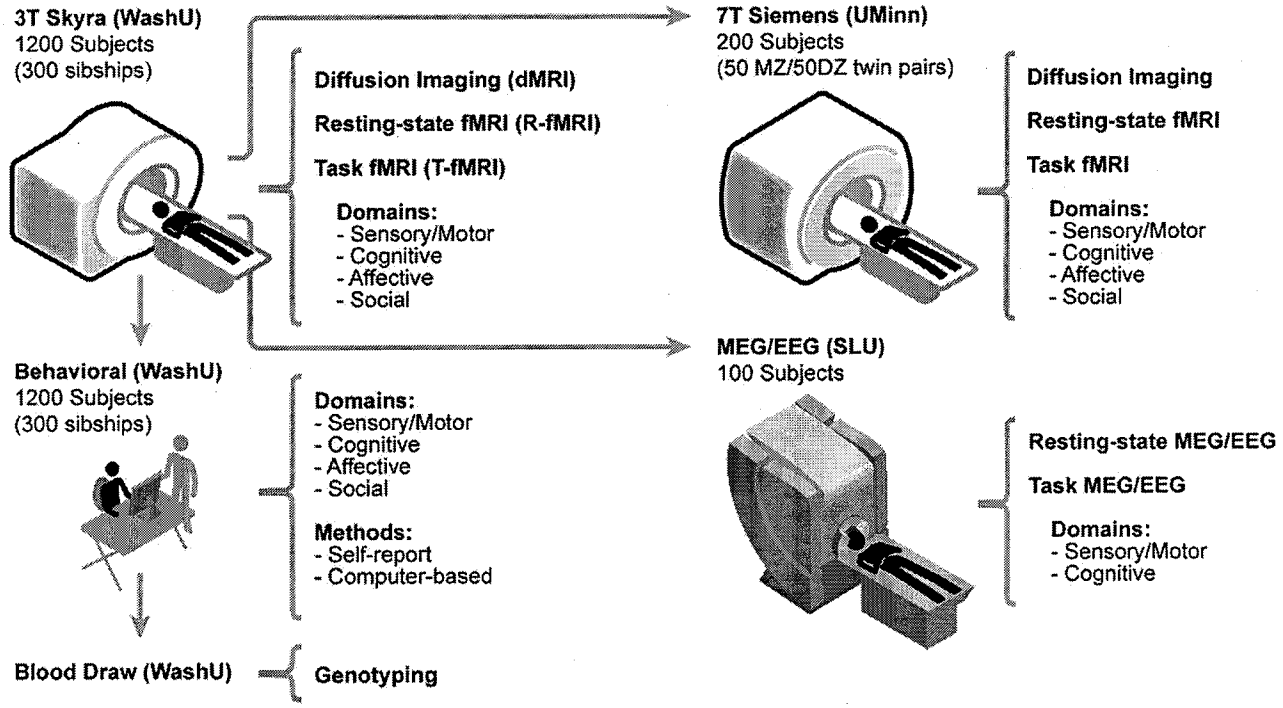

Fig. 1.

Schematic summary for acquiring imaging, behavioral, and genetic data using MR and MEG/EEG scanners at three HCP data acquisition sites. Left: Behavioral testing, blood draws for genotyping, and scanning on a 3T Skyra will be carried out on 1200 healthy adults at Washington University (WashU). Center: Major data acquisition modalities are indicated in the center column; for task-fMRI and behavior, major domains are listed. Top right: A subset of 200 subjects will be scanned on a 7T Skyra at the University of Minnesota (UMinn). Bottom right: A subset of 100 subjects will be scanned using magnetoencephalography (MEG) and perhaps electroencephalography (EEG) at St. Louis University (SLU).

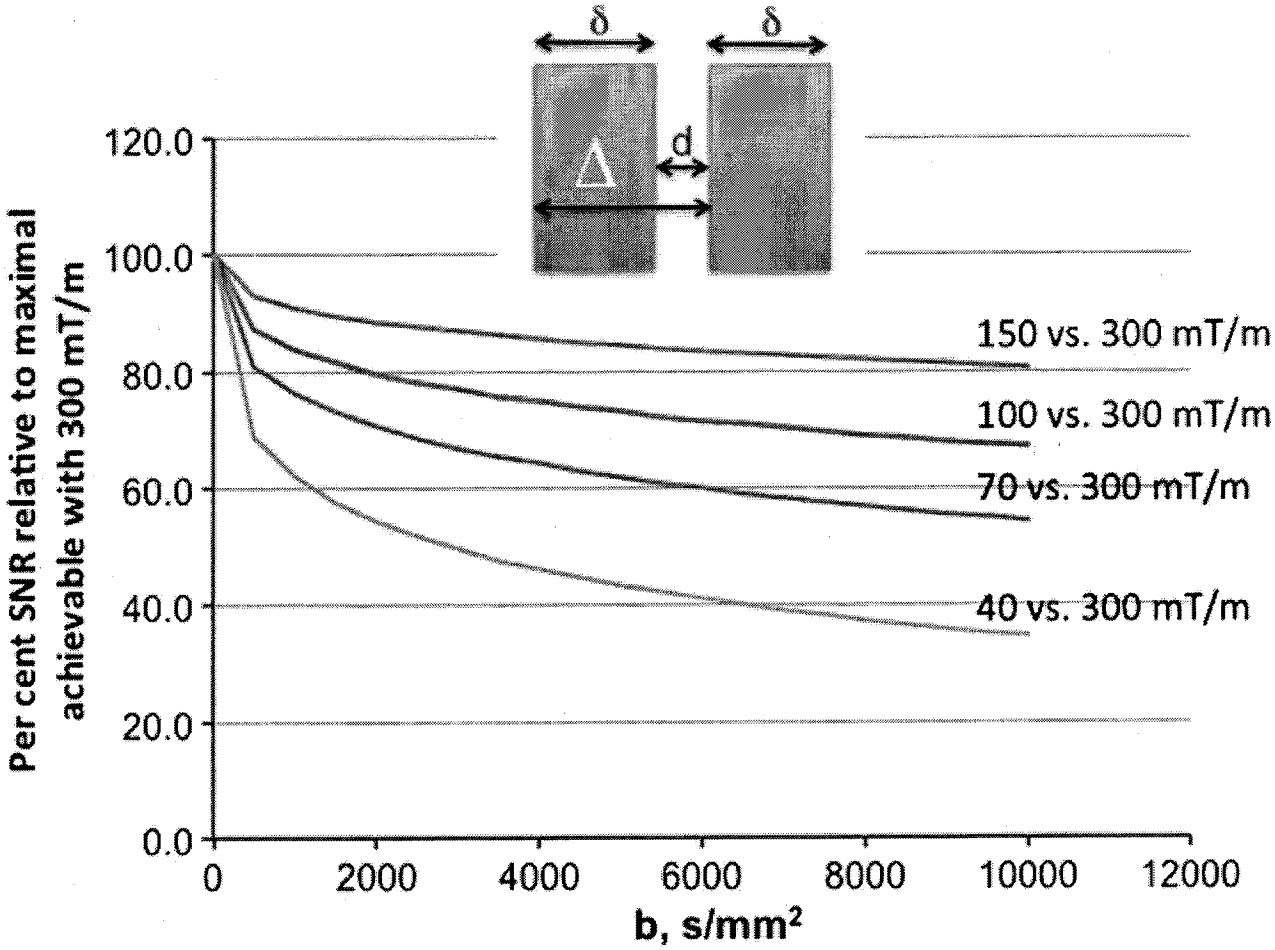

Fig. 2.

Relative SNR at the central k space point in diffusion imaging with 150, 100, 70, and 40 mT/m maximum gradients relative to maximum achievable with 300 mT/m when TE is minimized using the available gradient amplitude, calculated for white matter at different b-values ranging from 500 to 10,000.

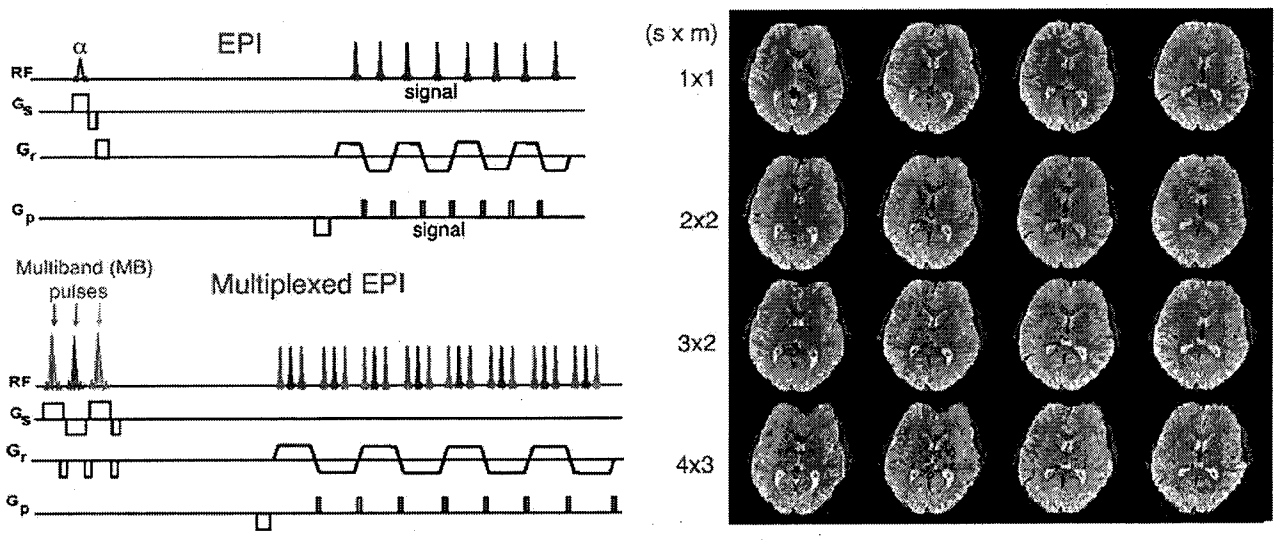

Fig. 3.

The M-EPI pulse sequence compared with conventional EPI. Top left: EPI pulse sequence generates a single slice image during each readout train, which is repeated for each slice to scan the whole brain. The multiband technique replaces the single slice excitation pulse with multiband (MB) pulses to excite several slices simultaneously, which are then unaliased using array coil sensitivity profiles. As such, far fewer repeats are required to scan the whole brain. Bottom left: Multiplexed-EPI (M-EPI) pulse sequence combines the SIR approach with the MB technique: SIR consecutively excites s slices ($s = 3$ is shown in the pulse sequence diagram with pulses in red, blue and green) and reads them out in a single echo train, separated in time. Using MB pulses to simultaneously excite m slices instead of exciting each single slice in the SIR approach produces the M-EPI sequence, with a "slice acceleration" of ($s \times m$) leading to ($s \times m$) number of slices collected in a single echo train. Right: Each column shows four (of 60) slices from a whole brain (2 mm isotropic resolution) 3T data set obtained with the M-EPI technique, shown with the ($s \times m$) acceleration factors ranging from 4 to 12.

Adapted with permission from Feinberg et al. (2010).

EXHIBIT 4

Curriculum Vitae - GODFREY D. PEARLSON

DATE OF BIRTH: January 30, 1950
PLACE OF BIRTH: Sunderland, England
TELEPHONE: (860) 545-7757
EMAIL: godfr@jhmi.edu
gpearls@harthosp.org
godfrey.pearlson@yale.edu

WEBSITE: http://www.nrc-iol.org/

OFFICES:

Olin Neuropsychiatry Research Center
The Institute of Living
200 Retreat Avenue
Hartford, CT 06106

Yale University
Clinical Neuroscience Research Unit
Abraham Ribicoff Research Facilities
Connecticut Mental Health Center
34 Park Street
New Haven, CT 06519

EDUCATION

1969-1974	Newcastle Upon Tyne University Medical School, England, M.B., B.S. Medicine: (equivalent to U.S. MD degree)
1976	Columbia University, Graduate School of Arts and Sciences, New York. M.A. (Philosophy of Science)

CAREER

2013- Present	Adjunct Faculty, Lieber Institute, Johns Hopkins University.
2009 – Present	Professor, Department of Neurobiology, Yale University School of Medicine.
2002 – Present	Professor, (fulltime, tenured) Department of Psychiatry, Yale University School of Medicine, New Haven, CT.
2002 – Present	Founding Director, Olin Neuropsychiatry Research Center, Institute of Living, Hartford, CT.
1993 – 2002	Professor, full-time faculty, Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, Maryland. (2002-present, part-time appt). Joint Appointment, Professor, Department of Mental Hygiene, Johns Hopkins University School of Public Health, Baltimore, Maryland.
1991 – 2002	Founding Director, Division of Psychiatry Neuro-Imaging, Department of Psychiatry, Johns Hopkins University School of Medicine, Baltimore, Maryland.
1987 – 1992	Associate Professor, full-time faculty, Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, Maryland.
1987 – 1992	Joint Appointment, Associate Professor, Department of Mental Hygiene, Johns Hopkins University School of Public Health, Baltimore, Maryland.
1981 – 1987	Assistant Professor, Full-time faculty, Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, Maryland.
1980 – 1981	Postdoctoral Instructor in Psychiatry. Laboratory of Dr. Robert G. Robinson, Johns Hopkins University School of Medicine. Baltimore, Maryland.

1979 – 2002	Psychiatrist, Active Staff, Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, Maryland.
2002 – Present	Psychiatrist, Part-Time Staff, Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, Maryland.
1978 – 1979	Chief Resident in Psychiatry, The Johns Hopkins Hospital, Baltimore, Maryland.
1976 – 1979	Resident in Psychiatry, Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine.
1974 – 1975	Intern in General Internal Medicine, Newcastle Royal Victoria Infirmary, and in General Surgery, Newcastle General Hospital, England.

CERTIFICATIONS

American Board of Neurology and Psychiatry (in psychiatry), 1980 (#21511)
Medical License State of Connecticut, 040622 (2002)
Medical License State of Maryland, D21805 (1977)
E.C.F.M.G. (#221-420-3)
F.L.E.X. (Maryland State Board of Medical Examiners) (#D-21805)

PROFESSIONAL HONORS AND AWARDS

1973	Distinction, Medical Finals Part I, University of Newcastle Upon Tyne, England.
1974	Dickinson Scholarship (Surgery), University of Newcastle Upon Tyne, England.
1974	Wilfred Kingdon Prize (Psychiatry), University of Newcastle Upon Tyne, England.
1986	Lundbeck Lecturer, University of Newcastle Upon Tyne, England
1987	Mental Health Sciences Affiliations, Principal Lecturer. Hahnemann University, Pennsylvania.
1987	Fellowship, American Psychopathological Association.
1989	Distinguished Fellow, American Psychiatric Association.
1990	Annual Lecture, American Academy of Clinical Psychiatrists.
1991	Invited Lectures - Annual NIMH CRC Directors Meeting; Royal College of Psychiatrists, and Institute of Psychiatry, U.K.
1993	Invited Authorship and Lecture - American Psychiatric Association 12th Annual Review of Psychiatry, 1993. "Psychiatric Applications of MRI".
1993	Membership, American College of Neuropsychopharmacology
1993	Invited Lectures - Royal College of Psychiatrists, Institute of Psychiatry, U.K.
1996	Ziskin-Somerfeld Award, Society of Biological Psychiatry, U.S.
1997	Martell Gold Medal, UK
1999	Fellowship, ACNP
2000	Michael Visiting Professorship, Weizmann Institute, Rehovot, Israel
2000	NARSAD Distinguished Investigator Award
2001	Bernard Sisskin Annual Neurology Lecture, Lenox Hill/NYU
2002	Mysell Lecture, Harvard University
2003	ISI – Most Highly Cited Publications,
2003	Israel Biological Psychiatry Mentor Program
2003 – 2005	Society of Biological Psychiatry- Scientific Program Ctee
2004	Program Chair, ECNS-ISNIP joint meeting, Irvine CA
	Frontiers of Science Lecturer, 2004 Annual APA Meeting
2005-Current	MERIT award, NIMH
2006	NARSAD Scientific Council, ACNP Program Ctee
2008	30th Albert Beile Memorial Award, Jefferson Medical College
2009	NeuroImage- Top 10 top cited scientific articles 2008
	American College of Psychiatrists, Member
2011	National Academy. of Neuropsychology. Nelson Butters Award for Research Contributions to Clinical Neuropsychology.
2013	APA Scientific Program Committee, ICOSR Scientific Program Committee

DEPARTMENTAL, MEDICAL SCHOOL AND UNIVERSITY COMMITTEES

YALE UNIVERSITY COMMITTEES

2002 –Present	Senior Faculty/Promotions Committee, Psychiatry
2003 – 2008	Donaghue/PRIME Research Committee

HARTFORD HOSPITAL COMMITTEES

2002 – Present	Research Committee
2002 – Present	Neuroscience Services Committee
2002 – Present	Psychiatry Research Committee
2002 – Present	Schizophrenia Research Committee

OTHER PROFESSIONAL ACTIVITIES

2003 – 2008	Donaghue Foundation Scientific Research Review Panel

NATIONAL REVIEW COMMITTEES

1994 – 1997	Review Panel: Scottish Rite Schizophrenia Research Program
1997 – Present	Ad Hoc scientific Review APA Annual Meeting
1991 – 1994	Reviewer, National Institute of Mental Health, Clinical Neurosciences Review Committee (formerly Clinical Biology Subcommittee, NPAS)
1989 – Present	Ad-hoc reviewer, National Institute on Drug Abuse.
1988	Advisor: Work group on Psychotic Disorders for DSM IV - Late life onset Schizophrenia. Advisor: DSM -IV work group on schizophrenia and related psychoses.
1986 – 1998	American Medical Association-Diagnostic and Therapeutic Technology Assessment Program of the Council on Scientific Affairs.
1985 – Present	Frequent ad-hoc reviewer, National Institute of Mental Health, Special Review Committees (PCB-2, TDA-3) NIMH/NIAAA

INTERNATIONAL SCIENTIFIC REVIEW

1995 – Present	Canadian Medical Research Council
1995 – Present	International Human Frontier Science Program (HFSP)
1995 – Present	Swiss National Science Foundation
1993 – Present	UK - Medical Research Council ad Hoc Scientific Review
1993 – Present	Wellcome Trust (UK)

ADVISORY COMMITTEES

1997 – 2002	NARSAD/Stanley Neurobiology review panel at JHU.
1988 – 2002	Depression and Related Disorders Association (DRADA), Scientific Advisory Committee.

SOCIETY MEMBERSHIPS

American Association for the Advancement of Science
American College of Neuropsychopharmacology. (Fellow)
American Federation for Aging Research
American Neuropsychiatric Association
American Psychiatric Association (Fellow)
American Psychopathological Association (Fellow)
Association for Research in Nervous and Mental Disease
Eastern Psychological Association
International Brain Research Organization
International Society for Neuroimaging in Psychiatry
Johns Hopkins Medical and Surgical Association
Society for Neuroscience
Society of Biological Psychiatry

MISCELLANEOUS

International Congress on Schizophrenia Research - Program Consultant 1996, 2013.
University of Pittsburgh Medical Center – Interventional Mental Health CRS for Study of Late - Life Mood Disorders: External Advisory Board 1995 - present
AAGP, Alzheimer's Association, American Geriatrics Soc. Expert Advisory Panel- Use of Neuroimaging in early diagnosis of Alzheimer's disease, (see report in JAMA, 278: 1363-1371, 1997).

EDITORIAL BOARDS

Frontiers in Neuropsychiatric Imaging
Biological Psychiatry
Schizophrenia Bulletin
Brain Imaging and Behavior
Psychiatry Research: Neuro-imaging.
J. Adv. Schizophrenia and Brain Research

REVIEWER - JOURNALS

Archives of General Psychiatry
Psychiatry Research
Neuroimage
Schizophrenia Bulletin
Archives of Neurology
Science
Journal of Abnormal Psychology
American Journal of Psychiatry
Journal of Nervous & Mental Disease
Psychosomatics
New England Journal of Medicine
PNAS, HBM

COMMUNITY SERVICE

The BrainDance Awards http://www.nrc-iol.org/Braindance/onrc_braindance.asp

Dr. Pearlson is co-founder of the annual BrainDance Competition, started in 2004, which is open to high school students across New England. The BrainDance Awards encourage students to gain knowledge about psychiatric diseases and to develop a more tolerant and realistic perspective toward people with severe psychiatric problems by offering awards for art, essays and scientific projects related to mental illness. Winners attend an annual lecture related to mental illness and/or stigma and showcase their work.

MENTORSHIP

1. **RESIDENT, RESEARCH ELECTIVE AND POSTDOCTORAL FELLOWSHIP SUPERVISOR (Representative Selection):**

	CURRENT STATUS
Dr. Paul Moberg. 1983-4. Olfactory Memory in HD and schizophrenia	Professor, Neuropsychiatry, University of Pennsylvania. NIH RO1s
Dr. Christopher Ross, 1988. Dopamine D2 receptor PET scans in schizophrenia vs. bipolar illness.	Professor, Psychiatry, Neuroscience, Johns Hopkins Univ., Director, Huntington's Disease Project, Neuroscience research, NIH awardee. Pew Scholar.
Dr. Jeffrey Moore, 1986-7. Negative symptoms in late-life onset schizophrenic patients.	Academic psychiatrist, Ohio.
***Dr. Alistair Burns**, 1986. Centrum semiovale white matter density in late life schizophrenia, AD, normal aging.	Deputy Dean for Clinical Affairs and Professor of Geriatric Psychiatry, Manchester University, U.K., formerly Wellcome Lectureship, Dr. Raymond Levy, Institute of Psychiatry (Geriatrics) London, U.K. 1989 IPA Psycho-geriatrics Research Award.
***Dr. Martin Deahl**, 1987. Cerebral atrophy measures in schizophrenia and affective disorder.	Consultant Psychiatrist, Researcher, Denis Hill Unit, Bethlem Hosp., London, U.K.
Dr. Richard Powers, 1987. MRI atlas construction.	Deputy Chief, Psychogeriatrics, University of Alabama, Birmingham. NIH awardee.
***Dr. Jeremy Broadhead**, 1987. Temporal ventricular horn assessment in schizophrenics versus controls.	Consultant psychiatrist, U.K. Research in neuropathology of amygdala.
Dr. Patrick Barta, 1988. Computer-based segmentation applied to MRI images in schizophrenia, MRI display software.	Associate Professor, Johns Hopkins Univ. NIH FIRST, R01's, NARSAD, Scottish Rite awardee.
Dr. Gordon Harris. 1988. Computer reconstruction and registration of SPECT image sets (Ph.D. thesis advisor)	Professor, Radiology, Harvard University/Director MGH 3-D Imaging Lab. NIH FIRST Awardee.
Dr. Elizabeth Aylward, 1989. Quantitative brain atrophy measures on MRI and CT. Measurement of suprasellar cistern.	Professor, Radiology, U. Washington Seattle, Quantitative MRI research NIH Awardee, HDSA Awardee
Dr. Laura Marsh, 1990. MRI in schizophrenia: Replication of post-mortem studies.	Professor, Dept of Neurology Baylor University, Texas. Prev. Johns Hopkins U. Parkinson's disease research. Research Fellowship, Dr. Daniel Weinberger, NIH Intramural. MRI research.Young Investigator Award, Third Internl. Congress on Schizophrenia Research, 1991. NIH Awardee.
***Dr. Raj Persaud**, 1990. MRI in schizophrenia: Basal ganglia.	Professor,Maudsley Hospital, London, U.K. MRI research in affective disorder. Author
Dr. Frederick Schaerf 1990. Brain imaging in AIDS dementia	Private practice, Ft. Myers, Fla.
Dr. Steven Machlin, 1989. MRI and SPECT changes in patients with obsessive-compulsive disorder.	Private practice, FL.
***Dr. Peter Woodruff**, 1991. MRI in schizophrenia: Corpus callosum.	Professor and Head of Psychiatry Neuroimaging, Sheffield U., UK Prev. Faculty, Maudsley Hospital, London, U.K. Brain Imaging Functional MRI Research, **Wellcome Awardee, Fulbright Awardee**

RESIDENT, RESEARCH ELECTIVE AND POSTDOCTORAL FELLOWSHIP SUPERVISOR Cont'd.

	CURRENT STATUS
Dr. Benjamin Greenberg, 1991, MRI of basal ganglia in AIDS dementia.	Associate Professor, Brown University Prev., prev. Research Faculty, Lab. of Dr. D. Murphy, NIMH. Society of Biological Psychiatry,Dista Fellowship, 1991.
***Dr. Rajiv Menon**, 1991. MRI of superior temporal gyrus in schizophrenia.	Senior Faculty, Psychogeriatrics, Chelsea, Maudsley Hospital, London, U.K.
Dr. J.Thomas Noga, 1991. MRI of cingulate gyrus in schizophrenia.	Faculty, Emory University Atlanta, GA. Prev. fellow, NIMH/St. Eliz., Washington, D.C. (Lab of Dr. D. Weinberger and Dr. Joel Kleinman).
***Dr. Iain McGilchrist**, 1992. Parietal cortical reconstruction from 3-D MRI.	Faculty, Maudsley Hospital, London, U.K. Brain Imaging Research.
Dr. Richard Petty, 1992. Planum temporale reconstruction from 3-D MRI	Faculty, University of Pennsylvania.
Dr. Thomas Schlaepfer, 1991-1992 and 1993-1996. PET in cocaine abusers, SPECT in opiate abuse	Dean, Research and Professor and Vice-Chair Psychiatry, U. Bonn, Germany. Awardee - **Swiss Nat. Sci. Foundation.**
***Dr. Sophia Frangou**, 1994. Superior temporal gyrus in schizophrenia and Down syndrome	Professor Psychiatry and Chief of Psychosis Research Program Mt. Sinai School of Medicine NYC. Prev. Research/Clinical Faculty, Institute of Psychiatry, London, U.K., **Awardee - Wellcome Foundation.**
* **Dr. Tonmoy Sharma**, 1994-1995. Cortical grey matter in schizophrenics and their families	Director, Cognitive Psychopharm. Lab. Previously Faculty, Institute of Psychiatry, London, U.K., **MRC Awardee**
Dr. Melissa Frederikse, 1995-1997. IPL in schizophrenia	Assistant Professor/UMDNJ, Quantitative MRI research
Dr. Nancy Honeycutt, 1995-1996. Amygdala and hippocampus in schizophrenia	Assistant Professor, Johns Hopkins Univ., Quantitative MRI research. **NIH Awardee**
Dr. Andrej Marusic, 1997. Statistical parametric mapping applied to SPECT rCBF in early AD	Deceased. Director, National Psychiatric Res. Inst. Republic of Slovenia
Dr. Paul Rivkin, 1997-1998. fMRI in presymptomatic AD	Assistant Professor, Johns Hopkins University, Department of Psychiatry Neuroimaging. fMRI research **NIH Awardee**
***Dr. Paula Dazzan**, 1997-1998. Cortical surface area in schizophrenia	Faculty, Institute of Psychiatry, London, U.K Head, Div of Early Psychosis Research
Dr. Sergio Nicastri 1998-99 rCBF in cocaine abusers	Psychiatry Faculty, Sao Paolo, Brazil Humphrey Fellow
Dr. Laura Amodei, 2000-2001. Diffusion tensor imaging of language circuits in schizophrenia.	Radiology resident. Johns Hopkins U.
Dr. Vince Calhoun 2000-2002. Application of Independent Component analysis to virtual driving/fMRI (Ph.D. thesis advisor)	Professor, University of New Mexico. **NIMH, NSF multiple RO1 awardee.** ISNIP junior investigator award 2004. ACNP Elkes Award Winner 2013.
Dr. Sarah Reading, 2001-2002. fMRI of attentional networks in schizophrenia	Asst. Prof, U of Florida **NIMH K Awardee**

-RESIDENT, RESEARCH ELECTIVE AND POSTDOCTORAL FELLOWSHIP SUPERVISOR Cont'd.

	CURRENT STATUS
***Dr. Richard Kanaan,** 2001-2002. fMRI of verbal binding in schizophrenia	Faculty, Dept of Psychiatry, London, UK DTI research
Dr. Jin-Suh Kim, 2001-2002. Diffusion tensor imaging (Current)	Asst. Prof Radiology, U. Iowa
Dr. Michal Assaf, 2001-2003. fMRI in thought disorder	Sr. Scientist ONRC, Asst Clin Professor, Yale U. Dept Psychiatry. NAAR, Donaghue Foundation Awardee. **NIMH R01 Awardee**
Dr. Kristen McKiernan, 2002- Task-induced deactivation in fMRI	Sr. Scientist ONRC, Asst Clin Professor, Yale U. Dept Psychiatry **NIA R21 Awardee**
Dr. Michael Stevens, 2004- fMRI of impulsivity, (K Award primary mentor)	Sr. Scientist ONRC, Assoc Clin Professor, Yale U. Dept Psychiatry. **NIMH K Awardee, RO1 Awardee**
Dr. Matthew Kurtz 2004- fMRI of cognitive rehabilitation in schizophrenia, (K Award advisor)	Associate Prof, Wesleyan U, Asst Clin Professor, Yale U. Dept Psychiatry. **NIMH K Awardee**
Dr. Beth Turner Anderson 2007 Amphetamine interactions with COMT Genotype	Current Staff Scientist, Olin Center IOL/HH **NIDA Awardee**
Dr. Sharna Jamadar 2010-2011, fMRI in Schizophrenia	Junior faculty, Monash University, Australia
Dr. Janet Ng 2012- Current. Neuroscience of Obesity	Institute of Living
Dr. Haley Yarosh 2012- Current. Neurobiology of Impulsive/Risky Choice.	Yale University

** Visiting fellows, Maudlsey Hospital, London, U.K.*

RESEARCH PROJECT SUPERVISION:

Loyola College Psychology MA Program

1988	D. Houlihan: Longitudinal follow-up of 350 chronic pain patients and controls.
1986	M. Haden: Electrodermal non-responding and VBR in schizophrenia.
1984 – 1985	N.J. Yatron: Cognitive distortion and depressed mood in chronic pain.
1982 – 1983	D.J. Garbacz: VBR-clinical correlates in bipolar disorder.

Howard University Neuropsychology Ph.D. Program

1983 – 1985	S.C. Levin: Structural CT change in bipolar disorder assessed by image processing. Relationship to cognitive abnormalities. Thesis advisor.

University of Maryland, Baltimore County Ph.D. Program

2000	V.D. Calhoun: Independent Component Analysis of fMRI applied to Complex Tasks.

RESEARCH FUNDING

Ongoing Research Support – Pearlson, Godfrey D.

5 R37 MH43775 (Pearlson) 08/01/0905/31/14
NIMH
Quantitative Neuroimaging in Psychosis MERIT Award
The major goals of this project are to investigate circuit-wide abnormalities in schizophrenia using functional and structural brain MRI in schizophrenia and healthy controls.

(Pearlson) 06/01/12-05/31/15
Competitive Supplement to above grant.

1R01MH096957-01A1 (Pearlson) 06/01/13-05/31/15
NIMH
Psychosis and Affective Research Domains and intermediate Phenotypes (**PARDIP** study)
This multisite, multiple-endophenotype project builds on and benefits from the extensive BSNIP consortium infrastructure. It will collect a comprehensive battery of biological, neuroanatomic, neurophysiologic, cognitive, and clinical measures from a large sample of non-psychotic Bipolar Disorder (BD) patients to determine whether BD patients with psychosis and without psychosis represent a difference in degree or a difference in kind.

HHC Research Institute (Pearlson) 07/01/2012-06/30/16
HH Interdisciplinary Center on Obesity Research
This project is collaboration between the Olin Center and the HH Surgical Weight Loss Center (SWLC) to examine the ability of pre-surgical neuroimaging & neuroendocrine testing to predict 12-month post-surgical outcome in patients undergoing surgical weight-loss procedures, (comprising laparoscopic gastric banding, sleeve gastrectomy and Roux-en-Y gastric bypass). The project assesses metabolic aspects of obesity and satiety, physiology of feeding behavior, impulsivity, and addiction measures and regulation of craving. Neuroimaging is re-assessed 12 months following surgery.

C0RR028654-01 (Project Liason- Pearlson) 01/29/10-01/28/13
NCRR
Olin Research Center: Major Building Addition for New MRI Scanner and Research Staff
Construct and /or renovate the following facilities on the Institute of Living Campus at Hartford Hospital, Hartford, CT:
1. To construct a new 1500 – 2000 square foot building addition (Magnet Addition) to house a new 3T Siemens Skyra wide-bore, fast MRI scanner at the North end of the existing White Hall Building
2. To construct a new 6700 square foot, two story research facility (Research Staff Addition) at the location of the existing Huntington Building, to accommodate scanner-related research staff and testing, exam and sample processing rooms for subjects who participate in MRI research.

R01AA016599 (Pearlson) 09/30/08 – 08/31/14
NIAAA
Alcohol Use in College Students: Cognition and fMRI (BARCS study)
US college students are at high risk for problem drinking. This project will recruit and test cognitively 2000 first-year students from local colleges in Connecticut, fMRI scan a representative sub-sample and assess alcohol and drug use by web-based reporting over 2 years, when all students will be retested/rescanned. Findings from this study will provide important insights on risk factors for problem drinking and how alcohol use impacts the developing adolescent brain.

R01 MH077945 (Pearlson) 9/29/07-5/31/13
NIMH
Bipolar & Schizophrenia Consortium for Parsing Endophenotypes (BSNIP study)
The major goals of this multi-site collaboration will enroll several hundred patients with schizophrenia, psychotic bipolar illness and their unaffected siblings, to assess multiple imaging physiologic and cognitive endophenotypes and examine specificity.

01EB005846 (Calhoun) 8/1/05- 5/30/13
NIH/NIBIB
Informed Data-Driven Fusion of Behavior, Brain Function, and Genes
To develop data fusion approaches for fMRI, EEG, behavior and whole genome SNP array & CNV data.

R01MH080956-01 (Stevens) 04/01/08-03/31/13
NIMH
Characterizing Two Distinct ADHD Neurobiologies with fMRI
This study uses functional imaging, genetic analysis, and neuropsychological assessment to examine whether there are two separate profiles of neurobiological impairment underlying impulsive behavior in ADHD.

R01 MH081969 (Stevens) 07/01/08-06/30/13
NIMH
Adolescent Maturation of Brain Network Integration for Executive Control Abilities
A study using fMRI analyses of neural network connectivity and neuropsychological assessment to examine the neural substrates of three domains of 'executive' cognitive abilities and to track their development across early adolescent to early adult maturation in healthy persons.

R01 MH082022 (Woods) 09/01/08 – 08/31/13
NIMH
8/8 Predictors and Mechanisms of Conversion to Psychosis
The major goals of this project are to identify predictors and mechanisms of conversion to psychosis in a new sample of adolescents.

R03 DA027893 (Anderson) 3/1/11 – 2/29/13
NIDA
Simulated Driving Under the Influence of Marijuana: an fMRI Study
The major goals of this project uses a psycho-pharmacologic repeated measures fMRI design to identify brain circuits used in driving that re most affected by marijuana in a dose-dependent manner and are related to intoxicated driving. Role: Investigator

R01HL098085 (Parker) 3/1/10 – 2/28/14
NHLBI
The Effect of High-Dose Atorvastatin on Neuronal Activity and cognition in Humans
The major goal of this study is to investigate the effects of atorvastatin therapy on neuronal activation and cognition in healthy adults. Role: Investigator

R01DA027615-03S1 (Petry/Pearlson) 09/01/11-08/31/13
NIH/NIDA
Reinforcing Exercise in Cocaine Abusers (Exercise and Cognition Supplement)
The purpose of this study is to examine the association between exercise and cognitive functioning.

1R01MH095888-01A1 (PI: Assaf) 07/01/12-06/30/17
NIMH
The Social Brain in Schizophrenia and Autism Spectrum Disorders

PARTICIPATION: NATIONAL/INTERNATIONAL CONSORTIA

BSNIP
ENIGMA

BIBLIOGRAPHY

H.index= 77. Most cited: Wong et al. Science/19:234 1986=764 citations

1. Slavney PR, Rich G, **Pearlson GD**, and Mchugh PR. Phencyclidine abuse and symptomatic mania. Biological Psychiatry, 12: 697-700, 1977

2. Wilkinson PW, Parkin JM, Strong M, **Pearlson GD,** Sykes P. Energy intake and physical activity in obese children. British Medical Journal, 756-758, March 19, 1977.

3. Wilkinson PW, Parkin JM, **Pearlson GD,** Philips PR, Sykes P. Obesity in childhood: A community study in Newcastle upon Tyne. Lancet, Feb 12, 8007: 350-352, 1977.

4. Tune LE, Creese I, Coyle JT, **Pearlson GD**, Snyder SH. Low neuroleptic serum levels in patients receiving fluphenazine decanoate. American Journal of Psychiatry, 137: 80-82, 1980.

5. **Pearlson GD**, Flournoy LH, Simonson M, Slavney PR. Body image in obese adults. Psychological Medicine, 11: 147-154, 1981.

6. **Pearlson GD**, Veroff AE. Computerized tomographic scan changes in manic-depressive illness. Lancet, 8244, II: 470 1981.

7. **Pearlson GD**. Psychiatric and medical syndromes associated with phencyclidine (PCP) abuse. Johns Hopkins Medical Journal, 148: 25-33, 1981.

8. **Pearlson GD** and Robinson RG. Suction lesions of the frontal cerebral cortex in the rat induce asymmetrical behavioral and catecholaminergic responses. Brain Research, 218: 233-242, 1981.

