FACILITIES & OTHER RESOURCES

UNIVERSITY OF MINNESOTA

Founded in 1851 as a public land-grant university, the University of Minnesota (U of MN) is the state's only research university and a major center of education, creative scholarship, research, and service. The U of M is one of the largest universities in the U.S., with more than 66,000 students and some 4,000 full-time faculty, and is one of the largest employers in Minnesota. The U of MN is also one of only four universities in the nation that have a Medical School, College of Veterinary Medicine, Engineering School, and Agricultural College on the same campus. This makes the U of MN one of the nation's largest campuses and it significantly facilitates interdisciplinary research and projects.

Collectively, the U of MN, through its commitment to the PI from both the Department of Pediatrics, the MIDB and other resources (described below) provides a collaborative and supportive environment to enable successful completion of the proposed studies.

University of Minnesota Masonic Institute for the Developing Brain (MIDB)

The MIDB represents the outstanding neuroscience, neuroimaging and bioinformatics research programs. The MIDB is dedicated to fostering the healthy brain function of children across the lifespan with the mission to set and maintain a healthy trajectory for all children toward positive life outcomes through early neurobehavioral and mental health assessment, innovative targeted interventions, informed policy-making, compassionate child-advocacy, and community education. Committed to collaboration, MIDB researchers are from numerous departments, including Pediatrics, Neuroscience, Child Psychology, Child Psychiatry and Psychology. Dr. Damien Fair and Dr. Michael Georgieff serve as co-directors of MIDB.

Facilities

1 Laboratory: The 100,000 square foot MIDB facility houses the Center for Neurobehavioral Development (CNBD) interdisciplinary clinical research center, the Child and Adolescent Psychiatry, Pediatric Neuropsychology and Pediatric Neurology clinics within MHealth-Fairview, and the Institute on Community Integration-a policy and educational outreach facility. The MIDB's mission of basic and clinical research in the field of neurobehavioral development is supported by multiple cores including: Analytics, Informatics, Neuroimaging, Human Phenotyping, Translational Neuroscience, Neurointervention, Community Integration and Education, Tele-outreach, and Global Health.

The MIDB provides administrative, educational, and physical space to support over 50 research projects. The MIDB is administratively housed in the Office of Academic and Clinical Affairs in the Medical School and the College of Education and Human Development (CEHD) and reports to the Deans of the Medical School and CEHD. It has academic associations with the Center for Magnetic Resonance Research (which administers the 3T magnet located in MIDB), the Genomics Center, the Stem Cell Institute, and the Minnesota Supercomputing Institute

2. Office Space: Researchers who are conducting studies at the CNBD are assigned space in one of nine 150 square foot research suites. Each office houses 4 computers and has ample locking file storage.

3. Clinical Research Area: The MIDB clinical research area occupies approximately 16,000 square feet in MIDB and consists of a family waiting room, 26 examination rooms and 9 research suites, 2 computer labs, and 5 conference rooms. The MIDB's examination rooms accommodate equipment and assessment tools which allow researchers to collect both behavioral, body composition, and electrophysiological (EEG) assessments. A 3T research MRI scanner is located within CNBD. Specific resources available for the study of children include 2 high density (128 channel) EEG systems, Tobii TX300 eye tracker; Biopac autonomic suite, NIH Toolbox devices, and , and standard child neurodevelopmental assessment batteries. Body composition assessment is available via PeaPod and BodPod Air Displacement Plethysmography (ADP) systems and GE Lunar iDXA machine. Pediatric phlebotomy and laboratory services are available via the MHealth Fairview Clinic located on the first floor of the MIDB. A Neuromodulation Laboratory providing both magnetic and low current electrical stimulation is located within MIDB (see Neurointervention Core). The MIDB also provides staff support to assist in the use of equipment and to process and analyze data. The MIDB is a core facility for the NIH –funded University of Minnesota Clinical and Translational Science Institute (CTSI).

