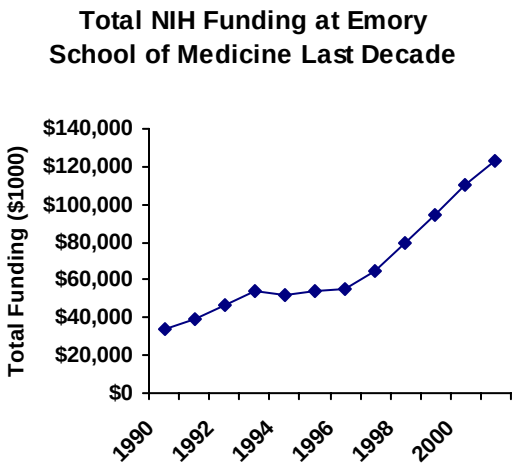
A.1 Rationale and History

Brain imaging has led to an explosion of knowledge about the brain and mechanisms underlying mental disorders over the past decade, however the complicated and rapidly changing nature of the imaging sciences limits progress in this area. More importantly, the complex and technical nature of the imaging sciences discourages clinicians with good research ideas that have clinical relevance from pursuing their ideas. Engineers, physicists and computer scientists with the technical know-how do not have exposure to clinical areas of mental health which would allow them to perform research translating into real gains for patients with mental disorders. Programs that combine medical and behavioral scientists with engineers and physicists have great potential to push forward the envelope in the imaging sciences in a way that will translate into real gains for patients with mental disorders. The technology of imaging is changing so rapidly that interdisciplinary programs are critical to make significant advances. Atlanta has a natural template to combine doctors and engineers, in the Georgia Institute of Technology and the Emory School of Medicine and relevant departments at Emory College. There is a critical need for training programs to address deficiencies in knowledge of the imaging sciences. The addition of a training program in neuroimaging sciences will be a value added addition to the Emory and Georgia Tech communities. The program will provide critical training for scientists from a wide range of backgrounds in the neuroimaging sciences. Trainees coming from diverse backgrounds including neuroscience, psychiatry, engineering, physics and computer science, will emerge with the tools they need to become independent investigators. What is more, the addition of courses in psychopathology, and interview sessions with patients with real mental disorders, will give all of the trainees a perspective that will enable them to become directed toward applying imaging research to an understanding of mental disorders in a way that will really help people with mental illness. Georgia Tech is a leader in biomedical engineering (BME) and other engineering areas, and Emory has up and coming psychiatry, neuroscience and neurology departments. Because of the obvious need to integrate BME with clinically relevant medical research, Georgia Tech and Emory recently formed a joint BME Department with $35 million in funding support, as described below. However, many investigators are physically and intellectually disparate. The Emory and Georgia Tech faculty do not have opportunities for exchange of ideas and information. Engineers at Georgia Tech are developing cutting edge technology, but they don't have the opportunity to translate this knowledge into real clinical gains because of their separation from clinical programs. If they do translate into clinical practice, it is in the areas of cancer or heart disease.



The proposed T-PINS will change all of that. The T-PINS will provide a structure for these clinicians and scientists to interact and cross-fertilize, through lectures, seminars, and joint supervision of trainees. The T-PINS will also re-direct the attention of imaging scientists toward the goals of mental health research, by providing support for trainees to work in their laboratories, and a forum to interact with scientists and clinicians focused on mental health. Finally, the T-PINS will produce an outstanding crop of young investigators, who have rubbed shoulders with scientists and clinicians from all areas, and have obtained training in everything from the details

of image processing, to kinetic modeling, structure of the synapse, to clinical psychopathology and real life encounters with patients with mental illness.

With the rapidly converging nature of diverse imaging technologies, including positron emission tomography (PET), magnetic resonance imaging (MRI), spectroscopy, optical imaging, and computed tomography (CT), it makes sense to have a program that provides training in all of these modalities, to prepare the individual to have the greatest flexibility in a rapidly changing field. Up until now the possibilities for rigorous training have been few and far between, and aspiring young investigators have performed a catch-as-catch can self-education while simultaneously trying to launch an independent research career. Thus it is no surprise that the majority of these enterprises do not lead to sustained independent research careers. The few areas where there is some opportunity for education, e.g. in radiology residencies or schools of engineering, are provided for individuals who may or may not be directed toward an independent research career in neuroimaging sciences. It is also desirable to have M.D.s and Ph.D.s in a common training program, to enhance translation from basic science to clinically relevant questions, and to permit clinical knowledge to inform basic science developments. Finally, there are no programs that adequately provide training in imaging sciences, neuroscience, cognitive psychology, and psychopathology, with a practical exposure to patients with real mental disorders, that will allow individuals from all backgrounds to emerge with the tools that they need to perform cutting edge research with real relevance to patients with mental disorders.

