

# Compensation in the brain could lead to new treatment

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New evidence indicates that Parkinson's disease is preceded by a period during which healthy regions of the brain take over the functions of damaged ones. Neurologist Bart van Nuenen performed a unique study involving people who are clinically still healthy and free from disease manifestations, but who have an increased risk of developing Parkinson's disease later in life due to their genetic predisposition. Van Nuenen will defend his PhD thesis based on this study on 22 November.

Parkinson's disease results from the death of [brain cells](#) that produce dopamine. Remarkably, the physical symptoms of Parkinson's disease (tremor, rigidity and slowness of movement) do not appear until 50% to 70% of the dopamine-producing cells have died. It has long been a mystery why the physical symptoms take so long to develop.

In recent years, multiple [genetic mutations](#) have been discovered that cause Parkinson's symptoms. In collaboration with various international research groups, the research group of Prof. Bas Bloem at the Radboud University Nijmegen Medical Centre conducted a study of families in Germany, Italy and Israel that have such a mutation in a Parkinson's gene. Parkinson's disease is very common in these families, but some family members do not yet show symptoms of the disease despite having the mutation. This allowed for an effective study of the preclinical phase of the disease, i.e. the period that precedes the manifestation of physical motor symptoms. The study was conducted with the aid of advanced [MRI scanners](#) for functional [brain research](#) (fMRI scanners).

## Healthy brain region

One of the investigators in the study, Bart van Nuenen - who currently works as a [neurologist](#) at the Catharina Hospital in Eindhoven - asked the [test subjects](#) to perform various tasks. At the same time, he conducted fMRI scans of their brain. He did the same with a control group of individuals who do not have Parkinson's disease in their family. Both groups were entirely healthy in clinical terms, and both groups performed the tasks equally well. However, the analysis of the MRI scans showed that the brain activity of the genetically predisposed group differed from that of the control group. In particular, the genetically predisposed group showed enhanced activity in a specific area of the brain -the extrastriate body area - that also remains unaffected in the late stages of Parkinson's disease. Apparently, in the genetically predisposed group this healthy brain area compensates for the declining function of brain areas that are already being affected by the disease. Due to this compensation, the test subjects could still move normally and suppress the Parkinson's symptoms.

## TMS

To conclusively demonstrate that this overactive brain area actually contributes to compensation, Van Nuenen conducted an additional experiment using transcranial magnetic stimulation (TMS). This technique can temporarily deactivate a specific area of the brain. When Van Nuenen deactivated the extrastriate body area by using TMS, Parkinson's patients were temporarily unable to perform certain hand motions correctly. In the healthy control group, the deactivation of the extrastriate body area did not have this effect. This makes it very likely that compensation in the brain occurs during the preclinical phase, and that this compensation delays the clinical manifestation of Parkinson's disease.

This finding is crucial for understanding the [brain](#) processes that play a role during the very early stages of Parkinson's disease. Van Nuenen explains: 'Conventional treatments have focused exclusively on correcting the dopamine deficiency. But now we have a starting point for a new type of therapy that focuses on stimulating the compensation mechanism. If this therapy is successful, not only can we suppress symptoms more effectively, but perhaps even postpone the clinical presentation of the disease in carriers of a Parkinson's gene mutation.'

**More information:** Bart F.L. van Nuenen. "Cerebral reorganization in premotor parkinsonism." PhD thesis. Date of PhD defence: 22 November 2012. PhD supervisors: Prof. B.R. Bloem, Prof. I. Toni, Prof. H.R. Siebner (University of Copenhagen).

Provided by Radboud University Nijmegen

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