4. Computer Hardware and Software: The CNBD has a computer lab which houses 12 computers, outfitted with software for data collection and analysis such as EPrime, SPSS, SAS, Brains2, Matlab, BESA, Procoder, and Netstation. The research suites (also containing software for data collection and analysis) house a total of 36 networked computers. The U of M Health Sciences Technology office supports all the machines including Apple based systems.

5. Analytics Core: The mission of the MIDB analytics core is to support data analytics, statistics, data harmonization and storage across a broad array of research activities relevant to brain health and brain development. The Core accomplishes its mission via: 1) consultation; 2) development of statistical methods and modeling, and 3) hands-on computational work. The Core also works closely with the Informatics Core to make developed tools and resources available to the broader community to facilitate research related to MIDB's mission.

6. Informatics Core: The mission of the MIDB Informatics Core is to support data acquisition, management, and interpretation needs across a broad array of research activities relevant to brain health. The guiding principle is that significant advances in brain health can only be made by harmonizing data across multiple large data sets with multiple modalities and species. The Core accomplishes its mission via: 1) Consultation; 2) Development of standardized data acquisition, processing, harmonization, and organization methods; 3) Aggregation, integration, and dissemination of basic, applied, clinical, and pre-clinical science data for MIDB stakeholders and collaborators. The Core works closely with other University of Minnesota informatics experts and individuals specializing in research and clinical care to facilitate research and training related to MIDB's mission. This core is directly embedded in the Universities Research Computing unit (https://research.umn.edu/resources/research-computing), which houses the Minnesota Super Computing Institute (https://www.msi.umn.edu/).

7. Neuroimaging Core: The mission of the MIDB imaging core is to equip investigators with the resources and knowledge base to conduct developmental neuroscience research of outstanding quality and significance. Alongside faculty and staff from the world-renowned Center for Magnetic Resonance Research (CMRR), we provide access to state-of-the-art approaches in 1) image acquisition; 2) experimental design; 3) preprocessing; 4) data analysis; 5) flexible data sharing. The imaging core fosters collaborations within departments at the University of Minnesota and across institutions to build teams with the highest possible degree of expertise. Ultimately, we seek to better understand the neural basis of cognition, emotion, and perception, discovering interactions between brain, behavior, and the environment that shape changes throughout typical and atypical development. The Core works closely with the Center for Magnetic Resonance Research (CMRR) (see below).

8. Human Phenotyping Core: The primary mission of the Measurement and Human Phenotyping (MAP) Core is to support the clinical research community. Anchoring this mission is the fundamental observation that adaptive and maladaptive functioning that define psychiatric and neurodevelopmental disorders is first and foremost determined by cognitive and behavioral assessment. The MAP core has assembled a team of experts to 1) optimize clinical, developmental, and experimental assessment of research participants; 2) train researchers on state-of-the-art and/or gold standard clinical, developmental, and experimental assessments; 3) execute clinical, developmental, and experimental assessments for research studies; 4) manage and cultivate continued expansion of research participant registries; 5) integrate and iterate with the informatics, neuroimaging, and neuromodulation cores to ensure effective synthesis across the units; and 6) establish a Biomarker Consultative Committee, constituted by key experts around campus but external to MIDB to ensure that MIDB investigators are leveraging the broader expertise of the University community as needed.

9. Translational Neuroscience Core: The mission of the translational core is to generate new laboratory discoveries about neurodevelopment that can be rapidly and safely translated to the clinical research and clinical care delivery settings in MIDB. The members of this core are involved in the flow of scientific information from "bench to bedside" and are responsive to research agendas driven from clinical care.