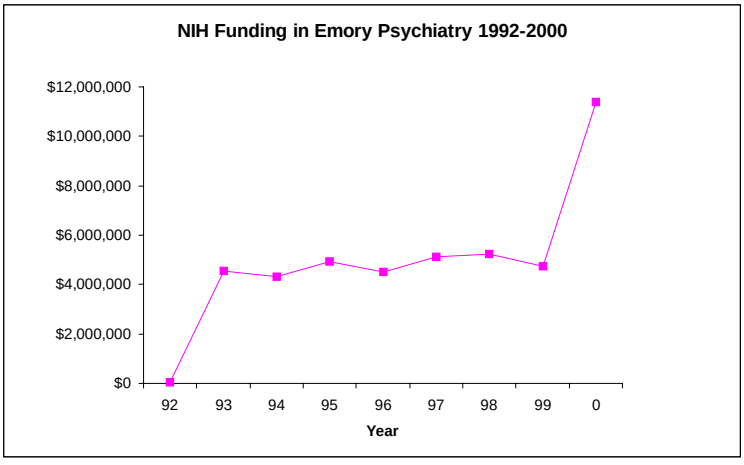
Emory and Georgia Institute of Technology represent an excellent environment for a training program in neuroimaging sciences. Emory has experienced an incredible increase in research productivity in the past decade. With the help of a large endowment from the Woodruff family in 1980, the single largest to any university in history at that time, Emory was positioned to grow into having a 5 billion dollar endowment, now one of the nations largest. Emory has used this to fund a $500 million capital development campaign, including funding for research infrastructure that has attracted research talent and led to a doubling of research dollars every few years with a total 333% increase over the last decade. This is ahead of the national trend, which did not quite see a doubling of funding in that period. Emory Psychiatry and Neurology have gone from having essentially no funding at the beginning of the 1990s to having exponential funding growth in the past decade. The number of training programs at Emory has grown from 2 15 years ago to 15, making it an increasingly excellent environment for training. The MD/PhD Program, HIV/AIDS Behavioral Training, and Neurosciences Training Program, are excellent training environments with trainees who would mutually benefit from interacting with the trainees in the current proposed program, and many of the faculty are overlapping. The Georgia Institute of Technology has also continued to grow in research funding, and consistently ranks in the top 10 nationally in several departments related to engineering. The proximity of Emory and Georgia Tech is especially germane to training in the technically involved area of neuroimaging sciences.

Emory has excellent departments of psychiatry and related disciplines such as neurology and radiology, PET and MRI Centers, and outstanding basic neuroscience research including the Yerkes Center for Non-Human Primate Research, the Center for Behavioral Neuroscience, Emory Conte Center for the Neurobiology of Mental Disorders, graduate programs at Emory in neurosciences and psychology. The Georgia Institute of Technology adds outstanding strengths in technical fields that are relevant to

imaging, including the joint Georgia Tech/Emory Biomedical Engineering Program, as well as psychology and computer science.

The program will involve training in one primary discipline with interaction, direct or collaborative, with other disciplines. We have greatly enriched and expanded our training curriculum. Although the number of faculty were reduced from 40 to 30 to focus the group into those most closely related to the aims of the program, we added three Georgia Tech faculty who are working in the area of imaging at the nanoparticle level. A key aim of the program is to provide fellows for them to train in their labs and ensure that these fellows receive an enhanced clinical and neuroscience training, so that their future work will be relevant to mental health. We increased the lecture series to 87 lectures, given twice a week, by adding lectures in optical imaging, imaging at the nanoparticle level, neuroscience, cognition, and clinical psychiatry (with practical forums in which a psychiatrist on the faculty interviews patients with mental disorders with the fellows). We also leveraged existing resources at Georgia Tech and Emory to add didactic courses in statistics, psychology (cognition), neuroscience, psychopathology, and imaging sciences. The Images of the Future monthly symposium will bring in outside speakers who will meet with the fellows. The revised curriculum will provide the broad range of tools needed for all trainees to go forward and perform cutting edge imaging research that is directly relevant to patients with mental disorders throughout their career. This program will be unprecedented in its breadth and scope, and promises to make important contributions to our knowledge of mental disorders. Planning the curriculum has generated enthusiasm and interest amongst the faculty members, and several have expressed an interest in attending the lectures for their own education. This multidisciplinary approach is the best way to perform cutting edge research in this rapidly changing and technology driven field. New approaches in physics, engineering and computer science lead to new methods and more successful strategies that are applied to image acquisition and processing, which facilitate the ability to answer clinical questions. Advances in organic and radiochemistry permit the development of radiopharmaceuticals which make it possible to answer for the first time questions about neurochemical changes in humans with neuropsychiatric disorders. The T-PINS includes strong participation in cognitive psychology from both Emory and Georgia Tech. Direct exposure to clinicians through joint training and collaboration allows basic scientists to work on problems and develop tools that are more applicable to the most important questions in mental health, thus increasing the relevance of their own work.

