Journal of the International Neuropsychological Society (2023), **29,** 670–676
doi:10.1017/S1355617722000704

Research Article

Utility of empathy informant report in FTD differential diagnosis

Carissa M. Lane[1,2], Mary Lee[1,3], Jacob Lowe[1,4], Corey Bolton[1,5] and Benjamin A. Pyykkonen[1]

[1]School of Psychology, Counseling and Family Therapy, Wheaton College, Wheaton, IL, USA, [2]Corporal Michael J. Crescenz VA Medical Center, Philadelphia, PA, USA, [3]University of Chicago Medical Center, Chicago, IL, USA, [4]Pine Rest Christian Mental Health Services, Grand Rapids, MI, USA and [5]Vanderbilt University Medical Center, Nashville, TN, USA

Abstract

Objective: Loss of empathy is a hallmark feature of behavioral variant frontotemporal dementia (bvFTD). Change in socioemotional functioning identified by others is often the primary initial presenting concern in this disorder, in contrast to more subtle early cognitive changes and limited patient insight. The present study examined the predictive utility of an empathy informant-report measure for discriminating clinician-diagnosed bvFTD from other dementia syndromes. **Method:** Data from the National Alzheimer's Coordinating Center (NACC) database were used to study individuals with bvFTD ($n = 406$) and other dementia syndromes ($n = 385$). Participants were administered neuropsychological measures and collateral informants completed an informant-report of empathy. **Results:** Informants reported that patients with bvFTD demonstrated significantly lower levels of empathic concern [$F(1, 789) = 120.91$, $p < .001$, $\eta^2 = 0.13$] and perspective taking [$F(1, 789) = 153.08$, $p < .001$, $\eta^2 = 0.16$] than patients with other dementia syndromes. These differences were not attributable to the level of global cognitive impairment. Empathy scores were not significantly associated with any neurocognitive measure when controlling for age. ROC curve analyses showed fair to good clinical utility of the informant-report empathy measure for distinguishing bvFTD from non-bvFTD, whereas a traditional measure of executive functioning failed to differentiate the groups. **Conclusions:** These findings indicate that informant ratings of empathy offer a unique source of clinical information that may be useful in detecting neurobehavioral changes specific to bvFTD before a clear neurocognitive pattern emerges on testing.

Keywords: frontotemporal; dementia; executive functioning; neurobehavioral; collateral informant; socioemotional; cognitive

(Received 2 May 2022; final revision 9 August 2022; accepted 24 August 2022; First Published online 26 September 2022)

Introduction

Frontotemporal lobar degeneration (FTLD) describes a heterogeneous group of neurodegenerative diseases that share a predominance of degeneration in the frontal and temporal lobes. Under the umbrella of FTLD are a number of neuropathologic subtypes, with the most common being FTLD-tau and FTLD-TDP (Cairnes et al., 2007; Mackenzie et al., 2010). Clinically, FTLD comprises distinct syndromes, one of which has been referred to as FTD. The FTD clinical syndrome is itself heterogenous, being composed of various distinct subtypes including behavioral variant FTD (bvFTD), motor neuron disease (FTD-MND), and the semantic and non-fluent variants of primary progressive aphasia (SV-PPA, NFV-PPA; Bang et al., 2015).

Most common among the FTD subtypes is bvFTD, a clinical syndrome marked by progressive deterioration of social comportment and executive functions. Behavioral symptoms supportive of a diagnosis of bvFTD include behavioral disinhibition, apathy or inertia, loss of empathy, perseverative or stereotyped behaviors, hyperorality, and dietary changes (Rascovsky et al., 2011). From a neuropsychological standpoint, diagnostic criteria of bvFTD specify evidence of executive/generation deficits with relative sparing of memory and visuospatial functions. Further diagnostic clarity may be reached with neuroimaging evidence of frontal and anterior temporal atrophy or hypometabolism/hypoperfusion, while a definitive diagnosis can be made only with evidence of a pathogenic mutation or histopathological features at autopsy.

Due to the heterogeneity of neuropathology in bvFTD, finding a targeted treatment is a monumental challenge, and recent work has therefore sought to identify clinical features of bvFTD that may differentiate underlying pathology. A study by Perry et al. (2017) found that early loss of empathy was found to be far more frequent in those with Pick's disease, TDP type C, and FTLD due to fused in sarcoma pathology (FTLD-FUS) compared to CBD or PSP tauopathies. The specific pattern of neurodegeneration was thought to be driving these distinctions, as Pick's disease, FTLD-FUS, and TDP-C are all typically associated with more anterior temporal involvement as opposed to the dorsal-frontal pattern of CBD and PSP (Perry et al., 2017). Other studies have found that the right anterior temporal lobe in particular is critical for empathic behavior (Rankin et al., 2006).