10. Neurointervention Core: The mission of Intervention Core of the Masonic Institute for the Developing Brain is to seek foundational knowledge about the developing brain and nervous system and to apply that knowledge towards integrated interventions that optimize pediatric outcomes, for a lifetime. To support this mission, the intervention core: 1) Conducts research to advance pediatric outcomes through valuable scientific discoveries in pediatric health and care. 2) Develops novel cutting-edge interventions such as neuromodulation. 3) Promotes the experience and backgrounds of a diverse team of experts for the individual care and development of the optimal intervention for each child. Within the Neurointervention Core, he non-invasive Neuromodulation Laboratories are equipped with the most advanced non-invasive neuromodulation devices/systems, including:

- Transcranial Magnetic Stimulation, TMS: The Magstim BiStim² and Magstim 200² set (The Magstim Co. Ltd., Carmarthenshire, UK).
- Repetitive TMS, rTMS, TBS: The Magstim Rapid^2 (The Magstim Co. Ltd., Carmarthenshire, UK)
- Electromyogram, EMG acquisition system: 4-ch bipolar EMG pre-amplifier (Y03-2, Motion Lab Systems, Inc., Baton Rouge, LA) (Gain: 300, band-pass filter: 20~2000Hz).
- Cadwell 4-ch EEG amplifier system.(Cadwell Industries Inc. WA, USA).
- High definitive Transcranical Direct/Alternative Current Stimulation, tDCS/tACS: Starstim NE wireless alternative/direct current stimulation system with 8-ch wireless EEG amplifier (Neuroelectrics SL, Massachusetts, USA).
- Electroencephalogram, EEG acquisition system: 64-ch EGI amplification system (EGI Magstim-EGI, UK).
- Neuronavigation system: frameless stereotactic BrainSight II neuronavigation system (Rogue Research Inc, Quebec, Canada).
- Medical grade isolation transformer: ISB-100W medical grade isolation transformer (Power Sources Unlimited, Inc, Massachusetts, USA).
- System control platform: including data acquisition system: NI 9234 Analog-to-digital converter (National Instruments, Austin, TX) with a sampling rate upto 100K Hz with a quantification resolution of 24-bit. Real-time data monitoring and analysis system powered by LabVIEW (v2012, National Instruments, Austin, TX). Equipment communication and control system powered by LabVIEW (National Instruments, Austin, TX).

With equipment and facilities, the Non-invasive Neuromodulation Laboratories are able to conduct almost all of the non-invasive TMS excitability assessments and neuromodulation paradigms including:

- *Cortical excitability assessment:*

- Single pulse: basic excitability assessment including single pulse test, S-R curve, CSP and cortical grid mapping.
    - Paired pulse: SICI, ICF, SICF, LICI, IHI, I-wave curve, ISI curve, CI curve and SAI.
- *Neuromodulation interventions:*
    - Low-frequency rTMS (inhibitory) and sham
    - High-frequency rTMS (facilitatory) and sham
    - PAS intervention which combines low-frequency rTMS with peripheral electrical stimulation. We can easily recorded the N20 SEP by customized fast EEG acquisition method, and use the N20 as a reference to induce LTD-/LTD-like PAS neuromodulation intervention (inhibitory and facilitatory respectively)
    - tDCS (StarStim, Neuroelectrics, Barcelona, Spain)
    - tACS (StarStim, Neuroelectrics, Barcelona, Spain)
- *Sensory function evaluation:*
    - N20 SEP latency
    - Temporal discrimination test
    - Electrical stimulation perceptual threshold
- *Customized experiment protocol:*
    - The system control platform is highly customizable to any new/tailored protocol design.

11. Community Integration & Education Core: The Community Engagement and Education (CEE) Core promotes healthy development by fostering strong community connections, inviting community input for MIDB services and research, linking the community to developmental services, promoting science-based policies and practices that result in tangible solutions that improve people's lives in the community, and grooming the next generation of URM scientists in developmental medicine and neuroscience.

12. Administrative Core: The MIDB Administration Core supports program management specific to the needs of mutli-PI/multi-site studies, including program management/project tracking software, web conferencing, coordination of subject testing and family accommodation, collaborative meeting spaces, and communication support. They have administrative support who assist in preparing presentations, manuscripts, and grant applications.

