Title

528 REM Sleep Without Atonia in Idiopathic REM Sleep Behavior Disorder in the North American Prodromal Synucleinopathy Cohort

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Neuropsychology/Early detection of cognitive decline with neuropsychological tests

The North American Prodromal Synucleinopathy (NAPS) Consortium: Baseline neuropsychological findings in 136 participants

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Abstract

Background: It is important to determine the natural history of individuals with RBD and generate clinical and neuropsychological data for planning disease-modifying trials to delay or prevent phenoconversion of RBD to an overt synucleinopathy such as dementia with Lewy bodies, Parkinson's disease, or multiple system atrophy. Our objective is to present initial neuropsychological data on 136 participants with REM sleep behavior disorder (RBD) without an overt synucleinopathy who are in the North American Prodromal Synucleinopathy (NAPS; R34AG056639) Consortium.

Method: As part of the NAPS protocol (www.naps-rbd.org), investigators at 10 centers in North America are enrolling a target of 360 participants with RBD. A comprehensive clinical battery and a set of neuropsychological measures (using the National Alzheimer Coordinating Center Uniform Data Set version 3 or UDS3) are performed at each visit.

Result: Participants were 82% male, ranging in age from 35-85 (Mean=65.9, SD=15.9) and education from 8-20 years (Mean=15.9, SD=3.1). Only 17 participants (13%) were impairment-free across all tests administered. The proportions of participants with impaired scores were tabulated as follows ($\leq$ -1.5 SD after adjustment for age, sex, and education): global cognition – 17%; attention/executive functioning – 10-20% across measures; language – 14-24% across measures; visuospatial – 16%; and episodic learning/memory – 18-25% across measures. Of all participants, 79 (58%) showed impairments $\leq$ -2 SD. Moreover, 53% of those with cognitive impairment involved impact in 2

domains, an additional 20% in 3 domains, and another 4% was impaired in all domains. The combination of attention/executive and language was most often observed.

Conclusion: Collection of a comprehensive set of clinical and neuropsychological measures is feasible and tolerated in RBD patients. Using the UDS3 neuropsychological test battery, impairment in one or more measures was present in 87% of participants, and 58% showed impairments greater than 2 SD below the mean in the absence of a clinical diagnosis of dementia. Impairments in $\geq$ 2 domains was common, most frequently involving attention/executive and language. Future longitudinal assessments will be required to determine the predictive utility of neuropsychological performance for phenoconversion of RBD to an overt synucleinopathy.