Corticomotor excitability in Progressive Supranuclear Palsy, Parkinson's disease and healthy controls, a TMS study

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Background and Objectives

Progressive Supranuclear Palsy (PSP) is the second most common parkinsonian syndrome after Parkinson's disease (PD), with some overlapping clinical features especially in the early phases, making diagnosis difficult until later stages. To date, no definite imaging, biochemical, or genetic diagnostic marker are available. Non-invasive neurophysiological techniques, such as transcranial magnetic stimulation (TMS), could prove useful to gain insight into these pathologies as widely available methods for differential diagnosis. The aim of this study is to assess corticospinal excitability in PSP and PD subjects.

Methods

Seventeen PD and 13 PSP were evaluated in OFF state (i.e. after overnight retrieval of dopaminergic drugs). Clinical scores were derived from MDS-UPDRS part III, a commonly used rating scale for severity assessment in PD. TMS evaluations included resting motor threshold (RMT), resting motor evoked potentials (MEP) amplitude, contralateral (CSP) and ipsilateral (iSP) silent period after TMS delivered during maximal voluntary ongoing contraction. Intracortical inhibition (SICI) and facilitation (ICF) were evaluated with paired pulse TMS, measuring MEP size modulation in response to conditioning stimuli. Eleven healthy volunteers were included as controls (CT). Statistical analysis was performed using either parametric or non-parametric ANOVA and post-hoc tests, according to data distribution. For paired-pulse, repeated measures ANOVA was adopted, using interstimulus interval (ISI) and group as factors, with ISI 1-3 testing intracortical inhibition (SICI) and ISI 10-15 intracortical facilitation (ICF).

Results

PSP and PD groups did not significantly differ in MDS-UPDRS part III. Non parametric one-way ANOVA showed significant group effect for RMT (p.008), post-hoc tests demonstrated different distribution across groups (p.002, PSP>CT>PD, Fig.1). Group effects were found on dominant iSP duration (p.016, Fig.2) that was longer in PSP compared with CT (p.005) – PD showing intermediate values – and on pre-iSP EMG activity on both sides (p<.001) that was higher in PSP compared with PD (for both sides p<.001), with intermediate values in CT.
PSP also had reduced paired-pulse intracortical inhibition and increased intracortical facilitation compared to PD subjects (p.017) and controls (p.032) (Fig.3; Conover non-parametric repeated measures ANOVA: significant effect for ISI: p<.001 and group: p.035, without significant interaction).

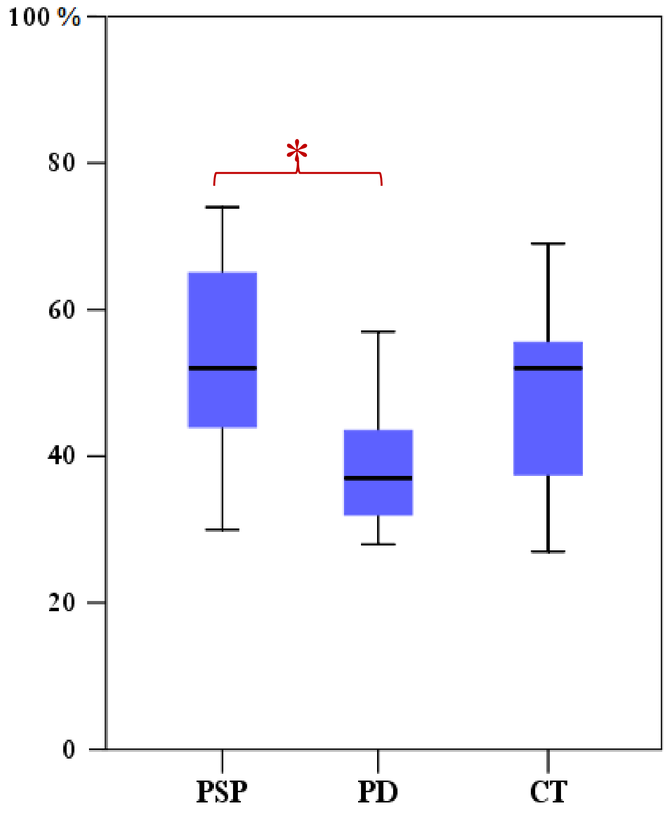

Figure 1.
*Resting motor threshold, expressed as % of max stimulator output, across groups. * p<.05*