The training program is related to the research objectives of the NIMH by fostering the training of researchers to produce new knowledge about mental disorders and maladaptive behavior. Basic and clinical research is carried out to apply neuroimaging technology to the study of neuropsychiatric disorders, including mood and anxiety disorders (depression, posttraumatic stress disorder (PTSD), panic disorder), and



neuropsychiatric aspects of neurological disorders (.e.g, depression in patients with Parkinson's disease, primary dystonia, and epilepsy).

A.2 Training Faculty and Facilities

The T-PINS benefits from the inter-disciplinary collaborative nature of physicians and basic scientists at Emory University and the Georgia Institute of Technology. There are already strong resources in place at Emory and Georgia Tech to support research training. The faculty in this program are PIs of $110 million ($25 million per year) worth of currently funded research grants (including total years of support) which is mostly from NIH (Table 3 in the appendix). The T-PINS faculty published 608 data oriented papers in peer reviewed journals since 1997, over half of which were written with their trainees (Appendix Table 5). Of these articles, 21% were written by faculty primarily involved in brain imaging in psychiatric disorders (both humans with mental disorders and non-human primate models), 20% imaging methods and development, 15% in biomedical engineering, 8% in brain mapping, 8% human cognition, and 4% radioligand development. These statistics show the broad range of involvement of the faculty in a range of interests that will enrich the experience of the trainees.

Strengths of the proposed training program include the opportunity for psychiatrists and behaviorally oriented neurologists to work directly with neuroscientists, cognitive psychologists, physicists, engineers, computer scientists, and radiochemists. This will permit an immersion in a complex and technological field that will benefit them in their future careers. Basic scientists also have the opportunity to participate in studies that have a direct and immediate clinical outcome, e.g. PET and MRI studies of the effects of selective serotonin reuptake inhibitors (SSRIs) on brain circuits and structures in patients with PTSD and depression, quantitative measurement of benzodiazepine receptor binding in the brain in patients with panic disorder, discovery of medications that block the behavioral effects of cocaine in non-human primates with correlations with dopamine receptor occupancy, or correlating depression with thalamic stimulation in patients with dystonia.

The T-PINS has a solid foundation in the relevant basic sciences. Georgia Tech had 7 engineering programs in the top 10 in the nation this year based on the US News and World Report rankings. Georgia Tech formed a joint venture with Emory to combine medical doctors and scientists with engineers and push forward the envelope of applied medical technology. The Wallace H. Couter Georgia Tech/Emory joint Biomedical Engineering (BME) Program is highly relevant to this training program and will be a cornerstone of the T32. BME was founded by Don Giddens, PhD, GRA Eminent Scholar, and currently Dean of Engineering at Georgia Tech, with the support of a $16 million leadership development grant from the Whitaker Foundation, and later a $25 million award from the Wallace H. Couter Foundation. BME is currently Chaired by Larry McIntire, PhD. BME jumped from #6 to #2 nationally in this year's US News and World Report rankings of BME departments nationwide. BME has research programs in Cellular and Tissue Engineering, Neuroengineering, Biomedical Imaging, Bioinformatics/System Biology, Cardiovascular Biomechanics and Biology, and Biomedical Engineering/Bionanotechnology.

Emory Psychiatry has also risen dramatically from having no NIH funding 15 years ago to having over 20 million dollars per year and rising at an annual increase of 35% per year. Emory Neurology has demonstrated a similar Cinderella story. The Georgia Research Alliance (GRA) is a partnership of business, the state's research universities, and state government that was founded in 1995 to promote biotechnology industry and the state economy by investing in technology that will lead to new biotechnology business in the State of Georgia. GRA supports 40 eminent scholars (including Dr Hu), research laboratories and equipment (including the Emory

HRRT through matching of NCRR funds, and the Emory 3T MRI), national centers for research and innovation, and technology transfer. GRA has invested $350 million, with 2 billion leveraged in federal funds. Drs Bremner and Hu, as Directors of PET and MR Biotechnology for Georgia Tech and Emory, are in excellent positions to capitalize on these resources and further the goals of imaging sciences for Georgia Tech and Emory. There is nowhere in the world where a technology-focused educational institution and a traditional university are in such close collaboration and proximity, not to mention an association with up and coming departments of psychiatry and neurology as well as the Yerkes Primate Center. Georgia Tech and Emory are therefore poised to become world leaders in the neuroimaging sciences, which will represent an excellent environment for training in neuroimaging sciences.

