Appendix 1: Review of research on dementia in Parkinson's disease, included in the review article.

Author (according to year)	Sample number (n)	Findings	Limitations
Hughes et al. (1992)	n(PD) = 100	• 76% of patients met the pathohistological criteria for PD after autopsy. • Among patients who had a misdiagnosis of PD in their lifetime, progressive supranuclear palsy (6%), multiple system atrophy (5%), and Alzheimer's disease (3%) were the most commonly identified pathohistologically. • The loss of cells in the substantia nigra correlated with the duration and intensity of PD. • After retrospective application of the recommended diagnostic criteria for PD, the accuracy of the diagnosis rose to 82%.	
Hughes et al. (2000)	n(PD) = 83 n(control) = 50 After 122 months: n(PD) = 57 n(control) = 26	• During the course of the study (122 months), 17 patients with PD (29%) developed dementia and none from the control group. • Predictors for the development of dementia were male sex, older age, severe motor impairment, and longer disease duration.	A larger sample is needed. A relatively large number of subjects did not complete their participation in the study.
Aarsland et al. (2001)	n(PDND) = 171 n(control) = 3062 After 4,2 years: n(PDND) = 130 n(control) = 1908	• After 4.2 years, 43 patients with PD had dementia (33% tested). • Patients with PD are 5.9 times more likely to develop dementia compared to the control group. • Predictive factors were the result on the MMSE test, which was lower than 29 points, performed at the first test, higher age, and more severe motor symptoms.	At the first test, patients did not undergo neuropsychological testing, so mild cases of dementia could have been overlooked. 21% of patients with PD were not screened after 4.2 years because they died. A relatively high number of control subjects no longer wanted to participate after 4.2 years.
Aarsland et al. (2003)	n(PD) = 224 n(PDD) = 51 n(control) = 3295 After 4 years: n(PD) = 139 After 8 years: n(PD) = 87	• After 4 years, 43 cases of PDD were newly diagnosed in the PD group. The overall diagnostic accuracy was 51.6%. • After 8 years, 28 cases of PDD were newly discovered in the PD group. The overall diagnostic accuracy was 78.2%. • In the control groups, the 5-year prevalence of dementia was 18.2%. • Patients with PD were three times more likely to develop dementia than healthy subjects. • Risk factors were pre-study hallucinations and akinetic dominant or mixed PD (tremor + akinesia).	A relatively high number of patients with PD left the study due to death or other rea-sons. At baseline, no neuropsychological testing was performed, so mild cases of dementia could have been overlooked.
Emre et al. (2004)	n(PDD) = 541 • n(rivastigmine) = 362 • n(placebo) = 179 After 24 weeks: n(PDD) = 410 • n(rivastigmine) = 263 • n(placebo) = 147	• Compared to placebo, rivastigmine showed a moderate but significant improvement in the global assessment of dementia, cognition and behavioural symptoms. • The most common side effects were nausea, vomiting and tremor.	
Inzelberg et al. (2004)	n(PD) = 240	• 12% of patients had a positive family history of PD, of which 20% were carriers of the Parkin mutation. • PD started in patients with a positive family history of PD at a younger age, but its course was milder.	
Aarsland et al. (2005)	n(LBD) = 15 n(PDD) = 36 n(PD) = 26 n(AD) = 17	• Neuroleptic sensitivity occurred in 53% of patients with LBD, 39% of patients with PDD, and 27% of patients with PD. • Neuroleptic sensitivity did not occur in patients with AD. • Neuroleptic malignant syndrome was not associated with other clinical or demographic characteristics.	A larger sample is needed.
Bronnick et al. (2006)	n(PDD) = 461	• Attention Deficit Disorder in Patients with PDD sigificantly affects the performance of daily activities.	Some attention tests could be affected by the patient's motor skills.
Goetz et al. (2006)	n(PD-BH) = 48	• In 81% of patients, benign hallucinations with preserved insight progressed to impaired insight and disillusionment within three years.	A larger sample is needed. Longitudinal studies would be needed to more accurately assess the progression of benign hallucinations.
Goris et al. (2007)	n(PD) = 659 n(control) = 2176 After 3,5 years: n(PD) = 109	• Simultaneous mutation of the MAPT and SNCA genes doubles the likelihood of developing PD. • Cognitive decline and the development of dementia in patients with PD are strongly associated with the inverted MAPT polymorphism.	

