Brain's mysteries unraveled through computational neuropsychiatry

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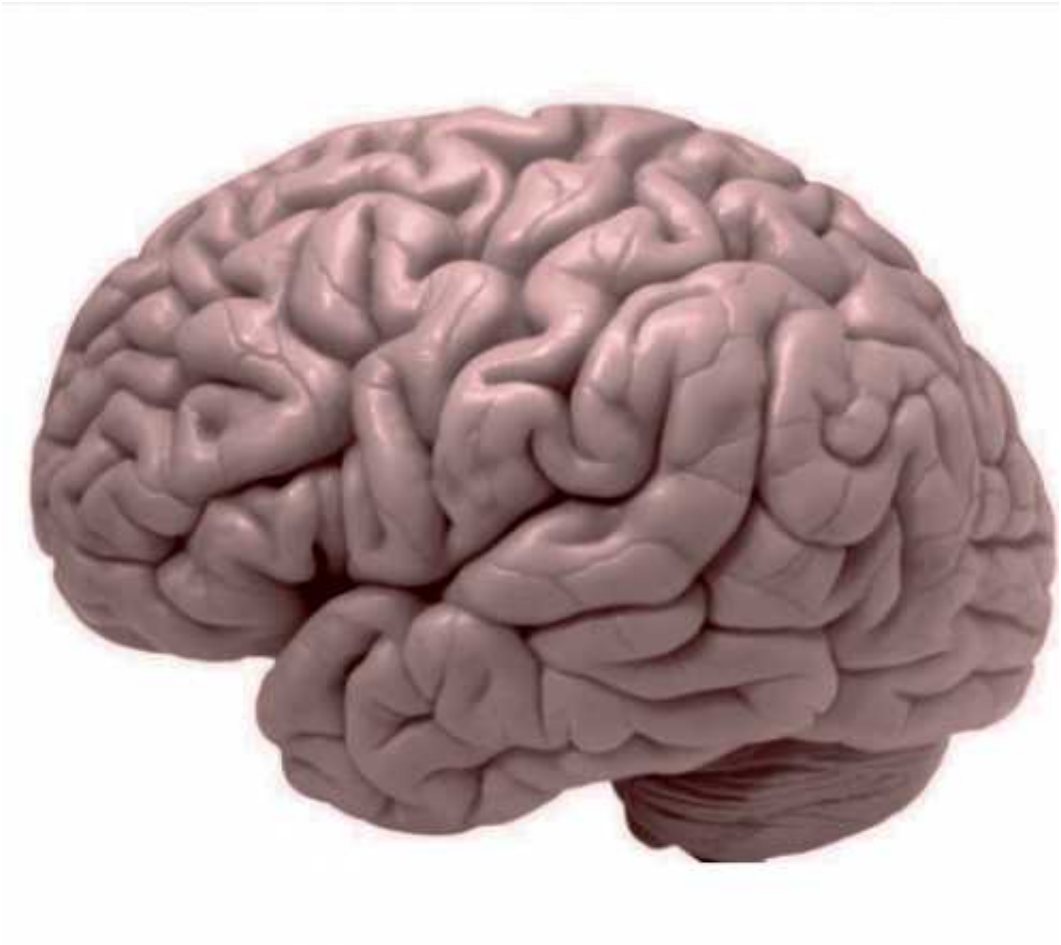

In new research published in the prestigious journal *Proceedings of the National Academy of Sciences* (*PNAS*), a team of scientists from the

Hebrew University Hadassah Medical School, in the Faculty of Medicine, unraveled a longstanding mystery of a fundamental property of the brain.

It has long been known that the brain uses topographic organization, meaning that parts of the brain that make similar types of computations are situated close to each other (also known as brain maps or spatial computation). However, in the case of pathology, these topographies may undergo re-organization. The researchers now show that it is the continuity of these brain maps which is disturbed. Moreover, this continuity can be quantified, allowing them to be used as a biomarker for detecting neuropsychiatric disease.

In order to understand this relationship, researchers from Hebrew University's Computational Neuropsychiatry Laboratory and the Edmond and Lily Safra Center for Brain Sciences (ELSC), as well as a neurosurgeon from Hadassah Medical Center, investigated the role of topographic organizational continuity.

Using functional MRI, they studied two types of unique patient populations: patients with injury to one side of the spinal cord, which enabled comparison of disturbed and non-disturbed body sides, and patients undergoing surgical repair.

