

Subthalamic nucleus role in behaviour and cognition: insights from tauopathies and synucleinopathies

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1. The subthalamic nucleus (STN) plays a role in behavioural symptoms of ageing and neurodegenerative diseases: i.e. inhibitory control and impulsivity
2. STN stimulation in PD, modulates neuropsychiatric symptoms and decreases measures of interpersonal reactivity (empathy)
3. In PSP, defined by STN phosphorylated-tau neuropathology, altered motor and cognitive impulsivity correlate with stage, and STN is functional hyperconnected

INTRODUCTION

The subthalamic nucleus (STN) is a major site of neurodegeneration in several diseases manifesting behavioural and cognitive symptoms, i.e. progressive supranuclear palsy (PSP), dementia with Lewy bodies, and Parkinson Disease (PD). STN has been proposed as a behavioural brake within frontal-striatal connectivity networks serving cognitive, affective, and motor functions in PD and animal models.

Goal: Which clinical outcomes can reflect STN dysfunction in ageing and other subcortical dementias?

METHODS

A series of studies evidenced:

1. Neuropsychiatric symptoms as prevalent in subcortical dementias (PSP, LBD) as in behavioural FTD
2. Healthy ageing deters inhibitory control reaction times and increases impulsivity
3. Behavioural symptoms change and empathy is reduced in PD patients with chronic STN neuromodulation
4. Motor/Cognitive impulsivity higher in patients with PSP than PD
5. In PSP, STN shows functional hyper-connectivity in resting-MRI

