Quantitative In Vivo Methods for Measuring Brain Networks

Summary
Researchers at the NICHD seek licensing and/or co-development research collaborations for a Magnetic Resonance Imaging (MRI) method to quantitatively measure in vivo the estimated conduction time of nerve impulses in the brain.

NIH Reference Number
E-226-2010

Product Type
• Diagnostics

Keywords
• Axon diameter distribution, DTI Tractography, Magnetic Resonance Imaging, MRI, connectome, MRI diagnostic

Collaboration Opportunity
This invention is available for licensing and co-development.

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Description of Technology
The pattern or latency connectome was hypothesized to change in physiological development and disease. For example, in amyotrophic lateral sclerosis (ALS), large diameter axons are damaged selectively – while in autism, small-diameter axons may be over-expressed. These anatomical changes are expected to alter the latency connectome or pattern of delays of information transmission between different gray matter areas involved in salient brain networks.

Researchers at the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) developed Magnetic Resonance Imaging (MRI) methods to measure the axon diameter distribution (ADD) within nerve fascicles (e.g., by AxCaliber MRI). A new technology extends this prior work by combining it with the non-invasive measurement of the path length of white matter fascicles (e.g., using DTI tractography or other tractography methods).
The technology combines and integrates information obtained from two different diffusion MRI methods (with the possible addition of other neurophysiological and imaging methods) to estimate the mean latency and latency distribution between different gray matter regions in the brain. The technology also uses AxCaliber MRI to estimate the ADD along white matter pathways, known to scale with conduction velocity. Diffusion-based tractography determines the path lengths of these white matter fascicles. Together, these data can be used to estimate the latencies or time delays for neural impulses travelling along these pathways, between the different gray matter areas they connect.

The technology is directed toward measuring the latency connectome in each subject *in vivo*. Data produced by this method include latency matrices. Latency matrices are data arrays that indicate the latency or latency distribution between any two functional gray matter regions in the brain. This method could be used to diagnose abnormalities in nerve conduction in brain regions and providing a neuroanatomical basis for many cognitive and behavior disorders. Techniques such as electroencephalography (EEG), magnetoencephalography (MEG), transcranial magnetic stimulation (TMS) and function MRI (fMRI) could be used in conjunction with this new invention - improving estimates of mean latencies and latency distributions.

**Potential Commercial Applications**
- Characterize normal and abnormal brain network function in development
- Diagnose brain network abnormalities in diseases and disorders of the brain such as Peripheral Nervous System (PNS), Alzheimer, autism, and Amyotrophic Lateral Sclerosis (ALS);
- A neuroanatomical basis for many cognitive and behavioral disorders.
- A basic tool in neuroscience and neuropsychological research to explore the dynamic functioning of the brain.

**Competitive Advantages**
- Diagnose several cognitive and behavioral abnormalities, disease and disorders that are currently only assessed using psychological or psychiatric testing;
- Provides new quantitative imaging biomarkers;
- Used to understand and follow brain changes during normal aging and in disorders and - diseases like MS and Alzheimer's disease;
- Used to explain motor deficits in ALS disease;
- Provides way of classifying and understanding various neurological and neuropsychiatric conditions per conduction delays.

**Inventor(s)**
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**Development Stage**
- Pre-clinical (in vivo)

**Publications**
Y. Assaf et al. [PMID 18506799]

D. Barazany et al. [PMID 19403788]

A.V. Avram, et al. [Abstract No. 6968]

R.D. Fields et al. [PMID 2968368]

**Patent Status**
- **PCT:** PCT Application Number 61/535,851, Filed 14 Sep 2012
- **Foreign Filed:** EP - Patent Application 127779598.5, Filed 14 Sep 2012
- **U.S. Patent Filed:** U.S. Patent Application Number 14/345,219, Filed 16 Jun 2014
- **U.S. Patent Issued:** U.S. Patent Number 10,996,303, Issued 04 May 2021
- **Foreign Issued:** Patent Number 2756324, Issued 14 Jul 2021

**Related Technologies**
- E-079-2003

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