

Summary

Parkinson disease (PD) is caused by degeneration of the dopaminergic neurones in the substantia nigra in the brain. When 50–70% of the neurones have degenerated, movement disturbances appear, tremor, rigidity, slowness of movement and postural instability being the most frequent symptoms. Most patients develop non-motor symptoms, such as depression, autonomic symptoms and dementia, later in the course of the disease. The etiology of PD is partly unknown; however, many hypotheses have been put forward. In this PhD, we investigated whether head injuries and autoimmune diseases increase the risk for PD. Both projects are related to the hypothesis that inflammation increases the risk. Further, we investigated whether patients with osteoarthritis are at reduced risk for PD as a consequence of the anti-inflammatory treatment they receive. All three projects are based on information from Danish registries.

Head injuries and risk for Parkinson disease: On the basis of the hypothesis that head injury increases the risk for PD, we conducted a case–control study based on data from the Danish Hospital Register. We included 13 695 patients and five controls for each case, matched on gender and year of birth. We found that PD patients had significantly more head injuries in the period before diagnosis than the control group (odds ratio (OR), 1.5; 95% confidence interval (CI), 1.4–1.7). When we looked at the time between head injury and a diagnosis of PD, however, we found that the head injuries occurred mainly just before the diagnosis of PD. For ≥ 10 years between head injury and PD, the risk estimate was neutral (OR, 1.1; 95% CI, 0.9–1.3). These results indicate that these patients had symptoms such as postural instability before the hospital diagnosis of PD, which probably increased the risk for head injuries. Our results therefore do not indicate that head injuries increase the risk for PD.

Autoimmune disease and risk for Parkinson disease: In a case–control study based on the same study population as above, we investigated whether patients with an autoimmune disease had an increased risk for PD as a consequence of increased inflammation. The occurrence of 32 autoimmune diseases, divided into systemic, organ-specific and nonspecific, was ascertained among cases and controls through the Danish Hospital Register. We observed a neutral risk for PD among patients with an autoimmune disease (OR, 0.96; 95% CI, 0.85–1.08) but a significantly decreased risk among patients with the systemic autoimmune

disease rheumatoid arthritis (OR, 0.7; 95% CI, 0.5–0.9). This finding might be due to the use of anti-inflammatory drugs by this group of patients or to underdiagnosis of PD because of the physical consequences of rheumatoid arthritis.

Risk for Parkinson disease among patients with osteoarthritis: We identified a cohort of 134 000 patients with a diagnosis of osteoarthritis and a subsequent hip or knee implant. This patient group, like patients with rheumatoid arthritis, receives large doses of anti-inflammatory drugs. The cohort was followed up for PD, and the incidence was compared with that expected from age-, sex- and calendar period-adjusted incidence rates for the general population. We found that the risk of patients with osteoarthritis for PD was comparable to that of the general population (standardized incidence ratio (SIR), 1.07; 95% CI, 0.99–1.16). As use of anti-inflammatory drugs is associated with a reduced risk for colorectal cancer, the patients with osteoarthritis were followed up for colorectal cancer in the Danish Cancer Registry. As expected, a reduced risk of colorectal cancer was observed (SIR, 0.92; 95% CI, 0.88–0.97). Our results do not support the hypothesis that use of anti-inflammatory drugs reduces the risk for PD.

In conclusion, inflammation is a highly complicated process, which might influence initiation or progression of PD, however, the three types of inflammation that we studied do not appear to influence the risk. We lacked information on factors that might affect the risk, such as smoking habits; this information would be useful for future studies.