This approach enabled direct comparison in human patients with respect to their own self or before and after surgical intervention. Instead of inducing lesions in animals, the team could repair the human patients and check them before and after. Importantly, unlike animals, patients could report their subjective experience, which is crucial for understanding high cognitive functions and neuropsychiatry.

The researchers developed an algorithm that quantifies continuity of the patients' brain maps. Their results showed that in each individual patient,

pathological processing was reflected by a discontinuity of topographic maps rather than signal reduction.

"These findings suggest that continuity is a primary principle in brain computation, but in pathological states the brain may give up on this principle in order to retrieve as much information as possible," said neuroscientist Dr. Shahar Arzy, director of the Computational Neuropsychiatry Laboratory, who led the team. "Moreover, this may serve as a biomarker for neurological pathologies that we are now investigating."

The researchers are now fine-tuning their findings in neurosurgical patients in order to enable a better patient-tailored diagnosis and follow-up. In addition they are extending their findings to other kinds of brain processing such as vision, hearing, number processing and memory.

Award-Winning Research May Enable Early Detection of Alzheimer's Disease

Earlier this year, the Hebrew University team published research in *PNAS* that earned them best scientific paper award by the Israeli Neurological Association for 2015. ('Brain system for mental orientation in space, time, and person'; *PNAS*, published ahead of print August 17, 2015)

In that paper, the Computational Neuropsychiatry Laboratory, together with researchers from the Swiss Institute of Technology (EPFL), in the framework of HUJI-EPFL collaboration, unraveled another mystery: the brain function that relates the behaving self to the environment, what they call "mental-orientation."

Through high-resolution functional MRI scanning, the team showed that

mental orientation in space, time and person produces a sequential and partially overlapping posterior-anterior pattern of activity in the brain.

Based on these findings, the researchers showed that mental orientation is managed by a specific brain system with a highly ordered internal organization.

The researchers hypothesized that it is this mental-orientation system that is disturbed in Alzheimer's disease.

"Behavioral and functional neuroimaging examination of this system may therefore enable early detection of Alzheimer's disease," said Dr. Arzy, "far before clinical signs are evident, which is crucial for presentation of preventive treatment." The researchers in the Neuropsychiatry Lab have already tested their hypothesis in patients. Their initial results have already won them the first prize by the International Neuropsychiatry Association for 2015. The researcher also designed an Android-based App for the developed test. Full results as well as the free App for diagnosis and follow up of Alzheimer's disease will be available in the coming months.

Research Highlights Unique Role of Computational Neuropsychiatry Laboratory as a Research and Clinical Center

The research was conducted in the Computational Neuropsychiatry Laboratory, co-located in both the Department of Clinical Neuroscience at Hebrew University Hadassah Medical School in the Faculty of Medicine, and the Department of Neurology at Hadassah Medical Center in Jerusalem. This unique lab combines clinical practice and research in neurology, psychiatry, computer science, physics and psychology, and applies state-of-the-art computational methods on

precious clinical data, enabling researchers to perform sophisticated analyses and modeling and improve scientific understanding of the human self in health and in disease.

Working with neurological and psychiatric patients in the department of neurology, neuropsychiatry clinic, invasive neurophysiological unit and in the operating room, the Lab uses state of the art computational methods applied directly to clinical data, particularly tailored to improve clinical management and scientific understanding of neuropsychiatric disorders. The multidisciplinary team of medical doctors, physicists, computer scientists and psychologists use tools including fMRI, multi-channel EEG, intracranial EEG, virtual reality, and direct cortical stimulation to investigate and help patients in real-time.

"Our main interests involve conditions including epilepsy, neurodegenerative diseases, conversive and dissociative disorders, amnesias, disorientation states and different cognitive disturbances and misperceptions," said Dr. Shahar Arzy, director of the Computational Neuropsychiatry Laboratory. "By combining direct clinical involvement and cutting-edge computational methods we are able to reframe neuropsychiatry and at the same time to develop effective patient-tailored clinical tools, which fits the new digital era of computational revolution and precision medicine."

"We have the best students available from both the natural sciences and The Hebrew University's MD-PhD program", said Dr. Arzy. "With high computational skills, medical insights and extreme motivation, they dedicate their talent to both understanding the mysteries of the human brain and at the same time solving the most crucial needs in clinical practice."

More information: Noam Saadon-Grosman et al. Discontinuity of cortical gradients reflects sensory impairment, *Proceedings of the*

National Academy of Sciences (2015). DOI: 10.1073/pnas.1506214112

Michael Peer et al. Brain system for mental orientation in space, time, and person, *Proceedings of the National Academy of Sciences* (2015). DOI: 10.1073/pnas.1504242112