9. **Pearlson GD**, Veroff AE, McHugh PR. The use of computed tomography in psychiatry: Recent applications to schizophrenia, manic-depressive illness and dementia syndromes. Johns Hopkins Medical Journal, 149: 194-202, 1981.

10. Veroff AE, **Pearlson GD**, Ahn HS. CT scan and neuropsychological correlates of Alzheimer's disease and Huntington's disease. Brain and Cognition, 1: 177-184, 1982.

11. Kubos KL, **Pearlson GD**, Robinson RG. Intracortical kainic acid induces an asymmetrical behavioral response in the rat. Brain Research, 239: 303-309, 1982.

12. **Pearlson GD**, Veroff AE, Wise TN. The use of CT scanning in psychiatry. Psychosomatics, 23: 993-1004,1982.

13. **Pearlson GD**, Garbacz DJ, Tompkins RH. Imaging of the brain: Aiding the search for physical correlates of mental illness. Integrative Psychiatry, 1: 134-138, 1983.

14. Lipsey JR, Robinson RG, **Pearlson GD**, Rao K, and Price TR. Mood change following bilateral hemisphere brain injury. British Journal Psychiatry, 293: 241-250, 1983.

15. **Pearlson GD**, Garbacz DJ, Tompkins RH, Ahn HS, Gutterman DF, DePaulo JR. Lateral ventricular enlargement in affective disorder: Clinical correlates. American Journal of Psychiatry, 141: 253-256, 1984.

16. **Pearlson GD**, Garbacz DJ, Breakey WR, Ahn HS, DePaulo JR. Relationship of lateral ventricular enlargement on CT scan to chronic unemployment in schizophrenia and affective disorder. Psychiatry Research, 12:1-9, 1984.

17. Lipsey JR, Robinson RG, **Pearlson GD**, Rao K, and Price TR. Nortriptyline treatment of post stroke depression: A double blind treatment trial. Lancet, I: 297-300, 1984.

18. Brady JY, Griffiths RR, Hienz RD, Bigelow GE, Emurian HH, Lukas SE, Ator NA, Nellis MJ, Ray RI, **Pearlson GD**. Abuse liability and behavioral toxicity assessment: Progress report from the behavioral biology laboratories of the Johns Hopkins University School of Medicine. NIDA Res Monogr. 1984 Mar;49:92-108.

19. **Pearlson GD**, McHugh PR. Significance of enlarged lateral ventricles, (ltr. to ed.) Psychosomatics, 25: 707, 1984.

20. Robinson RG, Lipsey JR, **Pearlson GD**. The occurrence and treatment of post-stroke mood disorders. Comprehensive Therapy, 10:19-24, 1984.

21. **Pearlson GD**, Kubos KL, Robinson RG. Effects of anterior-posterior lesion location on the asymmetrical behavioral and biochemical response to cortical suction ablations in the rat. Brain Research, 293: 241-250, 1984.

22. **Pearlson GD**, Garbacz DJ, Moberg P, Ahn HS, DePaulo JR. Symptomatic, familial, perinatal and social correlates of CT changes in schizophrenics and bipolars. Journal Nervous and Mental Disorders, 173: 42-50, 1985.

23. Lipsey JR, Robinson RG, **Pearlson GD**, Rao K, Price TR. The dexamethasone suppression test and mood following stroke. American Journal of Psychiatry, 142: 318-323, 1985.

24. Wong DF, Wagner HN, Jr., **Pearlson GD**, Dannals RF, Tune LE. Dopamine receptor binding of C-11 N Methylspiperone in the caudate in schizophrenia and bipolar illness: A preliminary report. Psychopharmacology Bulletin, 21: 595-598, 1985.

25. Robinson RG, Lipsey JR, Bolla-Wilson K, Bolduc PL, **Pearlson GD**, Rao K, Price TR. Mood disorders in left-handed stroke patients. American Journal of Psychiatry, 142: 1424-1429, 1985.

26. Wong DF, Wagner HN, Jr., Tune LE, Dannals RF, **Pearlson GD**. Positron emission tomography reveals elevated D2 dopamine receptors in drug-naive schizophrenics. Science, 239:1473-1624, 1986.

27. **Pearlson GD** and Tune LE. Cerebral ventricular size and cerebrospinal fluid acetylcholinesterase levels in senile dementia of the Alzheimer Type. Psychiatry Research, 17: 23-29, 1986.

28. Rabins PV, Brooks BR, O'Donnell P, **Pearlson GD**, Moberg PJ, Jubelt B, Coyle P, Dalos N, Folstein MF. Structural brain correlates of emotional and cognitive disorder in multiple sclerosis. Brain, 109: 585-597, 1986.

29. Moran TH, Zern KA, **Pearlson GD**, Kubos KL, Robinson RG. Cold water stress abolishes hyperactivity produced by cortical suction lesions without altering NE depletions. Behavioral Neuroscience, 100: 422-426, 1986.

30. Moberg PJ, **Pearlson GD**, Folstein SE, Speedie LJ, Lipsey JR. Olfactory recognition: Differential impairments in early and late Huntington's and Alzheimer's diseases. Journal of Clinical & Experimental Neuropsychology, 9: 650-664, 1987.

31. Rabins PV, **Pearlson GD**, Jayaram G, Steele CS, Tune LE. Elevated VBR in late-onset schizophrenia. American Journal of Psychiatry, 144: 1216-1218, 1987.

32. Starkstein SE, **Pearlson GD**, Boston J, Robinson RG. Mania after brain injury: A controlled study of etiological factors. Archives of Neurology. 44: 1069-1073, 1987.

33. Foltin RW, Fischman MW, Pedroso JJ, **Pearlson GD**. Marijuana and cocaine interactions in humans: Cardiovascular consequences. Pharmacology and Biochemical Behavior, 28:459-464, 1987.

34. Foltin RW, Fischman MW, Pedroso JJ, **Pearlson GD**. Repeated intranasal cocaine administration: Lack of tolerance to pressor effects. Drug & Alcohol Dependence, 22: 169-177, 1988.

35. Wong DF, Wagner HN Jr, Links JM, Dannals RF, Folstein S, Ravert HT, Tune L, **Pearlson GD**, Frost JJ, Folstein M, et al. Positron emission tomography imaging of dopamine and serotonin receptors in Huntington's chorea. Am J Physiol Imaging. 1988;3(1):51

36. Jeste DV, Harris MJ, **Pearlson GD**, Rabins PV, Lesser I, Miller B, Coles C, Yassa R: Late Onset Schizophrenia - Studying Clinical Validity. Psychiatric Clin. N. America, Psychosis and Depression in the Elderly, 11: 1-13, 1988.

37. Starkstein SE, Brandt J, Folstein SE, Strauss ME, Berthier ML, **Pearlson GD**, Wong DF, McDonnell A, Folstein MF. Neuropsychological and neuroradiological correlates in Huntington's disease. Journal Neurology, Neurosurgery and Psychiatry, 51: 1259-1263, 1988.

38. LaFrance ND, **Pearlson GD**, Schaerf FW, McArthur JC, Polk BF, Links JM, Bascom MJ, Knowles MC, Galen SS. Iodine-123 single photon emission computed tomography in HIV-related dementia. Advances in Functional Neuro-Imaging, 1: 9-15, 1988.

39. **Pearlson GD**, Rabins PV. The Late onset psychoses - possible risk factors. Psychiatric Clin. N. America, Psychosis and Depression in the Elderly, 11: 15-33, 1988.

40. Wong DF, Gjedde J, Wagner HN, Dannals RF, Links JM, Tune LE, **Pearlson GD**. Elevated D2 dopamine receptors in drug naive schizophrenics. (Ltr. to Ed.) Science, 241: 790-791, 1988.

41. **Pearlson GD**, Warren A. (ltr. to ed.) Brain atrophy in aging Down's syndrome patients. Neurology, 39: 1407-1408,1989.

42. **Pearlson GD**, Fischman MW, Foltin RW, Cornell E and Pedroso JJ. Cocaine-induced delirium versus delusional disorder. Biological Psychiatry, 26:847-858, 1989.

43. **Pearlson GD**, Warren AC. Aging and brain weight in Down's syndrome. Neurology. 1989 Oct;39(10):1407-8

44. **Pearlson GD**, Rabins PV, Kim WS, Speedie LJ, Moberg PJ, Burns A, and Bascom MJ. Structural brain CT changes and cognitive deficits in elderly depressives with and without reversible dementia. Psychological Medicine, 19: 573-584, 1989.

45. **Pearlson GD**, Kreger L, Rabins PV, Chase GA, Cohen B, Wirth JB, Schlaepfer TB, Tune LE. Late life onset schizophrenia: A chart review study. American Journal of Psychiatry, 146: 1568-1574, 1989.

46. Starkstein SE, Folstein SE, Brandt J, **Pearlson GD**, McDonnell A, Folstein MF. Brain atrophy in Huntington's disease. NeuroRadiology, 31: 156-159, 1989.

47. **Pearlson GD**, Kim WS, Kubos KL, Jayaram G, Heyler G, Chase, GA, Goldfinger AD, Tune LE. VBR, CT density and brain area in 50 schizophrenics. Archives of General Psychiatry, 46: 690-697, 1989.

48. **Pearlson GD**, Warren A, Starkstein SE, Aylward EH, Kumar AJ, Chase GA, Folstein MF. Brain atrophy in 18 patients with Down's syndrome. American Journal of Neuro-Radiology, 11: 811-816, 1990.

49. Foltin RW, Fischman MW, Nestadt G, Stromberger H, Cornell EE, **Pearlson GD**. Demonstration of naturalistic methods for cocaine smoking by human volunteers. Drug Alcohol Depend. 1990 Oct;26(2):145-54

50. Barta PE, **Pearlson GD**, Powers RE, Richards SS, Tune LE. Auditory hallucinations and smaller superior temporal gyral volume in schizophrenia. Am J Psychiatry. 1990 Nov;147(11):1457-62

51. Piven J, Berthier ML, Starkstein SE, Nehme E, **Pearlson GD**, Folstein SE. Magnetic resonance imaging evidence for a defect in cerebral cortical development in autism. American Journal of Psychiatry, 147: 734-739, 1990.

52. Fischman MW. Foltin RW, Nestadt G and **Pearlson GD**. Effects of desipramine maintenance on cocaine self-administration in humans. Journal of Pharmacology and Experimental Therapeutics, 253: 760-770, 1990.

53. Speedie L, Rabins PV, **Pearlson GD**, Moberg P. Confrontation naming deficit in dementia of depression. J. Neuropsychiatry & Clinical Neurosciences, 2: 59-63, 1990.

54. **Pearlson GD**, Rabins PV (ltr. to ed.) Late-life onset schizophrenia. American Journal of Psychiatry, 147: 1383, 1990.

55. Barta PE, **Pearlson GD**, Powers RE, Tune LE. Reduced superior temporal gyral volume on MRI in schizophrenia; Relationship to hallucinations. American Journal of Psychiatry, 147: 1457-1462, 1990.

56. **Pearlson GD**, Ross CA, Lohr WD, Rovner BW, Tune LE, Folstein MF. Family history of affective disorder is associated with the depressive syndrome of Alzheimer's disease American Journal of Psychiatry, 147: 452-456, 1990.

57. **Pearlson GD**, Ross CA. (ltr. to ed.) Family history of depression and alcoholism in Alzheimer patients and age-matched controls. International Journal of Geriatric Psychiatry 5: 344-345, 1990.

58. Harris GJ, Rhew EH, Noga JT, **Pearlson GD**. A user-friendly method for rapid brain and CSF volume calculation using transaxial MRI images. Psychiatry Research Brain Imaging, 40: 61-68, 1991.

59. Aylward EH, Schwartz J, Machlin SR and **Pearlson GD**. Bicaudate ratio as a measure of caudate volume in MRI. American Journal of Neuroradiology, 12: 1217-1222, 1991.

60. Harris GJ, Links JM, **Pearlson GD**, Camargo EE. Cortical circumferential profiles: An objective approach to the analysis of the distribution of radioactivity in cerebral emission computed tomography. Application to a study of Alzheimer's disease. Psychiatry Research NeuroImaging, 40: 167-180, 1991.

61. Hoehn-Saric R, Harris GJ, **Pearlson GD**, Cox CS, Machlin SR, and Camargo EE. A fluoxetine induced frontal lobe syndrome in an obsessive-compulsive patient. J Clinical Psychiatry, 52: 131-133, 1991.

62. Harris GJ, Rhew EH, Noga T, **Pearlson GD**. User-friendly method for rapid brain and CSF volume calculation using transaxial MRI images. Psychiatry Res. 1991 May;40(1):61-8

63. Machlin S, Harris GJ, **Pearlson GD**, et al. Elevated frontal cerebral blood flow in obsessive-compulsive patients: A SPECT study. American Journal of Psychiatry, 148: 1240-1242, 1991.

64. Hoehn-Saric R, **Pearlson GD**, Harris GJ, et al. Effects of fluoxetine on regional cerebral blood flow in obsessive-compulsive disorder. American Journal of Psychiatry, 148: 1243-1245, 1991.

65. **Pearlson GD**, Barta PE, Schraml FV, Chase GA, Tune LE. (ltr. to ed.) Brain size in schizophrenia. Archives of General Psychiatry, 48: 179-180, 1991.

66. Aylward EH, Schwartz J, Machlin S, **Pearlson G**. Bicaudate ratio as a measure of caudate volume on MR images. AJNR Am J Neuroradiol. 1991 Nov-Dec;12(6):1217-22

67. **Pearlson GD**.. PET scans in schizophrenia: What have we learned? Annals of Clinical Psychiatry, 3: 97-101, 1991.

68. Strauss ME, Novakovic T, Tien AY, Bylsma F, **Pearlson GD**. Disengagement of attention in schizophrenia. Psychiatry Research, 37: 139-146, 1991.

69. Aylward EA, Karagiozis H, **Pearlson GD**, and Folstein MF. Suprasellar cistern measures as a reflection of dementia in Alzheimer's disease but not Huntington's disease. Journal of Psychiatric Research, 25: 31-47, 1991.

70. Tune LE, Brandt J, Frost JJ, Harris G, Mayberg H, Steele C, Burns A, Sapp J, Folstein MF, Wagner HN, **Pearlson GD**. Physostigmine in Alzheimer's disease: effects on cognitive functioning, cerebral glucose metabolism analyzed by positron emission tomography and cerebral blood flow analyzed by single photon emission tomography. Acta Psychiatr Scand, Supplement 366: 61-65, 1991.

71. Cascella N, **Pearlson GD**, Wong DF, Brousolle E, Nagoshi C, Margolin RA, London ED. Effects of substance abuse on ventricular and sulcal measures assessed by computed tomography. British Journal of Psychiatry, 159: 217-221, 1991.

72. **Pearlson GD**, Rabins PV, Burns A. CT changes in centrum semiovale white matter in dementia of depression. Psychological Medicine, 21: 321-328, 1991.

73. Rabins PV, **Pearlson GD**, Aylward EH, Kumar AJ, Dowell K. Cortical MRI changes in elderly inpatients with major depression. American Journal of Psychiatry, 148: 617-620, 1991.

74. Piven J, Nehme E, Simon J, Barta P, **Pearlson GD**, Folstein SE. Magnetic resonance imaging in autism: Measurement of the cerebellum, pons and fourth ventricle. Biological Psychiatry, 31: 491-504, 1992.

75. Rabins PV, **Pearlson GD**, Aylward EH. Magnetic resonance imaging in the diagnosis of dementia (ltr. to ed.). American Journal of Psychiatry, 149: 419, 1992.

76. **Pearlson GD**, Harris GJ, Powers RE, Barta PE, Camargo EE, Chase GA, Noga JT, Tune LE. Quantitative changes in mesial temporal volume, regional cerebral bloodflow and cognition in Alzheimer's disease. Archives of General Psychiatry, 49: 402-408, 1992.

77. Harris GJ, **Pearlson GD**, Peyser C, Aylward E, Folstein SE. Putamen volume measured on MRI completely discriminates early Huntington's disease patients from controls. Annals of Neurology, 31: 69-75, 1992.

78. Tien AY, **Pearlson GD**, Machlin SR, Bylsma RW, Hoehn-Saric R. Oculomotor performance in obsessive compulsive disorder. American Journal of Psychiatry, 149: 641-646, 1992.

79. Schwartz J, Aylward E, Barta PE, Tune LE, **Pearlson GD**. Increased sylvian fissure size in schizophrenia using the CERAD MRI rating protocol. American J Psychiatry, 149: 1195-1198, 1992.

80. Woodruff P, **Pearlson GD**, Barta PE, Chilcoat H. Corpus callosum MRI measures in schizophrenia. Psychological Medicine, 23: 45-56, 1993.

81. Aylward EH, **Pearlson GD**, Rabins PV. Differences in early and late onset schizophrenia (letter to ed.). American Journal of Psychiatry, 150: 846-847, 1993.

82. Gur R and **Pearlson GD**. Neuroimaging in schizophrenia. Schizophrenia Bulletin, Special Issue, Schizophrenia, 19: 337-354, 1993.

83. Tune LE, Wong DF, **Pearlson GD**, Strauss ME, Young T, Shaya EK, Dannals RF, Wilson AA, Ravert HT, Sapp J, Cooper T, Chase GA, Wagner HN Jr. Dopamine D2 receptor density estimates in schizophrenia: A positron emission tomography study with 11C-N-Methylspiperone. Psychiatry Research, 49: 219-237, 1993.

84. Harris GJ, **Pearlson GD**, Hoehn-Saric R. Caudate nucleus in obsessive-compulsive disorder patients appears structurally and functionally normal using MRI and SPECT (Letter to ed.). Archives of General Psychiatry, 50: 498-499, 1993.

85. **Pearlson GD**, Jeffery P, Harris GJ, Ross CA, Fischman M, Camargo EE. Local cocaine-induced cerebral bloodflow changes: Correlation with subjective effects. American Journal of Psychiatry, 150: 495-497, 1993.

86. **Pearlson GD**, Tune LE, Wong DF, Aylward EH, Barta PE, Powers RE, Chase GA, Harris GJ, Rabins PV. Quantitative D2 dopamine receptor PET and structural MRI changes in late onset schizophrenia. Schizophrenia Bulletin, 19: 783-795, 1993.

87. Harris GJ, **Pearlson GD**. MRI-guided region of interest placement on emission computed tomograms. Psychiatry Research Neuroimaging, 50: 57-63, 1993.

88. Aylward EH, Henderer JD, McArthur JC, Brettschneider PD, Harris GJ, Barta PE, and **Pearlson GD**. Reduced basal ganglia volume in HIV-1 associated dementia complex: results from quantitative neuroimaging. Neurology, 43: 2099-3104, 1993.

89. Harris GJ, **Pearlson GD**, McArthur JC, Zeger S, LaFrance ND. Altered cortical blood flow in HIV seropositive individuals with and without dementia: A SPECT study. AIDS, 8: 495-499, 1994.

90. Harris GJ, Hoehn-Saric RH, Lewis R, **Pearlson GD**, Streeter G. Mapping of SPECT regional cerebral perfusion abnormalities in obsessive-compulsive disorder. Human Brain Mapping, 237-248, 1994.

91. Harris GJ, Barta PE, Peng L, Lee S, Brettschneider PD, Shah A, Henderer JD, **Pearlson GD**. MRI gray and white matter volume segmentation using manual thresholding: dependence on image brightness. American Journal Neuroradiology, 15: 225-230, 1994.

92. Aylward EH, Roberts-Twillie JV, Barta PE, Kumar AJ, Harris GJ, Geer M, Peyser CE, **Pearlson GD**. Basal ganglia volumes and white matter hyperintensities in bipolar disorder. American Journal of Psychiatry, 151: 687-693, 1994.

93. Habbak R, Warren A, Aylward E, Jerram M, **Pearlson GD**. Synkinesias are common in Down syndrome. Journal of Nervous and Mental Disease, 182: 667, 1994.

94. Harris GH, Schlaepfer TE, Peng LW, Lee S, Federman EB, **Pearlson GD**. Magnetic resonance imaging evaluation of the effects of aging on grey-white ratio in the human brain. Neuropathology and Applied Neurobiology, 20: 290-293, 1994.

95. Schlaepfer TE, Harris GJ, Tien AY, Federman EB, Peng LW, Lee S, and **Pearlson GD**. Pattern of decreased regional cortical gray matter volume using magnetic resonance imaging in schizophrenia. American Journal of Psychiatry, 151: 842-848, 1994.

96. Aylward E, Reiss A, Barta P, Tien A, Han W, Lee J, **Pearlson G**. MRI Measurement of posterior fossa structures in schizophrenia. American Journal of Psychiatry, 151: 1448-1452, 1994.

97. Petty RG, Barta PE, **Pearlson GD**, McGilchrist IK, Lewis RW, Tien AY, Pulver A, Vaughn DD, Casanova MF, Powers RE. Reversal of asymmetry of the planum temporale in schizophrenia. American Journal of Psychiatry, 152: 715-721, 1995.

98. Menon RR, Barta PE, Aylward EH, Richards SS, Vaughn DD, Tien AY, **Pearlson GD**. Posterior superior temporal gyrus in schizophrenia: grey matter changes and clinical correlates. Schizophrenia Research, 16: 127-135, 1995.

99. Noga JT, Aylward EH, Barta PE, **Pearlson GD**. Cingulate gyrus in schizophrenia and controls. Psychiatry Research Neuroimaging, 61: 201-208, 1995.

100. Schlaepfer TE, Harris GJ, Aylward EH, McArthur HC, Peng LW, Lee S, **Pearlson GD**. Structure differences in the cerebral cortex of normal male and female subjects. Psychiatry Research - Neuroimaging, 61: 129-135, 1995.

101. Barta PE, Petty RG, McGilchrist I, Lewis RW, Jerram M, Casanova MF, Powers RE, Brill, III LB, **Pearlson GD**. Asymmetry of the planum temporale: Methodologic considerations. Psychiatry Research Neuroimaging, 61: 137-150, 1995.

102. **Pearlson GD**, Wong DF, Tune LE, Ross CA, Chase GA, Links JM, Dannals RF, Wilson AA, Ravert HT, Wagner HN, Jr, DePaulo JR. C-11 NMSP PET scans in psychotic and non-psychotic bipolars. Archives of General Psychiatry, 52: 471-477, 1995.

103. Schlaepfer TE, **Pearlson GD**. Pitfalls of SPECT studies of acute ethanol-induced changes in cerebral blood flow. (Ltr. to the Editor) American Journal of Psychiatry, 152: 111, 1995.

104. Aylward E, Brettschneider PD, McArthur JC, Harris GJ, Schlaepfer TE, Henderer JD, Barta PE, Tien AY, **Pearlson GD**. MRI gray matter volumes reductions in HIV-1 dementia. American Journal of Psychiatry, 152: 987-994, 1995.

105. Davison SE, Aylward EH, McArthur JC, Selnes O, Lyketsos C, Barta PE, **Pearlson GD**. A quantitative MRI study of the basal ganglia in depression with HIV infection. Journal of Neuro-AIDS, 1: 29-41, 1996.

106. Schlaepfer TE, Strain EC, Bigelow GE, Lancaster E, Preston KL, **Pearlson GD**. Differential cerebral blood flow effects caused by mu versus kappa opioid agonists. NIDA Res Monogr, 162: 194, 1996.

107. Holder JL, Habbak RA, **Pearlson GD**, Aylward EA, Pulsifer M, Warren AC. Reduced survival of apolipoprotein E4 homozygotes in Down's syndrome? NeuroReport, 7: 2455-2456, 1996.

108. Aylward EH, Harris GH, Hoehn-Saric R, Barta PE, Machlin S, **Pearlson GD**. Normal caudate nucleus in obsessive compulsive disorder assessed by quantitative neuro-imaging. Archives of General Psychiatry, 53: 577-584, 1996.

109. Aylward EH, Rasmusson DX, Brandt J, Raimundo L, Folstein M, **Pearlson GD**. CT measurement of suprasellar cistern predicts rate of cognitive decline in Alzheimer's disease. Journal of the International Neuropsychological Society, 2: 89-95, 1996.

110. Hooten WM, **Pearlson GD**. Delirium caused by tacrine and ibuprofen interaction. (Letter to the Editor), American Journal of Psychiatry, 153: 6, 1996.

111. Lyketsos CG, Tune LE, **Pearlson GD**, Steele C. Major depression in Alzheimer's disease. An interaction between gender and family history. Psychosomatics, 37: 380-384, 1996.

112. **Pearlson GD**, Petty RG, Ross CA and Tien AY. Schizophrenia: A disease of heteromodal association cortex? Neuropsychopharmacology, 14: 1-17, 1996.

113. Ross CA, **Pearlson GD**. Schizophrenia, the heteromodal association neocortex and development: Potential for a neurogenetic approach. Trends In Neurosciences 19: 171-176, 1996.

114. Tien AY, Eaton WE, Schlaepfer TE, McGilchrist I, Menon RR, Powers RE, Aylward EH, Barta PE, Strauss ME, **Pearlson GD**. Exploratory factor analysis of MRI brain structure measures in schizophrenia. Schizophrenia Research, 19: 93-101, 1996.

115. Tune LT, Barta P, Wong D, Powers PE, **Pearlson G**, Tien A, Wagner HN. Striatal D2 receptor quantification and superior temporal gyrus volume determination in 14 chronic schizophrenic subjects. Psychiatric Research - Neuroimaging, 67: 155-158, 1996.

116. Tien, AY, Ross D, **Pearlson GD**, Strauss ME. Eye movements and psychopathology in schizophrenia and bipolar disorder. Journal of Nervous and Mental Disease, 184: 331-338, 1996.

117. Harris GJ, Aylward EH, Peyser CE, **Pearlson GD**, Brandt J, Roberts-Twillie JV, Folstein SE. Single photon emission computed tomographic blood flow and magnetic resonance volume imaging of basal ganglia in Huntington's disease. Archives of Neurology, 53: 316-324, 1996.

118. Aylward E, Codori AM, Barta PE, **Pearlson GD**, Harris G, Brandt J. Basal ganglia volume and proximity to onset in presymptomatic Huntington's disease. Archives of Neurology, 53: 1293-1296, 1996.

119. Tien AY, Spevack TV, Jones DW, **Pearlson GD**, Schlaepfer TE, Strauss ME. Computerized Wisconsin Card Sorting Test: Comparison With Manual Administration. Kaohsiung Journal of Medical Sciences, 12: 479-485, 1996.

120. Ross CA, **Pearlson GD**. (Letter to Editor) Glutamate receptors and schizophrenia. Trends In Neurosciences, 19: 416-417, 1996.

121. **Pearlson GD**, Barta PE, Powers RE, Menon RR, Richards SS, Aylward EH, Federman EB, Chase GA, Petty RG, Tien AY. Medial and superior temporal gyral volumes and cerebral asymmetry in schizophrenia versus bipolar disorder. Biological Psychiatry, 41: 1-14, 1997. **Winner, 1996 Ziskind-Somerfeldt Research Award.**

122. **Pearlson GD**, Schlaepfer TE. (Ltr. to the Ed.) Cortex and sex differences in schizophrenia. Archives of General Psychiatry, 54: 189, 1997.

123. Barta PE, **Pearlson GD**, Brill LB, Royall R, McGilchrist IK, Pulver AE, Powers RE, Casanova MF, Tien AY, Frangou S, and Petty RG. Planum temporale asymmetry reversal in schizophrenia: replication and relationship to gray matter abnormalities. Am J Psychiatry, 154: 661-666, 1997.

124. Frangou S, Sharma T, Sigmudsson T, Barta P, **Pearlson G**, Murray RM. The Maudsley Family Study 4. Normal planum temporale asymmetry in familial schizophrenia. British Journal of Psychiatry, 170: 328-333, 1997.

125. **Pearlson GD**. Superior temporal gyrus and planum temporale in schizophrenia. Prog. Neuro-Psychopharmacology and Biol. Psychiatry, 21: 1203-1229, 1997.

126. **Pearlson GD**. Schizophrenia. Editorial, International J. Psychiatry, 9: 317-319, 1997.

127. Aylward E, Habbak R, Warren A, Pulsifer MB, Barta PE, Jerram M, **Pearlson GD**. Cerebellar volume in adults with Down Syndrome. Archives of Neurology, 54: 209-212, 1997.

128. Frangou S, Aylward EH, Warren AC, Sharma T, Barta PE, **Pearlson GD**. Planum temporale in Down's syndrome. American Journal of Psychiatry, 154: 1424-1429, 1997.

129. Aylward E, Li Q, Habbak R, Warren A, Pulsifer MB, Barta PE, Jerram M, **Pearlson GD**. Basal ganglia volume in adults with Down Syndrome. Psychiatry Research - Neuroimaging, 74: 73-82, 1997.

130. Aylward EH, Augustine AM, Li Q, Barta PE, **Pearlson GD**. Measurement of frontal lobe volume on MRI scans. Psychiatry Research Neuroimaging, 75: 23-30, 1997.

131. Barta PE, **Pearlson GD**, Powers RE, Aylward EH, Chase GA, Harris GJ, Rabins PV, Raimundo LD, Tune LE. Quantitative MRI volume changes in late-onset schizophrenia and Alzheimer's disease compared to normal controls. Psychiatry Research - Neuroimaging, 68: 65-75, 1997.

132. Wong WF, **Pearlson GD**, Tune LE, Young LT, Meltzer CC, Dannals RF, Ravert HY, Reith J, Kuhar MJ, Gjedde A. Quantification of neuroreceptors in the living human brain. IV. Effect of aging in elevations of D2-like receptors in schizophrenia and bipolar illness. J Cereb Blood Flow Metab, 17: 331-342, 1997.

133. Schlaepfer TE, **Pearlson GD**, Wong DF, Marenco S, Dannals RF. Intravenous cocaine competes with [11C]-raclopride at dopamine receptors in human subjects: A PET study. American Journal of Psychiatry 154: 1209-1213, 1997.

134. Aylward EH, Li Q, Stine OC, Ranen N, Sherr M, Barta PE, Bylsma FW, **Pearlson GD**, Ross CA. Longitudinal change in basal ganglia volume in patients with Huntington's disease. Neurology, 48: 394-399, 1997.

135. Aylward EH, Anderson NB, Bylsma FW , Wagster MV, Barta PE, Sherr M , Feeney J, Davis A, Rosenblatt A, **Pearlson GD**, Ross CA. Frontal lobe volume in patients with Huntington's disease. Neurology, 50:252-258, 1998.

136. Rivkin P and **Pearlson GD**. An unusual presentation of Huntington's disease. Psychosomatics, 39:291-294, 1998.

137. Schlaepfer TE, Strain EC, Greenberg BD, Preston KL, Lancaster E, Bigelow GE, Barta PE, **Pearlson GD**. Site of opioid action in the human brain: mu and kappa agonists' subjective and cerebral blood flow effects. American Journal of Psychiatry 155:470-473, 1998.

138. Honeycutt NA, Smith PD, Aylward E, Li Q, Chan M, Barta PE, **Pearlson GD**. Mesial temporal lobe measurements on magnetic resonance imaging scans. Psychiatry Research: Neuroimaging, 83: 85-94, 1998.

139. Tien AY, Schlaepfer TE, Orr W, **Pearlson GD**. 1998 SPECT brain blood flow changes with continuous ligand infusion during previously learned WCST performance. Psychiatry Research 82: 47-52.

140. **Pearlson GD**, Breiter SN, Aylward EH, Warren AC, Grygorcewicz M, Frangou S, Barta PE, Pulsifer M. MRI brain changes in Down syndrome patients with and without dementia. Developmental Medicine and Child Neurology, 40:326-334, 1998.

141. Buchanan RW, Vladar K, Barta PE, **Pearlson GD**. Structural evaluation of the prefrontal cortex in schizophrenia. Am J Psychiatry 155: 1049-1055, 1998.

142. Sharma T, Lancaster E, Lee D, Lewis S, Sigmundsson T, Takei N, Gurling H, Barta P, **Pearlson GD**, Murray R. Brain changes in schizophrenia: Volumetric MRI study of families multiply affected with schizophrenia - The Maudsley Family Study 5. British J Psychiatry, 173: 132-138, 1998.

143. Aylward EH, Li Q, Honeycutt NA, Warren AC, Pulsifer MB, Barta PE, Chan MD, Smith PD, Jerram M, **Pearlson GD**. MRI volumes of the hippocampus and amygdala in adults with Down's syndrome with and without dementia. Am J Psychiatry, 156: 564-568, 1999.

144. Aylward EH, Minshew NJ, Goldstein G, Honeycutt NA, Augustine AM, Yates KO,Barta PE, **Pearlson GD**. MRI MRI volumes of amygdala and hippocampus in non-mentally retarded autistic adolescents and adults. Neurology 53: 2145-2150, 1999.

145. **Pearlson GD**. Structural and functional brain imaging in bipolar disorder: a selective review. Schizophrenia Research, 39: 133-140, 1999.

146. Frederikse ME, Lu A, Aylward EA, Barta PE, **Pearlson, GD**: Sex differences in the inferior parietal lobule. Cerebral Cortex 9: 896-901, 1999.

147. Barta PE, **Pearlson GD**, Vladar K, Buchanan RW. Demonstration of a simple, accurate method for measuring the volumes of cortical gyri, illustrated by an application to the frontal lobes. Psychiatry Research Neuroimaging, in press.

148. **Pearlson GD**, Marsh L. Structural brain imaging changes in schizophrenia. A selective review. Biological Psychiatry, 46: 627-649,1999

149. Sharma T, Lancaster E, Sigmundsson T, Lewis S, Takei N, Gurling H, Barta P, **Pearlson GD**, Murray R. Lack of normal pattern of cerebral asymmetry in familial schizophrenic patients and their relatives: The Maudsley Family Study. Schizophrenia Research, 40: 111-120, 1999.

150. **Pearlson GD**. New insights on the neuroanatomy of schizophrenia. Curr Psychiatry Rep. 1: 41-45, 1999.

151. Frederikse M, Lu A, Aylward EH, Barta PE, Sharma T, **Pearlson GD.** Sex differences in inferior parietal lobe volume in schizophrenia. American J. Psychiatry, 157: 422-427, 2000.

152. **Pearlson GD**. Neurobiology of Schizophrenia. Annals of Neurology, 48: 556-566, 2000.

153. Mori S, Kaufmann W, **Pearlson GD**, Crain BJ, Stieltjes B, Solaiyappan M, van Zijl PCM. In vivo visualization of human neural pathways by MRI. Annals of Neurology, 47: 412-4, 2000.

154. Calhoun V, Adali T, Kraut M, **Pearlson GD**. A weighted-least squares algorithm for estimation and visualization of relative latencies in event-related functional MRI. Magnetic Resonance in Medicine, 44: 947-954, 2000.

155. Rabins PV, Aylward E, Holroyd S, Chase GA, **Pearlson GD.** MRI findings differentiate between late-onset schizophrenia and late-life mood disorder. Journal of Nervous and Mental Disease, 15: 954-960, 2000.

156. Rivkin P, **Pearlson GD**, Barta PE, Anthony JC, Arria AM. Comparison of white matter hyperintensities in age-matched groups of controls and subjects with late-onset and early-onset schizophrenia. International Journal of Geriatric Psychiatry, 15: 1085-1089, 2000.

157. Honeycutt NA, Musick A, Barta PE, **Pearlson GD**. Measurement of the planum temporale on magnetic resonance imaging scans: Temporal PT alone and with parietal extension. Psychiatry Research: Neuroimaging, 98: 103-116, 2000.

158. Aylward, E.H, Codori, A.M., Rosenblatt, A., Sherr, M., Brandt, J., Stine,O.C., Barta, P.E., **Pearlson, G.D.**, Ross, C.A. Rate of caudate atrophy in presymptomatic and symptomatic stages of Huntington's disease. Movement Disorders, 15:552-560, 2000.

159. Schretlen D, **Pearlson GD**, Anthony JC, Aylward EH, Augustine AM, Davis A, Barta P. Elucidating the contributions of processing speed, executive ability, and frontal lobe volume to normal age-related differences in fluid intelligence. J Int Neuropsychol Soc., 6:52-61, 2000.

160. Schretlen DJ, **Pearlson GD,** Anthony JC, Yates KO. Determinants of Benton facial recognition test performance in normal adults. Neuropsychology, 15: 405-410, 2001.

161. Hoehn-Saric R, Schlaepfer TE, Greenberg BD, McLeod DR, **Pearlson GD**, Wong SH. Cerebral blood flow in obsessive-compulsive patients with major depression: effect of treatment with sertraline or desipramine on treatment responders and non-responders. Psychiatry Research, 108: 89-100, 2001.

162. Calhoun VD Adali T, Kraut M, **Pearlson GD.** Spatial and temporal independent component analysis of functional MRI data containing a pair of task-related waveforms. Human Brain Mapping, 13: 43-53, 2001.

163. Calhoun VD, Adali T, **Pearlson GD**, and Pekar JJ. A method for making group inferences from functional MRI data using independent component analysis. Human Brain Mapping, 14: 140-451, 2001.

164. Calhoun VD, Adali T, McGinty VB, Pekar JJ, Watson TD, and **Pearlson GD**. fMRI activation in a visual-perception task: Network of areas detected using the general linear model and independent components analysis. Neuroimage, 14: 1080-1088, 2001.

165. Stieltjes B, Kaufmann WE, van Zijl PC, Fredericksen K, **Pearlson GD,** Solaiyappan M, Mori S. Diffusion tensor imaging and axonal tracking in the human brainstem. Neuroimage, 14: 723-735, 2001.