Author (according to year)	Sample number (n)	Findings	Limitations
Buter et al. (2008)	n(PD) = 233 n(control) = 3295 After 12 years: n(PD) = 45	• After 12 years, 60% of patients developed dementia. • Life expectancy was shorter in male patients. • The overall incidence of PDD was 80-90% in patients up to the age of 90 years. • After 4 years, the probability of developing dementia in patients with PD was 5.9 times higher than in healthy subjects from control groups.	Four years elapsed between the first and second patient tests. During this time, 41 patients died for whom we do not know whether they had dementia or not. The control group was followed for only 5 years, so the comparison with the prevalence of dementia among the healthy is unreliable.
Hely et al. (2008)	n(PD) = 136 After 20 years: n(PD) = 36	• After 20 years, dementia was present in 83% of the surviving patients. • 87% of patients with PDD experienced falls (35% also had bone fractures), 81% had dysarthria, 71% had urinary incontinence, 70% had excessive daytime sleepiness, 74% had hallucinations, and 48% had postural hypotension and dysphagia.	
Zadikoff et al. (2008)	n(PDD) = 88	• MoCA is the more sensitive test for early detection of cognitive decline in PDD compared to MMSE. • Less than 26 points, which was the cut-off value for both tests, was achieved by 32% in the MoCA test and 11% in the MMSE test.	The implemented 26-point cross-sectional value was not verified to detect cognitive decline specifically for patients with PD. Longitudinal studies are needed to confirm the hypothesis that lower scores on the MoCA test are a more reliable predictor of cognitive decline than the results of the MMSE test.
Ibáñez et al. (2009)	n(families with ADPD) = 264 n(families with aADP) = 22	• 4 families with ADPD (1.5%) were carriers of SNCA duplication. • 1 family with aADP (4.5%) was a carrier of SNCA triplication. • The multiplied copies were of different sizes, meaning that the SNCA mutations developed independently of each other. • The severity of the disease was related to the number of SNCA copies but not to the number of amplified genes.	A larger sample of SNCA mutation carriers is required.
Kempster et al. (2010)	n(PD) = 125	• Visible hallucinations, dementia, frequent falls, and inability to self-care were indicators of advanced disease that began to appear about five years before the patient's death. • These indicators appeared 5 years before death regardless of the age of the patient or the duration of the disease. • The occurrence of dementia and visual hallucinations was closely related to the histopathological finding of Lewy bodies in the cerebral cortex.	
Riedel et al. (2010)	n(PD) = 1449	• At least one neuropsychiatric symptom was present in 71% of patients with PD. • The three most common neuropsychiatric symptoms were dementia (29%), depression (24%) and psychotic symptoms (13%). • Dementia was more common in the elderly. Other neuropsychiatric symptoms were not associated with age but with progression of PD.	The study did not have a control group. Only mobile patients were examined.
Posada et al. (2011)	n(GP) = 5262 • n(PD) = 81	• After 12 years, 2701 patients died (51.3%), of which 66 with PD (81.5%). • The probability of death of a patient with PD was approximately 2-fold higher compared to the other participants.	Only patients over 65 years of age were included. The study excluded patients with new-onset PD during the sample from the general population.
Reid et al. (2011)	n(PD) = 149 n(control) = 50	• Patients with poorer language skills developed dementia earlier than those with better vocabulary. • Dementia occurred in patients around age 70, regardless of when the disease started in an individual patient. • The patients who developed PD in their old age had a more aggressive course of the disease, a rapid cognitive decline, and a poorer prognosis of outcome.	Due to the 20-year duration of the study, a minority of test subjects survived until the last test, so the test results after 15 and 20 years are more or less speculative. The success of solving some tasks of neuropsychological tests could be influenced by the patient's motor skills.
Saleta et al. (2011)	n(PDND) = 33 • n(control group) = 15 • n(experimental group) = 18 After 4 weeks: n(PDND) = 28 • n(control group) = 12 • n(experimental group) = 16	• After four weeks of cognitive therapy, the experimental group performed better on tests for memory, attention, executive functions, verbal fluency, and visuospatial skills. • No changes in quality of life or improvement in day-to-day activities were reported by patients.	A larger sample is needed. A longitudinal study would be required to assess the long-term effect.
Srovnalova et al. (2011)	n(PDND) = 10	• Single rTMS stimulation of the left and right inferior frontal gyrus improved Stroop test results. • The FAB test result remained the same after stimulation.	A larger sample is needed.
Goker-Alpan et al. (2012)	n(PD+GD) = 7 n(PDNGBA) = 11 n(GD) = 14 n(GBANPD) = 7 n(control) = 68	• The PD + GD and PDNGBA groups showed the greatest loss of dopamine synthesis in the caudal striatum. • The PD + GD group had reduced blood flow in the lateral parieto-occipital association cortex and the praecuneus bilaterally. • The GD group, which did not have parkinsonism, also showed a decrease in dopamine in the striatum.	A larger sample is needed.