RESULTS

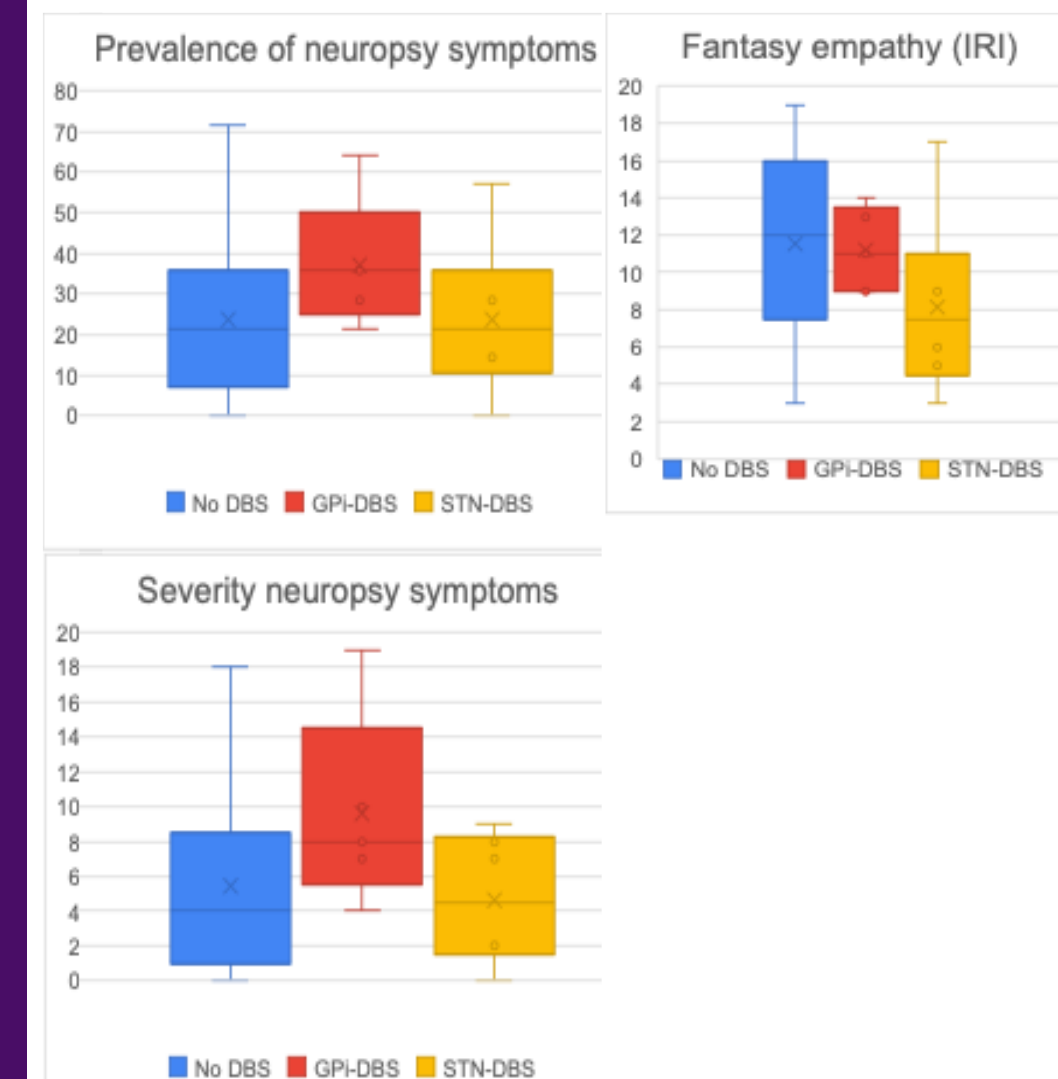
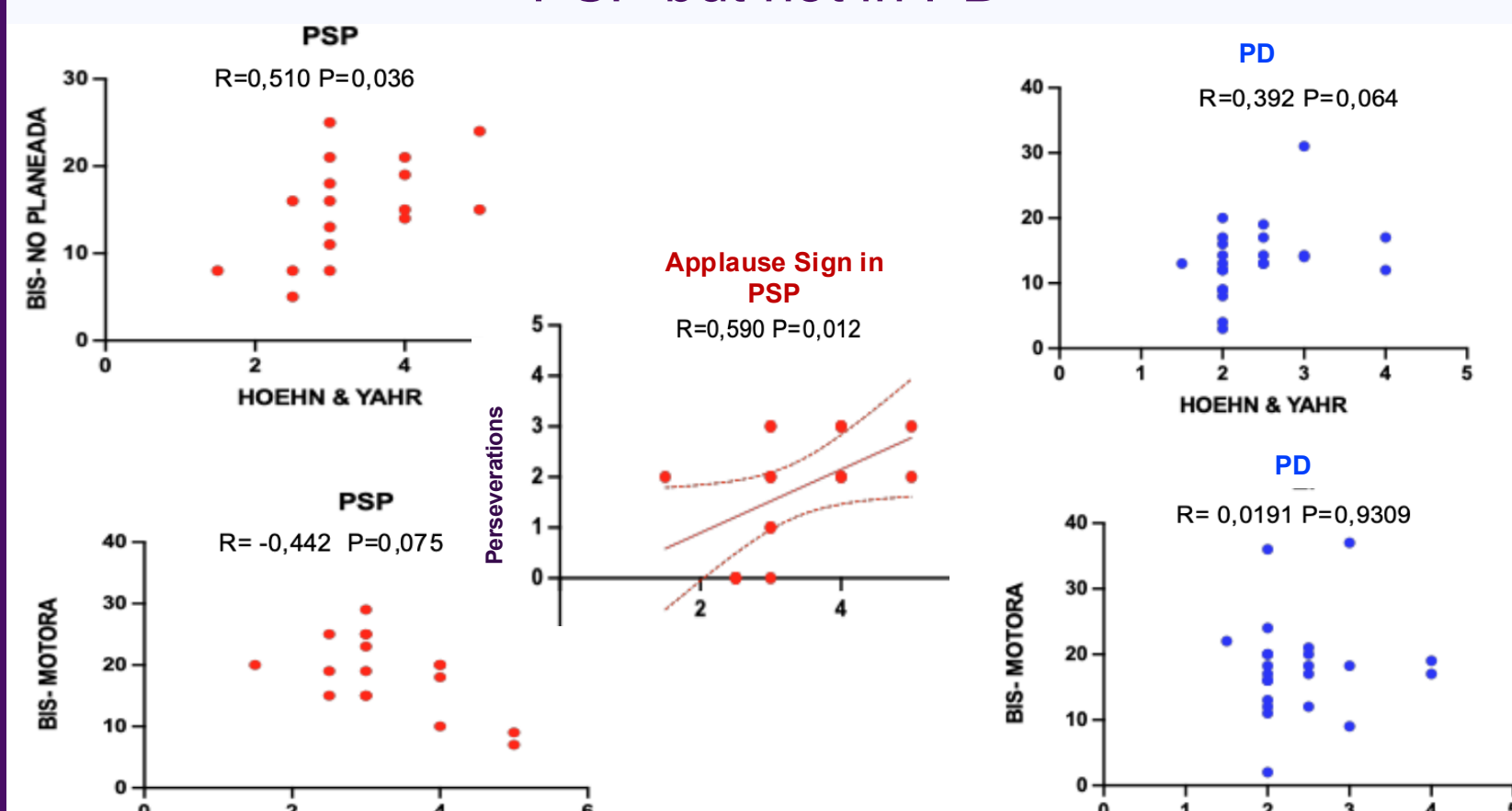


Fig. 3. In moderate stage-PD behavioral symptoms occur under chronic treatment with STN deep-brain stimulation.