166. Potash JB, Willour VL, Chiu YF, Simpson SG, MacKinnon DF, **Pearlson GD**, DePaulo JR Jr, McInnis MG. The familial aggregation of psychotic symptoms in bipolar disorder pedigrees. Am J Psychiatry, 158: 1258-1264, 2001.

167. WR Kates, CP Burnette, E Jabs, J Rutberg, AM Murphy, MA Grados, M, Geraghty, WE Kaufmann, **Pearlson, GD.** Regional cortical white matter reductions in velocardiofacial syndrome: A volumetric MRI analysis. Biological Psychiatry 49: 677-684, 2001.

168. Naidu S, Kaufmann WE, Abrams MT, **Pearlson GD,** Lanham DC, Fredericksen KA, Barker PB, Horska A, Golay X, Mori S, Wong DF, Yablonski M, Moser HW, Johnston MV. Neuroimaging studies in Rett syndrome. Brain Development S62-S71, 2001.

169. Calhoun V, McGinty V, Pekar J, Watson T, **Pearlson GD**. Investigation of Marinol (THC) Effects on fMRI activation during active and passive driving using independent component analysis and SPM. Neuroimage, 13: 6, 388, 2001.

170. Calhoun VD, Pekar JJ, McGinty VB, Adali T, Watson TD, **Pearlson GD.** Different activation dynamics in multiple neural systems during simulated driving. Hum Brain Mapping 16(3):158-67, 2002.

171. Kates WR, Frederikse M, Mostofsky SH, Folley BS, Cooper K, Mazur-Hopkins P, Kofman O, Singer HS, Denckla MB, **Pearlson GD**, Kaufmann WE. MRI parcellation of the frontal lobe in boys with attention deficit hyperactivity disorder or Tourette syndrome. Psychiatry Res,116(1-2):63-81, 2002.

172. Calhoun VD, Adali T, **Pearlson GD,** van Zijl PC, Pekar JJ. Independent component analysis of fMRI data in the complex domain. Magn Reson Med.; 48(1):180-92, 2002.

173. Mori S, Kaufmann WE, Davatzikos C, Stieltjes B, Amodei L, Fredericksen K, **Pearlson GD,** Melhem ER, Solaiyappan M, Raymond GV, Moser HW, van Zijl PC. Imaging cortical association tracts in the human brain using diffusion-tensor-based axonal tracking. Magn Reson Med.; 47(2):215-23, 2002.

174. Calhoun VD, Adali T, Pekar JJ, **Pearlson GD**. Latency (in)sensitive ICA. Group independent component analysis of fMRI data in the temporal frequency domain. Neuroimage. Nov;20(3):1661-9, 2003.

175. Ratnanather JT, Barta PE, Honeycutt NA, Lee N, Morris HM, Dziorny AC, Hurdal MK, **Pearlson GD**, Miller MI. Dynamic programming generation of boundaries of local coordinatized submanifolds in the neocortex: application to the planum temporale. Neuroimage, 20(1):359-77, 2003.

176. Schretlen DJ, Munro CA, Anthony JC, **Pearlson GD**. Examining the range of normal intra-individual variability in neuropsychological test performance. J Int Neuropsychol Soc,9(6):864-70, 2003.

177. Miller TJ, McGlashan TH, Rosen JL, Cadenhead K, Ventura J, McFarlane W, Perkins DO, **Pearlson GD**, Woods SW. Prodromal assessment with the structured interview for prodromal syndromes and the scale of prodromal symptoms: predictive validity, interrater reliability, and training to reliability. Schizophr Bull.;29(4):703-15, 2003.

178. Calhoun VD, Kiehl KA, Liddle PF, **Pearlson GD**. Aberrant localization of synchronous hemodynamic activity in auditory cortex reliably characterizes schizophrenia. Biol Psychiatry. Apr 15;55(8):842-9, 2004.

179. Kates WR, Burnette CP, Eliez S, Strunge LA, Kaplan D, Landa R, Reiss AL, **Pearlson GD.** Neuroanatomic variation in monozygotic twin pairs discordant for the narrow phenotype for autism. Am J Psychiatry, 161(3):539-46, 2004.

180. Kates WR, Burnette CP, Bessette BA, Folley BS, Strunge L, Jabs EW, **Pearlson GD**. Frontal and caudate alterations in velocardiofacial syndrome (deletion at chromosome 22q11.2). J Child Neurol, 19(5):337-42, 2004.

181. Buchanan RW, Francis A, Arango C, Miller K, Lefkowitz DM, McMahon RP, Barta PE, **Pearlson GD**. Morphometric assessment of the heteromodal association cortex in schizophrenia. Am J Psychiatry.;161(2):322-31, 2004.

182. Buchanan RW, **Pearlson GD.** Prefrontal cortex, structural analysis: segmenting the prefrontal cortex. Am J Psychiatry. Nov;161(11):1978, 2004.

183. Diaz-Asper CM, Schretlen DJ, **Pearlson GD**. How well does IQ predict neuropsychological test performance in normal adults? J Int Neuropsychol Soc. Jan;10(1):82-90, 2004.

184. Hawkins, K.A., Dean, D., & Pearlson, GD. Alternative forms of the Rey Auditory Verbal Learning Test: A review. Behavioural Neurology, 15(3-4):99-107, 2004.

185. Reading SA, Dziorny AC, Peroutka LA, Schreiber M, Gourley LM, Yallapragada V, Rosenblatt A, Margolis RL, Pekar JJ, **Pearlson GD**, Aylward E, Brandt J, Bassett SS, Ross CA. Functional brain changes in presymptomatic Huntington's disease. Ann Neurol, 55(6):879-83, 2004.

186. Kim JS, Reading SA, Brashers-Krug T, Calhoun VD, Ross CA, **Pearlson GD**. Functional MRI study of a serial reaction time task in Huntington's disease. Psychiatry Res,131(1):23-30, 2004.

187. Calhoun VD, Stevens MC, **Pearlson GD,** Kiehl KA. fMRI analysis with the general linear model: removal of latency-induced amplitude bias by incorporation of hemodynamic derivative terms. Neuroimage. May;22(1):252-7, 2004.

188. Calhoun VD, Altschul D, McGinty V, Shih R, Scott D, Sears E, **Pearlson GD**. Alcohol intoxication effects on visual perception: an fMRI study. Hum Brain Mapp. Jan;21(1):15-26, 2004. Erratum in: Hum Brain Mapp. Apr;21(4):298-9, 2004. (Cover issue)

189. Calhoun VD, Pekar JJ, **Pearlson GD**. Alcohol intoxication effects on simulated driving: exploring alcohol-dose effects on brain activation using functional MRI. Neuropsychopharmacology, 29(11):2097-17, 2004.

190. Schlaepfer TE, Lancaster E, Heidbreder R, Strain EC, Kosel M, Fisch HU, **Pearlson GD**. Decreased frontal white-matter volume in chronic substance abuse. Int J Neuropsychopharmacol, 1-7, 2005.

191. Calhoun VD, Carvalho K, Astur R, **Pearlson GD**. Using virtual reality to study alcohol intoxication effects on the neural correlates of simulated driving. Appl Psychophysiol Biofeedback, 30(3):285-306, 2005.

192. Hong B, **Pearlson GD,** Calhoun VD. Source density-driven independent component analysis approach for fMRI data. Human Brain Mapping. 2005.

193. Kiehl KA, Stevens MC, Laurens KR, **Pearlson GD,** Calhoun VD, Liddle PF. An adaptive reflexive processing model of neurocognitive function: supporting evidence from a large scale (n = 100) fMRI study of an auditory oddball task. Neuroimage, 15;25(3):899-915, 2005

194. Calhoun VD, Adali T, **Pearlson GD**, Kiehl KA. Neuronal chronometry of target detection: Fusion of hemodynamic and event-related potential data. Neuroimage, 2005.

195. Astur RS, St Germain SA, Baker EK, Calhoun V, **Pearlson GD**, Constable RT. fMRI hippocampal activity during a virtual radial arm maze. Appl Psychophysiol Biofeedback, 30(3):307-17, 2005.

196. Strasser HC, Lilyestrom J, Ashby ER, Honeycutt NA, Schretlen DJ, Pulver AE, Hopkins RO, Depaulo JR, Potash JB, Schweizer B, Yates KO, Kurian E, Barta PE, **Pearlson GD**. Hippocampal and ventricular volumes in psychotic and nonpsychotic bipolar patients compared with schizophrenia patients and community control subjects. Biol Psychiatry, 57:633-639, 2005.

197. Giuliani NR, Calhoun VD, **Pearlson GD**, Francis A, Buchanan RW. Voxel-based morphometry versus region of interest: a comparison of two methods for analyzing gray matter differences in schizophrenia. Schizophrenia Research.;74:135-147. 2005.

198. St. Germain SS, Astur RA, **Pearlson GD**. Driving in schizophrenia. Results on a driving simulator. Schizophrenia Research, 1;74(1):121-2, 2005.

199. Assaf M, Rivkin PR, Kuzu CH, Calhoun VD, Kraut MA, Groth KM, Yassa MA, Hart J Jr, **Pearlson GD.** Abnormal object recall and anterior cingulate over-activation correlate with formal thought disorder in schizophrenia. Biol Psychiatry. 2005.

200. Kanaan RA, Kim JS, Kaufmann WE, **Pearlson GD**, Barker GJ, McGuire PK. Diffusion tensor imaging in schizophrenia. Biol Psychiatry. 2005;58(12):921-929. (Cover Issue)

201. Schretlen DJ, Buffington AL, Meyer SM, **Pearlson GD**. The use of word-reading to estimate "premorbid" ability in cognitive domains other than intelligence. J Int Neuropsychol Soc., 11(6):784-7, 2005.

202. Calhoun VD, Adali T, Giuliani NR, Pekar JJ, Kiehl KA, **Pearlson GD.** Method for multimodal analysis of independent source differences in schizophrenia: Combining gray matter structural and auditory oddball functional data. Hum Brain Mapping. 27(1):47-62.2006.

203. Krystal JH, D'Souza DC, Gallinat J, Driesen N, Abi-Dargham A, Petrakis I, Heinz A, **Pearlson GD.** The vulnerability to alcohol and substance abuse in individuals diagnosed with schizophrenia. Neurotox Res. 2006;10(3-4):235-52.

204. Johnson MR, Morris NA, Astur RS, Calhoun VD, Mathalon DH, Kiehl KA, **Pearlson GD**. A functional magnetic resonance imaging study of working memory abnormalities in schizophrenia. Biol Psychiatry. 2006:60; 11-21.

205. Calhoun VD, Adali T, Kiehl KA, Astur R, Pekar JJ, **Pearlson GD**. A method for multitask fMRI data fusion applied to schizophrenia. Hum Brain Mapp. 2006:27(7):598-610.

206. Assaf M, Calhoun VD, Kuzu CH, Kraut MA, Rivkin PR, Hart J Jr, **Pearlson GD.** Neural correlates of the object-recall process in semantic memory. Psychiatry Res. 2006 Oct 30;147(2-3):115-26.

207. Jiang H, van Zijl PC, Kim J, **Pearlson GD**, Mori S. DTI-Studio: resource program for diffusion tensor computation and fiber bundle tracking. Comput Methods Programs Biomed. 2006;81(2):106-16.

208. Krystal J, D'Souza D, Gallinat J, Driesen N, Abi-Dargham A, Petrakis I, Heinz A, **Pearlson GD.** The vulnerability to alcohol and substance abuse in individuals diagnosed with schizophrenia. Neurotoxicology Research,10(3-4):235-252 2006.

209. Garrity AG, **Pearlson GD**, McKiernan K, Lloyd D, Kiehl KA, Calhoun VD. Aberrant "default mode" functional connectivity in schizophrenia. Am J Psychiatry. 2007;164 (3):450-7.

210. Schretlen DJ, Cascella NG, Meyer SM, Kingery LR, Testa SM, Munro CA, Pulver AE, Rivkin P, Rao VA, Diaz-Asper CM, Dickerson FB, Yolken RH, **Pearlson GD**. Neuropsychological functioning in bipolar disorder and schizophrenia. Biol Psychiatry. 2007;62(2):179-186.

211. Keshavan MS, Prasad KM, **Pearlson GD**. Are brain structural abnormalities useful as endophenotypes in schizophrenia? Int Rev Psychiatry. 2007;19(4):397-406.

212. Kurtz MM, Baker E, **Pearlson GD**, Astur RS. A virtual reality apartment as a measure of medication management skills in patients with schizophrenia: A Pilot Study. Schizophr Bull. 2007;33(5):1162-70.

213. **Pearlson GD**, Calhoun V. Structural and functional magnetic resonance imaging in psychiatric disorders. Can J Psychiatry. 2007 Mar;52(3):158-66.

214. Stevens MC, Kiehl KA, **Pearlson GD,** Calhoun VD. Functional neural circuits for mental timekeeping. Hum Brain Mapp. 2007 May;28(5):394-408.

215. Stevens MC, Kiehl KA, **Pearlson GD**, Calhoun VD. Functional neural networks underlying response inhibition in adolescents and adults. Behav Brain Res. 2007 Jul 19;181(1):12-22.

216. Ruano G, Blair CL, Bower B, Windemuth A, Kocherla M, Aleman Y, **Pearlson GD,** Goethe JW, Schwartz HI. Somatic complications of psychotropic medications in a patient with multiple CYP2 drug metabolism deficiencies. Conn Med. 2007 Apr; 71(4):197-200.

217. Stevens MC, **Pearlson GD**, Kiehl KA.An auditory oddball study of combined-subtype attention deficit hyperactivity disorder. Am J Psychiatry. 2007 Nov; 164(11):1737-49.

218. Manning KJ, Gordon B, **Pearlson GD**, Schretlen DJ. The relationship of recency discrimination to explicit memory and executive functioning. J Int Neuropsychol Soc. 2007 Jul;13(4):710-5.

219. Schretlen DJ, Inscore AB, Jinnah HA, Rao V, Gordon B, **Pearlson GD**. Serum uric acid and cognitive function in community-dwelling older adults. Neuropsychology. 2007;21(1):136-40.

220. Manning KJ, Gordon B, **Pearlson GD**, Schretlen DJ. The relationship of recency discrimination to explicit memory and executive functioning. J Int Neuropsychol Soc. 2007 Jul;13(4):710-5.

221. Schretlen DJ, Inscore AB, Vannorsdall TD, Kraut M, **Pearlson GD**, Gordon B, Jinnah HA. Serum uric acid and brain ischemia in normal elderly adults. Neurology. 2007 Oct 2;69(14):1418-23.

222. Windemuth A, Calhoun VD, **Pearlson GD**, Kocherla M, Jagannathan K, Ruaño G. Physiogenomic analysis of localized fMRI brain activity in schizophrenia. Annals of Biomedical Engineering, 2008; 36(6):877-88.

223. **Pearlson GD,** Folley BS. Schizophrenia, psychiatric genetics, and Darwinian psychiatry: an evolutionary framework. Schizophr Bull. 2008;34(4):722-33.

224. **Pearlson GD**, Folley BS. Endophenotypes, dimensions, risks: is psychosis analogous to common inherited medical illnesses? Clin EEG Neurosci. 2008;39(2):73-7.

225. Meda SA, Giuliani NR, Calhoun VD, Jagannathan K, Schretlen DJ, Pulver A, Cascella N, Keshavan M, Kates W, Buchanan R, Sharma T, **Pearlson GD.** A large scale (N=400) investigation of gray matter differences in schizophrenia using optimized voxel-based morphometry. Schizophr Res. 2008;101(1-3):95-105.

226. Arango C, McMahon RP, Lefkowitz DM, **Pearlson GD,** Kirkpatrick B, Buchanan RW. Patterns of cranial, brain and sulcal CSF volumes in male and female deficit and nondeficit patients with schizophrenia. Psychiatry Res. 2008 28;162(2):91-100.

227. Jafri MJ, **Pearlson GD,** Stevens M, Calhoun VD. A method for functional network connectivity among spatially independent resting-state components in schizophrenia. Neuroimage. 2008 15;39(4):1666-81.

228. Skelly LR, Calhoun V, Meda SA, Kim J, Mathalon DH, **Pearlson GD**. Diffusion tensor imaging in schizophrenia: relationship to symptoms. Schizophr Res. 2008;98(1-3):157-62.

229. Kim D, **Pearlson GD**, Kiehl KA, Bedrick E, Demirci O, Calhoun VD. A method for multi-group inter-participant correlation: abnormal synchrony in patients with schizophrenia during auditory target detection. Neuroimage. 2008 1;39(3):1129-41.

230. Calhoun VD, Maciejewski PK, **Pearlson GD**, Kiehl KA.Temporal lobe and "default" hemodynamic brain modes discriminate between schizophrenia and bipolar disorder. Hum Brain Mapp. 2008;29(11):1265-75

231. Cascella NG, Testa SM, Meyer SM, Rao VA, Diaz-Asper CM, **Pearlson GD**, Schretlen DJ. Neuropsychological impairment in deficit vs. non-deficit schizophrenia. J Psychiatr Res. 2008;42(11):930-7.

232. Kim D, Burge J, Lane T, **Pearlson GD**, Kiehl KA, Calhoun VD. Hybrid ICA-Bayesian network approach reveals distinct effective connectivity differences in schizophrenia. Neuroimage. 2008, 42;(4);1560-1568.

233. Caprihan A, **Pearlson GD**, Calhoun VD. Application of principal component analysis to distinguish patients with schizophrenia from healthy controls based on fractional anisotropy measurements. Neuroimage. 2008, 42(2)675-682.

234. Meda SA, Bhattarai M, Morris NA, Astur RS, Calhoun VD, Mathalon DH, Kiehl KA, **Pearlson GD**. An fMRI study of working memory in first-degree unaffected relatives of schizophrenia patients. Schizophrenia Res. 2008;104(1-3):85-95.

235. Demirci O, Clark VP, Magnotta VA, Andreasen NC, Lauriello J, Kiehl KA, **Pearlson GD**, Calhoun VD.A review of challenges in the use of fMRI for disease classification / Characterization and a projection pursuit application from multi-site fMRI schizophrenia study. Brain Imaging Behav. 2008 1;2:147-226.

236. Calhoun VD, Kiehl KA, **Pearlson GD**. Modulation of temporally coherent brain networks estimated using ICA at rest and during cognitive tasks. Hum Brain Mapp. 2008 Jul;29(7):828-38.

237. Skudlarski P, Jagannathan K, Calhoun VD, Hampson M, Skudlarska BA, **Pearlson G**. Measuring brain connectivity: diffusion tensor imaging validates resting state temporal correlations. Neuroimage. 2008 15; 43(3):554-61.

238. Meda SA, Gelernter J, Gruen JR, Calhoun VD, Meng H, Cope NA, **Pearlson GD**. Polymorphism of DCDC2 reveals differences in cortical morphology of healthy individuals- A preliminary voxel based morphometry study. Brain Imaging Behav. 2008;2(1):21-26.

239. Wilhelm S, Buhlmann U, Tolin DF, Meunier SA, **Pearlson GD**, Reese HE, Cannistraro P, Jenike MA, Rauch SL. Augmentation of behavior therapy with D-cycloserine for obsessive-compulsive disorder. Am J Psychiatry. 2008 Mar;165(3):335-41.

240. Schretlen DJ, Testa SM, Winicki JM, **Pearlson GD**, Gordon B. Frequency and bases of abnormal performance by healthy adults on neuropsychological testing. J Int Neuropsychol Soc. 2008 May;14(3):436-45.

241. Otto MW, Tolin DF, Simon NM, **Pearlson GD**, Basden S, Meunier SA, Hofmann SG, Eisenmenger K, Krystal JH, Pollack MH. Efficacy of D-cycloserine for enhancing response to cognitive-behavior therapy for panic disorder. Biol Psychiatry 2009

242. Testa SM, Winicki JM, **Pearlson GD**, Gordon B, Schretlen DJ. Accounting for estimated IQ in neuropsychological test performance with regression-based techniques. J Int Neuropsychol Soc. 2009;15(6):1012-22.

243. Meda SA, Stevens MC, Potenza MN, Pittman B, Gueorguieva R, Andrews MM, Thomas AD, Muska C, Hylton JL, **Pearlson GD**. Investigating the behavioral and self-report constructs of impulsivity domains using principal component analysis. Behav Pharmacol. Sep;20(5-6):390-399; 2009.

244. Meda SA, Calhoun VD, Astur RS, Turner BM, Ruopp K, **Pearlson GD**. Alcohol dose effects on brain circuits during simulated driving: an fMRI study. Hum Brain Mapp. 2009;30(4):1257-70.

245. Allen AJ, Meda SA, Skudlarski P, Calhoun VD, Astur R, Ruopp KC, **Pearlson GD**. Effects of alcohol on performance on a distraction task during simulated driving. Alcohol Clin Exp Res. 2009;33(4):617-25.

246. Stevens MC, Kiehl KA, **Pearlson GD**, Calhoun VD. Brain network dynamics during error commission. Hum Brain Mapp. 2009 Jan;30(1):24-37.

247. Hong CC, Harris JC, **Pearlson GD**, Kim JS, Calhoun VD, Fallon JH, Golay X, Gillen JS, Simmonds DJ, van Zijl PC, Zee DS, Pekar JJ. fMRI evidence for multisensory recruitment associated with rapid eye movements during sleep. Hum Brain Mapp. 2009 May; 30(5):1705-22.

248. Liu J, Kiehl KA, **Pearlson GD**, Perrone-Bizzozero NI, Eichele T, Calhoun VD. Genetic determinants of target and novelty-related event-related potentials in the auditory oddball response. NeuroImage. 2009 1;46(3):809-16.

249. Goldstein G, Panchalingam K, McClure RJ, Stanley JA, Calhoun VD, **Pearlson GD**, Pettegrew JW. Molecular neurodevelopment: an in vivo 31P-1H MRSI study. J Int Neuropsychol Soc. 2009;15:671-83

250. Stevens MC, Skudlarski P, **Pearlson GD**, Calhoun VD. Age-related cognitive gains are mediated by the effects of white matter development on brain network integration. Neuroimage. 2009;48:738-46.

251. Sui J, Adali T, **Pearlson GD**, Calhoun VD. An ICA-based method for the identification of optimal FMRI features and components using combined group-discriminative techniques. Neuroimage. 2009 15;46(1):73-86.

252. Assaf M, Jagannathan K, Calhoun V, Kraut M, Hart J Jr, **Pearlson G**. Temporal sequence of hemispheric network activation during semantic processing: a functional network connectivity analysis. Brain Cogn. 2009;70(2):238-46.

253. Stevens MC, **Pearlson GD**, Calhoun VD. Changes in the interaction of resting-state neural networks from adolescence to adulthood. Hum Brain Mapp. 2009;30 (8):2356-66.

254. Hong CC, Harris JC, **Pearlson GD**, Kim JS, Calhoun VD, Fallon JH, Golay X, Gillen JS, Simmonds DJ, van Zijl PC, Zee DS, Pekar JJ. fMRI evidence for multisensory recruitment associated with rapid eye movements during sleep. Hum Brain Mapp. 2009;30(5):1705-22.

255. Gordon RJ, Seamon JG, **Pearlson GD**. An fMRI study of neurocognitive functioning in schizophrenia with a mere exposure paradigm. Schizophr Res. 2009; 108(1-3):290-2.

256. **Pearlson GD**. Multisite collaborations and large databases in psychiatric neuroimaging: advantages, problems and challenges. Schizophrenia Bull. 2009; 35(1):1-2.

257. Liu J, **Pearlson GD**, Windemuth A, Ruano G, Perrone-Bizzozero NI, Calhoun V. Combining fMRI and SNP data to investigate connections between brain function and genetics using parallel ICA. Hum Brain Mapp. 2009; 30(1):241-55.

258. Calhoun VD, Eichele T, **Pearlson G.** Functional brain networks in schizophrenia: a review. Front Hum Neurosci. 2009; 3:17. In Press.

259. Demirci O, Stevens MC, Andreasen NC, Michael A, Liu J, White T, **Pearlson GD**, Clark VP, Calhoun VD. Investigation of relationships between fMRI brain networks in the spectral domain using ICA and Granger causality reveals distinct differences between schizophrenia patients and healthy controls. NeuroImage. 2009; 46(2):419-31.

260. Allen AJ, Griss ME, Folley BS, Hawkins KA, **Pearlson GD**. Endophenotypes in schizophrenia: a selective review. Schizophr Res. 2009; 109(1-3):24-37.

261. Sui J, Adali T, **Pearlson GD**, Clark VP, Calhoun VD. A method for accurate group difference detection by constraining the mixing coefficients in an ICA framework. Hum Brain Mapp. 2009; 30:2953-70.

262. Xu L, **Pearlson G**, Calhoun VD. Joint source based morphometry identifies linked gray and white matter group differences. Neuroimage. 2009 1; 44(3):777-89.

263. Meda SA, Stevens MC, Folley BS, Calhoun VD, **Pearlson GD**. Evidence for anomalous network connectivity during working memory encoding in schizophrenia: An ICA based analysis. PLoS One. 2009 Nov 19; 4(11).

264. **Pearlson G D**. Calhoun V D, Convergent approaches for defining functional imaging endophenotypes in schizophrenia, Frontiers in Human Neuroscience, 2009; 3:37 1-11.

265. Xu L, Groth KM, **Pearlson GD**, Schretlen DJ, Calhoun VD. Source-based morphometry: the use of independent component analysis to identify gray matter differences with application to schizophrenia. Hum Brain Mapp. 2009; 30(3):711-24.

266. Anderson BM, Rizzo M, Block RI, **Pearlson GD**, O'leary DS. Sex differences in the effects of marijuana on simulated driving performance. J Psychoactive Drugs. 2010 Mar; 42(1):19-30.

267. Otto MWW, Tolin DF, Simon NM, **Pearlson GD**, Basden S, Meunier SA, Hofmann SG, Eisenmenger K, Krystal JH, Pollack MH. Efficacy of D-cycloserine for enhancing response to cognitive-behavior therapy for panic disorder. Biol Psychiatry. 2010 Feb 15; 67(4):365-70.

268. Folley BS, Astur R, Jagannathan K, Calhoun VD, **Pearlson GD**. Anomalous neural circuit function in schizophrenia during a virtual morris water task. Neuroimage. 2010 Feb 15; 49(4):3373-84.

269. Christman AL, Vannorsdall TD, **Pearlson GD**, Hill-Briggs F, Schretlen DJ. Cranial volume, mild cognitive deficits, and functional limitations associated with diabetes in a community sample. Arch Clin Neuropsychol. 2010 Feb; 25(1):49-59.

270. Wakefield DB, Moscufo N, Guttmann CR, Kuchel GA, Kaplan RF, **Pearlson G**, Wolfson L. White matter hyperintensities predict functional decline in voiding, mobility, and cognition in older adults. J Am Geriatr Soc. 2010 Feb; 58(2):275-81.

271. Michael AM, Baum SA, White T, Demirci O, Andreasen NC, Segall JM, Jung REE, **Pearlson G**, Clark VP, L, Schulz SC, L, O, Ho BC, Bockholt HJ, Calhoun VD. Does function follow form? Methods to fuse structural and functional brain images show decreased linkage in schizophrenia. Neuroimage. 2010 Feb 1; 49(3):2626-37.

272. Rimol LM, et al; Alzheimer's Disease Neuroimaging Initiative. Sex-dependent association of common variants of microcephaly genes with brain structure. Proc Natl Acad Sci U S A. 2010 Jan 5;107(1):384-8. ADNI

273. Keihaninejad S, Heckemann RA, Fagiolo G, Symms MR, Hajnal JV, Hammers A; Alzheimer's Disease Neuroimaging Initiative. A robust method to estimate the intracranial volume across MRI field strengths (1.5t And 3t). Neuroimage. 2010 May 1;50(4):1427-37. ADNI

274. Vannorsdall TD, Cascella NG, Rao V, **Pearlson GD**, Gordon B, Schretlen DJ. A morphometric analysis of neuroanatomic abnormalities in traumatic brain injury. J Neuropsychiatry Clin Neurosci. 2010 Spring; 22(2):173-81.

275. Rzepecki-Smith CI, Meda SA, Calhoun VD, Stevens MC, Jafri MJj, Astur RS, **Pearlson GD**. Disruptions in functional network connectivity during alcohol intoxicated driving. Alcohol Clin Exp Res. 2010 Mar 1;34(3):479-87.

276. Ho Aj, Et Al; Alzheimer's Disease Neuroimaging Initiative. A commonly carried allele of the obesity-related Fto gene is associated with reduced brain volume in the healthy elderly. Proc Natl Acad Sci U S A. 2010 May 4;107(18):8404-9. ADNI

277. Meda SA, Jagannathan K, Gelernter J, Calhoun VD, Liu J, Stevens MC, **Pearlson GD**. A pilot multivariate parallel ICA study to investigate differential linkage between neural networks and genetic profiles in schizophrenia. Neuroimage. 2010 Nov 15;53(3):1007-15.

278. Assaf M, Jagannathan K, Calhoun VD, Miller L, Stevens MC, Sahl R, O'boyle JG, Schultz RT, **Pearlson GD**. Abnormal functional connectivity of default mode sub-networks in autism spectrum disorder patients. Neuroimage. 2010 Oct 15;53(1):247-56.

279. Jagannathan K, Calhoun VD, Gelernter J, Stevens MC, Liu J, Bolognani F, Windemuth A, Ruaño G, Assaf M, **Pearlson GD**. Genetic associations of brain structural networks in schizophrenia: A preliminary study. Biol Psychiatry. 2010 Oct 1;68(7):657-66.

280. Calhoun V, Wu L, Kiehl K, Eichele T, **Pearlson GD**. Aberrant processing of deviant stimuli in schizophrenia revealed by fusion of fMRI and EEG data. Acta Neuropsychiatr. 2010 Jun;22(3):127-138.

281. Witt ST, Lovejoy DW, **Pearlson GD**, Stevens MC. Decreased prefrontal cortex activity in mild traumatic brain injury during performance of an auditory oddball task. Brain Imaging Behav. 2010 Dec;4(3-4):232-47.

282. Schretlen DJ, Van Der Hulst EJ, **Pearlson GD**, Gordon B. A neuropsychological study of personality: Trait openness In relation to intelligence, fluency, and executive functioning. J Clin Exp Neuropsychol. 2010 Dec;32(10):1068-73.

283. *Vounou M, Nichols TE, Montana G; Alzheimer's Disease Neuroimaging Initiative. Discovering genetic associations with high-dimensional neuroimaging phenotypes: A sparse reduced-rank regression approach. Neuroimage. 2010 Nov 15;53(3):1147-59. ADNI*

284. Anderson BM, Rizzo M, Block RI, **Pearlson GD**, O'leary DS. Sex, drugs, and cognition: Effects of marijuana. J Psychoactive Drugs. 2010 Dec;42(4):413-24.

285. Folley BS, Astur R, Jagannathan K, Calhoun VD, **Pearlson GD**. Anomalous neural circuit function in schizophrenia during a virtual Morris water task. Neuroimage. 2010; 49 (4) 3373-3384.

286. Cascella NG, Fieldstone SC, Rao VA, **Pearlson GD**, Sawa A, Schretlen DJ. Gray-matter abnormalities in deficit schizophrenia. Schizophr Res. 2010 Jul;120(1-3):63-70.

287. Sakoğlu U, **Pearlson GD**, Kiehl KA, Wang YM, Michael AM, Calhoun VD. A method for evaluating dynamic functional network connectivity and task-modulation: application to schizophrenia. Magn Res Materials in Physics, Biology and Medicine (MAGMA). In Press, 2010.

288. Sui J, Adali T, **Pearlson GD**, Yang H, Sponheim SR, White T, Calhoun VD. A CCA+ICA based model for multi-task brain imaging data fusion and its application to schizophrenia. Neuroimage. 2010;15;51(1):123-34.

289. Skudlarski P, Jagannathan K, Anderson K, Stevens MC, Calhoun VD, Skudlarska BA, **Pearlson GD**. Brain connectivity is not only lower but different in schizophrenia: a combined anatomical and functional approach. Biol Psychiatry. 2010; 68(1):61-9.

290. Lui S, Li T, Deng W, Jiang L, Wu Q, Tang H, Yue Q, Huang X, Chan RC, Collier DA, Meda SA, **Pearlson G**, Mechelli A, Sweeney JA, Gong Q. Short-term effects of antipsychotic treatment on cerebral function in drug-naive first-episode schizophrenia revealed by "resting state" functional magnetic resonance imaging. Arch Gen Psychiatry. 2010;67(8):783-92.

291. Jia Z, Worhunsky PD, Carroll KM, Rounsaville BJ, Stevens MC, **Pearlson GD**, Potenza MN. An initial study of neural responses to monetary incentives as related to treatment outcome in cocaine dependence. Biol Psychiatry. 2011 Sep 15;70(6):553-60.

292. *Chiang GC, Insel PS, Tosun D, Schuff N, Truran-Sacrey D, Raptentsetsang S, Jack Cr Jr, Weiner MW; Alzheimer's Disease Neuroimaging Initiative. Identifying cognitively healthy elderly individuals with subsequent memory decline by using automated MR temporoparietal volumes. Radiology. 2011 Jun; 259(3):844-51. ADNI*

293. Parker BA, Thompson PD, Jordan KC, Grimaldi AS, Assaf M, Jagannathan K, **Pearlson GD**. Effect of exercise training on hippocampal volume in humans: A Pilot Study. Res Q Exerc Sport. 2011 Sep; 82(3):585-91.

294. Andrews MM, Meda SA, Thomas AD, Potenza MN, Krystal JH, Worhunsky P, Stevens MC, O'malley S, Book GA, Reynolds B, **Pearlson GD**. Individuals family history positive for alcoholism show functional magnetic resonance imaging differences in reward sensitivity that are related to impulsivity factors. Biol Psychiatry. 2011 Apr 1; 69(7):675-83.

295. Swanson N, Eichele T, **Pearlson GD**, Kiehl K, Yu Q, Calhoun VD. Lateral differences in the default mode network in healthy controls and patients with schizophrenia. Hum Brain Mapp. 2011 Apr; 32(4):654-64.

296. Castro E, Martínez-Ramón M, **Pearlson GD**, Sui J, Calhoun VD. Characterization of groups using composite kernels and multi-source fMRI analysis data: application to schizophrenia. Neuroimage. 2011 Sep 15; 58(2):526-36.

297. Sui J, **Pearlson GD**, Caprihan A, Adali T, Kiehl KA, Liu J, Yamamoto J, Calhoun VD. Discriminating schizophrenia and bipolar disorder by fusing fMRI and DTI in a multimodal CCA+ joint ICA model. Neuroimage. 2011 Aug 1; 57(3):839-55.

298. Abbott C, Juárez M, White T, Gollub RL, **Pearlson GD**, Bustillo J, Lauriello J, Ho B, Bockholt HJ, Clark VP, Magnotta V, Calhoun VD. Antipsychotic dose and diminished neural modulation: A multi-site fMRI study. Prog Neuropsychopharmacol Biol Psychiatry. 2011 Mar 30; 35(2):473-82.

299. Allen EA, Erhardt E, Damaraju E, Gruner W, Segall J, Silva R, Havlicek M, Rachakonda S, Fries J, Kalyanam R, Michael A, Caprihan A, Turner J, Eichele T, Adelsheim S, Bryan A, Bustillo J, Clark V, Ewing S, Filbey F, Ford C, Hutchison K, Jung R, Kiehl K, Kodituwakku P, Komesu Y, Mayer A, **Pearlson GD**, Phillips J, Sadek J, Stevens MC, Teuscher U, Thomas R, Calhoun V. A baseline for the multivariate comparison of resting-state Networks. Front Syst Neurosci. 2011 Feb 4;5:2.

300. Jamadar S, Powers NR, Meda SA, Gelernter J, Gruen JR, **Pearlson GD**. Genetic influences of cortical gray matter in language-related regions in healthy controls and schizophrenia. Schizophr Res. 2011 Jul;129(2-3):141-8

301. Hawkins KA, Cromer JR, Piotrowski AS, **Pearlson GD**. Mini-Mental State Exam performance of older African Americans: effect of age, gender, education, hypertension, diabetes, and the inclusion of serial 7s subtraction versus "world" backward on score. Arch Clin Neuropsychol. 2011 Nov;26(7):645-52.

302. Hawkins KA, **Pearlson GD**. Age and gender but not common chronic illnesses predict odor identification in older African Americans. Am J Geriatr Psychiatry. 2011 Sep;19(9):777-82.

303. Yu Q, Sui J, Rachakonda S, He H, Gruner W, **Pearlson G**, Kiehl KA, Calhoun VD. Altered topological properties of functional network connectivity in schizophrenia during resting state: a small-world brain network study. PLoS One. 2011;6(9):e25423.

304. Mattila J, Koikkalainen J, Virkki A, van Gils M, Lötjönen J; Alzheimer's Disease Neuroimaging Initiative. Design and application of a generic clinical decision support system for multiscale data. IEEE Trans Biomed Eng. 2012 Jan;59(1):234-40. ADNI

305. Keshavan MS, Morris DW, Sweeney JA, **Pearlson G**, Thaker G, Seidman LJ, Eack SM, Tamminga C. A dimensional approach to the psychosis spectrum between bipolar disorder and schizophrenia: the Schizo-Bipolar Scale. Schizophr Res. 2011 Dec;133(1-3):250-4.

