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Parkinsonism and Related Disorders

Altered transposition asymmetry in serial ordering in early Parkinson's disease☆

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ABSTRACT

I d c i : The ability to arrange thoughts and actions in an appropriate serial order is impaired in Parkinson's disease (PD). However, it is unclear how serial order is represented and manipulated and how the representation or manipulation is altered in the early stages of PD. We aimed to analyze the pattern of performance errors in serial ordering e serial recall in nondemented PD patients with mild clinical symptoms and healthy adults to identify the underlying principles of serial ordering.

Me h d : PD patients (N = 57) and healthy controls (N = 40) completed the adaptive digit ordering and digit span forward tests. We focused on items recalled in incorrect positions (transposition) and analyzed the tendency to recall transposed items too early (anticipation) e too late (postponement). We also analyzed the tendency to recall the item displaced by the error (fill-in) e the item following the error in the target output order (infill) after anticipation errors.

Re : PD patients not only made more transposition errors but also showed distinct error patterns. The pa-

post-error position, i.e. whether the error was followed by an item that preceded the error (fill-in) or an item that followed the error in the target output order (infill). Item errors were divided into repetition and non-repetition errors. A repetition error was the incorrect recall of an item already recalled in an earlier position. An increase in repetition errors reflects response suppression deficits.

Two researchers (S.M. and Z.Y.) coded error types independently. If an error fitted multiple types or the researchers did not agree on its type, the error was counted as ambiguous and excluded from further analyses. The proportion of ambiguous errors was less than 0.7% in either group and test.

2.4. Statistical analysis

Statistical inference was made using both null hypothesis significance testing and Bayesian model comparison with JASP. For each error type, the key parameter was the number of errors divided by the number of responses in the corresponding test. We first examined how transposition or item errors differed between groups using repeated measures ANOVAs. The ANOVA had a within-subject factor Test (DOT-A, forward), a between-subject factor Group (PD, PD-MCI, healthy control), and a covariate Age. The interaction between Test and Group was followed by two-sample -tests (two-tailed, Bonferroni-corrected threshold $p < 0.025$).

For transposition errors, we then examined how anticipation or postponement errors, and fill-in or infill errors, differed between groups. For item errors, we examined how repetition errors differed between groups. The analyses were conducted using similar ANOVAs with Test and Group as factors and Age as a covariate.

We finally examined the effect of D2/3 receptor agonists by correlating the levodopa equivalent dose for D2/3 receptor agonists with the percentage of anticipation and fill-in errors in each test (Bonferroni-corrected threshold $p < 0.013$). The levodopa equivalent dose for other dopaminergic drugs and age were controlled.

3. Results

3.1. Test performance

Table 1 shows demographic and clinical features and neuropsychological measures of the patients and healthy controls. The one-way ANOVA revealed a group effect in the DOT-A and forward test. Consistent with our previous study [6], PD patients with normal global cognition scored lower than healthy controls in the DOT-A (pairwise comparison, $p < 0.001$) but not in the forward test. PD-MCI patients scored lower than healthy controls in both tests (DOT-A: $p < 0.001$; forward: $p = 0.001$).

3.2. Error analysis

Having confirmed our previous finding, we examined the group effect on each error type, using repeated measures ANOVAs with Test and Group as factors and Age as a covariate. Fig. 2A presents the percentage of transposition and item errors in each group. For transposition errors, the ANOVA revealed a significant interaction between Test and Group ($F(2,93) = 7.48$, $p = 0.001$, $\eta^2 = 0.14$) in addition to the main effect of Group ($F(2,93) = 4.61$, $p = 0.012$, $\eta^2 = 0.09$). Post-hoc -

p

by the error in the forward test. The fill-in:infill ratio was approxi-

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