13. Other: Office space and furnishings for postdoctoral researchers and research assistants are provided by the division for all staff listed.

Minnesota Supercomputing Institute (MSI)
Established in 1983, the Minnesota Supercomputing Institute (MSI) is the University of Minnesota's principle center for computational research. MSI provides services to over 880 active groups that sponsor more than 4,500 unique users from 19 different university colleges, maintaining an array of systems dedicated to the computational and data intensive research needs of investigators in the state of Minnesota's higher education institutions and their collaborators.

Facilities
1. Data Centers, Network Connectivity, and Office Facilities**:** MSI enables interdisciplinary research through its robust data center facilities with over 1 MW of IT capacity to support leading edge computational and data storage systems. MSI supports two data centers, both of which are connected to the 10 Gbps campus network and the 100 Gbps dedicated science network called the Gopher Science Network (GSN). Dedicated 10 and 100 Gbps links to our regional optical network and Internet2 give our researchers the network capacity and capability needed to collaborate with researchers from around the world. Located in the Walter Library building, MSI office and data center space (~ 18,000 sq. ft) are centrally located on the Minneapolis campus. MSI also maintains office spaces on the Saint Paul campus where additional researchers are located. MSI also

provides computer and teaching laboratories that are routinely used for research by users but also for outreach and teaching workshops.

2. High Performance Computing**:** MSI's High Performance Computing (HPC) systems are designed with high speed networks, high performance storage, GPUs, and large amounts of memory in order to support some of the most compute and memory intensive programs developed today. MSI's HPC systems are comprised of over 40,000 X86 64-bit compute cores and 145 TB of RAM, which can support over 1.6 PFLOPS of peak performance. HPC nodes are equipped with between 64 GB and 2 Tb of RAM to support applications that require small and large amounts of memory, 32 nodes have Solid State Drives (SSDs) to support applications with demanding input and output (I/O) requirements, and 57 nodes include various configurations of the NVidia general purpose GPU accelerators (K40 and VT100), from 2- to 8-way. Besides the free resources that are available to all the PIs at the MSI, in this proposal we are budgeting 1 node with 128 cores and 2048 GB of RAM as dedicated resources.

3. Interactive Computing and Scientific Visualization**:** In collaboration with the Laboratory of Computational Science and Engineering, the MSI supports a visualization laboratory. The Lab can accommodate up to 24 people and is located in the same building as the MSI. MSI also supports specialized interfaces (i.e., NICE EnginFram and Jupyter Notebooks) and hardware for remote visualization and interactive computing. Interactive HPC systems allow real-time user inputs in order to facilitate code development, real-time data exploration, and visualizations. Interactive HPC systems are used when data are too large to download to a desktop or laptop, software is difficult or impossible to install on a personal machine, or specialized hardware resources (e.g.., GPUs) are needed to visualize large data sets.
1.3 Cloud Computing: MSI supports a cloud computing platform built on OpenStack to support special data use agreements and to allow quick deployment of web, database, and other non-High Performance Computing systems. The virtual instances in this environment are a variety of sizes depending on the number of processors and the amount of memory and disk space required for the project.

4. Data Storage**:** All MSI researchers have access to a high-performance parallel storage platform. This system provides 6.4 PB (PetaBytes) of storage with sustained read and write speeds of up to 48 GB/sec. The integrity of the data is protected by daily snapshots and tape backups. High value data sets are backed up to an off site facility as a part of the institute's disaster recovery plan. MSI also supports a second tier storage solution designed to address the growing need for resources that support data-intensive research. The system is tightly integrated with other MSI storage and computing resources in order to support a wide variety of research data life cycles and data analysis workflows and uses Amazon's S3 (Simple Storage Service) interface, so that researchers can better manage their data, more seamlessly share data with other researchers, and migrate entire data analysis pipelines to cloud-based platforms. In this proposal we are requesting 100TB of Dedicated Primary Storage. These data can be accessed from all MSI computing systems. We are also budgeting 100 TB of Dedicated Second-Tier Storage for storing less frequently used data.