306. Heister D, Brewer JB, Magda S, Blennow K, McEvoy LK; Alzheimer's Disease Neuroimaging Initiative. Predicting MCI outcome with clinically available MRI and CSF biomarkers. Neurology. 2011 Oct 25;77(17):1619-28. ADNI

307. Wolz R, Julkunen V, Koikkalainen J, Niskanen E, Zhang DP, Rueckert D, Soininen H, Lötjönen J; Alzheimer's Disease Neuroimaging Initiative. Multi-method analysis of MRI images in early diagnostics of Alzheimer's disease. PLoS One. 2011; 6(10):e25446. ADNI

308. White WB, Wolfson L, Wakefield DB, Hall CB, Campbell P, Moscufo N, Schmidt J, Kaplan RF, **Pearlson G**, Guttmann CR. Average daily blood pressure, not office blood pressure, is associated with progression of cerebrovascular disease and cognitive decline in older people. Circulation. 2011 Nov 22; 124(21):2312-9.

309. Vidoni ED, Townley RA, Honea RA, Burns JM; Alzheimer's Disease Neuroimaging Initiative. Alzheimer disease biomarkers are associated with body mass index. Neurology. 2011 Nov 22; 77(21):1913-20. ADNI

310. Yu Q, Plis SM, Erhardt EB, Allen EA, Sui J, Kiehl KA, **Pearlson G**, Calhoun VD. Modular organization of functional network connectivity in healthy controls and patients with schizophrenia during the resting state. Front Syst Neurosci. 2011; 5:103.

311. Calhoun VD, Sui J, Kiehl K, Turner J, Allen E, **Pearlson G**. Exploring the psychosis functional connectome: aberrant intrinsic networks in schizophrenia and bipolar disorder. Front Psychiatry. 2011; 2:75.

312. Caprihan A, Abbott C, Yamamoto J, **Pearlson G**, Perrone-Bizzozero N, Sui J, Calhoun VD. Source-based morphometry analysis of group differences in fractional anisotropy in schizophrenia. Brain Connect. 2011; 1(2):133-45.

313. Michael AM, King MD, Ehrlich S, **Pearlson G**, White T, Holt DJ, Andreasen NC, Sakoglu U, Ho BC, Schulz SC, Calhoun VD. A data-driven investigation of gray matter-function correlations in schizophrenia during a working memory task. Front Hum Neurosci. 2011; 5:71.

314. Khullar S, Michael AM, Cahill ND, Kiehl KA, **Pearlson G**, Baum SA, Calhoun VD. ICA-fNORM: spatial normalization of fMRI data using intrinsic group-ICA networks. Front Syst Neurosci. 2011; 5:93.

315. Allen EA, Liu J, Kiehl KA, Gelernter J, **Pearlson GD**, Perrone-Bizzozero NI, Calhoun VD. Components of cross-frequency modulation in health and disease. Front Syst Neurosci. 2011; 5:59.

316. Anderson BM, Stevens MC, Meda SA, Jordan K, Calhoun VD, **Pearlson GD**. Functional imaging of cognitive control during acute alcohol intoxication. Alcohol Clin Exp Res. 2011 Jan; 35(1):156-65.

317. Kim S, Et Al; Alzheimer's Disease Neuroimaging Initiative. Genome-wide association study of CSF biomarkers Abeta1-42, T-Tau, And P-Tau181p in The ADNI Cohort. Neurology. 2011 Jan 4;76(1):69-79. ADNI

318. Lo RY, Hubbard AE, Shaw LM, Trojanowski JG, Petersen RC, Aisen PS, Weiner MW, Jagust WJ; Alzheimer's Disease Neuroimaging Initiative. Longitudinal change of biomarkers in cognitive decline. Arch Neurol. 2011 Oct;68(10):1257-66. ADNI

319. Chu C, Hsu AL, Chou KH, Bandettini P, Lin C; Alzheimer's Disease Neuroimaging Initiative. Does feature selection improve classification accuracy? Impact of sample size and feature selection on classification using anatomical magnetic resonance images. Neuroimage. 2012 Mar;60(1):59-70. ADNI

320. Hamm JP, Ethridge LE, Shapiro JR, Stevens MC, Boutros NN, Summerfelt AT, Keshavan MS, Sweeney JA, **Pearlson G**, Tamminga CA, Thaker G, Clementz BA.I. Spatiotemporal and frequency domain analysis of auditory paired stimuli processing in schizophrenia and bipolar disorder with psychosis. Psychophysiology. 2012 Apr;49(4):522-30.

321. Dickerson BC, Wolk DA; Alzheimer's Disease Neuroimaging Initiative. MRI cortical thickness biomarker predicts AD-like CSF and cognitive decline in normal adults. Neurology. 2012 Jan 10;78(2):84-90. ADNI

322. Meda SA, Narayanan B, Liu J, Perrone-Bizzozero NI, Stevens MC, Calhoun VD, Glahn DC, Shen L, Risacher SL, Saykin AJ, **Pearlson GD**. A large scale multivariate parallel ICA method reveals novel imaging-genetic relationships for Alzheimer's disease in the ADNI cohort. Neuroimage. 2012 Apr 15; 60(3):1608-21.

323. Jamadar S, DeVito EE, Jiantonio RE, Meda SA, Stevens MC, Potenza MN, Krystal JH, **Pearlson GD**. Memantine, an NMDA receptor antagonist, differentially influences Go/No-Go performance and fMRI activity in individuals with and without a family history of alcoholism. Psychopharmacology (Berl). 2012 Jul;222(1):129-40.

324. Balodis IM, Kober H, Worhunsky PD, Stevens MC, **Pearlson GD**, Potenza MN. Diminished frontostriatal activity during processing of monetary rewards and losses in pathological gambling. Biol Psychiatry. 2012 Apr 15;71(8):749-57.

325. Fischer BA, Keller WR, Arango C, **Pearlson GD**, McMahon RP, Meyer WA, Francis A, Kirkpatrick B, Carpenter WT, Buchanan RW. Cortical structural abnormalities in deficit versus nondeficit schizophrenia. Schizophr Res. 2012 Apr;136(1-3):51-4.

326. Bakken TE, et al. Association of common genetic variants in GPCPD1 with scaling of visual cortical surface area in humans. Proc Natl Acad Sci U S A. 2012 Mar 6;109(10):3985-90. ADNI

327. Koikkalainen J, Pölönen H, Mattila J, van Gils M, Soininen H, Lötjönen J; Alzheimer's Disease Neuroimaging Initiative. Improved classification of Alzheimer's disease data via removal of nuisance variability. PLoS One. 2012;7(2):e31112. ADNI

328. Sui J, Yu Q, He H, **Pearlson GD**, Calhoun VD. A selective review of multimodal fusion methods in schizophrenia. Front Hum Neurosci. 2012;6:27.

329. Sung K, Gordon B, Vannorsdall TD, Ledoux K, Pickett EJ, **Pearlson GD**, Schretlen DJ. Semantic clustering of category fluency in schizophrenia examined with singular value decomposition. J Int Neuropsychol Soc. 2012 May;18(3):565-75.

330. Meda SA, Gill A, Stevens MC, Lorenzoni RP, Glahn DC, Calhoun VD, Sweeney JA, Tamminga CA, Keshavan MS, Thaker G, **Pearlson GD**. Differences in resting-state functional magnetic resonance imaging functional network connectivity between schizophrenia and psychotic bipolar probands and their unaffected first-degree relatives. Biol Psychiatry. 2012 May 15;71(10):881-9.

331. Chen J, Calhoun VD, **Pearlson GD**, Ehrlich S, Turner JA, Ho BC, Wassink TH, Michael AM, Liu J. Multifaceted genomic risk for brain function in schizophrenia. Neuroimage. 2012 Jul 16;61(4):866-75.

332. Luo L, Xu L, Jung R, **Pearlson G**, Adali T, Calhoun VD. Constrained source-based morphometry identifies structural networks associated with default mode network. Brain Connect. 2012;2(1):33-43.

333. Johnstone D, Milward EA, Berretta R, Moscato P; Alzheimer's Disease Neuroimaging Initiative. Multivariate protein signatures of pre-clinical Alzheimer's disease in the Alzheimer's disease neuroimaging initiative (ADNI) plasma proteome dataset. PLoS One. 2012;7(4):e34341. ADNI

334. Lo RY, Jagust WJ; Alzheimer's Disease Neuroimaging Initiative. Predicting missing biomarker data in a longitudinal study of Alzheimer disease. Neurology. 2012 May 1;78(18):1376-82. ADNI

335. Yuan L, Wang Y, Thompson PM, Narayan VA, Ye J; Alzheimer's Disease Neuroimaging Initiative. Multi-source feature learning for joint analysis of incomplete multiple heterogeneous neuroimaging data. Neuroimage. 2012 Jul 2;61(3):622-32. ADNI

336. Silver M, Montana G; Alzheimer's Disease Neuroimaging Initiative. Fast identification of biological pathways associated with a quantitative trait using group lasso with overlaps. Stat Appl Genet Mol Biol. 2012 Jan 6;11(1):Article 7. ADNI

337. Stein JL, et al; Enhancing Neuro Imaging Genetics through Meta-Analysis Consortium. Identification of common variants associated with human hippocampal and intracranial volumes. Nat Genet. 2012 Apr 15;44(5):552-61. ADNI

338. Desikan RS, McEvoy LK, Thompson WK, Holland D, Brewer JB, Aisen PS, Sperling RA, Dale AM; Alzheimer's Disease Neuroimaging Initiative. Amyloid-β—associated clinical decline occurs only in the presence of elevated P-tau. Arch Neurol. 2012 Jun;69(6):709-13. ADNI

339. Ethridge LE, Hamm JP, Shapiro JR, Summerfelt AT, Keedy SK, Stevens MC, **Pearlson G**, Tamminga CA, Boutros NN, Sweeney JA, Keshavan MS, Thaker G, Clementz BA. Neural

activations during auditory oddball processing discriminating schizophrenia and psychotic bipolar disorder. Biol Psychiatry. 2012 Nov 1;72(9):766-74.

340. Kerestes R, Bhagwagar Z, Nathan PJ, Meda SA, Ladouceur CD, Maloney K, Matuskey D, Ruf B, Saricicek A, Wang F, **Pearlson GD**, Phillips ML, Blumberg HP. Prefrontal cortical response to emotional faces in individuals with major depressive disorder in remission. Psychiatry Res. 2012 Apr 30;202(1):30-7.

341. Hyatt CJ, Assaf M, Muska CE, Rosen RI, Thomas AD, Johnson MR, Hylton JL, Andrews MM, Reynolds BA, Krystal JH, Potenza MN, **Pearlson GD**. Reward-related dorsal striatal activity differences between former and current cocaine dependent individuals during an interactive competitive game. PLoS One. 2012;7(5):e34917.

342. Jamadar S, Powers NR, Meda SA, Calhoun VD, Gelernter J, Gruen JR, **Pearlson GD**. Genetic influences of resting state fMRI activity in language-related brain regions in healthy controls and schizophrenia patients: a pilot study. Brain Imaging Behav. 2013 March:7(1):15-27.

343. Wang H, Nie F, Huang H, Risacher SL, Saykin AJ, Shen L; Alzheimer's Disease Neuroimaging Initiative. Identifying disease sensitive and quantitative trait-relevant biomarkers from multidimensional heterogeneous imaging genetics data via sparse multimodal multitask learning. Bioinformatics. 2012 Jun 15;28(12):i127-36. ADNI

344. Damoiseaux JS, Seeley WW, Zhou J, Shirer WR, Coppola G, Karydas A, Rosen HJ, Miller BL, Kramer JH, Greicius MD; Alzheimer's Disease Neuroimaging Initiative. Gender modulates the APOE ε4 effect in healthy older adults: convergent evidence from functional brain connectivity and spinal fluid tau levels. J Neurosci. 2012 Jun 13;32(24):8254-62. ADNI

345. Arbabshirani MR, Havlicek M, Kiehl KA, **Pearlson GD**, Calhoun VD. Functional network connectivity during rest and task conditions: A comparative study. Hum Brain Mapp. 2012 Jun 26. In press

346. Worhunsky PD, Stevens MC, Carroll KM, Rounsaville BJ, Calhoun VD, **Pearlson GD**, Potenza MN. Functional brain networks associated with cognitive control, cocaine dependence, and treatment outcome. Psychol Addict Behav. 2013 Jun;27(2):477-88.

347. Balodis IM, Kober H, Worhunsky PD, Stevens MC, **Pearlson GD**, Potenza MN. Attending to Striatal Ups and Downs in Addictions. Biol Psychiatry. 2012 Jul 11. In press

348. Tolin DF, Stevens MC, Villavicencio AL, Norberg MM, Calhoun VD, Frost RO, Steketee G, Rauch SL, **Pearlson GD**. Neural mechanisms of decision making in hoarding disorder. Arch Gen Psychiatry. 2012 Aug;69(8):832-41.

349. Holland D, Desikan RS, Dale AM, McEvoy LK; Alzheimer's Disease Neuroimaging Initiative. Rates of decline in Alzheimer disease decrease with age. PLoS One. 2012;7(8):e42325. ADNI

350. Patel KT, Stevens MC, **Pearlson GD**, Winkler AM, Hawkins KA, Skudlarski P, Bauer LO. Default mode network activity and white matter integrity in healthy middle-aged ApoE4 carriers. Brain Imaging Behav. 2012 Jul 25. In press

351. Jamadar S, O'Neil KM, **Pearlson GD**, Ansari M, Gill A, Jagannathan K, Assaf M. Impairment in semantic retrieval is associated with symptoms in schizophrenia but not bipolar disorder. Biol Psychiatry. 2012 Sep 15. In press

352. Anticevic A, Brumbaugh MS, Winkler AM, Lombardo LE, Barrett J, Corlett PR, Kober H, Gruber J, Repovs G, Cole MW, Krystal JH, **Pearlson GD**, Glahn DC. Global prefrontal and fronto-amygdala dysconnectivity in bipolar I disorder with psychosis history. Biol Psychiatry. 2013 March;73(6):565-73.

353. Jamadar S, Assaf M, Jagannathan K, Anderson K, **Pearlson GD**. Figural memory performance and functional magnetic resonance imaging activity across the adult lifespan. Neurobiol Aging. 2012 Aug 15. In press

354. *Ewers M, Schmitz S, Hansson O, Walsh C, Fitzpatrick A, Bennett D, Minthon L, Trojanowski JG, Shaw LM, Faluyi YO, Vellas B, Dubois B, Blennow K, Buerger K, Teipel SJ, Weiner M, Hampel H; Alzheimer's Disease Neuroimaging Initiative. Body Mass Index Is Associated With Biological Csf Markers Of Core Brain Pathology Of Alzheimer's Disease. Neurobiol Aging. 2012 Aug;33(8):1599-608. ADNI*

355. Xu J, Kober H, Carroll KM, Rounsaville BJ, **Pearlson GD**, Potenza MN. White matter integrity and behavioral activation in healthy subjects. Hum Brain Mapp. 2012 Apr;33(4):994-1002.

356. Moscufo N, Wolfson L, Meier D, Liguori M, Hildenbrand PG, Wakefield D, Schmidt JA, **Pearlson GD**, Guttmann CR. Mobility decline in the elderly relates to lesion accrual in the splenium of the corpus callosum. Age (Dordr). 2012 Apr;34(2):405-14.

357. Du W, Calhoun VD, Li H, MA S, Eichele T, Kiehl KA, **Pearlson GD**, Adali T. High classification accuracy for schizophrenia with rest and task fMRI Data. Front Hum Neurosci. 2012;6:145.

358. *Bonner-Jackson A, Okonkwo O, Tremont G; Alzheimers Disease Neuroimaging Initiative. Apolipoprotein E ε2 and functional decline in amnestic mild cognitive impairment and Alzheimer disease. Am J Geriatr Psychiatry. 2012 Jul;20(7):584-93. ADNI*

359. Urban NB, Slifstein M, Meda S, Xu X, Ayoub R, Medina O, **Pearlson GD**, Krystal JH, Abi-Dargham A. Imaging human reward processing with positron emission tomography and functional magnetic resonance imaging. Psychopharmacology (Berl). 2012 May;221(1):67-77.

360. *Gee DG, Karlsgodt KH, van Erp TG, Bearden CE, Lieberman MD, Belger A, Perkins DO, Olvet DM, Cornblatt BA, Constable T, Woods SW, Addington J, Cadenhead KS, McGlashan TH, Seidman LJ, Tsuang MT, Walker EF, Cannon TD; NAPLS Consortium. Altered age-related trajectories of amygdala-prefrontal circuitry in adolescents at clinical high risk for psychosis: a preliminary study. Schizophr Res. 2012 Jan;134(1):1-9. NAPLS*

361. Calhoun VD, **Pearlson GD**. A selective review of simulated driving studies: Combining naturalistic and hybrid paradigms, analysis approaches, and future directions. Neuroimage. 2012 Jan 2;59(1):25-35.

362. Kerestes R, Ladouceur CD, Meda S, Nathan PJ, Blumberg HP, Maloney K, Ruf B, Saricicek A, **Pearlson GD**, Bhagwagar Z, Phillips ML. Abnormal prefrontal activity subserving attentional control of emotion in remitted depressed patients during a working memory task with emotional distracters. Psychol Med. 2012 Jan;42(1):29-40.

363. *Rasmussen JM, Lakatos A, van Erp TG, Kruggel F, Keator DB, Fallon JT, Macciardi F, Potkin SG; Alzheimer's Disease Neuroimaging Initiative. Empirical derivation of the reference region for computing diagnostic sensitive ^{1}fluorodeoxyglucose ratios in Alzheimer's disease based on the ADNI sample. Biochim Biophys Acta. 2012 Mar;1822(3):457-66. ADNI*

364. Xu L, Adali T, Schretlen D, **Pearlson G**, Calhoun VD. Structural angle and power images reveal interrelated gray and white matter abnormalities in schizophrenia. Neurol Res Int. 2012;2012:735249.

365. Ginley MK, Whelan JP, Meyers AW, Relyea GE, **GD Pearlson**. Exploring a multidimensional approach to impulsivity in predicting college student gambling. Journal of Gambling Studies. March 2013. In press

366. Jamadar SD, **Pearlson GD**, O'Neil KM, Assaf M. Semantic association fMRI impairments represent a potential schizophrenia biomarker. Schizophr Res. 2013 Apr;145(1-3):20-6.

367. Sui J, He H, Liu J, Yu Q, Adali T, **Pearlson GD**, Calhoun VD. Three-way FMRI-DTI-methylation data fusion based on mCCA+jICA and its application to schizophrenia. Conf Proc IEEE Eng Med Biol Soc. 2012 Aug;2012:2692-5.

368. Yu Q, Allen EA, Sui J, Arbabshirani MR, **Pearlson GD**, Calhoun VD. Brain connectivity networks in schizophrenia underlying resting state functional magnetic resonance imaging. Curr Top Med Chem. 2012 Nov 1;12(21):2415-25.

369. Cope LM, Shane MS, Segall JM, Nyalakanti PK, Stevens MC, **Pearlson GD**, Calhoun VD, Kiehl KA.Examining the effect of psychopathic traits on gray matter volume in a community substance abuse sample. Psychiatry Res. 2012 Nov 30;204(2-3)

370. Tighe SK, Reading SA, Rivkin P, Caffo B, Schweizer B, **Pearlson GD,** Potash JB, Depaulo JR, Bassett SS. Total white matter hyperintensity volume in bipolar disorder patients and their healthy relatives. Bipolar Disord. 2012 Dec;14(8):888-93.

371. Sui J, He H, **Pearlson GD**, Adali T, Kiehl KA, Yu Q, Clark VP, Castro E, White T, Mueller BA, Ho BC, Andreasen NC, Calhoun VD. Three-way (N-way) fusion of brain imaging data based on mCCA+jICA and its application to discriminating schizophrenia. Neuroimage. 2012 Oct 26;66C:119-132.

372. Woods SW, Walsh BC, Hawkins KA, Miller TJ, Saksa JR, D'Souza DC, **Pearlson GD**, Javitt DC, McGlashan TH, Krystal JH. Glycine treatment of the risk syndrome for psychosis: Report of two pilot studies. Eur Neuropsychopharmacology. 2013 Aug;23(8):931-40.

373. Balodis IM, Kober H, Worhunsky PD, White MA, Stevens MC, **Pearlson GD**, Sinha R, Grilo CM, Potenza MN. Monetary reward processing in obese individuals with and without binge eating disorder. Biological Psychiatry. 2013 May 1;73(9):877-86.

374. Narayanan B, Stevens MC, Jiantonio RE, Krystal JH, **Pearlson GD**. Effects of memantine on event-related potential, oscillations, and complexity in individuals with and without family histories of alcoholism. J Stud Alcohol Drugs. 2013 Mar;74(2):245-57.

375. Yu Q, Sui J, Liu J, Plis SM, Kiehl KA, **Pearlson GD**, Calhoun VD. Disrupted correlation between low frequency power and connectivity strength of resting state brain networks in schizophrenia. Schizophr Res. 2013 Jan;143(1):165-71.

376. Dager AD, Anderson BM, Stevens MC, Pulido C, Rosen R, Jiantonio-Kelly RE, Sisante JF, Raskin SA, Tennen H, Austad CS, Wood RM, Fallahi CR, **Pearlson GD**. Influence of alcohol use and family history of alcoholism on neural response to alcohol cues in college drinkers. Alcohol Clin Exp Res. 2013 Jan;37 Suppl 1:E161-71.

377. Patel KT, Stevens MC, **Pearlson GD**, Winkler AM, Hawkins KA, Skudlarski P, Bauer LO. Default mode network activity and white matter integrity in healthy middle-aged ApoE4 carriers. Brain Imaging Behav. 2013 Mar;7(1):60-7.

378. Jamadar S, O'Neil KM, **Pearlson GD**, Ansari M, Gill A, Jagannathan K, Assaf M. Impairment in semantic retrieval is associated with symptoms in schizophrenia but not bipolar disorder. Biol Psychiatry. 2013 Mar 15;73(6):555-64.

379. Anticevic A, Brumbaugh MS, Winkler AM, Lombardo LE, Barrett J, Corlett PR, Kober H, Gruber J, Repovs G, Cole MW, Krystal JH, **Pearlson GD**, Glahn DC. Global prefrontal and fronto-amygdala dysconnectivity in bipolar I disorder with psychosis history. Biol Psychiatry. 2013 Mar 15;73(6):565-73.

380. Jamadar S, Assaf M, Jagannathan K, Anderson K, **Pearlson GD**. Figural memory performance and functional magnetic resonance imaging activity across the adult lifespan. Neurobiol Aging. 2013 Jan;34(1):110-27.

381. Han SD, Gruhl J, Beckett L, Dodge HH, Stricker NH, Farias S, Mungas D; Alzheimer's Disease Neuroimaging Initiative. Beta amyloid, tau, neuroimaging, and cognition: sequence modeling of biomarkers for Alzheimer's Disease. Brain Imaging Behav. 2012 Dec;6(4):610-20. ADNI

382. *Gibbons LE, Carle AC, Mackin RS, Harvey D, Mukherjee S, Insel P, Curtis SM, Mungas D, Crane PK; Alzheimer's Disease Neuroimaging Initiative. A composite score for executive functioning, validated in Alzheimer's Disease Neuroimaging Initiative (ADNI) participants with baseline mild cognitive impairment. Brain Imaging Behav. 2012 Dec;6(4):517-27. ADNI*

383. *Stricker NH, Dodge HH, Dowling NM, Han SD, Erosheva EA, Jagust WJ; Alzheimer's Disease Neuroimaging Initiative. CSF biomarker associations with change in hippocampal volume and precuneus thickness: implications for the Alzheimer's pathological cascade. Brain Imaging Behav. 2012 Dec;6(4):599-609. ADNI*

384. *Skinner J, Carvalho JO, Potter GG, Thames A, Zelinski E, Crane PK, Gibbons LE; Alzheimer's Disease Neuroimaging Initiative. The Alzheimer's Disease Assessment Scale-Cognitive-Plus (ADAS-Cog-Plus): an expansion of the ADAS-Cog to improve responsiveness in MCI. Brain Imaging Behav. 2012 Dec;6(4):489-501. ADNI*

385. *Holland D, Desikan RS, Dale AM, McEvoy LK; Alzheimer's Disease Neuroimaging Initiative. Rates of decline in Alzheimer disease decrease with age. PLoS One. 2012;7(8) ADNI*

386. *Ramanan VK, Kim S, Holohan K, Shen L, Nho K, Risacher SL, Foroud TM, Mukherjee S, Crane PK, Aisen PS, Petersen RC, Weiner MW, Saykin AJ; Alzheimer's Disease Neuroimaging Initiative (ADNI). Genome-wide pathway analysis of memory impairment in the Alzheimer's Disease Neuroimaging Initiative (ADNI) cohort implicates gene candidates, canonical pathways, and networks. Brain Imaging Behav. 2012 Dec;6(4):634-48. ADNI*

387. *Doecke JD, Laws SM, Faux NG, Wilson W, Burnham SC, Lam CP, Mondal A, Bedo J, Bush AI, Brown B, De Ruyck K, Ellis KA, Fowler C, Gupta VB, Head R, Macaulay SL, Pertile K, Rowe CC, Rembach A, Rodrigues M, Rumble R, Szoeke C, Taddei K, Taddei T, Trounson B, Ames D, Masters CL, Martins RN; Alzheimer's Disease Neuroimaging Initiative; Australian Imaging Biomarker and Lifestyle Research Group. Blood-based protein biomarkers for diagnosis of Alzheimer disease. Arch Neurol. 2012 Oct;69(10):1318-25. ADNI*

388. *Soares HD, Potter WZ, Pickering E, Kuhn M, Immermann FW, Shera DM, Ferm M, Dean RA, Simon AJ, Swenson F, Siuciak JA, Kaplow J, Thambisetty M, Zagouras P, Koroshetz WJ, Wan HI, Trojanowski JQ, Shaw LM; Biomarkers Consortium Alzheimer's Disease Plasma Proteomics Project. Plasma biomarkers associated with the apolipoprotein E genotype and Alzheimer disease. Arch Neurol. 2012 Oct;69(10):1310-7. ADNI*

389. *Crane PK, Carle A, Gibbons LE, Insel P, Mackin RS, Gross A, Jones RN, Mukherjee S, Curtis SM, Harvey D, Weiner M, Mungas D; Alzheimer's Disease Neuroimaging Initiative. Development and assessment of a composite score for memory in the Alzheimer's Disease Neuroimaging Initiative (ADNI). Brain Imaging Behav. 2012 Dec;6(4):502-16. ADNI*

390. *Park LQ, Gross AL, McLaren DG, Pa J, Johnson JK, Mitchell M, Manly JJ; Alzheimer's Disease Neuroimaging Initiative. Confirmatory factor analysis of the ADNI Neuropsychological Battery. Brain Imaging Behav. 2012 Dec;6(4):528-39. ADNI*

391. *Domoto-Reilly K, Sapolsky D, Brickhouse M, Dickerson BC; Alzheimer's Disease Neuroimaging Initiative. Naming impairment in Alzheimer's disease is associated with left anterior temporal lobe atrophy. Neuroimage. 2012 Oct 15;63(1):348-55. ADNI*

392. *Gross AL, Manly JJ, Pa J, Johnson JK, Park LQ, Mitchell MB, Melrose RJ, Inouye SK, McLaren DG; Alzheimer's Disease Neuroimaging Initiative. Cortical signatures of cognition and their relationship to Alzheimer's disease. Brain Imaging Behav. 2012 Dec;6(4):584-98. ADNI*

393. *Mukherjee S, Kim S, Gibbons LE, Nho K, Risacher SL, Glymour MM, Habeck C, Lee GJ, Mormino E, Ertekin-Taner N, Montine TJ, Decarli C, Saykin AJ, Crane PK; Alzheimer's Disease Neuroimaging Initiative. Genetic architecture of resilience of executive functioning. Brain Imaging Behav. 2012 Dec;6(4):621-33. ADNI*

394. *Reitz C, Tosto G, Mayeux R, Luchsinger JA; NIA-LOAD/NCRAD Family Study Group; Genetic variants in the Fat and Obesity Associated (FTO) gene and risk of Alzheimer's disease. Alzheimer's Disease Neuroimaging Initiative. PLoS One. 2012;7(12) ADNI*

395. *Swaminathan S, Huentelman MJ, Corneveaux JJ, Myers AJ, Faber KM, Foroud T, Mayeux R, Shen L, Kim S, Turk M, Hardy J, Reiman EM, Saykin AJ; Alzheimer's Disease Neuroimaging Initiative and NIA-LOAD/NCRAD Family Study Group. Analysis of copy number variation in Alzheimer's disease in a cohort of clinically characterized and neuropathologically verified individuals. PLoS One. 2012;7(12) ADNI*

396. *Habeck C, Risacher S, Lee GJ, Glymour MM, Mormino E, Mukherjee S, Kim S, Nho K, DeCarli C, Saykin AJ, Crane PK; Alzheimer's Disease Neuroimaging Initiative. Relationship between baseline brain metabolism measured using PET and memory and executive function in prodromal and early Alzheimer's disease. Brain Imaging Behav. 2012 Dec;6(4):568-83. ADNI*

397. *Mukherjee S, Trittschuh E, Gibbons LE, Mackin RS, Saykin A, Crane PK; Azheimer's Disease Neuroimaging Initiative.Dysexecutive and amnesic AD subtypes defined by single indicator and modern psychometric approaches: relationships with SNPs in ADNI. Brain Imaging Behav. 2012 Dec;6(4):649-60. ADNI*

398. *Casanova R, Hsu FC, Espeland MA; Alzheimer's Disease Neuroimaging Initiative. Classification of structural MRI images in Alzheimer's disease from the perspective of ill-posed problems. PLoS One. 2012;7(10). ADNI*

399. *Nho K, Risacher SL, Crane PK, DeCarli C, Glymour MM, Habeck C, Kim S, Lee GJ, Mormino E, Mukherjee S, Shen L, West JD, Saykin AJ; Alzheimer's Disease Neuroimaging Initiative--ADNI. Voxel and surface-based topography of memory and executive deficits in mild cognitive impairment and Alzheimer's disease. Brain Imaging Behav. 2012 Dec;6(4):551-67. ADNI*

400. *Kiddle SJ, Thambisetty M, Simmons A, Riddoch-Contreras J, Hye A, Westman E, Pike I, Ward M, Johnston C, Lupton MK, Lunnon K, Soininen H, Kloszewska I, Tsolaki M, Vellas B, Mecocci P, Lovestone S, Newhouse S, Dobson R; Alzheimers Disease Neuroimaging Initiative. Plasma based markers of [11C] PiB-PET brain amyloid burden. PLoS One. 2012;7(9) ADNI*

401. *Lo RY, Jagust WJ; Alzheimer's Disease Neuroimaging Initiative. Vascular burden and Alzheimer disease pathologic progression. Neurology. 2012 Sep 25;79(13):1349-55. ADNI*

402. *Augustinack JC, Huber KE, Stevens AA, Roy M, Frosch MP, van der Kouwe AJ, Wald LL, Van Leemput K, McKee AC, Fischl B; Alzheimer's Disease Neuroimaging Initiative. Predicting the location of human perirhinal cortex, Brodmann's area 35, from MRI. Neuroimage. 2013 Jan 1;64:32-42. ADNI*

403. Jamadar S, Powers NR, Meda SA, Calhoun VD, Gelernter J, Gruen JR, **Pearlson GD**. Genetic influences of resting state fMRI activity in language-related brain regions in healthy controls and schizophrenia patients: a pilot study. Brain Imaging Behav. 2013 Mar;7(1):15-27.

404. *Gray KR, Aljabar P, Heckemann RA, Hammers A, Rueckert D; Alzheimer's Disease Neuroimaging Initiative. Random forest-based similarity measures for multi-modal classification of Alzheimer's disease. Neuroimage. 2013 Jan 15. ADNI*

405. *Eskildsen SF, Coupé P, García-Lorenzo D, Fonov V, Pruessner JC, Collins DL; Alzheimer's Disease Neuroimaging Initiative. Prediction of Alzheimer's disease in subjects with mild cognitive impairment from the ADNI cohort using patterns of cortical thinning. Neuroimage. 2013 Jan 15;65:511-21. ADNI*

406. *Rajagopalan P, Toga AW, Jack CR, Weiner MW, Thompson PM; Alzheimer's Disease Neuroimaging Initiative. Fat-mass-related hormone, plasma leptin, predicts brain volumes in the elderly. Neuroreport. 2013 Jan 23;24(2):58-62. ADNI*

407. Ross DE, Ochs AL, Seabaugh JM, Shrader CR; Alzheimer's Disease Neuroimaging Initiative. Man versus machine: comparison of radiologists' interpretations and NeuroQuant volumetric analyses of brain MRIs in patients with traumatic brain injury. J Neuropsychiatry Clin Neurosci. 2013 Winter;25(1):32-9. ADNI

408. Keshavan MS, Clementz BA, **Pearlson GD**, Sweeney JA, Tamminga CA. Reimagining psychoses: An agnostic approach to diagnosis. Schizophr Res. 2013 May;146(1-3):10-6.

409. Devito EE, Meda SA, Jiantonio R, Potenza MN, Krystal JH, **Pearlson GD**. Neural correlates of impulsivity in healthy males and females with family histories of alcoholism. Neuropsychopharmacology. 2013 Sep;38(10):1854-63.

410. Xu J, Zhang S, Calhoun VD, Monterosso J, Li CS, Worhunsky PD, Stevens M, **Pearlson GD**, Potenza MN. Task-related concurrent but opposite modulations of overlapping functional networks as revealed by spatial ICA. Neuroimage. 2013 Apr 21. S1053-8119(13)00385-6.

411. Schretlen DJ, Peña J, Aretouli E, Orue I, Cascella NG, **Pearlson GD**, Ojeda N. Confirmatory factor analysis reveals a latent cognitive structure common to bipolar disorder, schizophrenia, and normal controls. Bipolar Disord. 2013 May 9. In press

412. Skudlarski P, Schretlen D, Thaker G, Stevens MC, Keshavan M, Sweeney J, Tamminga C, Clementz B, O'Neil K, **Pearlson GD**. Diffusion tensor imaging white matter endophenotypes in patients with schizophrenia or psychotic bipolar disorder and their relatives. American Journal of Psychiatry. In press

413. Ahmadi A, **Pearlson GD**, Meda S, Dager A, Potenza M, Rosen R, Austad CS, Raskin SA, Fallahi CR, Tennen H, Wood RM, Stevens MC. Influence of alcohol use on neural response to Go/No-Go task in college drinkers. Neuropsychopharmacology. 2013 Oct;38(11):2197-208.

414. Tamminga C, Ivleva E, Keshavan MS, **Pearlson GD**, Clementz BA, Witte B, Morris D, Bishop J, Elliott A, Thaker G, Sweeney J. Clinical phenotypes of psychosis in the bipolar and schizophrenia network on intermediate phenotypes (B-SNIP). American Journal of Psychiatry. In press

415. Khadka S, Meda S, Stevens MC, Glahn D, Calhoun V, Sweeney J, Tamminga C, Keshavan M, **Pearlson GD**. Is aberrant functional connectome as psychosis endophenotype? A resting state functional Magnetic Resonance Imaging study. Biological Psychiatry. 2013 Sep 15;74(6):458-66.

416. Patel K, Stevens MC, Meda SA, Muska C, Thomas AD, Potenza MN, **Pearlson GD**. Robust changes in reward circuitry during reward loss in current and former cocaine users during performance of a monetary incentive delay task. Biological Psychiatry. In press

417. Jahanshad N, Rajagopalan P, Hua X, Hibar DP, Nir TM, Toga AW, Jack CR Jr, Saykin AJ, Green RC, Weiner MW, Medland SE, Montgomery GW, Hansell NK, McMahon KL, de Zubicaray GI, Martin NG, Wright MJ, Thompson PM; the Alzheimer's Disease Neuroimaging Initiative. Genome-wide scan of healthy human connectome discovers SPON1 gene variant influencing dementia severity. Proc Natl Acad Sci U S A. 2013 Mar 19;110(12):4768-73. ADNI

418. Nanda P, Tandon N, Mathew IT, Giakoumatos CI, Abhishekh HA, Clementz BA, **Pearlson GD**, Sweeney J, Tamminga CA, Keshavan MS. Local gyrification index in Probands with psychotic disorders and their first-degree relatives. Biological Psychiatry. 2013 Nov 23. In press

419. He BJ, Nolte G, Nagata K, **Pearlson GD** et al. Abstracts of presentations at the International Conference on Basic and Clinical Multimodal Imaging (BaCI), a joint Conference of the International Society for Neuroimaging in Psychiatry (ISNIP), the International Society for Functional Source Imaging (ISFSI), the International Society for Bioelectromagnetism (ISBEM), the International Society for Brain Electromagnetic Topography (ISBET) and the EEG and Clinical Neuroscience Society (ECNS), in Geneva, Switzerland, September 5-8, 2013. Clinical EEG Neuroscience. 2013 Dec 24. In press

420. Dager AD, Anderson BM, Rosen R, Khadka S, Sawyer B, Jiantonio-Kelly RE, Austad CS, Raskin SA, Tennen H, Wood RM, Fallahi CR, **Pearlson GD**. fMRI Response to alcohol pictures predicts subsequent transition to heavy drinking in college students. Addiction. 2013 Dec 4. In press

421. Assaf M, Hyatt CJ, Wong CG, Johnson MR, Schultz RT, Hendler T, **Pearlson GD**. Mentalizing and motivation neural function during social interactions in autism spectrum disorders. Neuroimage Clinical. 2013 Sep 19;3:321-31.

