Newfound brain network ‘SCAN’ implicated in Parkinson’s disease

A study has uncovered previously elusive targets that could improve the efficacy of modulatory therapies for Parkinson’s; in a small trial with 18 people with the disease, those who received transcranial magnetic stimulation targeted at the brain’s SCAN regions had significantly less tremors and instability after two weeks

Parkinson’s disease affects more than 10 million people worldwide. A patient struggles to perform coordinated movement, requiring conscious effort and attention even for a simple task like buttoning a shirt. Natural movements like walking and turning have to be planned as the person will struggle to start and stop actions.

Over time, the person will move slower, become unstable, and suffer tremors.

Now, new research reveals a brain network promising precise targets for treatment.

Higher order networks

To date, various treatment options are available, but none are ideal. For example, pharmacological treatment with levodopa, a dopamine precursor, partially alleviates Parkinson’s symptoms. However, the effect of levodopa is variable and repeated use causes side-effects like uncontrolled movements. Another approved therapy is deep brain stimulation (DBS), wherein electrodes are surgically implanted inside specific brain regions.

“However, DBS is expensive and invasive, albeit not risky,” Prashanth Kukkle, consultant neurologist at the Parkinson’s Disease and Movement Disorders Clinic, Bengaluru, said.

Non-invasive therapies like transcranial magnetic stimulation (TMS), where magnetic fields are applied to stimulate nerve cells, are at an experimental stage and require “sweet spots, or precise targets that can bring about dramatic improvement, which are still being explored,” Dr. Kukkle added.

han 10 million people worldwide. | Photo Credit: Getty Images

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Until recently, neurologists were probing motor-effector areas of the motor cortex, which are surface-level brain areas controlling muscular activity of individual body parts like the foot, arm, and mouth. However, dysfunction in these regions has not been sufficient to explain the coordination deficits seen in Parkinson's.

A prevailing hypothesis has been that higher order networks — large-scale, interconnected clusters integrating information across brain regions for complex cognitive functions like planning and attention — may be involved. A new study in *Nature* addressed this hypothesis and found that Parkinson's disease is associated with the abnormal strengthening of a brain network called the somatic cognitive action network (SCAN).

The study's findings have uncovered previously elusive precise targets that could improve efficacy of modulatory therapies for Parkinson's.

Discovery of SCAN

Historically, neurologists have been interested in mapping the precise brain regions that directly control movement of specific body parts. Around a century ago, the American-Canadian neurosurgeon Wilder Penfield electrically stimulated the surface of the brain in awake patients and recorded which body parts moved in response. He found that neighboring parts of the body were represented in neighboring areas of the motor cortex, creating a continuous "map" of the body across the brain's surface.

Over time, however, this map has been questioned for its limited precision. Nico Dosenbach, a neurologist at Washington University School of Medicine in St. Louis and a co-author of the Parkinson's disease study, pioneered a method called precision functional mapping (PFM), which helped refine the Penfield map.

"Previously, most imaging studies relied on averaging data across individuals," he explained. "It's like averaging the faces of 100 people — you would end up with a cartoon face, not a real face."

PFM allowed functional mapping of individual brains, thus producing 'maps' of higher resolution.

Typically, in low-resolution maps, only the specific motor-effector area would be visible as a single dot when a particular body part moved. But in a 2023 paper, using PFM, Dr. Dosenbach and colleagues reported a new pattern where three additional zones appeared as "three dots" along the motor cortex whenever unrelated body parts were stimulated. These three zones were interspersed between the motor-effector regions controlling arm, foot, and mouth. Whether the ankle was stimulated or the elbow, the three-dots pattern would be activated.

"The regularity of the pattern across individuals made me suspect that there might be an entirely different organisational principle at work," Dr. Dosenbach said.

These patterns were later renamed SCAN, and they were found to connect to higher-order brain areas involved in coordinating movement.

Other experts agree that the discovery of SCAN changed their impression of the way the motor cortex is organised.

“We don’t only have a series of ‘effectors’ controlling individual body parts in the primary motor cortex. We also have integrative areas that oversee and coordinate movements,” Alfonso Fasano, a neurologist at the University of Toronto who wasn’t involved in the study, said.

SCAN in the picture

Using the same PFM technique, the authors examined functional MRI scans and electrocorticographs — records of electrical signals from the cortex — of 863 people with Parkinson’s disease, many of whom were receiving different approved therapies like DBS and levodopa.

“In Parkinson’s disease patients, the SCAN network is closely connected with key Parkinson’s-related brain regions such as the basal ganglia and thalamus, showing pathological abnormal strengthening of these connections,” Hesheng Liu, professor at Changping Laboratory, Beijing, and the lead author of the study, said.

In contrast, the SCAN network was not abnormally strengthened in patients with another motor disorder, amyotrophic lateral sclerosis (ALS).

A key strength of the paper was the sheer size of the datasets — which Dr. Liu and his team had been gathering since 2016.

“Hesheng Liu and team ran several complex clinical studies in record time and networked with other scientists around the world to pool data,” Dr. Dosenbach said.

“The other strength of the paper is that it uses multiple cohorts of patients treated with different modalities and shows a consistent finding: over-connectivity of SCAN to basal ganglia in Parkinson’s disease,” Dr. Fasano added. “Importantly, when a treatment has worked, there’s a common denominator: the reduction of SCAN over-connectivity.”

On the flip side, Dr. Fasano expressed belief that framing Parkinson’s disease as a SCAN disorder is an oversimplistic conclusion.

“First, Parkinson’s disease is heterogeneous. Second, other conditions such as parkinsonism or dystonia may involve similar network abnormalities,” he said.

Nevertheless, SCAN over-connectivity with basal ganglia represents a new network-level biomarker for Parkinson’s disease.

Cautious optimism

The findings have clinical implications. In the study, the authors conducted a preliminary trial where 18 people with Parkinson’s disease were randomly assigned to receive TMS directed at the SCAN regions. Compared to a control cohort whose brains were stimulated at the effector regions, the SCAN-targeted group showed significantly less tremors, rigidity, slowness, and instability within two weeks.

Both Dr. Dosenbach and Dr. Fasano agreed that a TMS therapy directed at SCAN for Parkinson’s disease patients is on the horizon.

”In future, there will be both non-invasive and minimally invasive neuromodulatory therapies aimed directly at SCAN in a personalized manner using PFM,” Dr. Dosenbach said.

Dr. Kukkle remained cautiously optimistic: “Being superficially located in the cortex, SCAN is easily accessible by TMS for non-invasive modulation.” However, he added that SCAN is also a newly discovered brain region that has yet to be included in standard medical textbooks and atlases: “While this paper shows rational, biological plausibility and early clinical evidence, it has to be seen whether it converts to routine clinical practice.”

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News Source:

https://www.thehindu.com/sci-tech/science/newfound-brain-network-scan-implicated-in-parkinsons-disease/article70801578.ece