Center for Magnetic Resonance Research (CMRR)
Center for Magnetic Resonance Research (CMRR), funded as a Biotechnology Research Center (BTRC) by the National Center for Research Resources (NCRR) until 2012 and by the National Institute of Biomedical Imaging and Bioengineering (NIBIB) since then, focuses on development of unique magnetic resonance (MR) imaging and spectroscopy methodologies and instrumentation for the acquisition of structural, functional, and biochemical information non-invasively in humans, and utilizing this capability to investigate organ function in health and disease.
The distinctive feature of this center is the emphasis on ultrahigh magnetic fields (7 Tesla and above), which was pioneered by this BTRC. This emphasis is based on the premise that there exists significant advantages to extracting biomedical information using ultrahigh magnetic fields, provided difficulties encountered by working at high frequencies corresponding to such high field strengths can be overcome by methodological and engineering solutions.

Facilities

1. MR Scanners: *The CMRR houses an array of high-field magnetic resonance scanners devoted to imaging and spectroscopy research.*

- ***Human systems (whole body):***
  - *3 Tesla/90 cm bore, Siemens Prisma console*
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  - *4 Tesla/90 cm bore, Varian/Siemens console*
  - *7 Tesla/90 cm bore, Passively Shielded (PS), Siemens console*
  - *7 Tesla/90 cm bore, Actively Shielded (AS), Siemens console*
  - *9.4 Tesla/65 cm bore, Varian console (human/animal system)*
  - *10.5 Tesla/82 cm bore, Siemens console (human/animal system)*
- ***Non-human systems:***
  - *9.4 Tesla/31 cm bore, Varian console, with attached 13C DNP hyperpolarizer*
  - *16.4Tesla/26 cm bore, Varian console*
  - *17 Tesla / 5 cm vertical bore levitating magnet*

2. Computing resources**:** Each of the MR instruments at the CMRR has a console host workstation along with physiologic monitoring and paradigm presentation computers. The scanners with Varian consoles (9.4T-31cm, 4T, 9.4T-65cm, 16.4T) use Linux workstations while the Siemens consoles (3T, 7T/AS & 7T/PS) use Windows based PCs. Each console host is connected by a 10 gigabit per second Ethernet network link for rapid transfer of image data to the data center for post- processing, analysis and storage.

3. Data center: The data center in the CMRR has 75 servers in a 750 sq. ft. room with redundant power (100KW Uninterruptible Power Supply and Diesel Generator) and redundant coiling systems (chilled water and glycol). To handle the enormous amount of image data generated by the 8 MR scanners, thirty (30) of these servers provide NFS file sharing with a total of 200 Terabytes of RAID data storage which supports not only fMRI research, but all other CMRR research, many of which are also quite data intensive, especially coil RF model simulations using the FDTD (Finite Difference Time Domain) method. Six (6) of the servers are dedicated to backups for disaster recovery contingency or long term archive and each has a 12 slot hot swappable hard drive bay attached that are filled with 2TB disks that are rotated offsite for safe keeping. Thirty two (32) of the CMRR servers are compute nodes, with an aggregate of over 460 CPU cores and 1.7 TB of memory where the largest single compute server node has 32 cores and 256GB of memory. Three (3) of these computes nodes each have a quad of Nvidia Tesla GPUs providing a peak double precision performance of over 2 Teraflops for accelerated computations which is becoming indispensable for the computation loads demands by both RF simulations and multichannel reconstruction.

In addition, as an fBIRN (functional Biomedical Informatics Research Network) grid point-of-presence, the CMRR houses a BIRN node, consisting of a gridftp server, HID (Human Imaging Database), and HID GUI interface server. The BIRN node supports distributed high-performance computing and data sharing between institutions at gigabit speeds over a nationwide network of Internet-2 connected computer systems.