422. Steele VR, Fink BC, Maurer JM, Arbshirani MR, Wilber CH, Jaffe AJ, Sidz A, **Pearlson GD**, Calhoun VD, Clark VP, Kiehl KA. Brain Potentials measured during a Go/NoGo Task predict completion of substance abuse treatment. Biological Psychiatry. 2013 Oct 11. In press

423. Sprooten E, Brumbaugh MS, Knowles EE, McKay DR, Lewis J, Barrett J, Landau S, Cyr L, Kochunov P, Winkler AM, **Pearlson GD**, Glahn DC. Reduced white matter integrity in sibling pairs discordant for bipolar disorder. American Journal of Psychiatry. 2013 Nov 1;170(11):1317-25.

424. Ivleva EI, Bidesi AS, Keshavan MS, **Pearlson GD**, Meda SA, Dodig D, Moates AF, Lu H, Francis AN, Tandon N, Schretlen DJ, Sweeney JA, Clementz BA, Tamminga CA. Gray matter volume as an intermediate phenotype for psychosis: Bipolar-Schizophrenia Network on Intermediate Phenotypes (B-SNIP). American Journal of Psychiatry. 2013 Nov 1;170(11):1285-96.

425. Cavallari M, Moscufo N, Skudlarski P, Meier D, Panzer VP, **Pearlson GD**, White WB, Wolfson L, Guttmann CR. Mobility impairment is associated with reduced microstructural integrity of the inferior and superior cerebellar peduncles in elderly with no clinical signs of cerebellar dysfunction. Neuroimage Clinical. 2013 Mar 1;2:332-40.

426. Yu Q, Sui J, Kiehl KA, **Pearlson G**, Calhoun VD. State-related functional integration and functional segregation brain networks in schizophrenia. Schizophrenia Research. 2013 Nov;150(2-3):450-8.

427. Reilly JL, Frankovich K, Hill S, Gershon ES, Keefe RS, Keshavan MS, **Pearlson GD**, Tamminga CA, Sweeney JA. Elevated antisaccade error rate as an intermediate phenotype for psychosis across diagnostic categories. Schizophrenia Bulletin. 2013 Sep 30. In press

428. Teeters JB, Ginley MK, Whelan JP, Meyers AW, **Pearlson GD**. The moderating effect of gender on the relation between expectancies and gambling frequency among college students. Journal of Gambling Studies. 2013 Sep 25. In press

429. Holt LJ, Armeli S, Tennen H, Austad CS, Raskin SA, Fallahi CR, Wood R, Rosen RI, Ginley MK, **Pearlson GD**. A person-centered approach to understanding negative reinforcement drinking among first year college students. Addictive Behaviors. 2013 Dec;38(12):2937-44.

430. Fryer SL, Woods SW, Kiehl KA, Calhoun VD, **Pearlson GD**, Roach BJ, Ford JM, Srihari VH, McGlashan TH, Mathalon DH Deficient Suppression of Default Mode Regions during Working Memory in Individuals with Early Psychosis and at Clinical High-Risk for Psychosis. Frontiers in Psychiatry. 2013 Sep 10;4:92.

431. Bryant C, Giovanello KS, Ibrahim JG, Chang J, Shen D, Peterson BS, Zhu H; Alzheimer's Disease Neuroimaging Initiative. Mapping the genetic variation of regional brain volumes as explained by all common SNPs from the ADNI study. PLoS One. 2013 Aug 28;8(8). ADNI

432. Rosenfeld ES, **Pearlson GD**, Sweeney JA, Tamminga CA, Keshavan MS, Nonterah C, Stevens MC. Prolonged hemodynamic response during incidental facial emotion processing in inter-episode bipolar I disorder. Brain Imaging Behaviors. 2013. In press

433. Arbabshirani MR, Kiehl KA, **Pearlson GD**, Calhoun VD. Classification of schizophrenia patients based on resting-state functional network connectivity. Frontiers in Neuroscience. 2013 Jul 30;7:133.

434. Castelluccio BC, Meda SA, Muska CE, Stevens MC, **Pearlson GD**. Error processing in current and former cocaine users. Brain Imaging Behavior. 2013 In press

435. Dager AD, Jamadar S, Stevens MC, Rosen R, Jiantonio-Kelly RE, Sisante JF, Raskin SA, Tennen H, Austad CS, Wood RM, Fallahi CR, **Pearlson GD**. fMRI response during figural memory task performance in college drinkers. Psychopharmacology (Berl). 2013 Aug 15. In press

436. Hamm JP, Ethridge LE, Shapiro JR, **Pearlson GD**, Tamminga CA, Sweeney JA, Keshavan MS, Thaker GK, Clementz BA. Family history of psychosis moderates early auditory cortical response abnormalities in non-psychotic bipolar disorder. Bipolar Disorders. 2013 Aug 14. In press

437. Ginley MK, Whelan JP, Relyea GE, Simmons JL, Meyers AW, **Pearlson GD**. College Student Beliefs About Wagering: An Evaluation of the Adolescent Gambling Expectancies Survey. Journal of Gambling Studies. 2013 Aug 11. In press

438. Book GA, Anderson BM, Stevens MC, Glahn DC, Assaf M, **Pearlson GD**. Neuroinformatics Database (NiDB)--a modular, portable database for the storage, analysis, and sharing of neuroimaging data. Neuroinformatics. 2013 Oct;11(4):495-505.

439. Giakoumatos CI, Tandon N, Shah J, Mathew IT, Brady RO, Clementz BA, **Pearlson GD**, Thaker GK, Tamminga CA, Sweeney JA, Keshavan MS. Are structural brain abnormalities associated with suicidal behavior in patients with psychotic disorders? Journal Psychiatry Research. 2013 Oct;47(10):1389-95.

440. Tamminga CA, Ivleva EI, Keshavan MS, **Pearlson GD**, Clementz BA, Witte B, Morris DW, Bishop J, Thaker GK, Sweeney JA. Clinical phenotypes of psychosis in the Bipolar-Schizophrenia Network on Intermediate Phenotypes (B-SNIP). American Journal Psychiatry. 2013 Nov 1;170(11):1263-74.

441. Liu CY, Iglesias JE, Tu Z; Alzheimer's Disease Neuroimaging Initiative. Deformable templates guided discriminative models for robust 3D brain MRI segmentation. Neuroinformatics. 2013 Oct;11(4):447-68. ADNI

442. Anticevic A, Cole MW, Repovs G, Murray JD, Brumbaugh MS, Winkler AM, Savic A, Krystal JH, **Pearlson GD**, Glahn DC. Characterizing thalamo-cortical disturbances in schizophrenia and bipolar Illness. Cerebral Cortex. 2013 Jul 3. In press

443. Unschuld PG, Buchholz AS, Varvaris M, van Zijl PC, Ross CA, Pekar JJ, Hock C, Sweeney JA, Tamminga CA, Keshavan MS, **Pearlson GD**, Thaker GK, Schretlen DJ. Prefrontal brain network connectivity indicates degree of both schizophrenia risk and cognitive dysfunction. Schizophria Bulletin. 2013 Jun 18. In press

444. Patel KT, Stevens MC, Meda SA, Muska C, Thomas AD, Potenza MN, **Pearlson GD**. Robust changes in reward circuitry during reward loss in current and former cocaine users during performance of a monetary incentive delay task. Biological Psychiatry. 2013 Oct 1;74(7):529-37.

445. Iglesias JE, Sabuncu MR, Van Leemput K; Alzheimer's Disease Neuroimaging Initiative. Improved inference in Bayesian segmentation using Monte Carlo sampling: application to hippocampal subfield volumetry. Medical Image Analysis. 2013 Oct;17(7):766-78. ADNI

446. Skudlarski P, Schretlen DJ, Thaker GK, Stevens MC, Keshavan MS, Sweeney JA, Tamminga CA, Clementz BA, O'Neil K, **Pearlson GD**. Diffusion tensor imaging white matter endophenotypes in patients with schizophrenia or psychotic bipolar disorder and their relatives. American Journal Psychiatry. 2013 Aug 1;170(8):886-98.

447. Steele VR, Aharoni E, Munro GE, Calhoun VD, Nyalakanti P, Stevens MC, **Pearlson G**, Kiehl KA. A large scale (N=102) functional neuroimaging study of response inhibition in a Go/NoGo task. Behavioral Brain Research. 2013 Nov 1;256:529-36.

448. Hill SK, Reilly JL, Keefe RS, Gold JM, Bishop JR, Gershon ES, Tamminga CA, **Pearlson GD**, Keshavan MS, Sweeney JA. Neuropsychological impairments in schizophrenia and psychotic bipolar disorder: findings from the Bipolar-Schizophrenia Network on Intermediate Phenotypes (B-SNIP) study. American Journal Psychiatry. 2013 Nov 1;170(11):1275-84.

449. Sui J, He H, Yu Q, Chen J, Rogers J, **Pearlson GD**, Mayer A, Bustillo J, Canive J, Calhoun VD. Combination of resting state fMRI, DTI, and sMRI data to discriminate schizophrenia by N-way MCCA+jICA. Frontiers Human Neuroscience. 2013 May 29;7:235.

450. Chen J, Calhoun VD, **Pearlson GD**, Perrone-Bizzozero N, Sui J, Turner JA, Bustillo JR, Ehrlich S, Sponheim SR, Cañive JM, Ho BC, Liu J. Guided exploration of genomic risk for gray matter abnormalities in schizophrenia using parallel independent component analysis with reference. Neuroimage. 2013 Dec;83:384-96.

451. Bradshaw EM, Chibnik LB, Keenan BT, Ottoboni L, Raj T, Tang A, Rosenkrantz LL, Imboywa S, Lee M, Von Korff A; Alzheimer Disease Neuroimaging Initiative, Morris MC, Evans DA, Johnson K, Sperling RA, Schneider JA, Bennett DA, De Jager PL. CD33 Alzheimer's disease locus: altered monocyte function and amyloid biology. Nature Neuroscience. 2013 Jul;16(7):848-50. ADNI

452. Martínez-Murcia FJ, Górriz JM, Ramírez J, Puntonet CG, Illán IA; Alzheimer's Disease Neuroimaging Initiative. Functional activity maps based on significance measures and Independent Component Analysis. Computer Methods and Programs in Biomedicine. 2013 Jul;111(1):255-68.

453. Fjell AM, McEvoy L, Holland D, Dale AM, Walhovd KB; Alzheimer's Disease Neuroimaging Initiative. Brain changes in older adults at very low risk for Alzheimer's disease. Journal Neuroscience. 2013 May 8;33(19):8237-42. ADNI

454. Dukart J, Kherif F, Mueller K, Adaszewski S, Schroeter ML, Frackowiak RS, Draganski B; Alzheimer's Disease Neuroimaging Initiative. Generative FDG-PET and MRI model of aging and disease progression in Alzheimer's disease. PLoS Computer Biology. 2013 Apr;9(4). ADNI

455. Dai Y, Wang Y, Wang L, Wu G, Shi F, Shen D; Alzheimer's Disease Neuroimaging Initiative. aBEAT: a toolbox for consistent analysis of longitudinal adult brain MRI. PLoS One. 2013;8(4):e60344. ADNI

456. Tong T, Wolz R, Coupé P, Hajnal JV, Rueckert D; Alzheimer's Disease Neuroimaging Initiative. Segmentation of MR images via discriminative dictionary learning and sparse coding: application to hippocampus labeling. Neuroimage. 2013 Aug 1;76:11-23. ADNI

457. Cheng B, Zhang D, Chen S, Kaufer DI, Shen D; Alzheimer's Disease Neuroimaging Initiative. Semi-supervised multimodal relevance vector regression improves cognitive performance estimation from imaging and biological biomarkers. Neuroinformatics. 2013 Jul;11(3):339-53. ADNI

458. Derado G, Bowman FD, Zhang L et al; Alzheimer's Disease Neuroimaging Initiative Investigators. Predicting brain activity using a Bayesian spatial model. UStatistical Methods in Medical Research. 2013 Aug;22(4):382-97. ADNI

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CERTIFICATION AND LICENSURE:

1998	American Board of Psychiatry and Neurology, Inc. Certification in the Subspecialty of Forensic Psychiatry
1989	Licensed in State of Connecticut
1984	Diplomate, American Board of Psychiatry and Neurology, Inc. (Psychiatry)
1980	Diplomate, National Board of Medical Examiners
1980	Licensed in New York State

EDUCATION AND TRAINING:

1983-1984	Fellowship in Psychiatry and Law, New York University-Bellevue Hospital Center, New York, New York
1979-1983	Internship and Psychiatric Residency, New York Hospital-Cornell Medical Center, Payne Whitney Clinic, New York, New York
1975-1979	M.D., Columbia University College of Physicians and Surgeons, New York, New York
1965-1969	B.A., Queens College, City University of New York, Flushing, New York

HOSPITAL APPOINTMENTS:

1999-	Psychiatrist-in-Chief and Vice President, Behavioral Health The Institute of Living/Hartford Hospital
1994-1999	Vice President, Clinical Affairs and Medical Director, The Institute of Living, Hartford Hospital's Mental Health Network

HOSPITAL APPOINTMENTS: (cont.)

1989-	Director, Department of Psychiatry, Hartford Hospital, Hartford, Connecticut
1987-1989	Chief, Psychiatric Outpatient Services, Beth Israel Medical Center, New York, New York
1985-1989	Chief, Program in Psychiatry and Law, Beth Israel Medical Center, New York, New York
1984-1987	Unit Chief, Adult Psychiatry Service, Beth Israel Medical Center, New York, New York

ACADEMIC APPOINTMENTS:

2010-	Professor, Adjunct, Department of Psychiatry, Yale University School of Medicine, New Haven, Connecticut
2004-2005	Visiting Clinical Professor (honorary), Smith College School for Social Work, Northampton, Massachusetts
2003-	Professor of Psychiatry and Associate Chairman, Department of Psychiatry, University of Connecticut School of Medicine, Farmington, Connecticut
1989-2003	Associate Professor of Psychiatry and Associate Chairman, Department of Psychiatry, University of Connecticut School of Medicine, Farmington, Connecticut
1987-1989	Associate Professor of Clinical Psychiatry, Mount Sinai School of Medicine, New York, New York
1984-1987	Assistant Professor of Clinical Psychiatry, Mount Sinai School of Medicine, New York, New York
1983-1984	Clinical Instructor of Psychiatry, New York University School of Medicine, New York, New York
1982-1983	Instructor of Clinical Psychiatry, Cornell University Medical College, New York, New York

AWARDS AND HONORS:

2013	Distinguished Life Fellow, American Psychiatric Association

AWARDS AND HONORS: (cont.)

2013	Listed in: *Best Doctors in America* (www.bestdoctors.com), 2012-2013; 2011-2012; 2009-2010; 2007-2008; 2006-2007; 2005-2006; 2003-2004
2013	Listed in: Top Docs (Psychiatry), *Connecticut Magazine,* consecutive years since inception
2007	Exceptional Leadership Award, The Institute of Living Board of Directors
2007	Excellence in Achievement Award for Public Service, Connecticut Coalition to Improve End-of-Life Care
2007	Award for Excellence in Continuing Medical Education (2007- The Institute of Living, Connecticut State Medical Society.
2005	Award for Distinguished Service, Connecticut Psychiatric Society
2004	Listed in: *Guide to America's Top Psychiatrists,* Consumers' Research Council of America, 2004-2005.
2003	Distinguished Fellow, American Psychiatric Association.
2003	Secretary of the State's Public Service Award, State of Connecticut, in recognition of service on the Advisory and Review Board for the Whiting Forensic Institute.
2001	Distinguished Alumni Award: New York University Forensic Psychiatry Fellowship Program
1999	Award for Excellence in Continuing Medical Education (1999- The Institute of Living, Connecticut State Medical Society.
1998	Listed in: *The Best Doctors in America* (National Edition), 1998-1999. Woodward/White, Inc. Aiken, South Carolina, 1998.
1997	Award for Excellence in Continuing Medical Education (1997- The Institute of Living), Connecticut State Medical Society.
1996	Listed in: *The Best Doctors in America: Northeast Region, 1996-1997.* Woodward/White, Inc., Aiken, South Carolina, 1996.
1996	Honorable Mention, Guttmacher Award Competition. Awarded to: Schwartz HI (Ed.) *Psychiatric Practice Under Fire: The Influence of Government, the Media and Special Interests on Somatic Therapies.* American Psychiatric Press, Inc., September 1994.

AWARDS AND HONORS: (cont.)

1993	Fellow, American Psychiatric Association
1988	Newsletter of the Year Award, American Psychiatric Association (Editor)
1986	Fellow, New York Academy of Medicine
1983	Resident Research Prize of the New York District Branch, American Psychiatric Association
1983	William T. Lhamon Research Award, Payne Whitney Clinic, New York-Cornell Medical Center, New York, New York
1978-1979	Rock Sleyster Memorial Scholar, American Medical Association

ORGANIZATIONS:

American College of Psychiatrists, Committee on Ethics, 2005-2007

American Psychiatric Association:
National:
Commissioner, Joint Commission on Government Relations, (Area I Representative), 1994-2001, Consultant, 2001-2009; Member, Confidentiality Committee, 1987-1993; Member, Manfred S. Guttmacher Award Committee, 2002-2003; Council on Advocacy and Public Policy, 2005-2006.

Connecticut Psychiatric Society:
Immediate Past President, 1997-1998; President, 1996-1997; President-Elect, 1995-1996; Secretary, 1994-1995; Treasurer, 1993-1994;
Legislative Committee Chair and State Legislative Representative, 1990-
Area II Council:
Vice-Chair, Psychiatry and Law Committee, 1986-1989.
New York County District Branch:
Executive Committee, 1988-1989; Newsletter Editor, 1986-1989; Public Affairs Network, 1986-1989.

American Academy of Psychiatry and the Law:
National:
Ethics Committee, 1998-
Task Force on Practice Guidelines for Forensic Evaluations, 1998-
Chair, Educational Oversight Committee, 1994-1995;

ORGANIZATIONS: (cont.)

Committee on Geriatric Psychiatry and the Law, 1986-1988; Chair, Learning Resources Committee, 1989-1992; Program Committee, 1986-1989; Faculty Liaison to the Education Steering Committee, 1993.

Tri-State Chapter:
President, 1992-1994; Vice President 1990-1992; Secretary 1986-1990.

Committee of Concerned Psychiatrists (PAC of the Connecticut Psychiatric Society), President, 1994- : Treasurer, 1991-1994.

National Association of Psychiatric Health Systems (NAPHS): Board of Trustees, 1999-2001 and 2006-2009; Committee on Behavioral Health Services within General Healthcare Systems, 1999- ; Selection Committee, 1999-2001; Payment Systems Committee, 2001-2003 ; Finance Committee, 2001-2002; Strategic Planning Committee, 2003-2005; Clinical Practice Committee, 2005-2007.

Joint Commission on the Accreditation of Health Care Organizations (JCAHO): Member, Hospital Professional and Technical Advisory Committee (representing NAPHS), 2001-

Central Neuropsychiatric Hospital Association:
President, 1995-1996; Councilor, 1996-1998.

American Association for Geriatric Psychiatry, 1989-1991.

The Hastings Center - Institute of Society, Ethics and the Life Sciences, 1982-

New York County Bar Association, Committee on Legal Problems of the Aged, 1988-1989.

Connecticut Hospital Association:
Member, Psychiatric Administrators Conference, 1989-present
Member, Conference of Ethics Committee Chairs, 1992-

American Association of General Hospital Psychiatrists, 1991-

Connecticut State Medical Society, 2000-

EDITORIAL:

Editorial Review Board, Textbook of Hospital Psychiatry, American Psychiatric Press, 2009.

Guest Editor, *Connecticut Medicine,* Vol. 64, No. 6, (Special Issue): Controversies in Psychiatry, June 2000.

Guest Editor: *Connecticut Medicine,* Vol. 61, No. 9, Special Issue Edition in honor of the 175th Anniversary of The Institute of Living, September 1997.

Editor, *Digest of Neurology and Psychiatry,* 1994-

EDITORIAL (cont.):

Peer Reviewer: *Psychiatric Services* (formerly *Hospital and Community Psychiatry),* 1982-
The Journal of Nervous and Mental Disease, 1985
The Journal of the American Academy of Psychiatry and the Law (formerly *The Bulletin of the American Academy of Psychiatry and the Law),* 1990-
Behavioral Sciences and the Law, 2006-

Editor, Newsletter of the New York County District Branch, American Psychiatric Association, 1986-1989.

TEACHING:

Beth Israel Medical Center Psychiatry Residency
Courses: Basic Psychiatry, Emergency Psychiatry
Psychotherapy (Course Co-Director)
Legal and Ethical Issues (Course Director)
Journal Club (Course Director)
Supervision: Case Management, Psychotherapy, Inpatient
Case conferences, special lectures, etc.
Coordinator: PGY 3 residency year.

Institute of Living/University of Connecticut Psychiatry Residency
Courses: Forensic Psychiatry
Supervision: Inpatient, Outpatient Psychotherapy
Case conferences, special lectures.

Faculty, Forensic Psychiatry Seminar of the American Academy of Psychiatry and the Law (Tri-State Chapter), 1984-1989.

University of Connecticut School of Medicine, "Mini-Medical School", 1994-95

Institute of Living Psychiatry Residency
Introduction to Psychiatry Course, Faculty, 2003-
Course: Forensic Psychiatry, Course Co-Director, 2005-
Seminar: Special Issues in Psychiatry, Law, Ethics and Public Policy, Seminar Director, 2006-
Case conferences, special lectures.
Psychotherapy supervisor.
Residency Training Committee (Executive), Member; Residency Selection Committee, Member

University of Connecticut School of Medicine, Human Development and Health Course, Faculty (Lecture on Psychodynamic Principles), 2003-

HARTFORD HOSPITAL COMMITTEES:

Executive Committee of the Medical Staff
Position Control Committee
Ethics Committee (Member, 1992- ; Chair, 2001-)
Capital Committee
Position Review Committee
Hartford Hospital Facilities Strategic Planning Committee
Hartford Hospital Neuroscience Oversight Committee
Hartford Hospital Balanced Scorecard Institute Model Steering Committee
Hartford Healthcare Corporation Strategic Planning Steering Committee
Hartford Healthcare Corporation Research Strategic Planning Committee (Co-Chair)
Hartford Healthcare Research Institute Executive Board
George Mead Fund Committee
Executive Committee of The Institute of Living (Chair)
Administrative Council of The Institute of Living (Chair)

GRANTS:

2010	NIH, National Center for Research Resources Grant # 1C06RR028654-01, PI Harold I. Schwartz, Project Title: Olin Research Center Addition for New MRI Scanner and Research Staff.

OTHER PROFESSIONAL ACTIVITIES:

2013	Governor's Sandy Hook Advisory Commission
2011-	Board of Trustees, The Mind Research Network, Albuquerque, New Mexico
2010	Search Committee, University of Connecticut School of Medicine - Senior Associate Dean for Education
2009	Faculty, The Scattergood Ethics Winter Institute for the Applied Ethics of Behavioral Health, Center for Bioethics, University of Pennsylvania, October 22-23, 2009.
2008	Faculty, The Scattergood Ethics Summer Institute for the Applied Ethics of Behavioral Health, Center for Bioethics, University of Pennsylvania, July10-11, 2008.
2007-	Advisory Board, The Scattergood Program for the Applied Ethics of Behavioral Health
2006-	Board of Directors, Chrysalis Centers, Inc.

OTHER PROFESSIONAL ACTIVITIES: (cont.)

2002	Maine Medical Center (Psychiatry) Departmental Review and Search Process. External Review Consultant. Maine Medical Center, Portland, Maine.
2001	Preferred Practices Advisory Group, Department of Mental Health and Addiction Services, Connecticut.
2000	Governor's Blue Ribbon Commission on Mental Health, Steering Committee.
1999	Behavioral Health Connecticut, LLC. Chair, Management Committee.
1998	Commissioner's Panel on Physical/Behavioral Intervention, Department of Children and Families.
1997	Medical Advisor, "Myths, Minds and Medicine: Two Centuries of Mental Health Care." A permanent exhibit on the history of the Institute of Living and the treatment of psychiatric illnesses. Supported by a grant from the Connecticut Humanities Council.
1994	Chief Proctor, American Board of Psychiatry and Neurology board examination, Part I. Hartford, CT
1993-	Member, Advisory and Review Board, Whiting Forensic Institute
1992-1993	Task Force to write Informed Consent - Treatment Refusal legislation, Connecticut Department of Mental Health.
1991-1994	Connecticut Department of Mental Health: Member, Committee on Involuntary Medication; Member, Committee on Outpatient Commitment.
1989-	Examiner, American Board of Psychiatry and Neurology, Inc.
1986	Member, Subcommittee on Legal/Ethical/Forensic Issues for Module B of the Psychiatric Knowledge and Skills Self-Assessment Program
1985-1989	Member, Ethics Committee, Beth Israel Medical Center
1984-1989	Member, Appellate Division Panel of Expert Psychiatrists, New York State Supreme Court
1984-	Forensic psychiatry consultations and expert witness testimony

RECENT MEDIA APPEARANCES:

2006	PBS Documentary: "Out of the Shadow." Panelist in discussion with filmmaker and sponsor.
2007	WGBY Documentary: "Darkest Hours: The Crisis in Children's Mental Health Care." Interviewee.
2009	WHYY Radio, Interviewee on "Voices in the Family," with Dr. Dan Gottlieb.

PRESENTATIONS:

1981	"Intern to Psychiatric Resident: Transition Issues." (Panel Moderator) Annual Meeting of the American Psychiatric Association, New Orleans, LA
1983	"Do Not Resuscitate Orders: Guidelines and Practices." Faculty Council Grand Rounds, Payne Whitney Clinic, New York Hospital-Cornell Medical Center
1983	"Clinical Judgments in the Decision to Commit: Psychiatric Discretion and the Law." Grand Rounds, Payne Whitney Clinic, New York Hospital-Cornell Medical Center and the New York District Branch, American Psychiatric Association
1986	"Legal Dangers and Ethical Pitfalls in Primary Care Psychiatry for Family Physicians." New York State Academy of Family Physicians, Bolton Landing, NY
1986	"Legal and Ethical Issues in Compliance." Annual meeting of the American Psychiatric Association, Washington, DC
1986	"DNR Orders - The Role of Clinicians' Attitudes." American Academy of Forensic Sciences, New Orleans, Louisiana and at the annual meeting of the American Academy of Psychiatry and the Law, Philadelphia, PA
1986	"Geriatric Psychiatry and the Law." (Panel Moderator) American Academy of Forensic Sciences, New Orleans, Louisiana
1986	"Legal and Ethical Issues in Neuroleptic Noncompliance." Grand Rounds, South Beach Psychiatric Center, Staten Island, New York
1986	"Noncompliance and Medication Refusal." Grand Rounds, Bronx Lebanon Hospital Center, New York

PRESENTATIONS: (cont.)

1987 "Do Not Resuscitate Decisions: Attitudes and Practice." Jersey City Medical Center, New Jersey

1987 "Patients' Attitudes Toward Involuntary Medication: An Assessment of Autonomy in Treatment Refusal." Grand Rounds, Payne Whitney Clinic, New York Hospital-Cornell Medical Center

1987 "The Right to Refuse Treatment, Update 1987." Workshop Chairman, and "Competence and Consent in the General Hospital" (panelist). American Psychiatric Association Annual Meeting, Chicago

1987 "Empirical Investigations of Involuntary Hospitalization and Treatment." Grand Rounds, New York State Psychiatric Institute, New York, NY

1987 "Involuntary Hospitalization and Treatment in New York 1987: The State of the Debate." Conference Co-Director and presenter, Beth Israel Medical Center, New York

1988 "Treatment Refusal and Involuntary Medication." Grand Rounds at Creedmore Psychiatric Center and Manhattan Psychiatric Center, New York

1988 "Patients' Attitudes After Involuntary Treatment" (paper) and "Supervision of Supportive Psychotherapy" (panelist). American Psychiatric Association Annual Meeting, Montreal, Canada

1989 "Is Geriatrics the Last Frontier for Informed Consent?" Annual Meeting of the American Association for Geriatric Psychiatry, Orlando, Florida

1989 "Patient Rights: A Double Edged Sword." Connecticut Alliance for the Mentally Ill, University of Connecticut/National Mental Illness Awareness Week Symposium

1989 "Autonomy and Medication Refusal: Clinical and Attitudinal Outcome of Involuntary Treatment." Grand Rounds, Hartford Hospital, Hartford, Connecticut

1989 "Informed Consent, Civil Commitment and Involuntary Treatment." Grand Rounds, Bergen Pines County Hospital, Paramus, New Jersey

1990 "The Erosion of Autonomy: Is Free Choice Dying in Psychiatric Practice?" Annual Meeting of the Hartford Psychiatric Society, Hartford, Connecticut

1990 "Predictions of Dangerousness in the Post-Tarasoff Era." Grand Rounds, North Shore University Hospital, Manhasset, New York

PRESENTATIONS: (cont.)

1990 "Informed Consent and Competency." Grand Rounds, Hartford Hospital, Hartford, CT

1990 Forensic Psychiatry. Paper session discussant. Annual Meeting of the American Psychiatric Association, New York, New York

1990 "Legal and Ethical Considerations in Stress Disorders." Presented at the Hartford Hospital Annual Psychiatry Symposium (Disorders of Extreme Stress: Diagnosis, Treatment, Legal and Ethical Issues), Hartford, CT

1991 "Negative Clinical Consequences of Triplicate Prescription Regulation of Benzodiazepines." At "Triplicate Prescription: Issues and Answers," symposium sponsored by the Medical Society of the State of New York

1991 "Influencing the Supreme Court on the Right to Refuse Treatment: Empirical Research in an Adversarial Process." Grand Rounds, The University of Connecticut School of Medicine, Farmington, CT.

1991 "Informed Consent and Competency in the General Hospital." Grand Rounds, Hospital of Saint Raphael, New Haven, CT.

1991 "Influencing the Courts on Psychiatric Issues," symposium chair and "Using 'Science' to Influence the Courts," paper presentation. American Psychiatric Association Annual Meeting, New Orleans, LA.

1991 "Advocating for Access to Medications." Workshop presentation. The National Alliance for the Mentally Ill Annual Meeting, San Francisco, CA.

1991 "The Management of Boundaries in Psychotherapeutic Relationships," panel moderator. Hartford Hospital Department of Psychiatry, Annual Symposium, Hartford, CT.

1991 "Regulation of Benzodiazepines Prescribing Practices: Clinical Implications." Paper presentation. American Academy of Psychiatry and the Law, Annual Meeting, Orlando, FL.

1991 "Irrational Regulation of Psychotropic Prescribing: Benzodiazepines in New York." Grand Rounds, Department of Psychiatry, Beth Israel Medical Center, New York, NY.

1992 "Triplicate Prescription of Benzodiazepines." Grand rounds, Baystate Medical Center, Springfield, MA.

PRESENTATIONS: (cont.)

1992 "Disclosure of Information About Famous Patients." Confidentiality Committee Workshop. Presenter, American Psychiatric Association Annual Meeting. Washington, DC.

1992 "Controversial Regulation of Somatic Therapies." Symposium chair. "Triplicate Prescriptions for Benzodiazepines." Symposium presentation: American Psychiatric Association Annual Meeting, Washington, DC.

1992 "Controversies in the Regulation of Psychiatric Practice," Grand Rounds, and "Regulation of Benzodiazepine Prescribing: Science vs. Politics," Research Seminar. Washington University School of Medicine, St. Louis, MO.

1992 "Irrational Benzodiazepine Regulation." Controversy in Pain Symposium. Hartford Hospital.

1994 "Shaping the Practice of Somatic Psychiatry: Regulation by Government, the Media and Special Interests." Grand Rounds, The Institute of Living, Hartford, CT.

1994 "Health Care Reform." Panelist, Annual Meeting of the Central Neuro-psychiatric Hospital Association, Austen Riggs Center, Stockbridge, MA.

1994 "Psychiatry." University of Connecticut School of Medicine "Mini-Medical School."

1994 "Prozac and Health Care Reform." Annual Meeting of the National Board of Governors, Institute of Living, Hartford, CT.

1994 "Health Care Reform: A Panel Presentation with Congresswoman Nancy Johnson." Panel moderator and presenter. Fairfield/Litchfield Chapter, Connecticut Psychiatric Society.

1994 "Crucial Legal and Ethical Issues in the Management of the Involuntary Patient." Grand Rounds, Fairfield Hills Hospital, Newtown, CT.

1995 "The Doctor's View of Civil Commitment and Involuntary Medication." Connecticut Bar Association Continuing Legal Education Program: Representing Clients with Psychiatric Disabilities in Probate Court. North Haven, CT.

1995 "The Right to Refuse Treatment." Connecticut Psychiatric Society Residents Day Symposium: Ethics in Psychiatry. Berlin, CT

PRESENTATIONS: (cont.).

1995 "Corporate Combination: Hartford Hospital/Institute of Living.' Keynote address, Central Neuropsychiatric Hospital Association, Dallas, TX.

1995 "Managed Care Legislative Forum." Moderator, American Psychiatric Association Federal Legislative Institute, Washington, D.C.

1995 "Current Dilemmas in Psychiatry." The National Board of Governors 22nd Annual Meeting, The Institute of Living, Hartford, CT.

1996 "Clinical Forensics in Psychiatric Practice." Contemporary Issues in Psychiatric Nursing. The Institute of Living, Hartford, CT.

1996 "The Evolution of Departments of Psychiatry and Their Chairmen - Relationships to Hospitals, PHO's, and Integrated Delivery Systems - What is the Future?" Connecticut Hospital Association, Psychiatric Administrators Conference, Wallingford, CT.

1997 "Transition from Medical to Professional Staffs," panelist. The Hamilton Workshop, Old Saybrook, CT.

1997 "Managed Care: At the Legislative Crossroads," Panel Moderator. American Psychiatric Association Federal Legislative Institute. Washington, D.C.

1998 "Physician-Assisted Suicide: Attitudes and Experience of Connecticut Physicians. Grand Rounds, The Institute of Living, Hartford, CT.

1998 "Physician-Assisted Suicide: Health Care Providers' Role in the Debate," panelist. Connecticut Hospital Association, Wallingford, CT.

1998 "Sexual Predator Laws: The Aftermath of Kansas v. Hendricks". Panel Moderator, American Psychiatric Association Joint Institute: State Legislative and Public Affairs, Fort Lauderdale, FL.

1998 "Assisted Suicide: Attitudes, Experience and Ethics." Research in progress paper presentation. American Academy of Psychiatry and the Law Annual Meeting. New Orleans, LA.

1998 "Physician-Assisted Suicide: The Views of Connecticut Physicians." The Hartford Medical Society. Hartford, CT.

1998 "The Oregon Experience of Physician-Assisted Suicide: What Are the Implications for Connecticut?" Panelist. Symposium by the Connecticut Association for Home Care, Inc. Southington, CT.

PRESENTATIONS: (cont.)

1999 "Violence in Our Schools: Practical Strategies for Keeping Our Children Safe," Panelist ("Predictions of Violence"), Community Forum, West Hartford, CT

2000 "Mind, Brain and Modern Psychiatry." Presented at "Psychiatry: Art and Life, Past and Present." The Institute of Living, Hartford, CT

2000 "Physician-Assisted Suicide in Connecticut: Experiences and Attitudes." The Hemlock Society of Connecticut. Farmington, CT

2000 "PAS or Voluntary Euthanasia: Any Distinction," Paper presentation.
American Academy of Psychiatry and the Law Annual Meeting. Vancouver, British Columbia.

2001 "Informed Consent and Competency in the General Hospital," Grand Rounds, Department of Medicine and Ethics Committee, Stamford Hospital, Stamford, CT

2001 "The Use of the Mock Trial in Psychiatric Staff Education," Panel discussant. American Psychiatric Association Annual Meeting, New Orleans, LA

2001 "Coping with Crises: What Resilient Families Need to Know." Public Forum (Moderator). West Hartford Meeting and Conference Center, West Hartford, CT

2002 "Violence: The Risk Assessment Challenge for Psychiatry." Grand Rounds, Silver Hill Hospital, New Canaan, CT

2003 "Medical Ethics and Women's Health." Grand Rounds, Department of Obstetrics and Gynecology, Hartford Hospital, Hartford, CT

2003 "Forensic Medicine in the Emergency Department," (panelist), Department of Emergency Medicine Grand Rounds, Hartford Hospital, Hartford, CT

2003 "Psychiatry: Past and Present," Co-presenter, University of Connecticut School of Social Work, Hartford, CT

2004 "The Role of the Emergency Room in Improving Acute Care for Psychiatric Disorders." Panel Discussant, National Association of Psychiatric Health Systems, "Hot Topics."

PRESENTATIONS: (cont.)

2004 "The Institute of Living's Tenth Anniversary as Hartford Hospital's Department of Psychiatry: Where We Have Been and Where We Are Going," Grand Rounds, The Institute of Living, Hartford, CT

2004 "Talking About Death Enhances Life: Improving Quality of Care Today for Tomorrow," (Moderator) Focus on Health Series, Hartford Hospital, Hartford, CT.

2005 "Overview of Behavioral Disorders, Treatments and Systems of Care," University of Connecticut School of Public Health, Farmington, CT.

2005 "The Institute of Living: 1822-2004 – Psychiatric Care from Moral Management to Neuroscience," The Robert U. Massey History of Medicine Society, University of Connecticut Health Center, Farmington, CT.

2005 "The Future of the End-of-Life: Reflections on the Right to Die Post-Schiavo," The Annual Lecture on the Humanities in Surgery honoring H. David Crombie, M.D., Grand Rounds, Department of Surgery, Hartford Hospital, Hartford, CT

2005 "From the Hartford Retreat for the Insane to The Institute of Living: A Model for Developments in American Psychiatry," Annual Combined Meeting of the Beaumont Medical Society (Yale University School of Medicine), the Hartford Medical Society and the Massey History of Medicine Society (University of Connecticut School of Medicine), Hartford, CT.

