UK PARKINSON'S Excellence Network

What pattern of cognitive deficit in Parkinson's mild cognitive impairment (PD-MCI) predicts progression to Parkinson's disease dementia (PDD)?

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Clinical bottom line

There is a burgeoning literature on this topic, but the evidence-base suffers from heterogeneity in terms of methodological approaches. A search focusing on the most appropriate study design and exacting diagnostic criteria identified a single good-quality study.[1] This indicated higher conversion to PDD among patients with deficits in episodic memory, visuospatial function, semantic fluency and mental flexibility. If the study were better powered, possible real differences in executive function and verbal naming might have been detected. Further high-quality, adequately powered, longitudinal population-based inception cohort studies are needed to address the question.

Background

Studies have reported that 75–80% of patients with PD may eventually develop Parkinson's disease dementia (PDD),[2] and PD-MCI is considered a harbinger of the condition.[3] Research has attempted to determine the pattern of cognitive decline in PD-MCI most likely to progress to PDD. This has proven challenging, because the cognitive changes described in Parkinson's are heterogeneous, including deficits in attention, executive, language, memory, and visuospatial functioning. This variation may be the result of differences between studies in the PD-MCI diagnostic criteria applied, the number of cognitive domains explored, and the selection and number of neuropsychological tests used.[4] In response, the Movement Disorder Society (MDS) commissioned a task force to develop formal diagnostic criteria for PD-MCI.[5] These are presented on the basis of both simplified (level 1) and more comprehensive (level 2) neuropsychological testing. This CAT addressed this issue of variation in criteria, domains and assessments by focusing only on studies employing MDS Task Force level 2 criteria. A further limitation was applied to the literature search in order to yield the best evidence: as the question is one of prognosis, longitudinal population-based inception cohort studies were sought. These have the advantage that they examine a representative sample of the population, at a common (early) point in the natural history of the condition, and they allow outcome criteria to be applied objectively.[6]

Search terms

idiopathic parkinson's disease [MeSH Terms] AND cognitive impairment, mild [MeSH Terms] AND (subtype* OR pattern* OR profile* OR neuropsycholog*) AND dementia [MeSH Terms]

Search strategy

PubMed, up to March 2018. Longitudinal population-based inception cohort studies were sought, that used MDS level 2 criteria for the diagnosis of PD-MCI. Only English-language studies were included. A hand-search sought additional articles from the bibliography of key articles.

Evidence

The search yielded 66 studies. The hand-search added a further five. From these 71, a single suitable study was found:

Domellof ME, Ekman U, Forsgren L, Elgh E. Cognitive function in the early phase of Parkinson's disease, a five-year follow-up. Acta Neurologica Scandinavica. 2015;132(2):79-88.

Summary

A community-based cohort study among 134 patients with previously undiagnosed Parkinson's. Patients were assessed at baseline and annually for up to 10 years. This study presents the five-year data. PD-MCI was diagnosed on the basis of MDS Task Force criteria at level two, and PDD according to criteria published by Emre.[7] Clinical assessment included DaTSCAN. Patients with PD-MCI converting to PDD differed from non-converters in episodic memory, visuospatial function, semantic fluency and mental flexibility, but not in executive function, working memory, phonemic fluency or language. The authors concluded that patients with PD-MCI at diagnosis should be monitored for further cognitive decline, especially those with deficits in episodic memory, visuospatial function, semantic fluency and mental flexibility.

The following points should be noted:

- The sample was assembled at a common (early) point in the course of Parkinson's. This improves the validity of inferences about the progression of the condition. The validity was also enhanced by the selection of a community-based cohort, which is representative of the patients a clinician is likely to encounter.
- Diagnosis of Parkinson's was based on UK Parkinson's Disease Society Brain Bank Criteria[8] and pathological dopaminergic function confirmed by DaTSCAN. The diagnosis of PD-MCI and PDD were based on MDS Task Force Criteria.[5,7] Diagnoses were by two independent movement disorder specialists, and the diagnoses were re-evaluated annually. Functional decline was investigated using several types of information including medical files, neuropsychological testing and interviews with patients and family. Investigators were not blind to baseline cognitive status when patients were assessed for PDD. Overall however, it is unlikely that patient groups or outcomes were incorrectly attributed.
- Follow-up was for an adequate period (five years), given what we know about the rate of cognitive decline in Parkinson's.[9] Losses to follow-up were numerous at 26 (almost 20%). Of those, 23 died and three withdrew. The characteristics of patients who declined neuropsychological testing (n=19) were compared with those who completed testing. They were on average older (77.5 years versus 70.2 years), had more severe Parkinson's (UPDRS 30.0 versus 25.0) and shorter follow-up (48 versus 60 months). This might have introduced a bias towards null, given that more fragile patients were less likely to participate in follow-up.
- No sample size calculation was published. A larger sample might have resulted in the power to detect real differences in executive function and verbal naming between PD-MCI converters and non-converters, both of which had wide interquartile ranges due to missing data and failed to reach statistical significance.

- Statistical adjustment was made for potential confounding due to age, sex and educational level.
- Overall, this was a well-conducted study. There were some limitations, namely that it was possibly underpowered to detect real differences in executive function and verbal naming, and that losses to follow-up were almost 20%, mainly among more fragile patients. With a larger sample and fewer losses to follow-up, the differences demonstrated in cognitive profile between PD-MCI converters and non-converters for these domains may have been greater. A further limitation was lack of blinding to baseline cognitive profile in subsequent assessments, possibly leading to attribution bias. Counter to this however, great effort was made to confirm diagnoses.

References

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