Schizophrenia in a Nutshell

Scientists in the Netherlands recently investigated how auditory hallucinations might be produced by the brain of these patients. The first thing to know about hearing is that it is mostly processed within the temporal lobe of the brain. This part of your brain lies just inside your ears. The scientists discovered that certain regions of the left temporal lobe were more active during an auditory hallucination, as compared to when the patient was not hallucinating. Essentially, the brains of hallucinating patients acted as though they were experiencing a "real" auditory experience. Their brains were generating the "voices or sounds" and they were "hearing" the sounds at the same time! Somehow the patients never made the connection that they were hearing their own voice. The patients believed that the voices were coming from someone else.

In order to understand how this happens, compare producing and hearing your own voice with producing and feeling your own tickle. Under normal circumstances, they always go together - never any surprises. Your brain always tells itself what it's about to experience. In the brains of people with schizophrenia this process seems to be malfunctioning. The scientists concluded that the brain signals originating in speech-generating regions of the brain were not bothering to tell the auditory regions that the forthcoming thought was actually self-generated. If the auditory part of the brain does not expect to hear its own voice, then any voices that are heard MUST belong to someone else.

The actual problem, for the psychology majors in the audience, which was discovered, was an anatomical error within the fiber bundle that connects speech-generating areas in the frontal lobe with auditory cortex in the temporoparietal lobe. Essentially, if you do not know with certainty that YOU are speaking then you will assume that the voices are talking TO you. Sadly, and **sometimes tragically, due to the underlying paranoia that these patients also experience, the voices instruct the patients to do disagreeable tasks.**

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VINCE CALHOUN, PHD

Executive Science Officer and Director, Image Analysis and MR Research

Professor of Translational Neuroscience

The Mind Research Network

Distinguished Professor, Departments of Electrical and Computer Engineering (primary), Neurosciences, Computer Science, and Psychiatry

The University of New Mexico

Dr. Calhoun develops techniques for making sense of complex brain imaging data. Because each imaging modality has limitations, the integration of these data is needed to understand the healthy and especially the disordered human brain.

Dr. Calhoun has created algorithms that map dynamic networks of brain function, structure and genetics, and how these are affected while being stimulated by various tasks or in individuals with mental illness such as schizophrenia.

For more information on Dr. Calhoun, please refer to his Curriculum Vitae or visit the Medical Image Analysis Lab. His CV includes his academic career, as well as grant history, professional service, a partial list of publications and a full bibliography.

Email Dr. Calhoun

Congratulations

Dr. Calhoun recently received fellowship designations for both the American Association for the Advancement of Science (AAAS) and the Institute of Electrical and Electronics Engineers (IEEE).

The organizations recognize Dr. Calhoun for his contributions to human brain research. One of Calhoun's most significant accomplishments is his development of advanced algorithms that identify how brain regions 'talk' to one another either during a specific task or when at rest.

He also recently earned the A. Earl Walker Neuroscience Research Award, which recognizes outstanding contributions to basic or clinical research in neuroscience by a member of the faculty in any UNM department.

Press Release

V.IMP

NIMH; 1 R01 MH072681-01 (Kiehl) 7/1/05-6/30/09
Abnormal functional connectivity in psychosis $250,000/year
To use functional brain imaging measures to differentially diagnose schizophrenia from psychotic bipolar illness.
Role: Co-Investigator

*NIH/NCRR; 1P20RR021938 (Calhoun) 8/1/08 – 7/31/13
COBRE: Neural Mechanisms of Schizophrenia: Use of Multiple Tools to Examine Dysfunctions in Neural Integration $1,725,415/year directs

Center grant funding 4 junior PIs and 4 cores which examines functional and anatomical connectivity in schizophrenia using multimodal neuroimaging analyses.
Role: Principle Investigator

*NSF; 1016619 (Calhoun) 8/15/2010–7/31/2013
III: Small: Collaborative Research: Canonical Dependence Analysis for Multi-modal Data Fusion and Source Separation $170,000/year directs