2005 "The Future of the End-of-Life: Reflections on the Right to Die Post-Schiavo," Grand Rounds, The Institute of Living, Hartford, CT.

2006 "The Future of the End-of-Life: Reflections on the Right to Die Post-Schiavo," Grand Rounds, Middlesex Hospital, Middletown, CT.

2007 "Physicians Involved in Executions: Is it Ethical?" (panelist), The Legal Medical Committee of the Hartford County Bar Association in conjunction with The Hartford County Medical Association, West Hartford, CT.

2007 "Outsider Art at The Institute of Living," Keynote Speaker, Mental Health Association of Connecticut, Hartford, Connecticut.

2007 "The Future of the End-of-Life: Reflections on the Right to Die Post-Schiavo," Keynote Speaker, Connecticut Coalition to Improve End-of-Life Care, Middletown, Connecticut.

PRESENTATIONS: (cont.)

2007 "The Institute of Living: Where We Are and Where We Are Going," Grand Rounds, The Institute of Living, Hartford, Connecticut.

2007 "The Right to Die in the Post-Schiavo Era." Grand Rounds, MidState Medical Center, Meriden, Connecticut.

2008 "The Paradox of Moral Treatment in Modern Times." Symposium Presentation: American Psychiatric Association Annual Meeting, Washington, DC.

2008 "Coercion and Compliance." The Scattergood Ethics Summer Institute for the Applied Ethics of Behavioral Health. Center for Bioethics, University of Pennsylvania.

2008 "Coercion, Compliance, Consent and Adherence: Autonomy vs. Paternalism in Mental Health Services," Grand Rounds, The Institute of Living, Hartford, Connecticut.

2009 Coercion and Compliance in Behavioral Health." The Scattergood Ethics Summer Institute for the Applied Ethics of Behavioral Health. Center for Bioethics, University of Pennsylvania.

2009 "The Institute of Living 2009: Where We Were, Where We Are and Where We Are Going," Grand Rounds, The Institute of Living, Hartford, Connecticut.

2009 "Ethical Challenges of the Recovery Movement." Scattergood Foundation, Annual Meeting of the Board of Directors, Philadelphia, Pennsylvania.

2010 "Involuntary Commitment and Medication: Balancing Liberty Interests and the Need for Treatment." The Scattergood Ethics Winter Institute for the Applied Ethics of Behavioral Health, Center for Bioethics, University of Pennsylvania.

2010 "Diagnosis and the DSM's: Use and Abuse of Nosology in Adult Psychiatry." Scattergood Foundation, Annual Meeting of the Board of Directors, Philadelphia, Pennsylvania

2011 "What's In a Name? The Controversial Evolution of our Nosology in DSM I Through DSM V." Grand Rounds, St. Vincent's Medical Center Behavioral Health Service, Westport, CT

2011 "What's In a Name? The Controversial Evolution of our Nosology in DSM I Through DSM V." Grand Rounds, The Institute of Living, Hartford, Connecticut.

2013 "Thoughts About Mental Illness in the Wake of Sandy Hook." Keynote speaker, Eastern Connecticut State University Foundation Luncheon for Natchaug Hospital, Willimantic, CT

2013 "Refusing Violence in our Cities: Stakeholder Discussion with Representatives Larson, Esty and Thompson. Invited participant. Faith Congregational Church, Hartford, CT

2013 Expert testimony to the Field Hearing of the Congressional Gun Violence Prevention Task Force (entered in the Congressional Record), Hartford, CT

2013 "Mental Health: Stigmas, Stereotypes and Solutions." Salons at Stowe featured guest. Harriet Beecher Stowe House Salon Series, Hartford, CT

PUBLICATIONS:

PEER REVIEWED ARTICLES:

Douglas CJ, Schwartz HI: ECT for Depression Caused by Lupus Cerebritis. *American Journal of Psychiatry* 139:1631-1632, 1982.

Schwartz HI*, Appelbaum PS, Kaplan RD: Clinical Judgments in the Decision to Commit: Psychiatric Discretion and the Law. *Archives of General Psychiatry* 41:811-815, 1984.

Perry SW, Schwartz HI*, Amchin J: Determining Resuscitation Status: A Survey of Medical Professionals. *General Hospital Psychiatry* 8:198-202, 1986.
Schwartz HI*, Blank K: Shifting Competency: A Model for Informed Consent Decisions. *Hospital and Community Psychiatry* 37:1256-1260, 1986.

Hoffman A, Schwartz HI, Novick R: Catatonic Reaction to Accidental Haloperidol Overdose: An Unrecognized Drug Abuse Risk. *Journal of Nervous and Mental Disease* 174:428-430, 1986.

Rachlin S, Schwartz HI: Unforeseeable Liability for Patients' Violent Acts. *Hospital and Community Psychiatry* 37:725-731, 1986.

Schwartz HI*, Pinsker H: Mediating Retention or Release of the Potentially Dangerous Patient. *Hospital and Community Psychiatry* 38:75-77, 1987.

Schwartz HI: Legal and Ethical Pitfalls in Family Practice Psychiatry. *American Family Physician* 35:4:103-108, 1987.
Reprinted in *Management of Violent Behavior: Collected Articles from Hospital and Community Psychiatry.* Hospital and Community Psychiatry Service, Washington, DC, 1988.

PEER REVIEWED ARTICLES: (cont.)

Taylor N, Schwartz HI: Neuroleptic Malignant Syndrome Following Amoxapine Overdose. *Journal of Nervous and Mental Disease* 176:249-251, 1988.

Schwartz HI: When Physicians Refuse to Treat AIDS Patients. *Medical Aspects of Human Sexuality,* April 1988:26-29.

Schwartz HI*, Vingiano W, Bezirganian Perez C: Autonomy and the Right to Refuse Treatment: Patients' Attitudes After Involuntary Medication. *Hospital and Community Psychiatry* 39:1049-1054, 1988.

Cited and paraphrased by the U.S. Supreme Court in Washington v. Harper, 494 U.S. 210 (1990).
Reprinted in Wexler, DB (Ed.): *Therapeutic Jurisprudence: The Law as a Therapeutic Agent.* Carolina Academic Press, Durham, NC, 1990.

Rachlin S, Schwartz HI: The Presence of Counsel at Forensic Psychiatric Examination. *Journal of Forensic Sciences* 33:1008-1014, 1988.

Schwartz HI: AIDS: Confidentiality versus the Duty to Warn. *Medical Aspects of Human Sexuality* 22:13, 1988.

Blank K, Vingiano W, Schwartz HI: Psychiatric Commitment of the Elderly. *Journal of Geriatric Psychiatry and Neurology* 2:140-144, 1989.

Schwartz HI*, Blank K: Regulation of benzodiazepine prescribing practices: Clinical implications. *General Hospital Psychiatry* 13:219-224, 1991.

Levine S, Blank K, Schwartz HI: Informed consent in the electroconvulsive treatment of geriatric patients. *The Bulletin of the American Academy of Psychiatry and the Law* 19:395-403, 1991.

Schwartz HI: Negative clinical consequences of triplicate prescription regulation of benzodiazepines. *New York State Journal of Medicine, Supplement: Proceedings of the Symposium, "Triplicate Prescription: Issues and Answers* 91:9S-12S, 1991.

Hellerstein DJ, Barron CT, Schwartz HI, Zolkind NA: A rating inventory for resident case presentations. *Academic Psychiatry* 15:146-152, 1991.

Schwartz, HI: An empirical review of the impact of triplicate prescription of benzodiazepines. *Hospital and Community Psychiatry* 43:382-385, 1992.

Schwartz HI*, Boland R: Using science to influence the Supreme Court on the right to refuse treatment: Amicus curiae briefs in Washington v. Harper. *Bulletin of the American Academy of Psychiatry and the Law* 23:135-146, 1995.

PEER REVIEWED ARTICLES: (cont.)

Goethe JW, Schwartz, HI, Szarek BL: Physician Compliance with Practice Guidelines. *Connecticut Medicine* 61:553-558, 1997.

Van Hoof TJ, Schwartz HI: When Consultants Write Orders: Physicians' Attitudes, Beliefs and Practices. *General Hospital Psychiatry* 21:333-339, 1999.

Schwartz HI*, Curry L, Blank K, Gruman C: The Physician-Assisted Suicide Policy Dilemma: A Pilot Study of the Views and Experiences of Connecticut Physicians. *Journal of the American Academy of Psychiatry and the Law,* 27:527-539, 1999.

Curry L, Gruman C, Blank K, Schwartz HI: Physician-Assisted Suicide in Connecticut: Physicians' Attitudes and Experiences. *Connecticut Medicine* 64(7):403-412, 2000.

Blank K, Fogel D, Robison J, Gruman C, Schwartz H: Late Life Depression: A Naturalistic Study of Inpatient Treatment. *Journal of Mental Health and Aging* 6:249-260, 2000.

Curry L, Schwartz HI, Gruman C, Blank K: Physician's Voices on Physician-Assisted Suicide: Looking Beyond the Numbers. *Ethics and Behavior* 10:337-361, 2000.

Blank K, Robison J, Doherty E, Prigerson H, Duffy J, Schwartz HI: Life Sustaining Treatment and Assisted Death Choices in Depressed Older Patients, *The Journal of the American Geriatric Society,* 49:153-161, 2001.

Schwartz HI*, Curry L, Blank K, Gruman C: Physician-Assisted Suicide or Voluntary Euthanasia: A Meaningless Distinction for Practicing Physicians. *The Journal of Clinical Ethics,* 12:51-63, 2001.

Blank K, Robison J, Prigerson H, Schwartz HI: Instability of Attitudes about Euthanasia and Physician-Assisted Suicide in Depressed, Older Hospitalized Patients. *General Hospital Psychiatry* 23:326-332, 2001.

Curry L, Schwartz HI, Gruman C, Blank K: Could Adequate Palliative Care Obviate Assisted Suicide. *Death Studies* 26:757-774, 2002.

Schwartz HI, Curry L: Physician-Assisted Suicide and Palliative Care: Beliefs and Empiricism in the Policy Debate. *Connecticut Medicine* 66(11): 699-702, 2002.

Blank K, Gruman C, Robison J, Hickey E, Hixon L, Schwartz HI: Determinants of Geropsychiatric Inpatient Length of Stay. *Psychiatric Quarterly*, 76:195-212, 2005.

Ruano G, Blair CL, Bower B, Windemuth A, Kocherla M, Aleman Y, Pearlson G, Goethe JW, Schwartz HI: Somatic Complications of Psychotropic Medications in a Patient with

PEER REVIEWED ARTICLES: (cont.)

Multiple CYP2 Drug Metabolism Deficiencies. *Connecticut Medicine* 71(4): 197-200, 2007.

Glick I, Sharfstein S, Schwartz HI: Inpatient Psychiatric Care in the 21st Century: The Need for Reform. *Psychiatric Services*,, 62(2): 206-209, 2011.

Villagra D, Goethe J, Schwartz HI, Szarek B, Kocherla M, Gorowski K, Windemuth A, Ruaño G: Novel Drug Metabolism Indices for Pharmacogenetic Functional Status Based on Combinatory Genotyping of CYP2C9, CYP2C19 and CYP2D6 Genes. *Biomarkers in Medicine,* 5(4):427-438, 2011.

Ruaño G, Villagra D, Szarek B, Windemuth A, Kocherla M, Gorowski K, Berrezueta C, Schwartz HI, Goethe J: Physiogenomic Analysis of *CYP450* Drug Metabolism Correlates Dyslipidemia with Pharmacogenetic Functional Status in Psychiatric Patients. *Biomarkers in Medicine,* 5(4):439-449, 2011.

Windemuth A, deLeon J, Goethe J, Schwartz HI, Woolley S, Susce M, Kocherla M, Bogaard K, Holford T, Seip R, Ruaño G: Validation of Candidate Genes Associated with Cardiovascular Risk Factors in Psychiatric Patients. *Progress in Neuro-Psychopharmacology & Biological Psychiatry,* 36:213-219, 2012.

Ruaño G, Szarek B, Villagra D, Gorowski K, Kocherla M, Seip RI, Goethe, JW, Schwartz HI. Length of Psychiatric Hospitalization Correlated with CYP2D6 Functional Status in Inpatients with Major Depressive Disorder. *Biomarkers in Medicine*, 2013, in press.

PEER REVIEWED ABSTRACTS, LETTERS AND POSTERS:

Schwartz HI*, Blank K: Intern to Psychiatric Resident: Transition Issues. (Abstract) *Syllabus and Scientific Proceedings of the 134th Annual Meeting of the American Psychiatric Association* 289-290, 1981.

Schwartz HI: Legal and Ethical Issues in Compliance (Abstract). *CME Syllabus, American Psychiatric Association 139th Annual Meeting 187*, 1986.

Schwartz HI: Using "Science" to influence the courts. (Abstract) CME Syllabus and Proceedings Summary, American Psychiatric Association, 144th Annual Meeting: 158, 1991.

Schwartz HI: Effects of Involuntary Medication. (Letter) *American Journal of Psychiatry* 148:1622, 1991.

Schwartz HI*, Blank K, Walker L, Gruman C: Assisted Suicide: Attitudes, Experience and Ethics. (Abstract) The American Academy of Psychiatry and the Law Annual Meeting, New Orleans, LA, 1998

EVIEWED ABSTRACTS, LETTERS AND POSTERS: (cont.)

Walker, L, Gruman C, Schwartz H, Blank K: Physician-Assisted Suicide: The Role of Practice Patterns and Professional Discipline. (Abstract) *The Gerontologist*, 38:30, 1998.

Gruman C, Walker L, Schwartz H, Blank K: Physician Perceptions of Physician-Assisted Suicide: The Influence of Values, Attitudes and Religion. (Abstract) *The Gerontologist*, 38:352, 1998.

Blank K, Robison JT, Schwartz H, Gruman C: Late-Life Depression: A Naturalistic Study of Inpatient Treatment. *The Gerontologist,* 38:373, 1998.
Walker L, Gruman C, Blank K, Schwartz HI: Physician Assisted Suicide: Attitudes and Experiences of Connecticut Physicians. *Journal of the American Geriatric Society 1999,* 47(9), S99.

Schwartz HI*, Curry Walker L, Gruman C, Blank K: Physicians' Views on Physician Assisted Suicide: Looking Beyond the Numbers. *The Gerontologist,* 39:215, 1999.

Walker L, Gruman C, Blank K, Schwartz HI: Physician Assisted Suicide: Religion Is Strongest Predictor of Physician Endorsement. *The Gerontologist,* 39:10, 1999.:

Schwartz HI, Curry L, Gruman C, Blank K: Palliative Care: An Alternative to Physician Assisted Suicide? *The Gerontologist,* 40:1:132, 2000.

Blank K, Robison J, Doherty E, Prigerson H, Schwartz, HI: Depression Increases Older Hospitalized Patients' Interest in Physician Assisted Death (PAD). *The Gerontologist,* 40(I):301, 2000.

Ruano G, Seip RL, Gorowski K, Szarek B, Schwartz HI, Goethe JW. Changes in Psychotropic Prescription during Hospitalization of Depressed Patients Correlated with Innate CYP2D6 Function. *American Psychiatric Association Annual Meeting,* 2013.

NON-REFEREED ARTICLES:

Schwartz HI: A person is a Person but a SHPOS is Not. *Man and Medicine* 5:3:226-228, 1980.

Schwartz HI: Informed Consent for Psychiatrists. *Bulletin of the Area II Council of the American Psychiatric Association* 27:5:7, 1985.

Schwartz HI: Resuscitation Decisions: The Impact on Clinicians' Attitudes. *Bulletin of the Area II Council of the American Psychiatric Association* 29:1:7-8, 1986.

Schwartz HI: Legal and Ethical Issues in Neuroleptic Noncompliance. *Psychiatric Annals* 16:588-595, 1986.

NON-REFEREED ARTICLES: (cont.)

Schwartz HI*, Rachlin S: The Growing "Right" to Access Mental Health Records. *Newsletter of the American Academy of Psychiatry and the Law* 12:2:28-29, 1987.

Schwartz HI: The Institute of Living: One Hundred and Seventy-Five Years of Innovation and Excellence (editorial). *Connecticut Medicine* 61:517-519, 1997.

Schwartz HI: Competent to Screen Competency? (article review) The Forensic Echo III:2:14-15, 1999.

Schwartz HI: Mental Health Services in Connecticut: Troubled Systems in a Time of Crisis (editorial). *Connecticut Medicine,* 64:325-327, 2000.

Schwartz HI: Death Row Syndrome and Demoralization: Psychiatric Means to Social Policy Ends (editorial). *Journal of the American Academy of Psychiatry and the Law*, 33:153-155, 2005.

BOOK CHAPTERS:

Schwartz HI*, Rachlin S: "Patient Access to Mental Health Records: Impact on Clinical Practice." *In* Rachlin S (Ed.) *Legal Encroachment on Psychiatric Practice.* New Directions for Mental Health. San Francisco, Jossey-Bass, March, 1985.

Schwartz HI: "DNR Orders: The Role of Clinicians' Attitudes." *In* Rosner R, Schwartz HI (Eds.) *Geriatric Psychiatry and the Law: Critical Issues in American Psychiatry and the Law, Volume 3.* Plenum Press, New York, 1987.

Schwartz HI*, Roth LH: "Informed Consent and Competency in Psychiatric Practice." *In* Tasman A. (Ed.) *American Psychiatric Press Review of Psychiatry, Volume 8*, American Psychiatric Press, Inc., Washington, D.C., 1989.

Blank K, Schwartz HI: "Inpatient Geriatric Psychiatry: Special Forensic Considerations." *In* Bluestone H, Travin S, Marlowe DB (Eds.) *Psychiatric-legal Decision Making by the Mental Health Practitioner: The Clinician as De Facto Magistrate.* John Wiley and Sons, Inc., New York, 1994.

Schwartz HI: "Informed Consent and Competency." *In* Rosner R. (Ed.) *Principles and Practice of Forensic Psychiatry.* Chapman and Hall, New York, 1994.

Zeman P, Schwartz HI: "Hospitalization: Voluntary and Involuntary." *In* Rosner R. (Ed.) *Principles and Practice of Forensic Psychiatry.* Chapman and Hall, New York, 1994.

BOOK CHAPTERS: (cont.)

Schwartz HI: "The Impact of Cost Containment Measures on Somatic Psychiatry." *In* Schwartz HI (Ed.) *Psychiatric Practice Under Fire: The Influence of Government, the Media and Special Interests on Somatic Therapies*. American Psychiatric Press, Inc., 1994.

Schwartz HI*, Greenblatt DJ: "The Misapplication of Controlled Substance Regulation to Benzodiazepines. *In* Schwartz HI (Ed.) *Psychiatric Practice Under Fire: The Influence of Government, the Media and Special Interests on Somatic Therapies*. American Psychiatric Press, Inc., 1994.

Anderson R, Klimek J, Tiernan C, Fagan JL, Schwartz HI: "Psychology of a Triad." *In* Stetler C and Charns M (Eds.) *Collaboration in Health Care: Hartford Hospital's Journey in Changing Management Practice.* American Hospital Association Publications, 1995.

Schwartz, HI, Mack DM: Informed Consent and Competency. *In* Rosner R. (Ed.) *Principles and Practice of Forensic Psychiatry, 2nd Edition.* Arnold Publishers, London, 2003.

Schwartz, HI, Mack DM, Zeman P: "Hospitalization: Voluntary and Involuntary." *In* Rosner R. (Ed.) *Principles and Practice of Forensic Psychiatry, 2nd Edition.* Arnold Publishers, London, 2003.

Schwartz, HI: Foreword to Goodheart, Lawrence. *Mad Yankees: The Hartford Retreat for the Insane and Nineteenth-Century Psychiatry.* University of Massachusetts Press, September 2003.

Schwartz, HI, Sharfstein S: "Administration and Leadership." *In* Sharfstein S. (Ed.) *The Textbook of Hospital Psychiatry.* American Psychiatric Press, Inc. 2009.

BOOKS:

Rosner R, Schwartz HI (Eds.) *Geriatric Psychiatry and the Law: Critical Issues in American Psychiatry and the Law, Volume 3*, Plenum Press, New York, 1987.

Rosner R, Schwartz HI (Eds.) *Juvenile Psychiatry and the Law: Critical Issues in American Psychiatry and the Law, Volume 4*, Plenum Press, New York, 1989.

Schwartz HI (Section Ed.) Section on Legal Regulation of Psychiatric Practice. *In* Rosner R. (Ed.) *Principles and Practice of Forensic Psychiatry.* Chapman and Hall, New York, 1994.

Awarded Honorable Mention, the American Psychiatric Association's Guttmacher Prize Competition, 1995.

BOOKS: (cont.)

Schwartz HI (Ed.) *Psychiatric Practice Under Fire: The Influence of Government, the Media and Special Interests on Somatic Therapies.* American Psychiatric Press, Inc. September 1994.

Awarded Honorable Mention, the American Psychiatric Association's Guttmacher Prize Competition, 1996.

Schwartz HI (Section Ed.) Section on Legal Regulation of Psychiatric Practice. *In* Rosner R. (Ed.) *Principles and Practice of Forensic Psychiatry, 2nd Edition.* Arnold Publishers, London, 2003.

BOOK REVIEWS:

Schwartz HI: Perspectives on Psychiatric Malpractice. *Contemporary Psychiatry* 2:2:108-110, 1983.

Schwartz HI: Terrorism and the Role of Psychiatry. *Contemporary Psychiatry* 3:3:172-174, 1984.

Schwartz HI: Review of *Ethics and Law in Mental Health Administration* by W.E. Barton and G.E. Barton. Hospital and Community Psychiatry 36:304, 1985.

Schwartz HI: Review of *A Time to Die: The Place for Physician Assistance* by Charles F. McKhann. Connecticut Medicine 63: 313-314, 1999.

Schwartz HI: Review of *Negotiating a Good Death: Euthanasia in the Netherlands* by Robert Pool. American Journal of Geriatric Psychiatry 11:376, 2003.

Revised 5/24/13

Stuart K Markowitz, MD, FACR

66 Berwyn Road
West Hartford, CT 06107
860.313.1121
smarkow@harthosp.org

Education

Yale University and University of Pennsylvania: Visiting Fellowships in Gastrointestinal Radiology	July-October 1985
Hartford Hospital: Diagnostic Radiology Residency	1982-1985
Hartford Hospital: Flexible Internship	1981-1982
University of Health Sciences – The Chicago Medical School Degree: M.D.	1977-1981
University of Pennsylvania – Degree: B.A.	1973-1977

Professional Work Experience

Hartford Hospital: President, Hartford Hospital & Hartford Region	2013 - present
Hartford Hospital: Chief Medical Officer and Vice President	2012-2013
Jefferson Radiology: Radiologist	1985-2011

Administrative and Professional Activities

Board of Directors, VNA Healthcare	2012-present
Board of Directors, HPA and HPHO, Hartford Hospital	2012-present
Hartford Healthcare Board Quality and Safety Committee	2010-present
Hartford Hospital Board Credentialing and Quality Committee	2010-present
Board of Directors, Hartford Hospital	2010-2011
Vice President, Medical Staff, Hartford Hospital	2010-2011
Chairman, Department of Radiology, Hartford Hospital	1995-2011
Vice Chair, Department of Radiology, Hartford Hospital	1992-1995
Medical Director, Radiology Technology Program, Hartford Hospital	1990-2011
Section Chief, Gastrointestinal Radiology, Hartford Hospital	1985-2011
Section Chief, Emergency Radiology, Hartford Hospital	1992-2007
Full Time Instructor in the Diagnostic Radiology Residency Program at Hartford Hospital	1985-present

Partner, Jefferson Radiology (Jefferson X-Ray Group)	1986-2011
Board of Directors, Jefferson Radiology	1988-2011
President, 937-941 Farmington Avenue Limited Partnership	1991-2011
American College of Radiology Practice Certification Reviewer	1985-1990
Statewide Healthcare Facilities Planning Advisory Body, Department of Public Health, CT	2010-present
Office of Healthcare Access CON Task Force	2009-present
Connecticut State Radiology Society Legislative Committee	2005-2009

Hospital Committee Experience : Medical Staff Council, Executive Committee of the Medical Staff, Joint Conference Committee, Mead Fund Committee, Library Committee, Credentials Committee, Radiation Safety Committee, Radiology Management Committee, Radiology Quality Council, Risk Management Committee, Claims Review Committee, Radiology/IT Steering Committee, Reimbursement Committee, Technology Advisory Group, Endovascular Credentialing Committee, OR Committee, EMR Committee, IS Physician Advisory Committee, Tumor Board

Hartford Hospital CEO Advisory Body	2009-present

Certifications

Medical License – State of Massachusetts	2011
Fellowship in the American College of Radiology: FACR	2009
American Board of Radiology	1985
Medical License – State of Connecticut	1983
National Board of Medical Examiners	1982

Hospital Appointments

Hartford Hospital, Senior Attending Staff – Hartford, Connecticut

Connecticut Children's Medical Center, Attending Staff – Hartford, Connecticut

University of Connecticut Health Center, Assistant Clinical Professor – Farmington, Connecticut

Johnson Memorial Hospital, Attending Staff – Stafford Springs, Connecticut

Windham Hospital, Attending Staff – Willimantic, Connecticut

Day Kimball Hospital, Attending Staff – Putnam, Connecticut

Noble Hospital, Attending Staff – Westfield, Massachusetts

Current Memberships

Society of Chairman of Academic Radiology Departments
American College of Radiology
American Society of Emergency Radiology – Fellow
Radiologic Society of North America
American Roentgen Ray Society
Connecticut State Radiology Society
Society of Breast Imaging – Fellow
American College of Physician Executives

Publications

ZITER FMH, MARKOWITZ SK, ZAMSTEIN J. LARGE RENAL PELVIC DEFECTS CAUSED BY SOUGHED PAPILLA. APPLIED RADIOLOGY, NOV. 1987.

PISTOIA F AND MARKOWITZ S. SPLENIC LYMPHANGIOMATOSIS: CT DIAGNOSIS. AJR 150: 121-22, JANUARY 1988.

MARKOWITZ S AND ZITER F. THE LATERAL CHEST FILM AND PNEUMOPERITONEUM. ANNALS OF EMERGENCY MEDICINE 15:4 APRIL 1986.

JACOBS J AND MARKOWITZ S. CT DIAGNOSIS OF UTERINE LIPOMA. AJR 150:1335-1336, JUNE 1988.

WOLF S AND MARKOWITZ S. SPONTANEOUS GAS FORMATION IN A STERILE RENAL CELL CARCINOMA. UROLOGIC RADIOLOGY 9:222-224, 1988.

PISTOIA F, MARKOWITZ S, SUSSMAN S. CONTRAST MATERIAL IN POSTERIOR VAGINAL FORNIX MIMICKING BLADDER RUPTURE: CT FEATURES. JCAT 13(1):153-155 JAN/FEB 1989.

MILICI L AND MARKOWITZ S. INTRAMURAL GASTRIC PSEUDOCYST: CT DIAGNOSIS. GASTROINTESTINAL RADIOLOGY, VOL 14:113-114, 1989.

TREEM WR, MARKOWITZ SK, SULLIVAN BM, HYAMS JS. DEFECOGRAPHY IN CHILDREN WITH PROLONGED CONSTIPATION. ABSTRACT SUBMITTED AT THE NORTH AMERICAN SOCIETY FOR PEDIATRIC GASTROENTEROLOGY AND NUTRITION, 1990.

MARKOWITZ SK, ZITER FMH. RADIOLOGIC DIAGNOSIS OF BOWEL OBSTRUCTION. IN: BOWEL OBSTRUCTION, CLINICAL DIAGNOSIS AND MANAGEMENT. J. WELCH, ED. SAUNDERS, 1990.

SAWHNEY R, REES JH, MARKOWITZ SK. CLOSTRIDIAL GAS GANGRENE COMPLICATING LEUKEMIA. ABDOMINAL IMAGING 19:45102, 1994.

SCAPPATICCI F AND MARKOWITZ SK. INTRAHEPATIC PSEUDOCYST COMPLICATING ACUTE PANCREATITIS: IMAGING FINDINGS. AJR, 1995; 165:873-4.

MARKOWITZ SK. DELAYED RUPTURE OF THE GALLBLADDER: DIAGNOSIS BY ERCP. SUBMITTED FOR PUBLICATION.

MARKOWITZ SK. BILIARY OBSTRUCTION DUE TO DUODENAL DIVERTICULUM: DIAGNOSIS BY CT AND ERCP. SUBMITTED FOR PUBLICATION.

MARKOWITZ SK. LONG TERM ALIMENTATION: COMPARISON

OF INTRAVENOUS AND NASOENTERIC ALIMENTATION. WORK IN PROGRESS.

ALLMENDINGER N, HALLISEY MJ, MARKOWITZ SK, ET AL. BALLOON DILATION OF ESOPHAGEAL STRICTURES IN CHILDREN. J. OF PEDIATRIC SURGERY, VOL 31, NO 3, P334-6, MARCH 1996.

CIRAULO DL, NIKKANEN HE, PALTER M, MARKOWITZ S, ET AL. CLINICAL ANALYSIS OF THE UTILITY OF REPEAT COMPUTED TOMOGRAPHIC SCAN BEFORE DISCHARGE IN BLUNT HEPATIC INJURY. JOURNAL OF TRAUMA 41(5):821-824, NOVEMBER 1996.

MARKOWITZ SK, KIRECZYK W. RADIOLOGIC EVALUATION OF DIVERTICULAR DISEASE OF THE SMALL AND LARGE INTESTINES. IN DIVERTICULAR DISEASE: MANAGEMENT OF THE DIFFICULT SURGICAL CASE. J. WELCH, ED. WILLIAMS AND WILKINS, 1997.

Recognitions Awards

Best Doctors in Hartford, Hartford Magazine	2004-2012
Best Doctors in Connecticut, Connecticut Magazine	2010-2012

Current Work Contact Information

Stuart K Markowitz, MD, FACR
Chief Medical Officer and Vice President
Hartford Hospital
80 Seymour Street
Hartford, CT 06102

860-545-5110
smarkow@harthosp.org

Personal

Born: April 22, 1955 – Brooklyn, New York

Wife: Debra Markowitz

Children: Melissa, Jessica, Nicole, Zachary
Stepson: Devin

GERALD J. BOISVERT, CPA, FHFMA
18 Alexander Place
South Windsor, CT 06074
860-644-6491 (Home)
860-545-0585 (Work)

Work Experience

April 2013	**Vice President & Chief Financial Officer**
To present	**Harford Hospital, Hartford, Connecticut**

Chief Financial Officer for 867 bed tertiary care academic medical center.

May 1997	**Executive Vice President & Chief Financial Officer**
To April 2013	**Connecticut Children's Medical Center, Hartford, Connecticut**

Executive Vice President & Chief Financial Officer for Connecticut's only independent Children's Hospital, and related entities (Faculty Practice Plan, School, and Foundation). Significant operational experience includes active financial oversight of 100 plus physician practice plan. Current responsibilities include Finance and Accounting, Revenue Cycle, Strategic Planning/Project Management/Process Improvement, Purchasing/Materials Management, Environmental Services, Facilities, Food Service, and Safety/Security. Previous responsibilities included oversight of IS, Community Relations, Rehabilitation Services, Pharmacy, Radiology and other ancillary services.

April 1996	**Vice President, Finance and Chief Financial Officer**
To May 1997	**US HomeCare Corp., Hartford, Connecticut**

Chief Financial Officer, reporting directly to the Chairman of the Board for publicly traded home care company. Responsibilities included direct supervision of accounting department, MIS department, and human resources department. Also responsible for investor relations, corporate secretary functions, SEC reporting, Medicare cost reporting, treasury and banking relationships. Worked in a turnaround/restructuring mode with crises management team and banks to stabilize and prepare company for sale.

August 1992	**Senior Vice President, Finance**
To April 1996	**Windham Community Memorial Hospital Willimantic, Connecticut**

Chief Financial Officer of 130-bed, acute care hospital, reporting to the President & CEO. Responsible for the following functions: Finance, Billing, Admitting/Registration, MIS, Medical Records, Personnel and Purchasing departments. Significant focus and

involvement with third party reimbursement, regulatory issues, banking/financing matters and union negotiations.

April 1988 To August 1992 — **Executive Vice President – Finance and Administration, Alden Design, Inc., Glastonbury, Connecticut**

Chief Financial and Administrative Officer of multi-location, full service communications company providing communications, consulting and production services to Fortune 1000 companies. Specific areas of responsibility included cash management, accounting, strategic planning, budgeting, human resources administration and company marketing/advertising.

September 1980 To April 1988 — **Senior Manager, Ernst & Whinney, Hartford, Connecticut**

Certified Public Accountant. Responsible for audit and special project consulting engagements for companies involved in manufacturing, banking, health care, education and non-profit services.

July 1979 To September 1980 — **Advanced Staff Accountant, Wolf & Company, Boston, Massachusetts**

Staff accountant for regional accounting firm located in Massachusetts. Served as staff accountant and in-charge accountant on savings bank, construction and small business audit engagements.

Education

Boston University School of Management
B.S. in Business Administration

Professional

Certified Public Accountant
Fellow, Health Care Financial Management Association

Member: American Institute of Certified Public Accountants; Connecticut Society of Certified Public Accountants; Health Care Financial Management Association; American College of Healthcare Executives

Community Service

Former Board Member and Finance Committee Chair of University of St. Joseph; Treasurer and member of the Board of Directors of the Capital Area Health Consortium; member of Committee of Hospital Finance for The Connecticut Hospital Association;

Community Service - continued

Former President and former Treasurer of Southside Institution Neighborhood Alliance (SINA) and former Chairman of the Board of The Learning Corridor Corporation; former Finance Chairman and Personnel Chairman of Canon Greater Hartford Open (PGA Tournament); former member of Vernon, Connecticut Economic Development Commission; and former Treasurer and Director of Sunshine Project, Inc. (a non-profit organization involved in housing and support services for the psychiatrically disabled).

Recognized as CFO of the year by Hartford Business Journal - 2011

Other Interests: Enjoy sailing, skiing, running, tennis and golf.

EXHIBIT 5

U. S. TREASURY DEPARTMENT
INTERNAL REVENUE SERVICE
WASHINGTON 25, D. C.

Vault

IN REPLY REFER TO
T:R:EO:4
VCJ

JAN 6 1960

Hartford Hospital
Hartford 15, Connecticut

Gentlemen:

This refers to your letter of November 13, 1959 in which you state that you received a ruling from this office dated August 11, 1953, exempting you from Federal income tax under the provisions of section 101(6) of the Internal Revenue Code. This ruling also had the effect of affirming prior rulings dated August 28, 1934, September 19, 1938 and January 27, 1941. You are now requesting that your status be brought up to date to conform with the 1954 Code, section 501(c)(3).

Treasury Regulations prescribed under the Internal Revenue Code of 1954 provide at section 1.501(a)-1(a)(2), as amended by Treasury Decision 6391, published June 26, 1959, for situations such as yours and read, in part, as follows:

> "Subject only to the Commissioner's inherent power to revoke rulings because of a change in the law or regulations or for other good cause, an organization that has been determined by the Commissioner or the district director to be exempt under section 501(a) or the corresponding provision of prior law may rely upon such determination so long as there are no substantial changes in the organization's character, purposes, or methods of operation. An organization which has been determined to be exempt under the provisions of the Internal Revenue Code of 1939 or prior law is not required to secure a new determination of exemption merely because of the enactment of the Internal Revenue Code of 1954 unless affected by substantive changes in law made by such Code."

In view of the present Regulations you are not required to have your existing exempt status affirmed under the 1954 Code in the absence of basic changes in your organization and/or operations. If you prefer, as a matter of convenience, to have a current ruling on your

status it will be necessary for you to file a new exemption application, Form 1023, with your District Director at Hartford, Connecticut, together with all supporting documents required by the application, as well as a statement in some detail concerning your activities subsequent to 1953. Inasmuch as we have on file the copies of your charter and by-laws submitted with your prior application, further copies of these documents need not be furnished, but any amendments subsequent to July 1953 should be supplied. For your use in this connection, there are enclosed three copies of Form 1023, two executed copies of which may be filed and the third may be retained for your use.

A cursory examination of your charter shows that it does not specify that you are organized as a nonprofit charitable hospital, contains no provision requiring you to be operated to the extent of your financial ability for those not able to pay for the services rendered, and other requirements of Revenue Ruling 56-185, published in Internal Revenue Bulletin 1956-1, page 202, which establishes the criteria to be met in determining whether a hospital qualifies for exemption as an organization described in section 501(c)(3) of the 1954 Code. Further, your charter does not contain any provision impressing your assets with a trust by providing that in the event of dissolution your assets are required to be distributed for one or more of the purposes described in section 501(c)(3). In this connection your attention is invited to section 1.501(c)(3)-1(b)(6) of the Regulations which reads, in part, as follows:

> "Applicability of the organizational test. A determination by the Commissioner or a district director that an organization is described in section 501(c)(3) and exempt under section 501(a) will not be granted after July 26, 1959 (regardless of when the application is filed), unless such organization meets the organizational test prescribed by this paragraph. If, before July 27, 1959, an organization has been determined by the Commissioner or district director to be exempt as an organization described in section 501(c)(3) or in a corresponding provision of prior law and such determination has not been revoked before such date, the fact that such organization does not meet the organizational test prescribed by this paragraph shall not be a basis for revoking such determination. Accordingly, an organization which has been determined to be exempt before July 27, 1959, and which does not seek a new determination of exemption is not required to amend its articles of organiza-

tion to conform to the rules of this paragraph, but any organization which seeks a determination of exemption after July 26, 1959, must have articles of organization which meet the rules of this paragraph.
* * *"

This office is also in receipt of a communication, dated April 16, 1959, from Shipmen & Goodwin, Counselors at law, Hartford, Connecticut, submitting in your behalf a request for a ruling on certain proposed transaction contemplated by you with respect to their effect on your exempt status. You are advised that our reply to this request will be held in abeyance pending receipt of advice from you as to what further action you intend to take with regard to having your status affirmed under the Internal Revenue Code of 1954.