CONCLUSIONS

Diverse evidence relates behavioural symptoms with STN dysfunction or its neuromodulation. Especially inhibitory control and impulsivity shed light on cortical-subcortical network changes. Understanding STN-networks' role in behavior would translate into better diagnostic tools and treatment for phospho-tau and α -synuclein-related neurodegeneration.

Fig. 4. Motor impulsivity correlates with disease stage in PSP but not in PD



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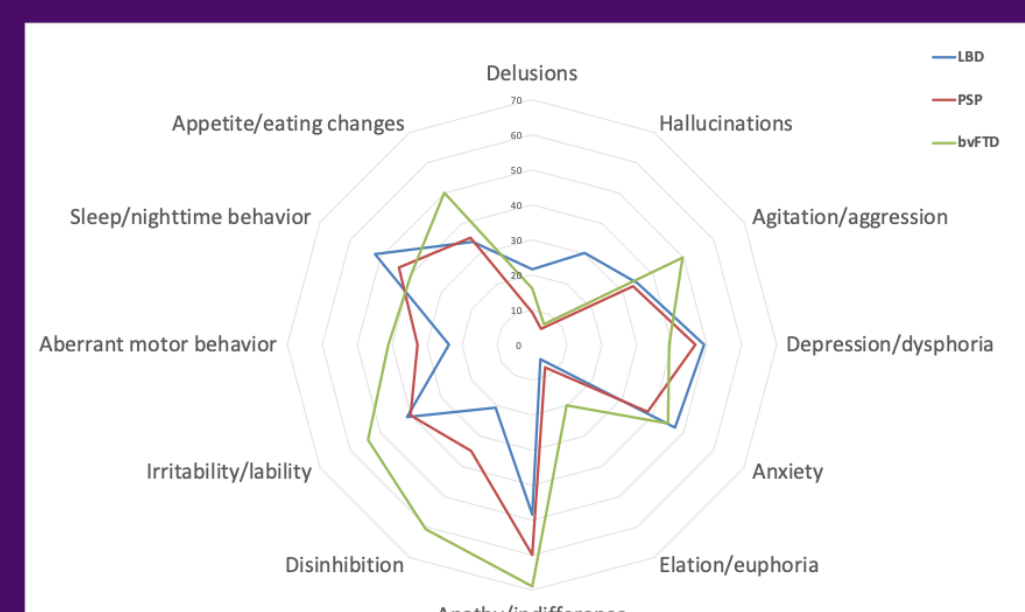


Fig. 1. Neuropsychiatric symptoms in NACC patients (NPI)