We will develop a set of powerful tools for multi-subject (multi-set) data analysis and multi-modal data fusion based on canonical dependence analysis that extends the power and flexibility of multiset canonical correlation analysis. We will study brain function and functional associations during simulated driving, a naturalistic task where data-driven methods have proven especially useful. We will also investigate genetic associations with good or poor driving behavior and will study the brain function variability at different blood alcohol levels.
Role: Principle Investigator [collaborative project with Tulay Adali @ UMBC]

RO1MH077945 (Pearlson) 12/1/2007–11/30/2012
NIH/NIMH $670,295/yr Direct
Bipolar & Schizophrenia Consortium for Parsing Endophenotypes

The overall goal of the proposed research is to examine a broad panel of putative endophenotypes in affected individuals with schizophrenia and bipolar and their unaffected relatives in order to: 1) characterize the degree of familial phenotypic overlap between SZ and psychotic BP; 2) identify patterns of endophenotypes unique to the two disorders, and 3) contrast the heritability of endophenotypes across the disorders.
Role: PI on Subcontract

NARSAD; (Calhoun) 4/1/04-3/31/09
Assessment of the State-Trait Specificity of Auditory Cortex fMRI Synchrony Maps in Schizophrenia and Bipolar Disorder $60,000 directs

Study of specificity of auditory cortex maps in acute psychotic bipolar patients and after 6 months of medication. Maps are generated using independent component analysis methods we have developed.
Role: Primary Investigator

Look Up his Resume – Very Renowned and Very Experienced. A whole one mile long list of research programs at leading research institutes while holding key positions.

VINCE CLARK, PHD

Professor of Translational Neuroscience

Dr. Clark has worked with MRN as Director of Neuroscience, then as Scientific Director recruiting scientists and helping MRN to increase its grant portfolio by expanding into new areas of research such as addiction, accelerated learning, and multimodal imaging. In association with the Department of Psychology at UNM (http://psych.unm.edu), where he is Founding Director of the new Clinical Neuroscience Center, he and his associates investigate the relationship between mind and brain. He employs structural and functional magnetic resonance imaging (fMRI), magnetoencephalography (MEG), event-related potentials (ERPs) and methods of transcranial brain stimulation, including transcranial direct current stimulation (tDCS) and transcranial alternating current stimulation (tACS), as well as other methods to examine human brain structure and function. Using these tools, he is investigating the basic organizational principles of perception, learning, memory, attention and language in healthy individuals. He also uses these methods to examine the neural basis of psychiatric disorders such as drug and gambling addiction, psychopathy and schizophrenia. He is developing new methods of data analysis for combining data from different imaging techniques to gain fundamentally new information on human brain structure and function, and is using this and other methods to expand the boundaries of brain imaging techniques. His recent area of research examines how tDCS can be used to increase learning and performance in healthy subjects, and the mechanisms by which tDCS produces changes in brain function and behavior. Brain stimulation may lead to a variety of innovations in classroom education and professional training, along with new treatments for psychiatric and neurological disorders.

Functional MRI Evaluation of Multiple Neural Networks Underlying Auditory Verbal Hallucinations in Schizophrenia Spectrum Disorders.

Functional MRI studies have identified a distributed set of brain activations to be associated with auditory verbal hallucinations (AVH). However, very little is known about how activated brain regions may be linked together into AVH-generating networks. Fifteen volunteers with schizophrenia or schizoaffective disorder pressed buttons to indicate onset and offset of AVH during fMRI scanning. When a general linear model was used to compare blood oxygenation level dependence signals during periods in which subjects indicated that they were versus were not experiencing AVH ("AVH-on" versus "AVH-off"), it revealed AVH-related activity in bilateral inferior frontal and superior temporal regions; the right middle temporal gyrus; and the left insula, supramarginal gyrus, inferior parietal lobule, and extranuclear white matter. In an effort to identify AVH-related networks, the raw data were also processed using independent component analyses (ICAs). Four ICA components were spatially consistent with an a priori network framework based upon published meta-analyses of imaging correlates of AVH. Of these four components, only a network involving bilateral auditory cortices and posterior receptive language areas was significantly and positively correlated to the pattern of AVH-on versus AVH-off. The ICA also identified two additional networks (occipital-temporal and medial prefrontal), not fully matching the meta-analysis framework, but nevertheless containing nodes reported as active in some studies of AVH. Both networks showed significant AVH-related profiles, but both were most active during AVH-off periods. Overall, the data suggest that AVH generation requires specific and selective activation of auditory cortical and posterior language regions, perhaps coupled to a release of indirect influence by occipital and medial frontal structures.

