

New study challenges the idea that early Parkinson's disease causes cognitive dysfunction

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Like many neurodegenerative diseases, Parkinson's disease (PD) is a thief that hacks into human operating systems and corrupts their



cognitive hard drives until they can no longer control their movements or perform activities of daily living.

Often, in its later stages, Parkinson's disease steals data too, leading to memory loss, confusion and dementia.

Both the cause and cure of Parkinson's disease remain elusive, but research has helped afflicted individuals manage their symptoms and lead healthier post-diagnosis lives. Individuals diagnosed with Parkinson's disease tend to have higher education than the general population and are often in their prime earning years, and the reasons for these two quirks are not well understood.

Large data sets

A recent study led by an MUSC neuropsychologist will help researchers in the field better evaluate whether their clinical trials are producing valuable outcomes in reducing the symptoms of individuals with PD.

Along with a team of collaborators, Travis Turner, Ph.D., assistant professor and director of the Neuropsychology Division at MUSC, dug deep into an existing treasure trove of data to clarify the cognitive impact of the early stages of PD. What he found initially seemed counterintuitive and challenges the notion of cognitive deficits in individuals experiencing PD for less than five years.

Turner and his colleagues determined that the disease generally does not reduce cognitive function during the first five years of the disease, at least not as measured by standardized tests on patients. This finding applies as well to those who were already experiencing mild cognitive impairment.

Specifically, Turner's team examined cognitive test results from the



Parkinson's Progression Markers Initiative (PPMI) on nearly 400 individuals, including 253 newly diagnosed PD patients and 134 healthy controls. Within the cohort, 84 of the individuals were identified as having pre-existing mild cognitive impairment. PPMI conducted a battery of tests on memory, visuospatial functions, processing speed, working memory and verbal fluency.

A small step back

Parkinson's disease patients performed normally on all but two tests, a measure of working memory and a processing speed test. Further examination of the results determined that the latter difference was entirely a function of motor decline: PD patients could not physically respond as quickly because of motor symptoms like tremor and rigidity. Employing a test to account for that variable eliminated the difference between PD patients and the control group.

For the memory test, individuals with PD experienced a mild dip, perhaps the source of what some who are diagnosed describe as brain fog. "Mild means some degree of subjective decline with more complicated tasks: doing bills, taxes, personal scheduling, non-routine work," said Turner. The difference, he says, would not generally be noticeable by anyone but the individual themselves.

The results were contrary to the team's expectations, particularly with regard to PD patients who were already experiencing mild impairment, Turner said. The data suggested that even those already affected suffered little-to-no further cognitive decline during the first five years after diagnosis.

Another surprise: that no other researchers had mined the repository of information and analyzed the results previously.



"Early cognitive decline is commonly reported by PD patients. There have been a lot of neuro-protective trials that look at non-motor symptoms like anxiety, depression and cognition, but no one had looked at this robust data set before," he said.

Earlier research

Previous tests on Parkinson's disease patients have produced a variety of results, some even somewhat contradictory according to Turner, but they lacked the controls or the sample size that his study included.

For example, one study that investigated mild cognitive impairment in PD patients did find more diminished ability, but it included individuals regardless of their time with the PD diagnosis. Individuals in later stages of PD often do exhibit cognitive impairment and even dementia, and their inclusion may have been clouding the results.

Another review employing the MOCA screening test produced similar findings as Turner's study, but with a single measure that offered a more global view of the disease's impact rather than his team's more specific findings.

Turner says the result of his analysis could have a far-reaching effect on future PD research. It suggests that researchers developing disease-modifying or neuroprotective interventions for PD should not use these neuropsychological tests as outcomes in clinical trials, as their paper suggests that they are not sensitive to the early subjective changes often reported by patients.

The impact

Turner is optimistic that he and his colleagues have unearthed something



important. "I feel like it is big news," he said. "I am hoping it can be used for industry trials that I really want to succeed. I'm a PD researcher, so if a drug comes along that slows or stops its progression, I want reliable outcome measures that are sensitive to that effect."

Turner has dedicated his career to studying Parkinson's disease and foresees a continuation of symptomatic therapies emerging in the next 5-10 years that can sustain and enhance the quality of life for individuals suffering with the disease and provide fewer and less-severe side effects. Therapies that modify some subtypes of this complex disease will be the next step towards a cure, something Turner believes researchers are moving closer to all the time.

More information: Travis H. Turner et al, <u>Are Standardized Tests</u> Sensitive to Early Cognitive Change in Parkinson's Disease? (2023)

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