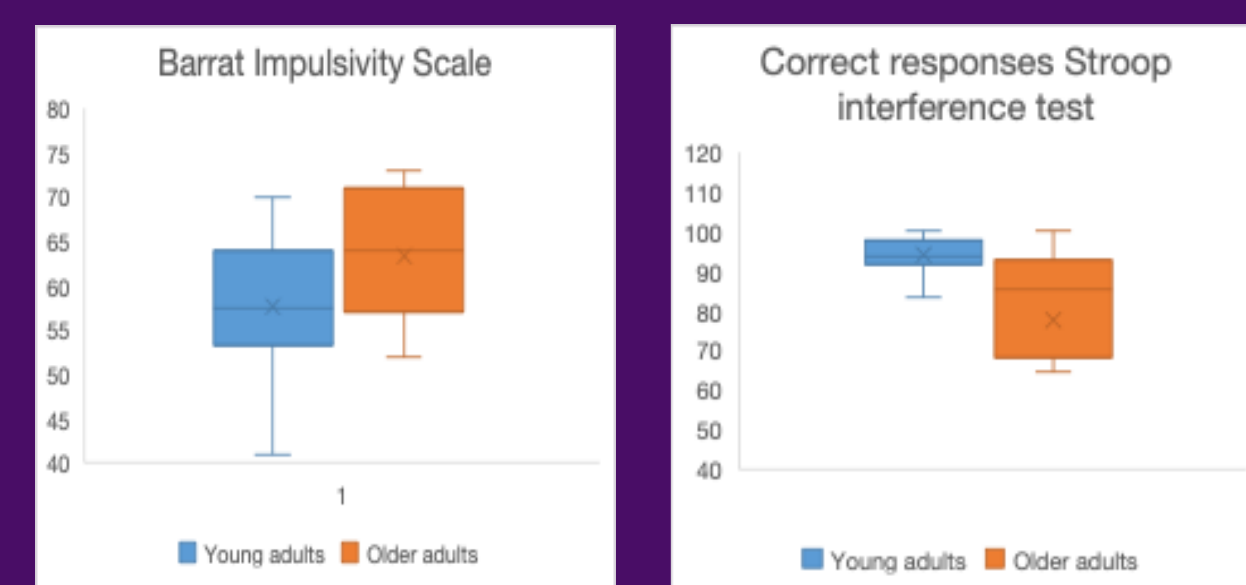


Fig. 2. Healthy ageing impacts on self-reported impulsivity and inhibitory control measures

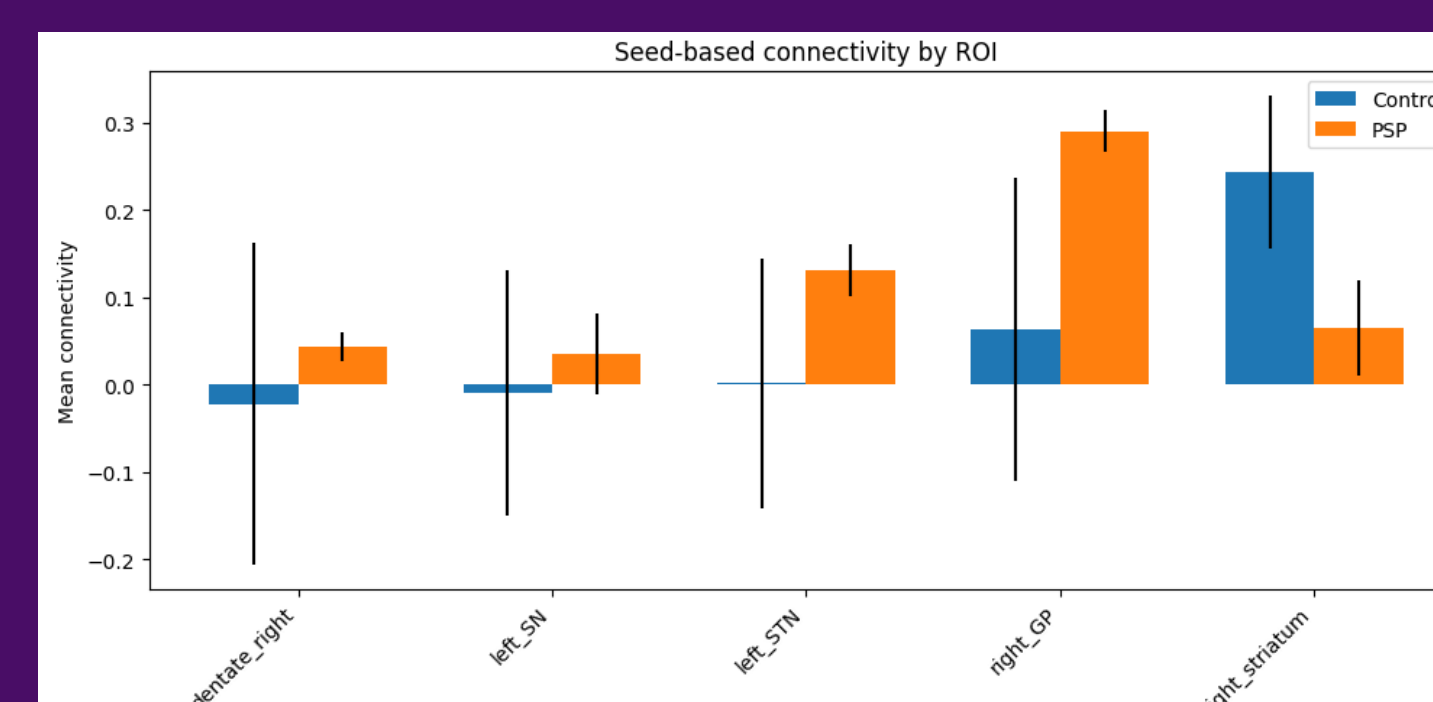


Fig. 5. In PSP, STN shows hyper-connectivity with other basal ganglia and cortex compared with healthy controls (4RTNI).