The Anti-NPI: A novel tool for assessment of neuropsychiatric symptoms in clinical trials for prodromal Alzheimer's disease

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Objectives: Expand the Neuropsychiatric Inventory (NPI) to reflect the continuum of neuropsychiatric symptoms across both standard NPI (focused on negative symptomatology) and the newly developed anti-NPI (focused on positive change in NPI variables).

Background: The NPI characterizes negative changes in neuropsychiatric symptom development in dementia, yet most understand that the variables examined in the NPI do not exist as present vs. absent, but rather are dependent on a continuum of symptomatology. The potential for positive changes in neuropsychiatric symptoms, not currently part of the NPI, needs to be studied.

Design/Methods: Observational study of the University of Kentucky Alzheimer's Disease Center cohort subjects with MCI and early dementia (n=48). Study partners were administered the NPI as well as our newly developed anti-NPI to examine the possibility of neuropsychiatric symptom change across both positive and negative axes. Standard descriptive statistical methods were used to evaluate neuropsychiatric symptom change in this preliminary study.

Results: Subjects were 78.9±8.6 years of age, 38% male, with 16.4±3.2 years of education, MMSE 26.0±2.8, CDR global score 0.5, and CDR sum of boxes 1.7±1.1. Total NPI symptoms reported as negatively changed were 2.5±2.7 out of 12, with total severity scores of 3.6±4.8, whereas positive change in NPI (Anti-NPI) total symptoms and extent of change were 7.9±3.1 and 11.7±7.7 out of 12 respectively ($p<0.001$ for both). NPI and anti-NPI symptom scores were negatively correlated with each other as expected ($r=-0.384$; $p<0.05$). No differences were seen between subjects on basic demographic or clinical variables based on diagnosis or presence/absence of NPI or anti-NPI symptoms.

Conclusion/Relevance: These data demonstrate that positive changes in neuropsychiatric symptoms are more common than the negative changes typically focused on using the NPI in MCI and early dementia. Further refinement and validation of the anti-NPI may allow a more complete assessment of neuropsychiatric symptom change in early cognitive impairment and dementia. As there are few current tools available for reliably measuring functional outcome in prodromal AD, the anti-NPI may prove extremely important in addressing this FDA-mandated outcome needed for drug approval for preclinical dementia and mild cognitive impairment, an area of extreme focus in drug development today.