AVH – Auditory Visual Hallicunations

Principal Investigator: Bruno Averbeck

Bruno Averbeck

Chief
Unit on Learning and Decision Making
Laboratory of Neuropsychology (LN)

https://www.nimh.nih.gov/labs-at-nimh/principal-investigators/bruno-averbeck.shtml

The work in Dr. Averbeck's group focuses on understanding the role of frontal-striatal circuits, and particularly the role of dopamine in these circuits, on learning and the representation of beliefs. The lab pursues these questions by establishing links between network dynamics at the level of neuronal ensembles and behavior. The overall strategy of the work in the lab is to carry out experiments in patient groups that have disordered dopamine signaling, including patients with schizophrenia and patients with Parkinson's disease. Specific behaviors that are affected in the patient groups can then be implemented in primate models, where in-vivo experiments allow detailed examination of mechanism. For example, recent work has examined the possibility that delusions in schizophrenia are driven by a change in the way evidence is gathered to support beliefs about the state of the world. Work by our group and others has shown that patients with schizophrenia make decisions after gathering less evidence than control groups. Recent work in the lab has examined this behavior in healthy human subjects using functional neuroimaging, and identified a network of areas that are involved in the task, including the intraparietal sulcus, the insula and the ventral striatum. Subsequent experiments in monkeys will follow up these findings by examining the effects of pharmacological manipulations, which are thought to model psychosis, on behavior and neural ensemble activity within the brain areas uncovered by the functional imaging..

Principal Investigator: Charles R Gerfen

Charles R Gerfen

Chief
Section on Neuroanatomy
Laboratory of Systems Neuroscience

https://www.nimh.nih.gov/labs-at-nimh/principal-investigators/charles-gerfen.shtml

Dr. Gerfen received a B.A. from Amherst College and Ph.D. from Northwestern University. His doctoral research was on neural substrates of reward involving the prefrontal cortex and basal ganglia. During a post-doctoral fellowship in the Laboratory of Max Cowan at the Salk Institute, he developed the PHA-L axonal tracing technique with Paul Sawchenko. In 1983, Dr. Gerfen was recruited by Ed Evarts to the Laboratory of Neurophysiology at NIMH to work on the neuroanatomy of the forebrain, where he established some of the functional principles of the organization of the basal ganglia. Dr. Gerfen is currently the Chief of the Laboratory of Systems Neuroscience at the NIMH.

Dr. Gerfen studies the functional organization of the cerebral cortex and basal ganglia. The basal ganglia are involved in transforming activity in the cerebral cortex into directed behavior. Using neuroanatomical tracing techniques, he mapped the connections of the circuits of this system, characterizing the compartmental nature of the input-output organization of the striatum, which is the main nucleus of the basal ganglia. His work established that the D1 and D2 dopamine receptors are segregated into two main pathways within the basal ganglia circuits. This finding forms a cornerstone of the predominant model of neurologic disorders affected by diseases of the basal ganglia, including movement disorders such as Parkinson's disease, chorea, and dystonia, and mental disorders such as attention deficit hyperactivity disorder and depression. Current work is focused on development of BAC-Cre transgenic mouse lines to study the functional organization of the cerebral cortex and basal ganglia. Dr. Gerfen is a Co-Investigator on the Gene Expression Nervous System Atlas (GENSAT) project, with Nat Heintz at Rockefeller University. This project provides transgenic mouse lines to the neuroscience research community with neuron specific expression of Cre recombinase. Over 200 Cre-driver lines have been characterized with expression limited to specific neuron types or specific brain regions. Characterization of these lines is provided on the lab website: http://genebrainsystems.nimh.nih.gov/. **mapping of mouse lines within the brain characterizing specific neuron types for specific regions within the brain which translates to biomarkers i.e. specific neuron types firing for schizophrenic brains.**

http://stanford.edu/~knutson/

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CV

My lab and I seek to elucidate the neural basis of emotion (affective neuroscience), and explore implications for decision-making (neuroeconomics) and psychopathology (neurophenomics).

