

Studies on the Etiology of Parkinson's Disease

Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentlig försvaras i Hörsal Arvid Carlsson, Medicinaregatan 3, fredagen den 23 oktober, klockan 9:00

av
Camilla Fardell

Fakultetsopponent: Docent Sven Pålhagen,
Lunds Universitet

Avhandlingen baseras på följande delarbeten:

- I. **Camilla Fardell**, Anna Zettergren, Caroline Ran, Andrea Carmine Belin, Agneta Ekman, Olof Sydow, Lars Bäckman, Björn Holmberg, Nil Dizdar, Peter Söderkvist and Hans Nissbrandt. S100B polymorphisms are associated with age of onset of Parkinson's disease. *BMC Med Genet.* 2018;19(1):42.
- II. **Camilla Fardell**, Maria Åberg, Linus Schiöler, Hans Nissbrandt, Kjell Torén. High IQ in early adulthood is associated with Parkinson's disease. *J Parkinsons Dis.* 2020;10.3233/JPD-202050.
- III. **Camilla Fardell**, Linus Schiöler, Hans Nissbrandt, Kjell Torén, Maria Åberg. The erythrocyte sedimentation rate in male adolescents and subsequent risk of Parkinson's disease – an observational study. *Submitted.*
- IV. **Camilla Fardell**, Linn Persson, Henrik Zetterberg, Björn Holmberg, Radu Constantinescu, Tomas Bergström, Hans Nissbrandt. Decreased levels of antibodies against Varicella-zoster virus in patients with Parkinson's disease – A pilot study. *Manuscript.*

Studies on the Etiology of Parkinson's Disease

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Abstract

Parkinson's disease (PD) is the second most common neurodegenerative disorder in the world and affects around 1% of the population over 60 years of age. The main symptoms of PD include bradykinesia, resting tremor and rigidity, caused to a large extent by degeneration of the dopaminergic neurons in substantia nigra. Aggregates of the protein α -synuclein can be seen in dopaminergic cells and other neurons. The pathogenesis starts up to 20 years before the patients notice any motor symptoms. Idiopathic PD is a complex multi-factorial disease and the etiology is largely unknown but several genetic and environmental risk factors have been identified. Treatments of PD aim to alleviate motor symptoms but there is no cure or any treatment to slow down disease progression.

The aim of this thesis was to investigate different factors in relation to PD risk. In Paper I, we investigated the relation between genetic polymorphisms in the S100B gene and the age at onset of PD in two independent Swedish populations. The main finding in Paper I is that the SNP rs9722 is associated with an earlier age at onset of PD. rs9722 has previously been shown to be associated with higher S100B levels. S100B can activate inflammatory pathways through RAGE and may be able to speed up progression of PD.

The work in Paper II and III consisted of population-based prospective studies of late-adolescent men who underwent compulsory military conscription. The main finding of Paper II was that high scores on IQ tests were associated with an increased risk of being diagnosed with PD later in life. In paper III, we found that higher erythrocyte sedimentation rate (ESR) was associated with lower PD risk.

The study in Paper IV investigated the antibody response to measles- and VZV-specific antigens in serum and CSF samples of patients with PD. PD patients had a lower antibody response to VZV-specific antigen in serum and CSF samples.

In conclusion, we present new risk factors for PD in the present thesis. Our findings suggest that inflammation may not be a risk factor for PD, but merely a secondary phenomenon that speeds up disease progression. On the contrary, our data rather suggest that a greater premorbid inflammatory reaction can play a protective role against PD. A decreased immune and inflammatory reaction against pathogens or protein aggregates could contribute to the progression of PD.

Keywords: Parkinson's disease, S100B, age at onset, conscription, IQ, Varicella zoster, measles

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