4. Orr SL, Friedman BW, Christie S, et al. Management of adults with acute migraine in the emergency department: the American Headache Society evidence assessment of parenteral pharmacotherapies. *Headache* 2016;56:911–940.
5. Roberto G, Raschi E, Piccinni C, et al. Adverse cardiovascular events associated with triptans and ergotamines for treatment of migraine: systematic review of observational studies. *Cephalalgia* 2015;35:118–131.
6. Magis D, Schoenen J. Advances and challenges in neurostimulation for headaches. *Lancet Neurol* 2012;11:708–719.

COGNITION AND NEUROPSYCHIATRY IN BEHAVIORAL VARIANT FRONTOTEMPORAL DEMENTIA BY DISEASE STAGE

Maxime Bertoux, Norwich, UK; Marie Sarazin, Paris; Florence Pasquier, Lille; Michel Bottlaender, Orsay, France; Leonardo Cruz de Souza, Belo Horizonte, Brazil; Eneida Mioshi, Michael Hornberger, Norwich, UK: We read the article by Ranasinghe et al. characterizing neuropsychological profiles of behavioral variant frontotemporal dementia (bvFTD) as a function of disease staging¹ with interest. This is an important study with an impressive sample size, paving the way for cognitive outcomes measures in future disease intervention trials.

The finding of relative intactness of episodic memory in early bvFTD is of particular interest as episodic memory is regarded as the neuropsychological gold standard to distinguish bvFTD and Alzheimer disease (AD). However, there is increasing evidence from many independent cohorts (some with pathologic diagnosis) that severe memory impairment can occur in some patients with bvFTD,^{2,3} even at the earliest disease stages,⁴ with concomitant hippocampal atrophy.⁵

The question is whether disease staging via the Clinical Dementia Rating (CDR) might have potentially led to an underrepresentation of memory deficits in both bvFTD and AD, as the memory component of the CDR should be strongly correlated to neuropsychological episodic memory performance. For future studies, it might be more appropriate to apply the frontotemporal lobar degeneration–specific CDR (FTLD-CDR) as a stage measure or use disease staging tools relying only on functional and neuropsychiatric features (e.g., Frontotemporal Dementia Rating Scale) to allow a clearer delineation of neuropsychological deficits by disease staging.

Author Response: Kamalini G. Ranasinghe, Katherine P. Rankin, Iryna V. Lobach, Joel H. Kramer, Virginia E. Sturm, San Francisco; Brianne M. Bettcher, Aurora, CO; Katherine Possin, San Francisco; S. Christine You, Los Angeles; Amanda K. Lamarre, San Francisco; Tal Shany-Ur, Tel Aviv, Israel; Melanie L. Stephens, David C. Perry, Suzee E. Lee, Zachary A. Miller, Maria L. Gorno-Tempini,

Howard J. Rosen, Adam Boxer, William W. Seeley, Gil D. Rabinovici, Keith A. Vossell, Bruce L. Miller, San Francisco: We thank Bertoux et al. for their comments on our article,¹ and agree that the issue of memory deficits in early bvFTD has historically been complicated.^{6,7} In our sample,¹ *average* free recall and recognition scores at CDR = 0.5 were in the unimpaired range ($z = -1.1$ and -0.6 , respectively). However, this may reflect clinical heterogeneity within the bvFTD syndrome, with a minority subset impaired, while others retained intact recognition memory and even free recall, a diversity previously observed by Bertoux et al.³

Data from our other related study provide further explanation for this heterogeneity.⁸ There, we did use FTLD-CDR to stratify patients with bvFTD, agreeing that this tool is superior for bvFTD disease staging, and discovered that approximately 40% of our patients with the lowest FTLD-CDR sum of boxes (4.0–7.5) had memory deficits. We further found that this heterogeneity in memory was partly accounted for by the anatomic diversity within bvFTD, similar to findings in other cohorts.⁹ The 2 subgroups with the greatest temporal lobe involvement had the most significant memory deficits, and these were the only patients with bvFTD in whom memory was sometimes the first affected symptom domain. Thus, we recommend that future studies use both FTLD-CDR and anatomic subclassification to understand memory in this complex syndrome.

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1. Ranasinghe KG, Rankin KP, Lobach IV, et al. Cognition and neuropsychiatry in behavioral variant frontotemporal dementia by disease stage. *Neurology* 2016;86:600–610.
2. Hornberger M, Piguet O, Graham AJ, Nestor PJ, Hodges JR. How preserved is episodic memory in behavioral variant frontotemporal dementia? *Neurology* 2010;74:472–479.
3. Bertoux M, de Souza LC, Corlier F, et al. Two distinct amnesic profiles in behavioral variant frontotemporal dementia. *Biol Psychiatry* 2014;75:582–588.
4. Schubert S, Leyton CE, Hodges JR, Piguet O. Longitudinal memory profiles in behavioral-variant frontotemporal dementia and Alzheimer's disease. *J Alzheimers Dis* 2016;51:775–782.
5. de Souza LC, Chupin M, Bertoux M, et al. Is hippocampal volume a good marker to differentiate Alzheimer's disease from frontotemporal dementia? *J Alzheimers Dis* 2013;36:57–66.
6. Rascovsky K, Hodges JR, Knopman D, et al. Sensitivity of revised diagnostic criteria for the behavioural variant of frontotemporal dementia. *Brain* 2011;134:2456–2477.
7. Diehl J, Monsch AU, Aebi C, et al. Frontotemporal dementia, semantic dementia, and Alzheimer's disease: the contribution of standard neuropsychological tests to differential diagnosis. *J Geriatr Psychiatry Neurol* 2005;18:39–44.
8. Ranasinghe KG, Rankin KP, Pressman PS, et al. Distinct subtypes of behavioral-variant frontotemporal dementia based on patterns of network degeneration. *JAMA Neurol* Epub 2016 Jul 18.
9. Irish M, Piguet O, Hodges JR, Hornberger M. Common and unique gray matter correlates of episodic memory dysfunction in frontotemporal dementia and Alzheimer's disease. *Hum Brain Mapp* 2014;35:1422–1435.