Emory University and Georgia Tech are in a unique position to provide a quality training program for M.D.s and Ph.D.s in the neuroimaging sciences. There is a wealth of scientific talent in neurosciences, psychiatry, neurology, engineering, physics, chemistry, computer science, and related disciplines. In addition, established programs at Emory in relevant areas will provide a rich environment for trainees in translational neuroimaging sciences to interact. The Center for Behavioral Neuroscience (CBN) (Albers, Director; Zola, Co-Director) was created by a $20 million grant from the National Science Foundation (NSF), one of the largest grants ever awarded by NSF, as one of five neuroscience centers in the country. CBN is a collaboration of eight Atlanta universities, including Emory and Georgia Tech. Other programs include the Emory Conte Center for Early Life Stress (C. Nemeroff, PI), Program Project Grants in Parkinson's Disorder (M. DeLong, PI), Primary Dystonia (J. Vitek, PI), the Yerkes Center for Primate Research (S. Zola, Director), and the Emory/Georgia Tech Biomedical Engineering Program (McIntire, Chair).

Another strength of the T-PINS is the outstanding convergence of excellent researchers in clinical and basic neuroscience and imaging sciences-related fields. The Department of Psychiatry at Emory has excellent leadership under Charles Nemeroff MD, PhD. Dr Nemeroff is a world leader in the field of psychiatry internationally both in research and clinical domains, and is Director of the Emory Conte Center for Early Life Stress. Emory recently recruited Stuart Zola PhD to direct the Yerkes Primate Center. The Department of Neurology (Allen Levey, MD, PhD, MD, Chair) has several program project grants and other NIH funding sources in Parkinson's disease, Dystonia, and epilepsy, with a major focus being collaboration with psychiatry to understand neural correlates of behavioral manifestations of these disorders. The Emory Department of Psychology under the leadership of Darryl Neill, Ph.D., is strongly committed to participating in the T-PINS, as is Randall Engle, Ph.D., Chair of Psychology of Georgia Tech. This involvement will provide a rich experience in training in applications of memory and cognition to neuroimaging.

There are several facilities who will participate in the T-PINS. The training faculty and fellows located in these facilities will interact with each other on a regular basis through collaborative research projects, seminars, and workshops as described below. Emory and Georgia Tech, with the help of the GRA, have invested heavily in imaging technology, including two 3T MRIs, 4.8T animal magnet, 9.8T animal magnet, MicroPET, Brain PET HRRT, cyclotron and two PET-CTs at Emory Hospital, optical imaging equipment at Georgia Tech, and a MicroPET and cyclotron at Yerkes, all of which are described in more detail below and in the Resources section. The joint Georgia Tech/Emory Biomedical Engineering is planning construction of a Biocomplex building on Emory's campus.

The Office of Postdoctoral Education (POE), Emory University School of Medicine, is an important resource for postdoctoral fellows and their training programs. The OPE currently supports approximately 470 postdoctoral fellows as well as their advisors in the School of Medicine, and serves as liaison to postdoctoral programs in other units of the University and in collaborating institutions. OPE postdoctoral programs and services include oversight of institutional postdoctoral policies and benefits, provision of postdoctoral career development and professional skills workshops, and support of postdoctoral communication via orientation activities, postdoctoral listserv and website services, and postdoctoral alumni tracking. Training in grant writing and review, in the responsible conduct of research via the University course *Values in Science* and structured guidance in job searches for academic research careers are important functions. The OPE also supports postdoctoral recruitment through national and regional recruitment activities, including participation in national minority career events, and assists in fellowship and other postdoctoral funding applications.