Your reply should also contain information concerning any implementing action which you may have taken subsequent to April 1959 with regard to the proposed transactions.

Your reply should be directed to the attention of T:R:EO:4-VCS.

Very truly yours,

G. F. Worley

Chief, Exempt Organizations Branch

Enclosure:
Form 1023 (3)

EXHIBIT 6

STATE OF CONNECTICUT

Department of Public Health

LICENSE

License No. 0046

General Hospital

In accordance with the provisions of the General Statutes of Connecticut Section 19a-493:

Hartford Hospital of Hartford, CT d/b/a Hartford Hospital is hereby licensed to maintain and operate a General Hospital.

Hartford Hospital is located at 80 Seymour Street and 200 Retreat Avenue, Hartford, CT 06106.

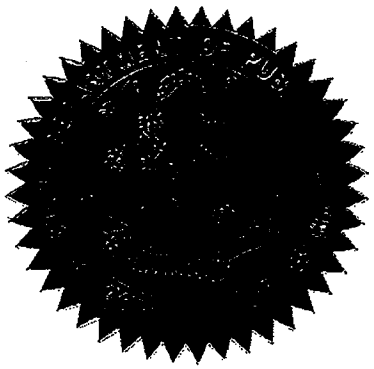
The maximum number of beds shall not exceed at any time:

48 Bassinets
819 General Hospital Beds

This license expires **December 31, 2015** and may be revoked for cause at any time.
Dated at Hartford, Connecticut, January 1, 2014. RENEWAL.

Satellites:
West Hartford Surgery Center, 65 Memorial Road, Suite 500, West Hartford
Hartford Hospital, 505 Willard Avenue, Bldg. 3, Newington

License Revised to Reflect:
Removed (1) Satellite - Duncaster Primary Care Satellite, 40 Loeffler Road, Bloomfield effective 10/1/13.



Jewel Mullen, MD, MPH, MPA
Commissioner

EXHIBIT 7

Olin Building 3T-MRI Scanner

ARCHITECTURAL NARRATIVE

The Institute of Living
Hartford, Connecticut

November 12, 2013

Prepared by:

Tecton Architects, PC
One Hartford Square West
Hartford CT, 06106

Tecton Project No. IL5301

Reports and Calculations

1) Basis of Design Report:

   a) MRI Addition building description (commonly known as Olin Center Building)

      i) A new building single story addition to house a new MRI is proposed at the north end of the existing Whitehall Building in the IOL campus. The new addition will be a single story structure with prefabricated steel truss roof. The new addition will be 1,322 S.F. gross area and will consist of load bearing walls supporting prefabricated steel trusses. The new eave and ridge heights will match the existing roof heights. The slab on grade under the MRI unit will be isolated physically from the parent structure and sound isolated as well. The MRI suite will be independent of the adjacent MRI with its own computer, control rooms and redundant MEP systems. There will be no basement.

2) Code Analysis:

   a) New additions design shall meet minimum requirements of the following:
      i) 2003 International Building Code (2005 Connecticut Supplement & 2009 Amendment)
      ii) 2005 Connecticut State Fire Safety Code (2009 Amendments)
      iii) 2006 International Energy Conservation Code.
      iv) ICC/ANSI A177.1 / 2003 Accessible and usable buildings and facilities & UFAS
      v) International Fire Code / 2003 ICC

2) Building Type:

   a) MRI Addition: IIIB

3) Use Category:

   a) MRI Addition: B - Business

4) Area analysis:

   a) Gross Area:

      i) MRI Addition: 1,322 S.F.

   b) Net Area:

      i) MRI Addition: 809 S.F.

5) Growth potential:

   a) No building growth is being forecasted at this time as the area on the campus in the vicinity of the new additions is very limited.

6) Description of Green/Sustainable Design elements included:

a) The project is designed to meet LEED certification; however the building will not be applied for through the USGBC.

7) Building envelope analysis:

   a) Overall building envelope.

      i) The overall Olin Building envelope will consist of bearing and non-bearing CMU walls insulated within: continuous insulation on the outside of the wall with an exterior air barrier and interior vapor barrier. The building will be clad with a combination of "EIFS", brick veneer and stone veneer.

   b) Thermal vapor flow and moisture:

      i) A combination of soffit vents, eave vents, ridge vents, roof vents and proper vents have been incorporated into the design to provide air circulation at all roof locations.

   c) Recommendations for vapor barriers.

      i) Vapor barriers will be located on the warm in winter side of all walls, slab on grade and ceiling locations. They will be made of sheet plastic, all seams and penetrations will be taped.

8) Asbestos report:

   a) Asbestos remediation is part of the owner's responsibilities and is not addressed in these documents.

9) MRI Addition:

   a) Non-ferrous construction requirements:

      i) The magnet will be shimmed accordingly and the gauss line will be adjusted to compensate for any stationary ferrous metals. The 0.5 mT gauss line will be contained within the magnet room.

      ii) Metal studs can be used without interfering with the magnet. Wood studs are not required.

      iii) Fiberglass reinforcing in the concrete slab and foundation walls is not required, steel can be used.

      iv) Aluminum ceiling grid will be specified for the magnet room.

   b) Magnetic shielding requirements:

      i) Not required as the 0.5 mT line is within the walls containing the magnet.

   c) RF shielding requirements:

      i) The magnet room is shielded as designed and provided by ETS Lindgren.

d) Acoustical requirements:

   i) Followed section 1.2-6 of the Guidelines for Design and Construction of Health Care Facilities 2010 and have mirrored the acoustical design of the sister magnet operational since 2007 functioning at 100% of owners desired performance.

e) Vibration requirements:

   i) Designed and provided by Siemens.

   ii) The magnet slab has been isolated from the adjacent slab and foundation wall with a 2" isolation joint.

f) Noise requirements:

   i) Provided by Siemens.

g) Magnet cooling:

   i) The magnet is cooled with in internal H_e circulation tied to the chiller located in the computer room. No external storage is required.

h) Magnet utilities:

   i) The magnet utilities are provided overhead, no trenches are required for cabling or cooling.

i) Quench vent:

   i) Siemens provides the Cryogen vent serving the MRI magnet with direct connection to the magnet and piped to the exterior of the building above the low roof.

   ii) The Scan Room / Exam Room Ventilation Fan is equipped with an Oxygen deprivation sensor on battery back-up power installed within the room. If the level of oxygen in the room is below set point (indicating a release of cryogen refrigerant) fan EF-10 shall start and an alarm shall sound.

End

EXHIBIT 8

12. C (i). Please provide one year of actual results and three years of projections of **Total Facility** revenue, expense and volume statistics without, incremental to and with the CON proposal in the following reporting format:

Total Facility: Description	FY 2012 Actual Results	FY 2013 Actual Results	FY 14 Projected W/out CON	FY 14 Projected Incremental	FY 14 Projected With CON	FY 15 Projected W/out CON	FY 15 Projected Incremental	FY 15 Projected With CON	FY 2016 Projected W/out CON	FY 16 Projected Incremental	FY 16 Projected With CON
NET PATIENT REVENUE											
Non-Government	$421,071,330	$439,164,968	$504,994,994		$504,994,994	$521,407,331		$521,407,331	$540,125,854		$540,125,854
Medicare	$381,926,070	$376,476,032	$375,474,280		$375,474,280	$387,677,194		$387,677,194	$401,594,805		$401,594,805
Medicaid and Other Medical Assistanc	$114,354,648	$99,237,056	$111,971,347		$111,971,347	$115,610,416		$115,610,416	$119,760,830		$119,760,830
Other Government	$9,281,003	$6,374,332	$6,084,024		$6,084,024	$6,281,755		$6,281,755	$6,507,270		$6,507,270
Total Net Patient Patient Revenue	$926,633,051	$921,252,388	$998,524,645	$0	$998,524,645	$1,030,976,696	$0	$1,030,976,696	$1,067,988,759	$0	$1,067,988,759
Other Operating Revenue	$172,515,114	$163,350,558	$145,471,573	$268,439	$145,740,012	$148,453,740	$284,545	$148,738,285	$153,738,693	$304,464	$154,043,157
Revenue from Operations	$1,099,148,165	$1,084,602,946	$1,143,996,218	$268,439	$1,144,264,657	$1,179,430,436	$284,545	$1,179,714,981	$1,221,727,453	$304,464	$1,222,031,917
OPERATING EXPENSES											
Salaries and Fringe Benefits	$604,512,881	$633,026,330	$606,093,983	$138,036	$606,232,019	$637,732,089	$142,177	$637,874,266	$667,705,497	$147,153	$667,852,650
Professional / Contracted Services	$44,286,457	$49,630,461	$51,410,354	$12,672	$51,423,026	$53,980,872	$12,059	$53,992,931	$56,679,915	$12,903	$56,692,818
Supplies and Drugs	$133,308,976	$166,401,219	$153,687,097	$2,076	$153,689,173	$164,445,194	$2,139	$164,447,333	$175,956,357	$2,203	$175,958,560
Bad Debts	$22,645,968	$17,467,613	$22,740,654		$22,740,654	$23,479,725		$23,479,725	$24,322,647		$24,322,647
Other Operating Expense	$173,935,441	$133,659,193	$189,269,610	$292,571	$189,562,181	$193,055,002	$293,997	$193,348,999	$196,916,102	$295,481	$197,211,583
Subtotal	$978,689,723	$1,000,184,816	$1,023,201,698	$445,355	$1,023,647,053	$1,072,692,882	$450,372	$1,073,143,254	$1,121,580,519	$457,740	$1,122,038,259
Depreciation/Amortization	$46,274,726	$48,796,972	$45,855,088	$545,974	$46,401,062	$64,731,581	$545,974	$65,277,555	$66,756,581	$545,974	$67,302,555
Interest Expense	$4,517,043	$5,704,487	$5,649,775		$5,649,775	$5,483,210		$5,483,210	$5,943,000		$5,943,000
Lease Expense	$17,167,465	$34,920,187	$17,960,797		$17,960,797	$18,320,013		$18,320,013	$18,686,413		$18,686,413
Total Operating Expense	$1,046,648,957	$1,089,606,462	$1,092,667,358	$991,329	$1,093,658,687	$1,161,227,686	$996,346	$1,162,224,032	$1,212,966,514	$1,003,714	$1,213,970,228
Gain/(Loss) from Operations	$52,499,208	($5,003,516)	$51,328,860	($722,890)	$50,605,970	$18,202,750	($711,801)	$17,490,949	$8,760,939	($699,250)	$8,061,689
Plus: Non-Operating Revenue	$56,285,568	$42,330,877	$20,461,000		$20,461,000	$20,461,000		$20,461,000	$20,461,000		$20,461,000
Revenue Over/(Under) Expense	$108,784,776	$37,327,361	$71,789,860	($722,890)	$71,066,970	$38,663,750	($711,801)	$37,951,949	$29,221,939	($699,250)	$28,522,689
FTEs	6,033	6,125	5,872		5872	5872		5872	5,872		5872
									25,000		

*Volume Statistics:
Provide projected inpatient and/or outpatient statistics for any new services and provide actual and projected inpatient and/or outpatient statistics for any existing services which will change due to the proposal.

EXHIBIT 9

12.C(ii). Please provide **three** years of projections of incremental revenue, expense and volume statistics **attributable to the proposal** in the following reporting format:

Type of Service Description **Neuroscience research - MRI**
Type of Unit Description: **Siemens Skyra 3T MRI scanner**
# of Months in Operation 12

FY 14 **FY Projected Incremental** Total Incremental Expenses: **$991,329** **Total Facility by Payer Category:**	(1)	(2) Rate	(3) Units	(4) Gross Revenue Col. 2 * Col. 3	(5) Allowances/ Deductions	(6) Charity Care	(7) Bad Debt	(8) Net Revenue Col.4 - Col.5 -Col.6 - Col.7	(9) Operating Expenses Col. 1 Total * Col. 4 / Col. 4 Total	(10) Gain/(Loss) from Operations Col. 8 - Col. 9
Medicare				$0				$0	$0	$0
Medicaid		$0		$0				$0	$0	$0
CHAMPUS/TriCare		$0		$0				$0	$0	$0
Total Governmental			0	$0	$0	$0	$0	$0	$0	$0
Commericial Insurers		$0		$0				$0	$0	$0
Uninsured		$0		$0				$0	$0	$0
Total NonGovernment		$0	0	$0	$0	$0	$0	$0	$0	$0
Total All Payers		$0	0	$0	$0	$0	$0	$0	$991,329	($991,329)

12.C(ii). Please provide **three** years of projections of incremental revenue, expense and volume statistics **attributable to the proposal** in the following reporting format:

Type of Service Description	**Neuroscience research - MRI**
Type of Unit Description:	**Siemens Skyra 3T MRI scanner**
# of Months in Operation	12

FY 15 **FY Projected Incremental** Total Incremental Expenses:	(1) **$996,346**	(2) Rate	(3) Units	(4) Gross Revenue Col. 2 * Col. 3	(5) Allowances/ Deductions	(6) Charity Care	(7) Bad Debt	(8) Net Revenue Col.4 - Col.5 -Col.6 - Col.7	(9) Operating Expenses Col. 1 Total * Col. 4 / Col. 4 Total	(10) Gain/(Loss) from Operations Col. 8 - Col. 9
Total Facility by Payer Category:										
Medicare				$0				$0	$0	$0
Medicaid		$0		$0				$0	$0	$0
CHAMPUS/TriCare		$0		$0				$0	$0	$0
Total Governmental			0	$0	$0	$0	$0	$0	$0	$0
Commericial Insurers		$0		$0				$0	$0	$0
Uninsured		$0		$0				$0	$0	$0
Total NonGovernment		$0	0	$0	$0	$0	$0	$0	$0	$0
Total All Payers		$0	0	$0	$0	$0	$0	$0	$996,346	($996,346)

12.C(ii). Please provide **three** years of projections of incremental revenue, expense and volume statistics **attributable to the proposal** in the following reporting format:

Type of Service Description: **Neuroscience research - MRI**
Type of Unit Description: **Siemens Skyra 3T MRI scanner**
# of Months in Operation: 12

FY 16 **FY Projected Incremental** Total Incremental Expenses:	(1) **$1,003,714**	(2) Rate	(3) Units	(4) Gross Revenue Col. 2 * Col. 3	(5) Allowances/ Deductions	(6) Charity Care	(7) Bad Debt	(8) Net Revenue Col.4 - Col.5 -Col.6 - Col.7	(9) Operating Expenses Col. 1 Total * Col. 4 / Col. 4 Total	(10) Gain/(Loss) from Operations Col. 8 - Col. 9
Total Facility by Payer Category:										
Medicare				$0				$0	$0	$0
Medicaid		$0		$0				$0	$0	$0
CHAMPUS/TriCare		$0		$0				$0	$0	$0
Total Governmental			0	$0	$0	$0	$0	$0	$0	$0
Commericial Insurers		$0		$0				$0	$0	$0
Uninsured		$0		$0				$0	$0	$0
Total NonGovernment		$0	0	$0	$0	$0	$0	$0	$0	$0
Total All Payers		$0	0	$0	$0	$0	$0	$0	$1,003,714	($1,003,714)

STATE OF CONNECTICUT

DEPARTMENT OF PUBLIC HEALTH

Office of Health Care Access

March 14, 2014

VIA FAX ONLY

Barbara A. Durdy
Director, Strategic Planning
Hartford Healthcare
181 Patricia Genova Drive
Newington, CT 06111

RE: Certificate of Need Application, Docket Number 14-31901-CON
Hartford Hospital
Acquisition of a Magnetic Resonance Imaging Scanner for research study

Dear Ms. Durdy:

On February 14, 2014, the Office of Health Care Access ("OHCA") received your Certificate of Need ("CON") application filing on behalf of Hartford Hospital ("Applicant") proposing to acquire a Magnetic Resonance Imaging ("MRI") scanner, with a total associated cost of $3,342,905.

OHCA has reviewed the CON application and requests the following additional information pursuant to Connecticut General Statutes §19a-639a(c):

1. On page 14 of the CON application, the Applicant states that the proposed 3T MRI may be used for clinical patients who require a wide-bore scanner. Please provide further discussion on this as well as additional supporting documentation.

2. On pages 14-15 of the CON application, the Applicant provided the actual 2013 utilization for the proposed MRI that indicates that the proposed MRI was placed in service in 2013. Please provide additional documentation to answer the following:

    a. What date did the proposed MRI become operational?

3. Where do the Applicant's research study participants come from? Please elaborate on how participants are recruited for the Applicant's research studies.

4. On page 10 of the CON application, the Applicant states that the original intent was to replace the existing MRI scanner with the new proposed scanner. However, after filing the Determination letter with OHCA, the Applicant decided not to take the existing MRI scanner off-line as originally planned. Please elaborate and explain the need for the Applicant to have two MRI scanners for its studies.

5. Please address the following questions regarding the existing Allegra 3T scanner:

   a. How long does the Applicant plan to utilize the scanner?
   b. The Applicant states that parts and maintenance for this scanner will be provided until December 31, 2016.What is the Applicant's intent for this scanner after 2016?

6. Please address the following a through c below regarding your Medicaid population. If not applicable to your proposed MRI acquisition, please indicate so in your response and provide an explanation.

   a. Whether the Applicant has satisfactorily demonstrated how the proposal will improve quality, accessibility and cost effectiveness of health care delivery in the region, including, but not limited to, (1) provision of or any change in the access to services for Medicaid recipients and indigent persons, and (2) the impact on the cost effectiveness of providing access to services provided under the Medicaid program;

   b. The Applicant's past and proposed provision of health care services to relevant patient populations and payer mix, including, but not limited to, access to services by Medicaid recipients and indigent persons;

   c. Whether the Applicant, who has failed to provide or reduced access to services to Medicaid recipients or indigent persons, has demonstrated good cause for doing so, which shall not be demonstrated solely on the basis of differences in reimbursement rates between Medicaid and other health care payers.

In responding to the questions contained in this letter, please repeat each question before providing your response. Paginate and date your response, i.e., each page in its entirety. Information filed after the initial CON application submission (e.g., completeness response letter, prefile testimony, late file submissions and the like) must be numbered sequentially from the Applicant's document preceding it. Please begin your submission using Page 145 and reference "Docket Number: 14-31901-CON." Submit one (1) original and three (3) hard copies of your response. In addition, please submit a scanned copy of your response, in an Adobe format (.pdf)

including all attachments on CD. If available, a copy of the response in MS Word should also be copied to the CD.

Pursuant to Section 19a-639a(c) of the Connecticut General Statutes, you must submit your response to this request for additional information no later than sixty days after the date that this request was transmitted. Therefore, please provide your written responses to OHCA no later than May 13, 2014, otherwise your application will be automatically considered withdrawn. If you have any questions concerning this letter, please feel free to contact me by email or at (860) 418-7007.

Sincerely,

Alla Veyberman
Health Care Analyst

* * * COMMUNICATION RESULT REPORT (MAR. 14. 2014 9:03AM) * * *

FAX HEADER:

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E-1) HANG UP OR LINE FAIL
E-2) BUSY
E-3) NO ANSWER
E-4) NO FACSIMILE CONNECTION

STATE OF CONNECTICUT
OFFICE OF HEALTH CARE ACCESS

FAX SHEET

TO: BARBARA DURDY

FAX: 860.972.9025

AGENCY: HARTFORD HOSPITAL

FROM: OHCA

DATE: 3/14/14 **Time:**

NUMBER OF PAGES: 4
(including transmittal sheet

Comments:
Docket Number: 14-31901

PLEASE PHONE IF THERE ARE ANY TRANSMISSION PROBLEMS

Phone: (860) 418-7001 ***Fax: (860) 418-7053***

410 Capitol Ave., MS#13HCA
P.O.Box 340308
Hartford, CT 06134

STATE OF CONNECTICUT

DEPARTMENT OF PUBLIC HEALTH

Office of Health Care Access

May 2, 2014

VIA FAX ONLY

Barbara A. Durdy
Director, Strategic Planning
Hartford Healthcare
181 Patricia Genova Drive
Newington, CT 06111

RE: Certificate of Need Application, Docket Number 14-31901-CON
Hartford Hospital
Acquisition of a 3T Magnetic Resonance Imaging Scanner

Dear Ms. Durdy:

On April 4, 2014, the Office of Health Care Access ("OHCA") received completeness responses to the Certificate of Need ("CON") application proposing to acquire a Magnetic Resonance Imaging ("MRI") scanner, with a total associated cost of $3,342,905.

OHCA has reviewed the responses and requests the following additional information pursuant to General Statutes §19a-639a(c).

1. The Applicant provided a table with the number of research slots available per week on page 11 of the application. On page 15 of the application, the Applicant provided historic utilization showing a decline in volume. Please explain the following:

    a. The decline in utilization from 2011-2012 and the overall decline from 2011 to 2013.
    b. The relationship between decreasing historical volume and the need for the second scanner.

2. Provide updated actual utilization in Table 2a-b (Oct-Apr) for current fiscal year.

3. Provide documentation from the manufacturer demonstrating the end of development and maintenance availability in December 2016 for the Allegra 3T MRI.

4. The Applicant did not provide responses to Questions 3a and 3f on pages 16-17 of the application concerning projected volume.

a. Please provide projections and a detailed explanation of all assumptions used in the calculation of the projected volume.
b. Please provide an update on the pending NIH grants listed in Table A on page 11 of the application indicating if the applicant has been awarded any of the pending grants to date.

In responding to the questions contained in this letter, please repeat each question before providing your response. Paginate and date your response, i.e., each page in its entirety. Information filed after the initial CON application submission (e.g., completeness response letter, prefile testimony, late file submissions and the like) must be numbered sequentially from the Applicant's document preceding it. Please begin your submission using Page 148 and reference "Docket Number: 14-31901-CON." Submit one (1) original and two (2) hard copies of your response. In addition, please submit a scanned copy of your response, in an Adobe format (.pdf) including all attachments on CD. If available, a copy of the response in MS Word should also be copied to the CD.

Pursuant to Section 19a-639a(c) of the Connecticut General Statutes, you must submit your response to this request for additional information not later than sixty days after the date that this request was transmitted. Therefore, please provide your written responses to OHCA no later than July 1, 2014, otherwise your application will be automatically considered withdrawn. If you have any questions concerning this letter, please feel free to contact me by email or at (860) 418-7007.

Sincerely,

A. Veyberman

Alla Veyberman
Health Care Analyst

* * * COMMUNICATION RESULT REPORT (MAY. 2. 2014 2:43PM) * * *

FAX HEADER:

TRANSMITTED/STORED : MAY. 2. 2014 2:42PM FILE MODE	OPTION	ADDRESS	RESULT	PAGE
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REASON FOR ERROR
E-1) HANG UP OR LINE FAIL
E-2) BUSY
E-3) NO ANSWER
E-4) NO FACSIMILE CONNECTION

STATE OF CONNECTICUT
OFFICE OF HEALTH CARE ACCESS

FAX SHEET

TO: BARBARA DURDY

FAX: 860.972.9025

AGENCY: HARTFORD HOSPITAL

FROM: OHCA

DATE: 5/2/14 **Time:**

NUMBER OF PAGES: 3
(including transmittal sheet

Comments:
Docket Number: 14-31901

PLEASE PHONE IF THERE ARE ANY TRANSMISSION PROBLEMS

Phone: (860) 418-7001 ***Fax: (860) 418-7053***

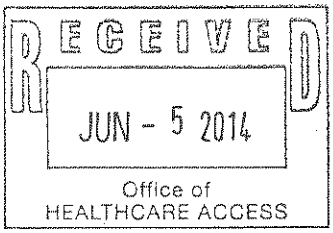
410 Capitol Ave., MS#13HCA
P.O.Box 340308
Hartford, CT 06134

SHIPMAN & GOODWIN LLP®

COUNSELORS AT LAW

Joan W. Feldman
Phone: 860-251-5104
Fax: 860-251-5211
Jfeldman@goodwin.com

June 5, 2014



Alla Veyberman
Health Care Analyst
Department of Public Health
Office of Health Care Access
410 Capital Avenue, MS#13 HCA
P.O. Box 340308
Hartford, Connecticut 06134-0308

Re: Completeness Questions/Responses (Round 2): Hartford Hospital Acquisition of a Magnetic Resonance Imaging Scanner for Research Study; Docket Number 14-31901-CON

Dear Ms. Veyberman:

On behalf of Hartford Hospital (the "Applicant"), enclosed please find the original and 3 hard copies of the Applicant's responses to your Certificate of Need Completeness Letter dated May 2, 2014. As requested, I have also included a CD with a scanned copy of the Applicant's entire response, and electronic versions of any Microsoft Word or Excel documents, as applicable.

Please do not hesitate to contact me at 860-251-5104 if you have any questions.

Sincerely,

Joan Feldman (VC)

Joan W. Feldman

Enclosures

000149 (06/05/14)

Hartford Hospital
Docket Number **14-31901-CON**
Completeness Letter Responses

---

1. The Applicant provided a table with the number of research slots available per week on page 11 of the application. On page 15 of the application, the Applicant provided historic utilization showing a decline in volume. Please explain the following:

    a. The decline in utilization from 2011-2012 and the overall decline from 2011 to 2013.
    b. The relationship between decreasing historical volume and the need for the second scanner.

    a. The decline in utilization from 2011-2012 along with some decline from 2011 to 2013 is due to the fact that existing studies at the time were beginning to wind down during this period and new studies were less available due to the increasing obsolescence of the Allegra 3T. However, with the proposed new Skyra 3T, the Applicant is now eligible to participate in a greater number of studies that will increase the volume of scans that will be performed by the Applicant. Nevertheless, the Applicant continues to require the operation of the Allegra 3T so that it can continue current studies while transitioning new studies to the Skyra 3T. Please also note on Exhibit 1 attached hereto that there are several research studies that have been awarded to the Applicant, but that have not begun. Once these studies begin, the volume dip that occurred during the period of 2011 through 2013 will be fully corrected.

    b. The need for the second scanner was not primarily based on volumes, but rather the obsolescence of the Allegra 3T. However, with the addition of the Skyra 3T, the Applicant is very confident that its volumes will increase and that the Skyra 3T will be fully utilized. See Exhibit 1 attached hereto.

2. Provide updated actual utilization in Table 2a-b (Oct-Apr) for current fiscal year.

Table 2a: Historical, Current, and Projected Volume, by Equipment Unit

	Actual Volume (Last 3 Completed FYs)			**CFY Volume***	**Projected Volume (First 3 Full Operational FYs)****		
	FY 2011	FY 2012	FY 2013	FY2014 (7 months) Annualized	FY 2015	FY 2016	FY 2017
Allegra 3T MRI	914	698	583	250	650	300	300
Skyra 3T MRI	N/A	N/A	183	450	1953	1884	1516
Total	**914**	**698**	**766**	**700**	**2603**	**2184**	**1816**

* For periods greater than 6 months, report annualized volume, identifying the number of actual months covered and the method of annualizing. For periods less than six months, report actual volume and identify the period covered. **Volume for FY 2014 is annualized based on 7 months of actual volume.**

** If the first year of the proposal is only a partial year, provide the first partial year and then the first three full FYs. Add columns as necessary.
*** Identify each scanner separately and add lines as necessary. Also break out inpatient/outpatient/ED volumes if applicable.
**** Fill in years. In a footnote, identify the period covered by the Applicant's FY (e.g. July 1-June 30, calendar year, etc.). **Please note that the period covered by the Applicant's FY is Oct. 1 - Sept. 30).**

Based on the foregoing projections, it is expected that the volume will increase by at least threefold. These projections not only include pending applications for research studies, but also include approved studies that have yet to be initiated.

The projections reflect volumes associated with grant applications submitted as of the date the CON application was filed and do not include volumes from grant applications submitted subsequent to filing the CON application.

Table 2b: Historical, Current, and Projected Volume, by Type of Scan/Exam

	Actual Volume (Last 3 Completed FYs)			**CFY Volume***	**Projected Volume (First 3 Full Operational FYs)****		
	FY2011	FY 2012	FY 2013	FY2014 (3 months) FYTD December 2013.	FY 2015	FY 2016	FY 2017
Allegra / Skyra pre-surgical brain mapping	14	25	17	20	20	20	20
Allegra Functional brain scans	900	673	566	228	630	280	280
Skyra Functional brain scans	N/A	N/A	183	452	1953	1884	1516
Total	**914**	**698**	**766**	**700**	**2603**	**2184**	**1816**

* For periods greater than 6 months, report annualized volume, identifying the number of actual months covered and the method of annualizing. For periods less than six months, report actual volume and identify the period covered. **Volume for FY 2014 is annualized based on 7 months of actual volume.**

** If the first year of the proposal is only a partial year, provide the first partial year and then the first three full FYs. Add columns as necessary.
*** Identify each type of scan/exam (e.g. orthopedic, neurosurgery or if there are scans/exams that can be performed on the proposed piece of equipment that the Applicant is unable to perform on its existing equipment) and add lines as necessary.

**** Fill in years. In a footnote, identify the period covered by the Applicant's FY (e.g. July 1-June 30, calendar year, etc.). **Please note that the period covered by the Applicant's FY is Oct. 1 - Sept. 30).**

3. Provide documentation from the manufacturer demonstrating the end of development and maintenance availability in December 2016 for the Allegra 3T MRI.

   Please see Exhibit 2 attached hereto for the relevant letter from Siemens.

4. The Applicant did not provide responses to Questions 3a and 3f on pages 16-17 of the application concerning projected volume.

   a. Please provide projections and a detailed explanation of all assumptions used in the calculation of the projected volume.

      The projected volumes are described by study in Exhibit 1 attached hereto. The projections include current research studies by scanner along with pending studies by scanner.

   b. Please provide an update on the pending NIH grants listed in Table A on page 11 of the application indicating if the applicant has been awarded any of the pending grants to date.

      See Exhibit 1 attached hereto for the current status of the studies indicated pending on page 11 of the Application, along with additional studies that are pending and awaiting approval.

Hartford Hospital, Olin Center
Acquisition of 3T MRI
Docket No: 14-31901-CON

Response to Completeness Letter

Exhibit 1

Schedule of Current and Pending Grant Funded Research Studies
Table A, Page 11 CON Application – Updated Status of Grant Applications

Hartford Hospital
Olin Center
Schedule of Current and Pending Grant Funded Research Studies
Table A, Page 11 CON Application

red = Allegra
blue = Skyra

1) Table A - Current Research Studies:

			Projected Volume from Current Studies				
Study Time Period (From Date / To Date)	**Study Description**	**Scans per week**	**ALLEGRA**	**SKYRA**	**FY15 Scans**	**FY16 Scans**	**FY17 Scans**
2013-2017	UCONN Steffens	2	0	2	100	100	100
2013-2017	Tolin Hoarding	1	0	1	77	77	77
2009-2015	College Alcohol	2	2	0	100	0	0
2014-2017	Pearlson PARDIP Bipolar Study	2	2	0	100	100	100
2013-2016	HH Obesity	3	0	3	150	150	0
2013-2017	Assaf Autism/Schizophrenia	2	0	2	100	100	100
2012-2017	Yale CTNA	4	4	0	200	200	200
2014-2017	Glahn Bipolar	1	0	1	50	50	50
2004-2015	Pearlson Psychosis NIMH MERIT Award	2	2	0	100	0	0
2011-2015	Pearlson COG Rehab	1	1	0	50	0	0
2013-2016	HH Neurosurgery	0.5	0	0.5	25	25	0
2012-2015	HH Cardiology/Lipid	1	1	0	50	0	0
2013-2015	UCONN MJ	1	0	1	50	0	0
2012-2015	UCONN HIV Exercise	1	1	0	50	0	0
2014-2017	Karen Blank Alzheimer	2	0	2	100	100	0
2013-2016	HH Cardiology Alzheimer	0.5	0	0.5	25	25	0
ongoing	QC Studies	4	2	2	200	200	200
	TOTAL CURRENT	30	15	15	1527	1127	827

2) Table A - Pending Research Applications Submitted to OHCA in Table A , page 11 of CON Application

			Projected Volume from Pending Funded Research				
Status of Grant Application: (Still Pending or Grant Awarded)	**Study Description**	**Scans per week**	**ALLEGRA**	**SKYRA**	**FY15 Scans**	**FY16 Scans**	**FY17 Scans**
Pending	PearlsonAlcohol/Driving # 2	3		3	150	150	150
Pending	Stevens Emotion Adolescence	2		2	67	64	15
Pending	Pearlson BSNIP-2	3		3	150	150	150
Pending	Oncology/Chemo-Memory	2		2	100	100	100
Pending	Pearlson/Stevens Driving MJ	1.5		1.5	58	57	58
Pending	Stevens/ADHD	1		1	121	121	121
Pending	Pearlson/Stevens Affective	1		1	50	50	50
Relocated*	Skudlarski	0.5		0.5	0	0	0
Pending	Dager K Award (Spectro)	1		1	50	50	50
Pending	Glahn UO1	3		3	200	185	165
Pending	Stevens/Pearlson- Driving Alcohol (NSF)	<1		<1	30	30	30
Pending**	K. Carroll	2		2	100	100	100
	TOTAL PENDING	19		19	1076	1057	989
Table A -Projected Scan Volume Current Studies and Pending Research Studies		**49**	**15**	**34**	**2603**	**2184**	**1816**

* Principal Investigator has moved the study to a different institution and will not be performing the study at the OLIN Center.
** Received verbal notification of grant/study approval

3) Pending Research Applications Submitted Subsequent To the Filing of the CON Application (not included in Table A, page 11 of CON)

			Projected Volume from Subsequent Research Applications				
Status of Grant Application: (Still Pending or Grant Awarded)	**Study Description**	**Scans per week**	**ALLEGRA**	**SKYRA**	**FY15 Scans**	**FY16 Scans**	**FY17 Scans**
Pending	Pearlson PerR01 Impulsivity NIMH	1.5		1.5	75	75	75
Pending	Pearlson NIDA Obesity NIDA	1.5		1.5	70	70	70
Pending	Pearlson NIMH Alcohol/Behavioral NIAAA	2		2	100	100	100
Pending	Diefenbach TMS Research NIMH	1		1	50	50	50
Pending	Glahn Bipolar	1		1	50	50	50
Awarded	Assaf HHC Functional Neurosurgery	1		1	50	50	50
Awarded	Assaf HHC TMS Research	0.5		0.5	30	30	30
	TOTAL PENDING	8.5		8.5	425	425	425
Grand Total Projected Scan Volume - All Funded Research Current & Pending		**57.5**	**15**	**42.5**	3028	2609	2241
				Allegra	650	300	300
				Skyra	1953	1884	1516
					2603	2184	1816
					3028	2609	2241

Hartford Hospital, Olin Center
Acquisition of 3T MRI
Docket No: 14-31901-CON

Response to Completeness Letter

Exhibit 2

Obsolescence Letter from Siemens Regarding the Allegra 3T

SIEMENS Healthcare

5/16/2014

Godfrey Pearlson
Hartford Hospital
Institute of Living
200 Retreat Ave
Hartford CT 06106

Dear Siemens Customer,

As your solutions provider, we take a proactive approach in notifying you when particular Siemens equipment is approaching an end-of-support status, so you can manage your medical equipment requirements and maintain the highest level of healthcare services for your patients. Migration decisions take time, and we can assist you by providing the information you need to meet your long-term planning goals.

According to our records, the equipment, or one or more components of the equipment, listed in the attached document has reached or will reach end-of-support status as of the date(s) indicated.

What is the impact of a product reaching end-of-support status?
Siemens prides itself on providing customers with state-of-the-art technology with our highest levels of service and support. When a product has reached end-of-support status, several issues arise:

- Spare parts availability can no longer be guaranteed and therefore, Siemens may be unable to complete a required service repair due to the unavailability of needed parts.
- As the number of systems in use declines, there may be fewer Siemens Engineers available to maintain and repair these products.
- Siemens cannot ensure that application training will be available on products for which support has ended.

Collectively, these factors greatly impact Siemens' ability to deliver the high level of service and support you have come to expect.

What options exist for replacing an end-of-support product?
Through Siemens' comprehensive customer care approach, we can help you migrate to the latest imaging technology. We offer trade-in programs with attractive incentives tailored exclusively for long-standing Siemens customers, as well as leasing plans to help you transition to the next product generation. For your convenience, please visit www.usa.siemens.com/eos for information regarding Siemens products and services to assist you in planning your imaging equipment strategy.

Siemens Medical Solutions USA, Inc.
51 Valley Stream Parkway
Malvern, PA 19355-1406
USA
Tel.: +1-888-826-9702
www.usa.siemens.com/healthcare

SIEMENS

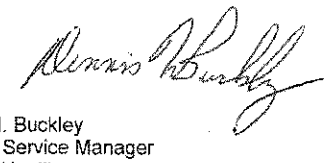
What if an end-of-support product currently has a service agreement?
If any of the equipment included in the attached table is currently covered by a Siemens service agreement, we may be able to continue to provide a limited level of service support without a guarantee of spare parts availability, although Siemens will no longer be able to deliver comprehensive service for these products or provide product enhancements, updates, or upgrades (other than safety updates).