4. Patient and Research Subject Spaces: The recently completed CMRR expansion was primarily designed to support translational clinical research. Towards achieving this goal, great care was taken for accommodating patient/subject handling facilities with over a 1000 sq. ft of space for waiting/reception area plus conference rooms for subject interview and staging rooms adjacent to each magnet suite. In addition 3,000 sq. ft. is dedicated to clinical research for patient and human subject preparation and nursing support.

5. Specialized Laboratory Space: The expanded building includes over 4000 sq. ft. of laboratory space for chemistry, histology and physiology research support.

6. Animal care and housing: CMRR includes 5000 sq. ft. dedicated space for animal care and housing. The animal housing are is fully equipped and managed by the University of Minnesota Research Animal

Resources (RAR). In addition, an 80,000 rodent vivarium is under construction in the Biomedical Discovery District and will be completed in 2014.

7. Machine Shops/Electronics Shop: Machine shops are available at the Physics Department and at the CMRR. A 1500 sq. ft. full electronics shop is located within the CMRR and is used for building RF probes, and developing physiological monitoring and recording systems for use in the MR scanner.

8. MRI Scanner Peripheral Equipment: The Prisma scanner room contains the necessary equipment to present experimental stimuli and acquire responses including (1) a rear projection system; (2) an S14 fMRI Compatible Insert Earphones system (Sensimetrics Corporation, Malden, MA); and (3) ergonomic subject response devices. Physiological Recording in the MR Scanner: During all EPI scans, recording of respiratory and pulse oximeter measurements is conducted using the built-in Prisma Siemens Physiological Monitoring Unity (PMU). The PMU records data from three sources: 1) respiratory bellows attached to the Physiologic ECG and Respiratory Unit (PERU), 2) pulse sensor attached to the Peripheral Pulse Unit (PPU), and 3) the external scanner trigger signal attached to the PMU input. The PMU records timestamps and scanner trigger information in each of the files, allowing synchronization of the recordings with the image acquisition.

9. Mock Scanner: If desired, participants may undergo a session in the mock scanner environment. The mock scanner acclimates participants to the scanner environment, thereby reducing anxiety, sensitization to noise, and head motion. The mock scanner environment is equipped with hardware to simulate the MR scanner environment: a 53cm bore and scanner opening, replica of the Siemens 32-channel head coil, coil-mounted mirror, fiber-optic button box, LCD projector, and Lucite screen.

Division of Biostatistics

The Division of Biostatistics at the University of Minnesota operates its own computer facilities, including a network of PCs and UNIX workstations connected by a divisional Ethernet for numerically intensive computing and database storage. Divisional computing is a University internal service organization with University approved rates; support staffs are available for software and hardware support, as well as day-to day maintenance and file backup. The Division of Biostatistics will provide standard office equipment, including copiers and a fax machine. Library facilities at the University of Minnesota will provide excellent support for background reading and research; in particular, many important books and journals are physically housed in the Division of Biostatistics reading room. The Division will provide necessary secretarial support for photocopy and limited technical typing as needed.

Division of Biostatistics Computing Resources. Research and teaching activities in the division are supported by an array of computer systems including high-end PC's, Unix/Linux-based workstations, and departmental file/application server. A wide variety of software and hardware supports the biostatistical needs for biomedical/health sciences investigators across the campus. There is access to excellent cluster-based computing facilities within the division. Further computational facilities are provided through the Minnesota Supercomputing Institute (MSI). Various application software packages and a comprehensive program development environment provide users with the means to analyze large scientific databases and run intensive parallel computations. The department is fully networked through its own LAN and the university communication backbone. The divisional network server is linked via a modem to a state-of-the-art personal computer located in the PI's office on which the data analyses will be performed using R and WinBUGS statistical software along with manuscript writing. Other software applications on the personal computer include spreadsheet, graphics and word processing capabilities. A laser printer is also available together with facilities for scanning and fax. There is a system administrator who is responsible for the domain, backup and web servers, department workstations, peripherals, and software.