Author (according to year)	Sample number (n)	Findings	Limitations
Leroi et al. (2012)	n(PD-NC) = 54 n(PD-MCI) = 48 n(PDD) = 25 n(caregivers) = 102	• The quality of life of the patients and burden of the caregivers did not differ significantly between the PD-NC and PD-MCI groups. • The quality of life and burden of caregivers was significantly higher in the group of patients with PDD. • General impairment and decline in ability to perform daily tasks escalated with decline in cognition (PD-NC < PD-MCI < PDD).	A larger sample is needed. More precise neuropsychological testing and categorisation by PD-MCI subtypes is needed to allow observation of the progression of cognitive decline to dementia.
Melzer et al. (2012)	n(PD-NC)= 57 n(PD-MCI)= 23 n(PDD)= 16 n(control) = 34	• There were no changes between the grey matter of control subjects and that of PD-NC patients. • In patients with PD-MCI, limited grey matter atrophy was seen in the temporal, parietal, and frontal cortex, and in the bilateral caudal hippocampus, the amygdala, and the right putamen. • In patients with PDD, atrophy was significantly more pronounced at the same locations as in patients with PD-MCI, and grey matter volume in the parahippocampus and posterior cingulate gyrus was also reduced. • The degree of atrophy correlated with the degree of cognitive, but not also motor preservation.	A larger sample is needed. Longitudinal studies will be required to assess the progression of atrophy and cognitive decline in patients with preserved cognition.
Willis et al. (2012)	n(PD) = 138000	• 35% of patients with PD lived longer than 6 years. • Women and patients of Hispanic or Asian descent were less likely to die. • In six years, dementia was diagnosed in 69.9%, and of those, more commonly in black people and women. • Patients with dementia died almost twice as often as patients without dementia. • Patients with PD were most often hospitalized for infections (20.9%) or cardiovascular disease (18.5%). • Patients living in urban industrial environments died 1-fold more often than those living in rural areas.	Because the study was based on administrative data, it is likely that some patients have been misdiagnosed.
Nalls et al. (2013)	n(LBD) = 721 n(PDD) = 151 n(control) = 1962	• Compared with the control group, patients with LBD were carriers of GBA1 more than 8 times more often. • Patients with PDD were carriers more than 6 times more frequently compared to the control group. • Patients with LBD and the GBA1 mutation became ill younger, had a more severe course of the disease, and died earlier than patients with LBD who were not carriers of the mutation.	The participating centres used different genotyping methods.
Anang et al. (2014)	n(PD) = 80 After 4,4 years: n(PD) = 80	• Dementia developed after 4.4 years in 34% of patients with PD. • Negative prognostic factors were older age, male sex, sleep disturbances in the REM phase, cognitive decline at the start of testing, high blood pressure, orthostatic hypotension, colour vision disorders, and poorer motor test results.	A larger sample is needed. Relatively short patient follow-up period.
Costa et al. (2014)	n(PDaMCI) = 16 n(aMCINPD) = 20 n(control) = 20	• Compared with the control group, patients with PDaMCI performed worse on spontaneous recall but not on hint recall. • Patients with aMCINPD performed worse in both forms of recall than patients with PDaMCI. • In patients with PD, the prognostic factor for spontaneous recall results was the result of an executive function test. • In patients with PD, the memory impairment is located at the level of recall rather than consolidation, probably due to executive dysfunction associated with frontal lobe function.	A larger sample is needed. Different criteria for inclusion in the experimental group.
Cummings et al. (2014)	n(PDP) = 199 • n(pimavanserin) = 105 • n(placebo) = 94 After 6 weeks: n(PDP) = 176 • n(pimavanserin) = 87 • n(placebo) = 89	• Compared with the placebo group, improvement in psychotic symptoms was observed in patients with pimavanserin treatment.	Relatively short period of receiving the drug.
Van Hartevelt et al. (2014)	n(PD) = 1 n(control) = 9	• Deep brain stimulation caused functional and structural changes in the sensory, motor, prefrontal, limbic, and olfactory parts of the brain in a patient with PD.	More patients will need to be monitored after deep brain stimulation. Due to the lead artifact, only the right hemisphere can be monitored and not the interhemispheric connections.
Kehagia et al. (2014)	n(PD) = 25	• Intake of 40 mg atomoxetine reduced impulsivity and disinhibition in patients with PD.	A larger sample is needed.
Lawson et al. (2014)	n(PD) = 219 n(control) = 99	• Patients with PD-MCI had more severe motor symptoms, poorer quality of life, and were more likely to suffer from depression. • Among patients with PD-MCI, those with more severe cognitive decline had a poorer quality of life.	Use of older guidelines for diagnosing PD-MCI.
