

- 1 Miller, J. B., Banks, S. J., Leger, G. C., & Cummings, J. L. (2014). Randomized controlled trials in frontotemporal dementia: cognitive and behavioral outcomes. *Transl.Neurodegener.*, 3, 12.
Notes: Progress has been made in understanding the genetics and molecular biology of frontotemporal dementia (FTD). Targets for intervention have been identified, therapies are being developed, and clinical trials are advancing. A major challenge for FTD research is that multiple underlying pathologies can be associated with heterogeneous phenotypes. The neuropsychological profiles associated with FTD spectrum disorders often include executive dysfunction, language impairments and behavioral disturbance. Behavioral variant FTD is characterized by an initial presentation of changes in personality, behavior and/or emotion, which are often difficult to objectively capture using traditional neuropsychological measures. The two principal language variants of FTD are Progressive Nonfluent Aphasia (PNFA) with predominant agrammatic/non-fluent impairments and Semantic Dementia (SD) with semantic impairments and visual agnosia. Selection of appropriate endpoints for clinical trials is critical to ensure that the measures are adequately sensitive to detect change, yet specific enough to isolate signal from noise, and acceptable to regulatory agencies. Given the anticipated potential for small effect sizes, measures must be able to identify small incremental changes over time. It is also imperative that the measures provide adequate coverage of the constructs or behaviors of interest. Selected outcome measures should be suitable for repeat administration, yet relatively robust to practice effects to ensure that observed changes reflect true signal variance and not residual effects due to repeated measurement or poor reliability. To facilitate widespread adoption as an endpoint, measures should be readily accessible. We provide several examples of potential global, composite, and individual cognitive measures, as well as behavioral measures promising for FTD trials. Development and application of appropriate trial outcomes is critically important to success in advancing new treatments for FTD patients
- 2 Leger, G. C. & Banks, S. J. (2014). Neuropsychiatric symptom profile differs based on pathology in patients with clinically diagnosed behavioral variant frontotemporal dementia. *Dementia and Geriatric Cognitive Disorders*, 37, 104-112.
Notes: BACKGROUND: Behavioral variant frontotemporal dementia (bvFTD) is pathologically heterogeneous. With emerging therapeutics, determining underlying pathology during life is increasingly important. Neuropsychiatric symptoms are prevalent and diagnostic in bvFTD. METHODS: We assessed the neuropsychiatric profile of patients with clinically diagnosed bvFTD as a function of pathology at autopsy. Patients with a clinical diagnosis of bvFTD at the initial visit were selected from the National Alzheimer's Coordinating Center (NACC) database. Neuropsychiatric symptoms endorsed on the Neuropsychiatric Inventory Questionnaire (NPI-Q) were analyzed. RESULTS: Of 149 patients with clinically diagnosed bvFTD, pathology was primarily Alzheimer's disease (AD) in 20.5%. These patients differed from those with underlying frontotemporal lobar degeneration: patients with AD pathology (plaques and tangles) were more likely to have hallucinations, delusions, or agitation. Patients were further differentiated into tau-positive (30% of cases, including Pick's disease, FTD and parkinsonism with tau-positive or argyrophilic inclusions, and other tauopathies) or tau-negative cases (70% of cases, including bvFTD tau-negative ubiquitin-positive inclusions). These patients also differed in some of the neuropsychiatric symptoms seen. Tau-negative cases were more likely to demonstrate depression, delusions, and changes in appetite and eating. CONCLUSIONS: These preliminary findings contribute to our increasing ability to predict, using simple clinical tools, the neuropathological underpinnings of bvFTD during life
- 3 Banks, S. J., Obuchowski, N., Shin, W., Lowe, M., Phillips, M., Modic, M. et al. (2014). The protective effect of education on cognition in professional fighters. *Archives of Clinical Neuropsychology*, 29, 54-59.
Notes: Education has a protective effect against cognitive deficits following various forms of brain insult. Professional fighting (boxing and mixed martial arts) provides a model for assessing the impact of cumulative brain injuries on cognition and brain health. In the current cross-sectional observational study, we explore whether education would be protective against

cognitive loss in fighters. We tested 141 professional fighters using a computerized neurocognitive battery, in addition to structural MRI. We used automated segmentation software to compute the volumes of various brain structures. We found fighters with high school education or less to show more associations between fight exposure and cognitive test scores. The relationship between brain structure volume and exposure did not differ based on education. These results are interpreted as putatively showing a protective effect of education on functional integrity in fighters, although longitudinal data and a larger sample size are required to further understand this relationship

- 4 Banks, S. J. & Weintraub, S. (2009). Generalized and symptom-specific insight in behavioral variant frontotemporal dementia and primary progressive aphasia. *Journal of Neuropsychiatry and Clinical Neuroscience*, 21, 299-306.

Notes: Behavioral variant frontotemporal dementia (FTD) and primary progressive aphasia (PPA) are related dementias with different presenting symptoms but with increasing symptom overlap as they progress. Loss of insight is associated with early behavioral variant FTD, but not PPA. This study used the Frontal Behavioral Inventory to compare patient and caregiver concepts of symptom presence and severity. Patients with behavioral variant FTD were found to have worse insight overall than PPA patients. However, the PPA group showed reduced insight into behavioral symptoms, and the behavioral variant FTD groups had intact insight into some language symptoms. Theoretical and clinical implications are discussed

- 5 Banks, S. J. & Weintraub, S. (2008). Neuropsychiatric symptoms in behavioral variant frontotemporal dementia and primary progressive aphasia. *Journal of Geriatric Psychiatry and Neurology*, 21, 133-141.

Notes: Neuropsychiatric symptoms are well defined in behavioral variant frontotemporal dementia but are not as well studied in primary progressive aphasia. This study compared caregiver reported neuropsychiatric symptoms in these 2 forms of dementia at short and long disease duration. Patients with behavioral variant frontotemporal dementia had more symptoms than patients with primary progressive aphasia. However, when divided by duration of disease, patients with primary progressive aphasia with long duration had a similar number of symptoms to patients with behavioral variant frontotemporal dementia at either duration. Furthermore, this group of patients with primary progressive aphasia had more symptoms typical of behavioral variant frontotemporal dementia and less mood-related symptoms which were more common in patients with primary progressive aphasia with shorter duration. This study illustrates the emergence of neuropsychiatric symptoms as primary progressive aphasia progresses and highlights the increasing overlap with behavioral variant frontotemporal dementia because the disease affects areas outside of the language network