Movement Disorders
CLINICAL PRACTICE

Strategy Adherence: A Specific and Rapidly Progressive Deficit in Progressive Supranuclear Palsy

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Progressive Supranuclear Palsy (PSP) is a rapidly progressive neurodegenerative tauopathy[1] without any disease-modifying treatment. To aid development and evaluation of new treatments, we need a clear understanding of the deficits PSP produces and their progression.

PSP patients develop multiple deficits in executive function (cognitive inflexibility, problems with planning, distractibility and impulsivity), apathy, and language problems.[2–4] Here we describe a novel cognitive measure, "strategy adherence", derived from an analysis of how a subject completes the well known cancellation task (Fig. 1). We used OCS-Plus, a tablet-based cognitive testing tool.[5] The participant is presented with a screen displaying 30 vegetables (10 cabbages, 10 peppers, 10 carrots) mixed with 30 fruits (10 bananas, 10 pears, 10 apples) and has to select the fruits with a stylus. Plotting the selection order reveals the system used by the participant to work their way through the task. Some proceed in an orderly geographic pattern through the screen of symbols. Others cancel by category (eg, apples then pears etc). Participants following any such strategy throughout the task are deemed "strategy adherent". Those switching strategy or to a random cancellation part way through the task, or canceling randomly from the outset, are deemed non-adherent.

We studied 27 PSP patients (17 Richardson's syndrome, 10 PSP-parkinsonism, all in clinically probable or possible diagnostic certainty categories), 51 idiopathic Parkinson's disease (PD) patients, and 21 healthy controls (HC). Participants were tested five times at three-monthly intervals.

At baseline, only 52% of PSP participants were strategy adherent, versus 96% of PD and 100% of HC participants ($P < 0.001$ for PSP vs. PD and for PSP vs. HC, chi squared test). The strategy adherence rate for PSP participants decreased rapidly, from 52% at visit 1 to 30%, 22%, 15% and 11% at visits 2 to 5. There was no decrease in strategy adherence in PD or HC groups. Deterioration from baseline in the PSP group was significant at all visits (Related Samples McNemar Test, vs. baseline, V2 $P = 0.031$, V3 $P = 0.008$, V4 $P = 0.002$, V5 $P = 0.001$). Once an individual lost strategy adherence, they never regained it at any subsequent visit, suggesting irreversible crossing of a significant threshold in cognitive decline. There was no significant difference between PSP phenotypes in strategy adherence at any visit (Fisher's exact test).

Conventional cognitive measures were insensitive to PSP progression in this short timeframe: Mini Mental State Evaluation ($P = 0.86$), and Montreal Cognitive Assessment ($P = 0.88$) (Friedman's test). The PSP rating scale showed significant change from baseline only at visit 5 ($P = 0.04$ Friedman's test; visit 1 vs. visit five pairwise comparison $P = 0.039$).

The decline in group level performance in PSP is both large and rapid. For trials, if intact SA at baseline were a criterion for entry, a reduction of 58% could be expected in 6 months. This is an extremely strong signal of progression and a potential disease modifying drug could be shown to successfully retard the progression of the cognitive effects of PSP in a short period of time.

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Author Roles

(1) Research project: A. Conception, B. Organization, C. Execution; (2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique; (3) Manuscript: A. Writing of the first draft, B. Review and Critique.

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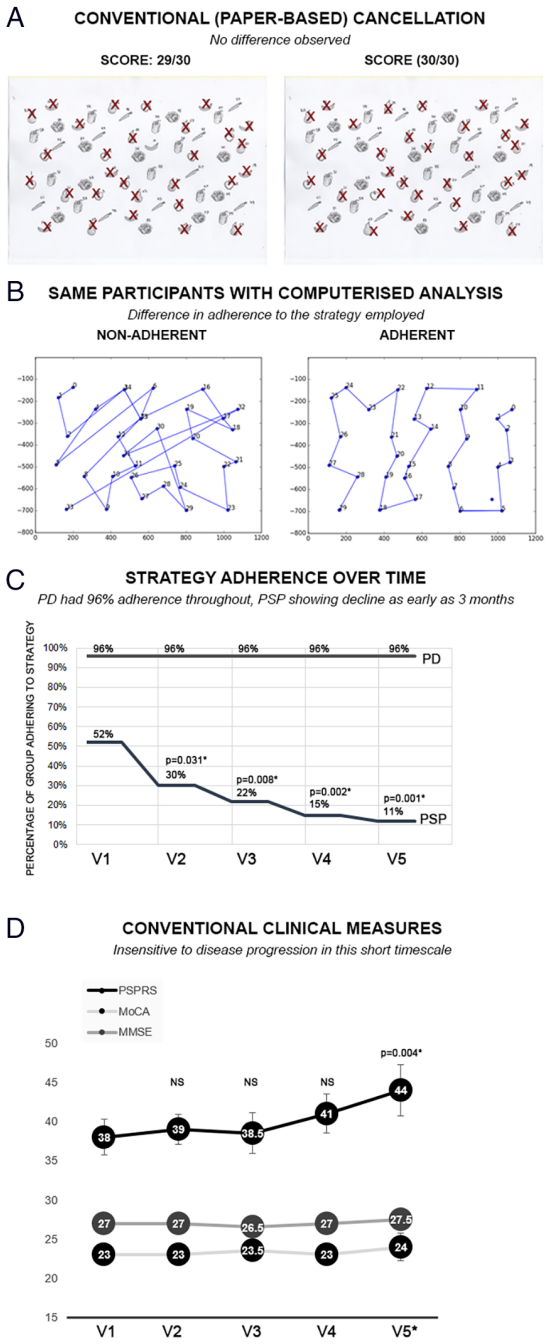

FIG. 1. (**A**) Cancellation task performed by two participants in the study, showing near identical performance when attention is pain only to which symbols have been selected; (**B**) The pathway through the symbols used by the same two participants appear dramatically different, with only the one on the right following a clear strategy; (**C**) Rapid decline in strategy adherence rate in the PSP group over time, compared to no decline in the PD group; (**D**) Changes in the PSPRS and conventional cognitive scales over time.

M.A.B.: 1C, 2A, 2B, 2C, 3A, 3B
M.B.: 1C, 3B
T.P.: 3B
J.J.F.: 1A, 1B, 1C, 2A, 2B, 2C, 3A, 3B
C.A.A.: 1A, 1B, 1C, 2A, 2B, 2C, 3A, 3B

Disclosures

Ethical Compliance Statement: The measurements were obtained during the Oxford study of QUantification In Parkinsonism (OxQUIP), a longitudinal study conducted at the John

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Radcliffe Hospital in Oxford, UK. The study was approved by the research ethics committee and the Health Research Authority (REC 16/SW/0262). The aim of OxQUIP is to develop novel methods of objective disease progression measurement. This is achieved by repeated administration of a battery of tests, according to a structured protocol, at three-monthly intervals. All participants were given written information about the study, and informed consent was obtained prior to participating. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

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