(Third-person): Brian Knutson is a Professor of Psychology and Neuroscience at Stanford University. His research focuses on the neural basis of emotional experience and expression. He investigates the topic with a number of methods including self-report, measurement of nonverbal behavior, comparative ethology, psychopharmacology, and neuroimaging. His long-term goal is to understand the neurochemical and neuroanatomical mechanisms responsible for emotional experience, and to explore the implications of these findings for the assessment and treatment of clinical disorders as well as for economic behavior. Knutson has received Young Investigator Awards from the National Alliance for Research on Schizophrenia and Depression and the American Psychiatric Association, and is a fellow of the Academy for Behavioral Medicine Research as well as the Association for Psychological Science. He received BAs in experimental psychology and comparative religion from Trinity University, a PhD in experimental psychology from Stanford University, and has conducted postdoctoral research in affective neuroscience at UC-San Francisco and at the National Institutes of Health.

Volunteer for Research

The Schizophrenia Center

The ultimate goal of our research in the Schizophrenia Center's research program is better understand the causes and progression of schizophrenia and related disorders. We routinely seek participants to help us in these research projects. The studies listed below are currently actively recruiting participants.

First Episode Psychosis: Longitudinal Characterization of Molecular Biomarker Changes Over the Early Course of Psychotic Disease
Researchers are seeking individuals diagnosed with a psychotic disorder to participate in a research study being done to study the cells of patients with psychotic disorders. Your participation may help improve the treatment of psychotic disorders for patients like you. This study is a longitudinal study over the course of three years (only a few visits required per year): you can earn up to $1740. To be eligible for this study, you must be between 13-35 years of age with a psychotic disorder diagnosis – this may include schizophrenia, bipolar disorder, and mood disorders. Qualified participants have the option of undergoing: blood draw, skin biopsy, nasal biopsy, lumbar puncture, and two sessions of brain scanning with MRI technology. To learn more, please call Patricia at 443-287-4986 or email at Pgraf2@jhmi.edu (NA_00082086, Principal Investigator: Akira Sawa, MD, PhD)

Cell and MRI Study of Patients with Schizophrenia
Do you have Schizophrenia? Are you between 18-65 years of age? You may be the perfect candidate for our study! Researchers are seeking individuals diagnosed with Schizophrenia to participate in a research study being done to study the cells of patients with schizophrenia. The study takes place over the course of two weeks, during which you can earn a compensation of up to $500! Qualified participants will have the option of undergoing neuropsychological testing with a study team member, a blood draw, a nasal biopsy, and three sessions of brain scanning

using MRI technology.To learn more, please call Cecilia Higgs, chiggs@jhmi.edu 443-287-2981. (Principal Investigator: Akira Sawa, M.D., Ph.D., (IRB # NA_00037204)

Using a Novel PET Ligand for Imaging Brains

Earn up to $350 in only three visits! The purpose of our study is to validate the use of a new technique to image inflammation in brains of patients with recent onset Schizophrenia. In particular, we aim to image inflammatory activation using Positron Emission Tomography (PET). We are recruiting patients with recent onset Schizophrenia (and in the first five years of the disease). To be eligible for the study, you must be over 18 years old. As a study participant, you will be asked to undergo preliminary tests including: a blood draw, a urine sample, a pregnancy test (if applicable), an EKG test (painless measurement of your heart's electrical activity), neuropsychological testing and a physical exam. In addition, we will schedule 2 imaging visits, 1 MRI and 1 PET scan visit. Participants will receive compensation of up to $350, paid in segments after completion of each portion of the study. To learn more, please call Dr. Coughlin at 443-287-4701or email at jcoughl2@jhmi.edu. (NA_00023849, Principal Investigator: Martin Pomper, M.D., Ph.D)