Nombela et al. (2014)	n(PD) = 168 n(control) = 85	• In patients with PD, neurocognitive changes associated with the fronto-striatal and parietal-temporal systems are seen soon after diagnosis on fMR. • COMT, MAPT, and APOE gene polymorphisms are associated with differences in regional brain activity. Patients with COMT polymorphism performed worse on executive function tests, MAPT on visuospatial function tests, and APOE on memory tests.	

Author (according to year)	Sample number (n)	Findings	Limitations
Wang et al. (2014)	n(PD) = 901	• 21.4% of examined patients with PD met the criteria for dementia and 22.8% for mild cognitive impairment. A general decline in cognitive abilities was observed in 44.3% of patients. • Patients performed the poorest at tasks related to visuospatial and executive function. • Severe cognitive impairment correlated with severe motor impairment. • Patients with psychiatric symptoms were more likely to have dementia. • MoCA was more sensitive to cognitive decline than MMSE.	Only mobile patients treated at selected centres were examined.
Djukic et al. (2015)	n(GP) = 160	• 59.6% of patients already had dementia diagnosed. The reversible cause was found in 18.2% of these patients. • In other patients, dementia was established. Among them, 31.1% were potentially reversible causes. • The most common causes were pseudodementia due to depression and vitamin B12 deficiency.	
Gan-Or et al. (2015)	n(RBD) = 265 n(PD) = 120 n(control) = 2240	• Patients with sleep disorders in the REM phase were carriers of the GBA mutation more than 6-fold more often than the control group. • Among patients with PD, those who were carriers of the GBA mutation were 3 times more likely to develop sleep disorders.	A larger cohort group of patients with PD will be required.
Hughes et al. (2015)	n(GP) = 864	• After almost two years of follow-up, MCI was developed by 8.3% of participants. • Cognitive and physical activity in combination protected against the development of MCI. • In separate treatment, physical activity was a more important protective factor than cognitive activity.	Longitudinal studies will be required for long-term impact on the development of MCI.
Oh et al. (2015)	n(PD) = 1200	• Mild cognitive impairment was observed in 38.9% of patients and dementia in 38.3%. The overall prevalence of cognitive decline in patients with PD was 77.2%. • Risk factors for the development of cognitive decline were older age, longer disease duration, sleep disorders in the REM phase, and more severe motor symptoms.	Use of other criteria for diagnosing PD-MCI.
Pigott et al. (2015)	n(PD) = 141	• Approximately half of patients with PD (47.7%) developed a cognitive decline within 6 years. • All new cases of PD-MCI progressed to dementia within 5 years.	The cohort group was selected from one centre and was in 99% comprised of Caucasians. Narrow age range (62-73 years). Variable duration of PD between patients before the start of testing. 20% of patients left the study before the 6 years ended.
Srivatsal et al. (2015)	n(PD) = 1447	• 29 (less than 2%) patients had the LRRK2 mutation. • Carriers of the mutation performed better in neuropsychological tests. • Fewer mutation carriers developed PDD.	Longitudinal studies will be required to demonstrate a slower development of cognitive decline. Despite the large number of patients with PD, there were few carriers of the mutation. A larger sample will need to be found.
Biundo et al. (2016)	n(PDND) = 197 n(PDD) = 40 n(LBD) = 27 After one year: n(PDND) = 132 n(PDD) = 7 n(LBD) = 14	• MMSE and MoCA are equally useful in assessing the progression of cognitive decline over time in patients with LBD. • In patients with PDND, MoCA is the more appropriate test.	A small sample of patients with LBD. Short patient follow-up period.
Chiu et al. (2016)	n(PDD) = 125 n(control – LBD) = 250 n(control – AD) = 500	• 95.2% of patients with PDD, 99.2% of patients with LBD and 96.8% of patients with AD had one or more psychiatric symptoms. • Patients with PDD had a psychiatric profile that was more similar to that of patients with AD than those with LBD. • Predictors of more severe, more pronounced psychiatric symptoms were lower age, advanced dementia, and LBD.	95.2% of patients with PDD were over 65 years of age, and for almost half of them, PD lasted only for 2–3 years. The clinical presentation in a more advanced form of the disease could be different from that found.
Takemoto et al. (2016)	n(PDD) = 52 n(LBD) = 46	• Compared with patients with PDD, neuroradiological imaging of patients with LBD showed greater cerebral blood flow to the entire cingulate gyrus and less blood flow to the praecuneus. • Patients with PDD performed better on the FAB test than patients with LBD, and performed worse on the language fluency, recall, and repetition tests. • Patients with PDD had significantly better results in spatial orientation, recognition of similarities between objects, and inhibition tests.	A larger sample is needed.