Grants from the NIH Awarded to T-PINS Faculty as PI

Grant Number	PI	Title
R01 NS44409	Bellamkonda, Ravi	A novel multiple ligand approach to targeting brain tumors
R01 NS043486	Bellamkonda, Ravi	Chondroitin sulfate GAG inhibition of growth cones
R01 NS045072	Bellamkonda, Ravi	Strain-induced scarring and its effects on microelectrodes
R01 DC06849	Bellamkonda, Ravi	Neurointegrative coatings for improved neural recordings
K08 DA00367	Berns, Greg	Neuroimaging of Novelty Detection in Cocaine Dependence
R01 MH61010	Berns, Greg	Integration of Bifurcation Theory and Continuous fMRI
R21DA014883	Berns, Greg	Hyperscan: Simultaneous fMRI Across the Internet
R01 DA016434	Berns, Greg	The Neurobiology of Uncertainty
K25 MH0654731	Bowman, Dubois	Statistical Methods for Neuroimaging Data
S10 RR16917	Bremner, J. Douglas	Shared Instrumentation for a Research PET Brain Device
R01 MH56120	Bremner, J Douglas	Neural Circuits in Women with Abuse and PTSD
P50 MH58922	Bremner, J Douglas	HPA Axis and Hippocampus in Women with Early Life Stress (Project #7)
R01 NS30212	Crutcher, Michael	Cortical Mechanisms Of Motor Processing
P50 NS38399	DeLong, Mahlon	Models Of Parkinson’s Disease – Therapeutic Implications
AT00610	DeLong, Mahlon	Center for Alternative Medicine in Neurodegenerative Diseases
R01 HL068904	Faber, Tracy	Detecting changes in myocardial perfusion and function

R21 MH066622	Goodman, Mark	Development and Applications of Novel SERT PET Ligands
R01 DA10344	Howell, Leonard	PET Imaging and Cocaine Pharmacology in Primates
R01 DA12514	Howell, Leonard	Cocaine Use and Monoamine Function in Nonhuman Primates
K02 DA000517	Howell, Leonard	Neuropharmacology of Cocaine in Nonhuman Primates
U19 DA13326	Howell, Leonard	Novel pharmacotherapies for treatment of cocaine addiction (project leader)
R01 MH055346	Hu, Xiaoping	Improvement and Applications of Functional MRI
RR 08079	Hu, Xiaoping	fMRI of neuronal activity
R01 DA 015229	Kilts, Clint	Cocaine dependence and cognitive control of behavior
T32 DA15040	Kuhar, Michael	Training program in the neurobiology of drug abuse
R01 DA010732	Kuhar, Michael	CART: A Novel Cocaine Regulated Neurochemical
R01 DA015162	Kuhar, Michael	Promoter Characterization of the CART Gene
K05 MH069124	Miller, Andrew	Pathology and treatment of cytokine induced depression
R01 HL073921	Miller, Andrew	Pathophysiology of IFN-alpha-induced sleep disturbances
R01 MH060723	Miller, Andrew	IFN Alpha-Induced Depression
T32 MH020018	Miller, Andrew	HIV/AIDS Clinical Research Training Program
R01 MH067990	Miller, Andrew	Frontal striatal dysfunction in IFNa induced depression
P50 MH58922	Nemeroff, Charles	Emory Conte Center for Neuroscience of Mental Disorders
N01 MH90001	Nemeroff, Charles	Comparative effectiveness of antipsychotic medications (CATIE)
U19 MH69056	Nemeroff, Charles	Emory GSK NIMH collaborative disorders initiative
R01 MH039415	Nemeroff, Charles	Neurotensin, An Endogenous Neuroleptic-Like Peptide
R01 MH042088	Nemeroff, Charles	Psychobiology of Corticotropin-releasing Factor
R01 HL059345	Oshinski, John	Development of navigator echo based magnetic resonance angiography
R01 HL158147	Oshinski, John	Robust contrast for auto analysis of cardiac cine images
R01 NS038628	Potter, Steve	Multielectrode & Imaging Analysis of Cultured Networks

R01 EY12440	Sathian, Krish	Cross Modal Interactions in Vision and Touch
R01 HL66287	Vaccarino, Viola	Mechanisms Linking Depression to Cardiovascular Risk
PO1 NS37470	Vitek, Jerrold	Functional mapping of normal and Parkinsonian basal ganglia
R29 NS30719	Vitek, Jerrold	Thalamic Mechanisms Underlying Parkinsonian Signs
R01 NS037959	Vitek, Jerrold	Deep brain stimulation for Parkinsons Disease
R01 NS037019	Vitek, Jerrold	Deep brain stimulation in the Parkinsonian monkey
R01 MH58922	Votaw, John	Cognitive effects of anesthetics and dopamine transport
R01 AI38282	Zhu, Cheng	Ligand binding kinetics and cell adhesion by Fc receptor
R03 TW05774	Zhu, Cheng	Kinetic analysis of the PSGL-1 molecule
P51 RR00165	Zola, Stuart	Support of the Yerkes Regional Primate Center (Johns PI, Zola Dir.)