If you have an IT product with a software Extended Support Agreement (ESA) and have not maintained the product at the most currently released version of software, you will be required to upgrade to the newest version of released software prior to the end-of-support date. If the upgrade is not performed by that date, Siemens will be required to cancel the ESA, as of the end-of-support date, per the terms of the ESA/software support agreement.

What if an end-of-support product listed is no longer installed?
If you no longer have some of the equipment included in this notification, please visit **www.usa.siemens.com/systemremovalform**. You will be asked to provide some basic information to keep our records up-to-date and ensure that our communications are tailored to your needs.

We greatly appreciate your business and welcome the opportunity to continue our relationship. To begin the transition to the latest Siemens technology, please visit **www.usa.siemens.com/eos** and contact your local Siemens account executive or call us at 1-888-826-9702.

Best regards,



Dennis M. Buckley
Regional Service Manager
Siemens Healthcare

Ellen Joyner
MRI Product Manager
Business Management and Support
Siemens Healthcare

Siemens Medical Solutions USA, Inc.
Customer Solutions Group
221 Gregson Dr
Cary, NC 27511

SIEMENS

Product End of Support (EOS) Notification

Facility	End of Support (EOS) Date	Equipment Type	Description	Functional Location #
Institute of Living	12/31/2016	MRI	Magnetom Allegra	400-119861

STATE OF CONNECTICUT

DEPARTMENT OF PUBLIC HEALTH

Office of Health Care Access

June 27, 2014 VIA FACISIMILE ONLY

Barbara A. Durdy
Director, Strategic Planning
Hartford Healthcare
181 Patricia Genova Drive
Newington, CT 06111

RE: Certificate of Need Application, Docket Number 14-31901-CON
Hartford Hospital
Certificate of Need Application Deemed Complete

Dear Ms. Durdy,

This letter is to inform you that, pursuant to Section 19a-639a (d) of the Connecticut General Statutes, the Office of Health Care Access has deemed the above-referenced application complete as of June 27, 2014.

If you have any questions regarding this matter, please feel free to contact me at (860) 418-7007.

Sincerely,

A. Veyberman

Alla Veyberman
Health Care Analyst

* * * COMMUNICATION RESULT REPORT (JUN. 27. 2014 12:00PM) * * *

FAX HEADER:

TRANSMITTED/STORED : JUN. 27. 2014 11:59AM FILE MODE	OPTION	ADDRESS	RESULT	PAGE
418 MEMORY TX		98609729025	OK	2/2

REASON FOR ERROR
E-1) HANG UP OR LINE FAIL
E-2) BUSY
E-3) NO ANSWER
E-4) NO FACSIMILE CONNECTION

STATE OF CONNECTICUT
OFFICE OF HEALTH CARE ACCESS

FAX SHEET

TO: BARBARA DURDY

FAX: 860.972.9025

AGENCY: HARTFORD HOSPITAL

FROM: OHCA

DATE: 6/27/14 **Time:**

NUMBER OF PAGES: 2
(including transmittal sheet

Comments:
Docket Number: 14-31901

PLEASE PHONE IF THERE ARE ANY TRANSMISSION PROBLEMS

Phone: (860) 418-7001 ***Fax: (860) 418-7053***

410 Capitol Ave., MS#13HCA
P.O.Box 340308
Hartford, CT 06134

STATE OF CONNECTICUT

DEPARTMENT OF PUBLIC HEALTH

Office of Health Care Access

September 24, 2014

IN THE MATTER OF:

An Application for a Certificate of Need filed Pursuant to Section 19a-638, C.G.S. by:	Notice of Agreed Settlement Office of Health Care Access Docket Number: 14-31901-CON
Hartford Hospital	**Acquisition of a 3T Magnetic Resonance Imaging Scanner**

To:

Barbara A. Durdy
Director, Strategic Planning
Hartford Healthcare
181 Patricia Genova Drive
Newington, CT 06111

Dear Ms. Durdy:

This letter will serve as notice of the approved Certificate of Need Application in the above-referenced matter. On September 24, 2014, the Agreed Settlement, attached hereto, was adopted and issued as an Order by the Department of Public Health, Office of Health Care Access.

Kimberly R. Martone
Director of Operations

Enclosure
KRM:lkg, amv

Department of Public Health
Office of Health Care Access
Certificate of Need Application

Agreed Settlement

Applicant: **Hartford Hospital**

Docket Number: **14-31901-CON**

Project Title: **Acquisition of a 3.0 Tesla MRI Scanner to Conduct Research Studies**

Project Description: Hartford Hospital, Olin Center for Neuropsychiatry ("Hospital" or "Applicant") seeks authorization to acquire a new 3.0 Tesla ("3T") Magnetic Resonance Imaging ("MRI") scanner to use for functional research. The total capital expenditure associated with this proposal is $3,342,905.

Procedural History: The Applicant published notice of its intent to file a Certificate of Need ("CON") application in the *Hartford Courant* on November 19, 20 and 21, 2013. On February 14, 2014, the Office of Health Care Access ("OHCA") received the CON application from the Applicant for the above-referenced project and deemed the application complete on June 27, 2014. OHCA received no responses from the public concerning the Applicant's proposal and no hearing requests were received from the public pursuant to Connecticut General Statutes ("Conn. Gen. Stat.") § 19a-639a. Deputy Commissioner Davis considered the entire record in this matter.

Findings of Fact and Conclusions of Law

To the extent the findings of fact actually represent conclusions of law, they should be so considered, and vice versa. *SAS Inst., Inc., v. S & H Computer Systems, Inc.*, 605 F.Supp. 816 (Md. Tenn. 1985).

1. The Applicant is an 867-bed[1] non-profit acute care hospital located at 80 Seymour Street and 200 Retreat Avenue in Hartford, Connecticut. Ex. A, p. 133.

2. The Institute of Living ("IOL") is a division of the Hospital. IOL is a not-for-profit center for comprehensive patient care, research and education in the fields of behavioral, psychiatric and addiction disorders. Ex. A, p.8.

3. The Olin Center for Neuropsychiatry Research ("Olin Center") is an integral component of the IOL. It is located at 400 Washington Street in Hartford, Connecticut. The Olin Center conducts continuing research studies in the areas of cognitive function including normal aging, working and long term memory, error monitoring, language and attention. The Olin Center is also involved in research on multiple neuropsychiatric diseases including depression, schizophrenia, Alzheimer's disease, manic-depressive illness and alcohol/drug abuse. Ex. A, p. 8.

4. The Olin Center is the only neuropsychiatry research facility within the Hospital's service area. Ex. A, p. 13.

5. On June 3, 2002, OHCA granted the Olin Center approval (DN 02-502-CON) to operate an Allegra 3T MRI ("Allegra MRI") scanner to conduct research studies on humans. OHCA CON Determination, Report Number 13-31871-DTR.

6. On November 27, 2012, the Applicant purchased a Siemens Skyra 3T MRI ("Skyra MRI") scanner to replace the existing Allegra MRI. Ex. A, pp. 9-10, 28.

7. The Skyra MRI was placed in service in January 2013. Ex. C, p. 146.

8. The Applicant initially intended to use the Allegra MRI until May 2016 due to the requirement that the same scanner be used throughout each research study to ensure a consistent and accurate study comparison. Ex. A, pp. 9-10, OHCA CON Determination, Report Number 13-31871-DTR.

9. Under Report Number 13-31871-DTR, issued on October 28, 2013, OHCA determined that the Hospital was required to file a CON application for the acquisition of the above-mentioned MRI scanner. OHCA CON Determination, Report Number 13-31871 -DTR.

[1] Includes 48 bassinets

10. After Report Number 13-31871-DTR was issued by OHCA, the number of funded research applications requiring the use of MRI scanning, as well as anticipated applications, has increased by over 60%. Ex. A, pp. 10-11.

11. The Applicant intends to retain the Allegra MRI rather than take it off-line, as originally planned. Ex. A, pp. 10-11.

12. While conventional MRI results in snapshots of what is inside the body, functional[2] MRI ("fMRI") technology "produces movies starring the brain." It shows researchers where the blood is rich in oxygen and where it is not, resulting in images that help to diagnose disorders related to speech, hearing, vision and motor skills. Ex. A, p. 9; www.apa.org/research/tools/fmri-adult.pdf

13. An article submitted by the Applicant, "Toward Discovery Science of Human Brain Function" published in the Proceedings of the National Academy of Sciences, March 9, 2010, supports the use of the Skyra 3T platform required for running Connectome[3] research sequences for neurosciences in need of fMRI scanning. Connectome is the flagship MRI brain anatomy project being performed at the Olin Center. Ex. A, p. 17 at Exhibit 3, pp. 30-36.

14. The need for a second MRI at the Olin Center is based on the following factors:
    a. Increase in the number of funded research studies;
    b. Inability to accommodate all ongoing studies with a single MRI scanner; and
    c. Obsolescence of the Allegra MRI.
    Ex. A, p. 11.

15. In the last several years, the number of scientific research projects at the Olin Center has grown substantially. The Olin Center currently supports multiple National Institutes of Health ("NIH") funded research projects and funded research sponsored by the Brain and Behavior Research Foundation, the Donoghue Foundation, Autism Speaks and local funders. There are several proposals currently submitted to NIH from Olin Center investigators awaiting funding decisions. Ex. A, p.12.

16. Current research studies include a 2,000-person study of alcoholism in college students, a 700-person study of psychosis endophenotypes and a 325-person study of imaging endophenotypes of bipolar disorder. Ex. A, p. 14.

17. Current funding from primary projects and from collaborator subcontracts represent a broad array of research ranging from schizophrenia, bipolar disorder, alcohol, cannabis and cocaine

[2] Functional magnetic resonance imaging or functional MRI (fMRI) is a functional neuroimaging procedure using MRI technology that measures brain activity by detecting associated changes in blood flow. http://fmri.ucsd.edu/Research/whatisfmri.html

[3] A Connectome is a comprehensive map of neural connections in the brain. The Human Connectome Project aims to provide an unparalleled compilation of neural data, an interface to graphically navigate this data and the opportunity to achieve never before realized conclusions about the living human brain. *www.humanconnectomeproject.org/*

abuse, autism spectrum disorders, Alzheimer's disease, multiple disease endophenotypes, normal adolescent brain development, ADHD, pathological hoarding, OCD, conduct disorder, exercise? and other topics. Ex. A, p.12.

18. The maximum number of MRI research subject slots available per week on one scanner is twenty-five (25), based on one scanner running five days a week and up to ten hours per day. Typical slots are from 1.5 to 3 hours.[4] Ex. A, p.11.

19. Currently, there are seventeen research studies utilizing 30 slots per week; 15 slots on each of the two MRIs. The Olin Center also has pending grants for eleven NIH research studies. These studies will require utilizing an additional 5.5 slots on the Allegra MRI and 13.5 slots on the Skyra MRI for a total of 28.5 slots. Combining the current and pending studies will require a total of 49 slots. Ex. A, p. 11.

20. With the introduction of the Skyra MRI, the Olin Center will be able to conduct additional large-scale projects or support other planned research studies. Ex. A, pp. 13, 17.

21. Over the past several years, the scale and type of research conducted by the Olin Center has grown substantially, creating a need for enhanced technological capacity and cutting edge imaging. Current research protocols require a variety of magnetic resonance techniques, including structural MRI, fMRI, proton spectroscopy and angiography. The Skyra MRI will accommodate these various techniques. Ex. A, p. 18.

22. Siemens will only guarantee the maintenance of the Allegra MRI scanner until December 31, 2016. Ex. A, pp. 9, 156.

23. The Allegra MRI is over ten years old and will not undergo any further development or updating by Siemens. Parallel-coil imaging required for high quality images in a shortened acquisition time and without compromising the ability to acquire meaningful data will not be made available for this scanner. Without the updated coil, the Allegra MRI will lag technologically and scan times will be prolonged, creating a problem for the majority of the research subject population: restless children/teenagers, claustrophobic patients or patients with ADHD and anxiety disorders, anxious/paranoid patients with major mental illnesses and patients with drug-induced restlessness. Ex. A, p. 9.

24. The Skyra MRI is equipped with parallel-coil imaging. The fMRI technology uses a combination of magnet and radio frequencies to study oxygen flow and metabolism in areas of the brain. The Skyra MRI provides access to additional neuroimaging techniques that facilitate existing studies and enable scanning new types of subjects. Ex. A, p. 9.

25. The Skyra MRI offers software options for online movement visualization or correction, and methods for real-time fMRI modeling to ensure data quality for research participant groups who are hard to recruit, or who refuse to be re-scanned in an additional session should they provide poor data because of movement. Ex. A, p.12 .

[4] Based on 3 hours per scan time the maximum number of scans than can be performed during 10 hours per day, 5 days per week for a 50-week year is 833 scans and based on 1.5 hours the maximum number is 1,666 scans.

26. Since the Skyra MRI is a wide-bore scanner, and wide-bore scanning capacity is limited on the main campus of the Hospital, on rare occasions, there may be a need for clinical usage. Clinical use will be limited to no more than ten percent (10%) of the total usage and will most likely be less, as it is projected that the research studies will keep the new scanner at or near full capacity. Ex. A, pp. 14; Ex. C, p. 148.

27. The Olin Center's historical and projected MRI utilization is as follows:

TABLE 1
HISTORICAL AND PROJECTED MRI UTILIZATION
BY NUMBER OF SCANS BY FISCAL YEAR

	Fiscal Year						
Description	**2011**	**2012**	**2013**	**2014***	**2015**	**2016**	**2017**
Allegra 3T MRI	914	698	583	250	650	300	300
Skyra 3T MRI**	-	-	183	450	1,953	1,884	1,516
Pending research studies	-	-	-	-	425	425	425
Total Scans	**914**	**698**	**766**	**700**	**3,028**	**2,609**	**2,241**

*Annualized utilization based on actual 7 months utilization from October 2013 to April 2014.
** The Skyra MRI scanner was placed in service in January 2013.
Ex. A, pp. 15-16; Ex. C, pp. 150, 154.

28. The decline in utilization from 2011-2013 is due to the winding down of existing studies at the time and new studies were less available due to the increasing obsolescence of the Allegra MRI scanner. Ex. C, p. 150.

29. The following table reports the projected number of scans for FY 2015, 2016 and 2017 including current research studies, studies awarded but not yet implemented, and pending applications.

TABLE 2
HISTORICAL AND PROJECTED MRI UTILIZATION

Research Study Grants	Current			Projected by Fiscal Year		
	Allegra	Skyra	Total Scans per week	2015	2016	2017
Current						
UCONN Steffens	0	2	2	100	100	100
Tolin Hoarding	0	1	1	77	77	77
College Alcohol	2	0	2	100	0	0
Pearlson PARDIP Bipolar Study	2	0	2	100	100	100
HH Obesity	0	3	3	150	150	0
Assaf Autism/Schizophrenia	0	2	2	100	100	100
Yale CTNA	4	0	4	200	200	200
Glahn Bipolar	0	1	1	50	50	50
Pearlson Psychosis NIMH MERIT Award	2	0	2	100	0	0
Pearlson COG Rehab	1	0	1	50	0	0
HH Cardiology/Lipid	1	0	1	50	0	0
UCONN MJ	0	1	1	50	0	0
UCONN HIV Exercise	1	0	1	50	0	0
Karen Blank Alzheimer	0	2	2	100	100	0
O.C. Studies	2	2	4	200	200	200
Additional Studies, combined	0	1	1	50	50	0
Total Current Slots	**15**	**15**	**30**	**1,527**	**1,127**	**827**
Total Current Scans			**1,500***			
Pending or Awarded						
Pearlson Alcohol/Driving #2	0	3	3	150	150	150
Stevens Emotion Adolescence	0	2	2	67	64	15
Pearlson BSNIP-2	0	3	3	150	150	150
Oncology/Chemo-Memory	0	2	2	100	100	100
Pearlson/Stevens Driving MJ	0	1.5	1.5	58	57	58
Stevens/Pearlson ADHD	0	1	1	121	121	121
Pearlson/Stevens Affective	0	1	1	50	50	50
Dager K Award (Spectro)	0	1	1	50	50	50
Glahn UO1	0	3	3	200	185	165
K. Carroll	0	2	2	100	100	100
Pearlson PerR01 Impulsivity NIMH	0	1.5	1.5	75	75	75
Pearlson NIDA Obesity NIDA	0	4.5	4.5	70	70	70
Pearlson NIMH Alcohol/Behavioral NIAAA	0	2	2	100	100	100
Diefenbach TMS Research NIMH	0	1	1	50	50	50
Glahn Bipolar	0	1	1	50	50	50
Assaf HHC Functional Neurosurgery	0	1	1	50	50	50
Additional Studies, combined	0	0.5	0.5	60	60	60
Total Pending or Awarded Slots	**0**	**28.5**	**28.5**	**1,501**	**1,482**	**1,414**
Total Pending or Awarded Scans			**1,425****			
Grand Total			**1,925**	**3,028**	**2,609**	**2,241**

*30 scans per week times 50 weeks.
**28.5 scans per week times 50 weeks.
Ex. C, pp. 152, 154.

30. The Applicant anticipates an operational loss associated with the Skyra MRI in FY 2014 through FY 2016 due in part to the annual depreciation[5] expense of $545,974 resulting from the acquisition of the scanner.

TABLE 3
PROJECTED INCREMENTAL REVENUES AND EXPENSES

Description	FY 2014	FY 2015	FY 2016
Revenue from Operations	$268,439	$284,545	$304,464
Total Operating Expenses	$991,329	$996,346	$1,003,714
Gain/(Loss) from Operations	**($722,890)**	**($711,801)**	**($699,250)**

Ex. A, p.140.

31. The Applicant projects overall operational gains of $50.6 million in FY 2014, $17.49 million in FY2015 and $8.06 million in FY2016.

TABLE 4
APPLICANT'S PROJECTED REVENUES AND EXPENDITURES WITH THE PROPOSAL

	FY 2014	FY 2015	FY 2016
Revenue from Operations	$1,144,265	$1,179,715	$1,222,031
Total Operating Expenses	$1,093,659	$1,162,224	$1,213,970
Gain/(Loss) from Operations	**$ 50,606**	**$ 17,491***	**$ 8,061****

Note: figures are in thousands.

* Decline in gain from operation is due to projected increases in the following expenses: supplies and drugs, salaries and fringe benefits and depreciation.

**Decline in gain from operation is due to projected increases in the following expenses: supplies and drugs and salaries and fringe benefits.

Ex. A, p.140.

32. The proposed scanner will be used primarily for research purposes and will have no impact on payer mix or access to clinical services at the Olin Center. Ex. C, p.148.

33. There will be no change in access for the patient population served by this proposal, in particular Medicaid patients. Ex. C, p.148.

34. OHCA is currently in the process of establishing its policies and standards as regulations. Therefore, OHCA has not made any findings as to this proposal's relationship to any regulations adopted by OHCA. (Conn .Gen. Stat. § 19a-639(a)(1))

35. This CON application is consistent with the overall goals of the Statewide Health Care Facilities and Services Plan. (Conn. Gen. Stat. § 19a-639(a)(2))

36. The Applicant has established that there is a clear public need for its proposal. (Conn. Gen. Stat. § 19a-639(a)(3))

37. The Applicant has satisfactorily demonstrated that its proposal is financially feasible. (Conn. Gen. Stat. § 19a-639(a)(4))

[5]A method of allocating the cost of a tangible asset over its useful life.

38. The Applicant has satisfactorily demonstrated that its proposal is primarily for research purposes. Therefore, it has no impact on the accessibility and cost effectiveness of health care delivery in the region. The proposal has the potential to improve the quality of health care delivery in the region. (Conn. Gen. Stat. § 19a-639(a)(5))

39. The Applicant has shown that there will be no change in access to the provision of health care services to the relevant populations and payer mix since the proposed equipment is mainly for research purposes. (Conn. Gen. Stat. § 19a-639(a)(6))

40. The Applicant has satisfactorily identified the population to be served and has satisfactorily demonstrated that this population has a need. (Conn. Gen. Stat. § 19a-639(a)(7))

41. The utilization of existing health care facilities and health care services in the Applicant's service area supports this application. (Conn. Gen. Stat. § 19a-639(a)(8))

42. The Applicant has satisfactorily demonstrated that the proposal will not result in an unnecessary duplication of existing services in the area. (Conn. Gen. Stat. § 19a-639(a)(9))

43. The Applicant has satisfactorily demonstrated that the proposal will not result in a reduction or change in access to services for Medicaid recipients or indigent persons. (Conn. Gen. Stat. § 19a-639(a)(10))

Discussion

CON applications are decided on a case by case basis and do not lend themselves to general applicability due to the uniqueness of the facts in each case. In rendering its decision, OHCA considers the factors set forth in Conn. Gen. Stat. § 19a-639(a). The Applicant bears the burden of proof in this matter by a preponderance of the evidence. *Jones v. Connecticut Medical Examining Board, 309 Conn. 727 (2013).*

The Applicant is an 867-bed non-profit acute care hospital located at 80 Seymour Street and 200 Retreat Avenue in Hartford, Connecticut. *FF1* The Olin Center is a component of the Institute of Living, a division of the Hospital. *FF2,3* The Olin Center currently supports multiple NIH-funded research projects and funded research sponsored by the Brain and Behavior Research Foundation, the Donoghue Foundation, Autism Speaks and local funders. Specifically, it is involved in research on multiple neuropsychiatric diseases including schizophrenia, bipolar disorder, alcohol, cannabis and cocaine abuse, autism spectrum disorders, Alzheimer's disease, multiple disease endophenotypes, normal adolescent brain development, ADHD, pathological hoarding, OCD, conduct disorder, exercise and other topics. *FF16,17*

On November 27, 2012, the Applicant purchased a Siemens Skyra 3T MRI ("Skyra MRI") scanner to replace the existing Allegra MRI. *FF6* Originally, the Skyra MRI scanner was meant to replace the existing Allegra MRI scanner for human research purposes. The Applicant initially intended to use the Allegra MRI until May 2016 due to the requirement that the same scanner be used throughout each research study to ensure a consistent and accurate study comparison. *FF7* Under Determination Report Number 13-31871-DTR, OHCA determined that the acquisition of the Skyra MRI required CON approval. *FF6-9* Subsequent to OHCA's determination, the scale and type of research conducted by the Olin Center grew substantially, creating a need for enhanced technological capability and additional capacity. *FF10, 21* As a result, the Applicant proposes retaining the Allegra MRI and receiving authorization for the acquisition of the Skyra MRI. *FF11* Though the Allegra MRI is over ten years old and will not undergo any further development or updating by Siemens, the researchers must use it to complete ongoing studies that are longitudinal in nature and must be conducted over time using the same MRI scanner. *FF10, 23* Due to the technological limitations of the Allegra MRI, the scanner has increasingly become "out-of-step" with techniques used by other neuroimaging researchers. This will decrease the likelihood of Olin Center investigators participating in future multi-site projects, which have become a valuable tool to increase the pace and impact of NIH-sponsored neuropsychiatric research. Ex. A, p. 13

The Skyra MRI is equipped with technological capacity required for advanced research studies such as parallel-coil imaging that produces high quality images in a significantly shortened acquisition time without compromising the ability to acquire meaningful data. In addition, the scanner has software options for online movement visualization or correction, and methods for real-time fMRI modeling to ensure data quality. *FF24,25* Unlike conventional MRI scanners that provide results in snapshots of what is inside the body, fMRI technology produces videos of the brain. It shows researchers where the blood is rich in oxygen and where it is not, resulting in images that will help in the diagnosis of disorders related to speech, hearing, vision and motor skills. *FF12*

Along with the enhanced technology, the Olin Center needs the Skyra MRI due to the increasing number of current, pending and awaiting approval research studies. *FF14,15* The maximum number of MRI research subject slots available per week on one scanner is twenty-five based on one scanner operating five days a week. *FF18* Currently, the Olin Center is running above capacity for one scanner with an average demand of thirty subject slots per week with another 28.5 slots pending approval. *FF19* The number of scans to be performed on the Skyra MRI has been projected to be 3,028, 2609 and 2,241 scans in Fiscal Years 2015, 2016 and 2017, respectively, tripling the 700 scans expected to be performed in FY 2014. *FF27* The additional MRI scanner capacity will enable the Olin Center to conduct additional large-scale projects, support further planned research studies and attract additional faculty. *FF20* While it is unlikely that many of the pending grant applications will be granted, the Olin Center will continuously apply for research study grants to maximize the usage of the scanners. Ex. A, p. 17 That said, the real need for the Skyra MRI is based upon its advanced technology, not speculative grants. Therefore, OHCA mandates that the Applicant take certain actions as stated in the attached Order.

The proposed Skyra MRI will be used primarily for research to be conducted at The Olin Center, the only neuropsychiatry research facility located within the Hospital's service area. *FF4,32* On occasion there may be a clinical need for the Skyra MRI due to the limited wide-bore scanning capacity on the main campus of Hartford Hospital. *FF26* Overall, this proposal will not have an impact on existing clinical MRI service providers in the area or access to care. Moreover, the proposal will have no impact on the services provided to the Medicaid population since it is being used primarily for research purposes. *FF32,33*

Even though the Applicant has projected an operational loss due to the depreciation expense resulting from the acquisition of the Skyra MRI, this proposal is financially feasible as the acquisition of the Skyra MRI was funded with the Applicant's operating capital and will be supported by the Applicant's overall operational gains of $50.6 million, $17.49 million and $8.06 million for Fiscal Years 2014, 2015 and 2016, respectively. *FF30,31*

This research-oriented MRI will indirectly benefit the strength of the state's health care system by contributing to the quality of health care delivery in the region by facilitating the advancement of neuropsychiatry research. The research conducted will allow the researchers to enhance their knowledge about neuropsychiatric disorders and has the potential to improve future treatment and quality of life outcomes for individuals suffering from these disorders. Therefore, OHCA concludes the Applicant has demonstrated clear public need for the proposal.

Order

NOW, THEREFORE, the Department of Public Health, Office of Health Care Access ("OHCA") and Hartford Hospital ("Applicant") hereby stipulate and agree to the terms of settlement with respect to the acquisition of a 3.0 Tesla MRI scanner to conduct research studies within Hartford Hospital's Olin Center for Neuropsychiatry, as follows:

1. Applicant's request to acquire a Siemens Skyra 3.0 Tesla MRI scanner to conduct research studies within the Olin Center for Neuropsychiatry is **approved.**

2. Not later than ten (10) business days after the signing of this Agreed Settlement, the Applicant shall provide OHCA with a complete list of research studies currently being performed on the Allegra 3T MRI scanner. The list shall include the name of the study; the name of the Grant approved for the study, the start date of the study; and the anticipated end date for the study.

3. Upon completion of all the research studies currently being conducted on the Allegra 3T MRI scanner, such list being provided to OHCA pursuant to Stipulation #2 herein, the Applicant shall terminate its use of the Allegra 3T MRI scanner and dispose of same.

4. The Applicant shall notify OHCA, in writing, of the disposal of the Allegra 3T MRI scanner not later than ten (10) business days after it has been disposed. Such notification shall provide specifics regarding the date of disposition and how it was disposed.

5. This Agreed Settlement is an order of OHCA with all rights and obligations attendant thereto, and OHCA may enforce this Agreed Settlement under the provisions of Conn. Gen. Stat. §§ 19a-642 and 19a-653 with all fees and costs of such enforcement being the responsibility of the Applicant.

6. OHCA and the Applicant agree that this Agreed Settlement represents a final agreement between OHCA and all parties with respect to this Application. The signing of this Agreed Settlement resolves all objections, claims and disputes that may have been raised by the Applicant with regard to Docket Number: 14-31901-CON.

7. This Agreed Settlement shall be binding upon the Applicant and its successors and assigns.

Signed by STUART K. MARKOWITZ, MD, PRESIDENT
(Print name) (Title)

9-24-14
Date

Duly Authorized Agent for
Hartford Hospital

The above Agreed Settlement is hereby accepted and so ordered by the Department of Public Health Office of Health Care Access on September 24, 2014.

9/24/14
Date:

Lisa A. Davis, MBA, BS, RN
Deputy Commissioner

* * * COMMUNICATION RESULT REPORT (SEP. 24. 2014 3:32PM) * * *

FAX HEADER:

TRANSMITTED/STORED : SEP. 24. 2014 3:30PM FILE MODE	OPTION	ADDRESS	RESULT	PAGE
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REASON FOR ERROR
E-1) HANG UP OR LINE FAIL
E-2) BUSY
E-3) NO ANSWER
E-4) NO FACSIMILE CONNECTION

STATE OF CONNECTICUT
OFFICE OF HEALTH CARE ACCESS

FAX SHEET

TO: BARBARA DURDY

FAX: 860.972.9025

AGENCY: HARTFORD HOSPITAL

FROM: OHCA

DATE: 9/24/14 **Time:**

NUMBER OF PAGES: 13
(including transmittal sheet

Comments:
Docket Number: 14-31901

PLEASE PHONE IF THERE ARE ANY TRANSMISSION PROBLEMS

Phone: (860) 418-7001 Fax: (860) 418-7053

410 Capitol Ave., MS#13HCA
P.O.Box 340308
Hartford, CT 06134

Huber, Jack

From: Huber, Jack
Sent: Friday, October 17, 2014 1:43 PM
To: 'Durdy, Barbara'
Subject: RE: Notice of CON Expiration Date for the Decision Rendered under Docket Number: 14-31901-CON

Good afternoon Barbara - Thank you for your letter dated October 15, 2014, concerning the reporting requirements associated with the Allegra 3T MRI scanning studies at the Olin Center. OHCA has reviewed the CON compliance and monitoring information you filed and finds the list of research studies currently being conducted on the Allegra 3T MRI scanner reports elements that meets the informational requirements as specified in Stipulation #2 of the agreed settlement authorization. Future compliance and monitoring reporting required by Stipulation # 4 of the agreed settlement may be sent to my attention when the Allegra 3T MRI scanner is no longer being used for the studies that have been identified. Thank you for your attention to this matter.

Sincerely,

Jack A. Huber

Jack A. Huber
Health Care Analyst
Department of Public Health
Office of Health Care Access
410 Capitol Avenue
P.O. Box 340308 MS #13HCA,
Hartford, CT 06134
Office: (860) 418-7069
Fax: (860) 418-7053
Email: Jack.Huber@ct.gov

From: Durdy, Barbara [mailto:Barbara.Durdy@hhchealth.org]
Sent: Wednesday, October 15, 2014 10:07 AM
To: Huber, Jack
Cc: Roberts, Karen
Subject: RE: Notice of CON Expiration Date for the Decision Rendered under Docket Number: 14-31901-CON

Jack,

Good morning.

The following is a list of research studies currently being conducted on the Allegra 3T MRI scanner at the Olin Center:

1. 1RO1MH096957-01 NIMH- Psychosis and Affective Research Domains and Intermediate Phenotypes; funded through 3/31/2016

2. Functional Brain Mapping in Neurosurgery; funded through 7/31/2016

3. Center for the Translational Neuroscience of Alcoholism NIAAA – funded through 5/31/2016

Please note that any of the studies listed above which are currently being conducted on the Allegra 3T scanner may receive an extension if one is needed to complete the study. We cannot predict at this time whether or not an extension will be needed but will keep OHCA apprised of progress toward completion.

Please do not hesitate to contact me if you have any questions or need additional information.

Sincerely,

Barbara

From: Huber, Jack [mailto:Jack.Huber@ct.gov]
Sent: Tuesday, October 14, 2014 1:46 PM
To: Durdy, Barbara
Cc: Roberts, Karen
Subject: RE: Notice of CON Expiration Date for the Decision Rendered under Docket Number: 14-31901-CON

Dear Ms. Durdy:

On September 24, 2014, in an agreed settlement under Docket Number: 14-31901-CON, the Office of Health Care Access authorized a Certificate of Need ("CON") to Hartford Hospital for the acquisition of a 3.0 tesla-strength magnetic resonance imaging scanner to be used at the Hospital's Olin Center for Neuropsychiatry in Hartford. Pursuant to Section 19a-639b of the Connecticut General Statutes ("C.G.S."), *"a certificate of need shall be valid for two years from the date of issuance by this office."*

With this letter, please be advised that pursuant to Section 19a-639b, C.G.S., the current CON authorization issued under Docket Number: 14-31901-CON will expire on September 24, 2016. Please contact me at (860) 418-7069 or Karen Roberts, Principal Health Analyst at (860) 418-7041, if you have any questions regarding this notification.

Additionally, please provide me with a progress update as to how the Hospital's project satisfies agreed-upon stipulation two of the agreed settlement, specifically with regard to the filing of a complete list of neuropsychiatric research studies currently being performed. A copy of the order is attached for your convenience. Thank you for your assistance in this matter.

Sincerely,

Jack A. Huber

Jack A. Huber
Health Care Analyst
Department of Public Health

Office of Health Care Access
410 Capitol Avenue
P.O. Box 340308 MS #13HCA,
Hartford, CT 06134
Office: (860) 418-7069
Fax: (860) 418-7053
Email: Jack.Huber@ct.gov

User, OHCA

From: Clarke, Ormand
Sent: Tuesday, September 05, 2017 9:51 AM
To: Barbara.Durdy@hhchealth.org
Cc: Roberts, Karen; User, OHCA
Subject: Queries related to Decision Rendered under Docket Number: 14-31901-CON

Dear Ms. Durdy:

On September 24, 2014, pursuant to Docket Number 14-31901-CON, the Office of Health Care Access (OHCA) issued a Certificate of Need (CON) authorization to Hartford Hospital for the Acquisition of a 3T Magnetic Resonance Image Scanner. As per your letter of August 13, 2013 to OHCA, at the conclusion of all studies in progress at the time of the new Skyra 3T's acquisition, the aging Allegra 3 T will be decommissioned as required by the CON conditions. So to substantiate the records:

(a) Please verify whether the above referenced studies were terminated at the end of July 3, 2016.
(b) If the studies were concluded at the end of July 3, 2016 was the Allegra 3 T decommissioned as planned?
(c) If the studies were not terminated consistent with your projections, please state the date of actual termination.
(d) If the Allegra 3 T was decommissioned consistent with your projections, please provide details of the means of disposition.

Please be sure to contact me if there are any questions.

Sincerely,

Ormand Clarke
Health Care Analyst
Office of Health Care Access
Connecticut Department of Public Health
410 Capitol Avenue, MS #13HCA, P.O. Box 340308, Hartford, CT 06134-0308
P: (860) 418-7047 / F: (860) 418-7053 / E: ormand.clarke@ct.gov

User, OHCA

From: Clarke, Ormand
Sent: Tuesday, September 05, 2017 2:24 PM
To: Durdy, Barbara
Cc: Roberts, Karen; User, OHCA; Clarke, Ormand
Subject: RE: Queries related to Decision Rendered under Docket Number: 14-31901-CON

Dear Ms. Durdy:

Thank you for your prompt response. Considering the 3T Magnetic Resonance Image Scanner exists in your custody, it remains indisposed, albeit inoperable. In order to substantiate the records, it is respectfully requested that on its occurrence, you notify OHCA of the date and means of final removal from your custody.

If there are any questions, please do not hesitate to contact me.
Sincerely,
Ormand.

From: Durdy, Barbara [mailto:Barbara.Durdy@hhchealth.org]
Sent: Tuesday, September 5, 2017 1:26 PM
To: Clarke, Ormand <Ormand.Clarke@ct.gov>
Cc: Roberts, Karen <Karen.Roberts@ct.gov>; User, OHCA <OHCA@ct.gov>
Subject: RE: Queries related to Decision Rendered under Docket Number: 14-31901-CON

Ormand,
Please see responses to your compliance questions below in Blue. If you have any questions or need additional information, please let me know.
Thank you
Barbara

From: Clarke, Ormand [mailto:Ormand.Clarke@ct.gov]
Sent: Tuesday, September 05, 2017 9:51 AM
To: Durdy, Barbara
Cc: Roberts, Karen; User, OHCA
Subject: Queries related to Decision Rendered under Docket Number: 14-31901-CON

Dear Ms. Durdy:

On September 24, 2014, pursuant to Docket Number 14-31901-CON, the Office of Health Care Access (OHCA) issued a Certificate of Need (CON) authorization to Hartford Hospital for the Acquisition of a 3T Magnetic Resonance Image Scanner. As per your letter of August 13, 2013 to OHCA, at the conclusion of all studies in progress at the time of the new Skyra 3T's acquisition, the aging Allegra 3 T will be decommissioned as required by the CON conditions. So to substantiate the records:
(a) Please verify whether the above referenced studies were terminated at the end of July 3, 2016.

Response: The last study on the Allegra 3 T was completed on March 9, 2016.

(b) If the studies were concluded at the end of July 3, 2016 was the Allegra 3 T decommissioned as planned?

Response: The equipment was decommissioned on March 30, 2016 by Siemens, who siphoned off the helium from the MRI scanner, rendering it inoperable. Hartford Hospital has attempted to sell the device on the market to a used equipment vendor and has had individuals visit to inspect it, but thus far there have been no viable offers.

(c) If the studies were not terminated consistent with your projections, please state the date of actual termination.

N/A.

(d) If the Allegra 3 T was decommissioned consistent with your projections, please provide details of the means of disposition.

Please see response to Question b above.

Please be sure to contact me if there are any questions.

Sincerely,

Ormand Clarke
Health Care Analyst
Office of Health Care Access
Connecticut Department of Public Health
410 Capitol Avenue, MS #13HCA, P.O. Box 340308, Hartford, CT 06134-0308
P: (860) 418-7047 / F: (860) 418-7053 / E: ormand.clarke@ct.gov