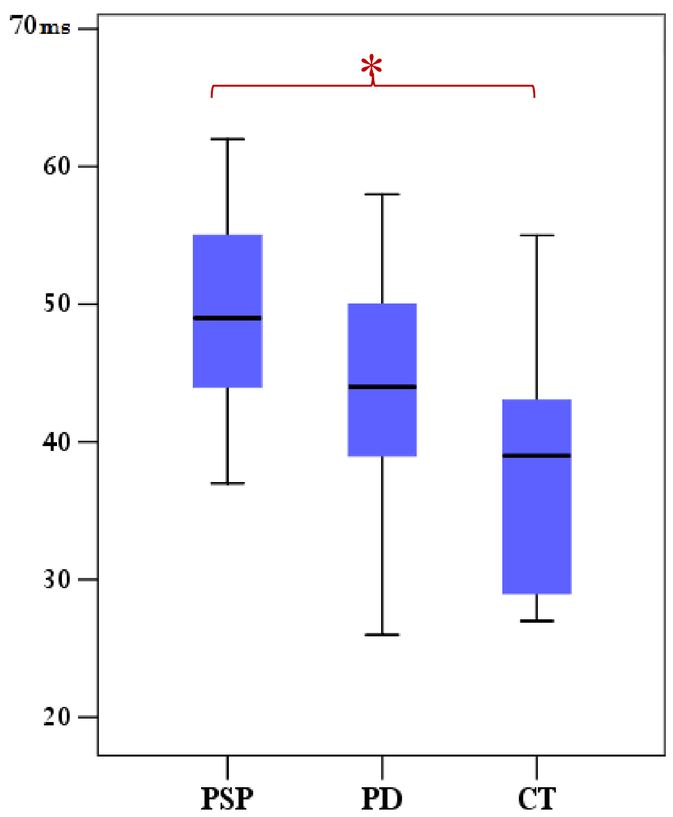

Figure 2.
*Duration (msec) of iSP duration of the dominant hemisphere across groups *p<.05*

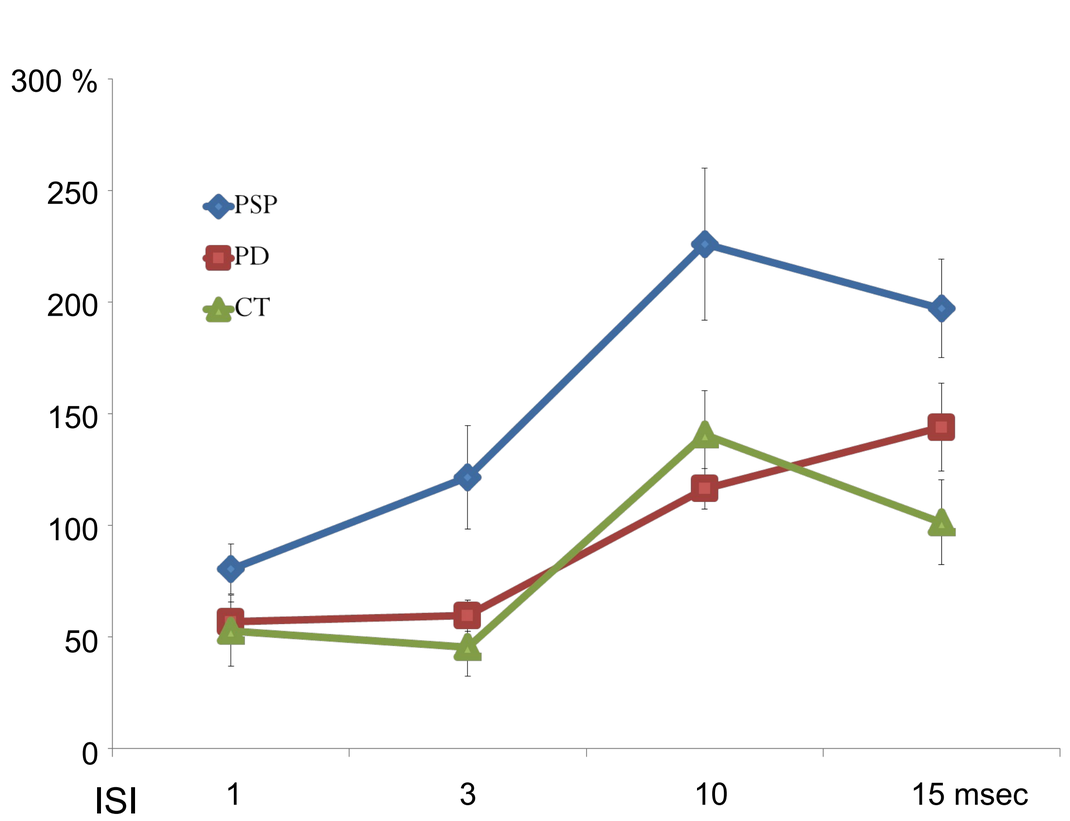

Figure 3
Paired-pulse conditioned MEP amplitudes (expressed as % of test MEP) testing inhibitory (ISI intervals 1-3 msec) and excitatory (ISI intervals 10-15 msec) inter-stimulus intervals-ISI.

Conclusions

RMT exhibited opposite behavior relative to controls in our PSP and PD groups, with significantly higher values in PSP, perhaps owing to more severe frontal cortical atrophy in PSP and to compensatory hyperexcitability for dysfunctional basal ganglia network in PD [1]. iSP duration was longer in PSP group compared with controls but not compared to PD, consistently with previous findings in PSP [2] and linked to involvement of GABA circuitry, although it is possible that differences in pre-stimulus voluntary contraction and different resting motor threshold may have contributed [3]. Increased intracortical excitability in PSP, as from the balance of paired-pulse intracortical facilitation and inhibition, consistently with previous reports [4] can also be linked to functional loss of GABAergic neurotransmission.
Taken together, these findings point to impairment of inhibitory mechanisms which is more evident in PSP compared with PD, despite higher resting motor thresholds. In this setting, TMS, as a low-cost, highly applicable neurophysiologic techniques can be helpful in the assessment of parkinsonian syndromes. Further investigations are however required to validate our results in larger cohorts, possibly in early stages in order to follow-up abnormalities over the course of the diseases.

Bibliography

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