Early bilateral caudate involvement in Parkinson’s disease is predictive of cognitive decline

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Objective

• To establish the prevalence of early caudate dopaminergic dysfunction in a large cohort of recently diagnosed (<2 years disease duration) and untreated patients with Parkinson’s disease (PD) using 123I-FP-CIT SPECT.

• To determine if differential patterns of early caudate dopaminergic dysfunction correlate with subsequent clinical outcomes.

Introduction

In patients with PD, autopsy and neuroimaging studies have demonstrated that the dopaminergic deficit within the striatum is unevenly distributed with the putamen relatively more affected than the caudate nucleus, particularly in the early stages of the disease. However, some imaging studies have shown that an early involvement of the caudate nucleus can be found in PD patients. Therefore, the prevalence of caudate dysfunction in early PD and its possible relationship to clinical phenotype remains to be established.

Methods

• PD patients and healthy controls (HC) were identified from the Parkinson’s Progression Markers Initiative (PPMI) database.

• The caudate signal was considered to be abnormal in PD patients if its level of 123I-FP-CIT binding fell two standard deviations or more below the mean caudate binding of the HC.

• Three PD groups were constructed as follows: those with no reduced 123I-FP-CIT binding either caudate (PD-NC), those with reduced 123I-FP-CIT binding in one caudate only (PD-UC) and those with bilaterally reduced caudate binding (PD-BC).

• To assess differences in gait impairment between groups at 4 years’ follow up, we calculated an index of gait severity by using the product of patient’s self-reported walking and balance score (sub-item 2.12 of part II of the MDS-UPDRS) and freezing score (2.13 of part II of the MDS-UPDRS) (Max disability score=16).

Results

• Imaging was available on 405 PD patients and 177 HC.

• Of PD patients, 53.1% had no impaired caudate function (PD-NC), 24.4% had a unilateral impaired caudate function (PD-UC) and 22.5% had a bilaterally impaired caudate (PD-BC).

• At 4 year follow-up:
  • Depression was more prevalent in the PD-BC compared with PD-NC (34.3% vs 13.8%, p=0.011). (Figure 2A)
  • The prevalence of cognitive impairment was higher in the PD-BC (45.7%) group compared to the PD-NC (20%, p=0.005) and PD-UC (17.6%, p=0.012). (Figure 2B)
  • Gait impairment was more severe in the PD-BC compared to the PD-NC but had similar severity to PD-UC. (Figure 2C)

Conclusion

• Early bilateral caudate involvement on 123I-FP-CIT SPECT increases the risk of subsequent cognitive decline, depression and gait impairment in PD patients.

References


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