While loss of empathy has been shown to be a useful marker for distinguishing between distinct subtypes of FTLD neuropathology, it may also be effective for distinguishing between bvFTD and other neurodegenerative disorders. This kind of marker could be particularly helpful because bvFTD can be difficult to discriminate

Corresponding author: Carissa M. Lane, email: carissa.lane@va.gov
Cite this article: Lane C.M., Lee M., Lowe J., Bolton C., & Pyykkonen B.A. (2023) Utility of empathy informant report in FTD differential diagnosis. *Journal of the International Neuropsychological Society*, **29:** 670–676, https://doi.org/10.1017/S1355617722000704

Table 1. Sample characteristics and IRI scores by diagnostic group

	n	Age***	Sex (M/F)*	Education (years)	IRI-PT***	IRI-EC***
bvFTD	406	62.63 (*8.39*)	247/159	15.62 (2.74)	13.75 (*5.34*)	20.08 (*6.82*)
Non-bvFTD	385	65.83 (*8.13*)	203/182	15.57 (*2.67*)	19.06 (*6.68*)	25.26 (*6.41*)
nfvPPA	68	66.56 (*8.50*)	31/37	15.28 (*2.38*)	21.19 (*6.88*)	26.12 (*5.67*)
svPPA	61	64.97 (*7.31*)	35/26	15.95 (*3.02*)	16.80 (*6.86*)	23.95 (*6.90*)
lvPPA	54	65.70 (*7.84*)	23/31	15.90 (*2.73*)	19.57 (*6.08*)	26.72 (*5.48*)
PPA NOS	17	66.29 (*10.25*)	7/10	14.47 (*2.70*)	17.88 (*4.15*)	23.88 (*7.22*)
FTLD-MND	4	62.50 (*22.31*)	2/2	15.00 (*2.58*)	15.75 (*9.47*)	24.00 (*6.98*)
FTLD-NOS	8	68.38 (*8.48*)	5/3	16.57 (*2.99*)	17.50 (*3.85*)	23.13 (*6.88*)
AD	58	64.84 (*8.52*)	34/24	15.28 (*2.56*)	19.19 (*7.08*)	25.86 (*6.81*)
PCA	13	60.92 (*3.86*)	6/7	14.69 (*1.97*)	22.15 (*5.06*)	29.23 (*4.51*)
PSP	44	68.77 (*7.29*)	23/21	15.73 (*2.56*)	19.70 (*6.23*)	24.48 (*6.13*)
DLB	15	65.27 (*5.11*)	14/1	16.27 (*2.89*)	18.27 (*7.89*)	25.20 (*5.60*)
CBD	32	66.97 (*7.46*)	16/16	16.03 (*2.69*)	18.88 (*7.05*)	24.13 (*7.03*)
Unknown/Other	11	62.18 (*7.49*)	7/4	14.70 (*2.50*)	14.64 (*4.59*)	22.91 (*8.20*)

Note. IRI, interpersonal reactivity index; PT, perspective taking; EC, emotional control; bvFTD, behavioral-variant frontotemporal dementia (Rascovsky et al., 2011); PPA, primary progressive aphasia (Gorno-Tempini et al., 2011); nfvPPA, nonfluent/agrammatic variant PPA; svPPA, semantic variant PPA; lvPPA, logopenic variant PPA; NOS, not otherwise specified; FTLD-MND, frontotemporal lobar degeneration with motor neuron disease (Brooks et al., 2000); AD, Alzheimer's disease (McKhann et al., 2011); PCA, posterior cortical atrophy (Crutch et al., 2013); PSP, Progressive Supranuclear Palsy (Bensimon et al., 2009); DLB, dementia with Lewy bodies (Litvan et al., 2003 and McKeith et al., 2017); CBD, corticobasal degeneration (Armstrong et al., 2013). Data are complete for all variables except for education, where bvFTD $n = 398$ and non-bvFTD $n = 371$. Data presented in Mean (*SD*) format where relevant. Primary groups are significantly different at $^{*}p < .05$, $^{***}p < .001$.

neuropsychologically, especially early in the disease course. Desmarais et al. (2018) found that socially inappropriate behaviors, including loss of empathy, were present in bvFTD and AD but absent in idiopathic Parkinson's disease and Lewy body dementia. Although AD patients may experience loss of cognitive empathy due to general cognitive decline, bvFTD patients experience loss of empathy as a primary feature, typically before other cognitive domains are affected (Dermody et al., 2016). In fact, a recent meta-analysis emphasized the importance of loss of empathy as a core feature of bvFTD and highlighted the paucity of studies that assess affective empathy (Carr & Mendez, 2018).

Therefore, the present study seeks to determine the utility of an informant-report measure of empathy in the diagnosis of bvFTD in comparison to commonly used measures of executive functioning using data from the National Alzheimer's Coordinating Center (NACC) database. Because bvFTD patients underreport empathy-related behavioral changes in comparison to caregiver observations (Eslinger et al., 2011), and informants may be most likely to observe lack of empathy in everyday contexts, we utilize a standardized informant-report measure to assess empathy. First, we examined differences in empathy between individuals with bvFTD and those with non-bvFTD dementia syndromes. Next, because studies using smaller samples suggested that certain aspects of neurocognitive functioning, including verbal fluency and mental flexibility, contribute to empathy capacity (Eslinger, 1998; Rankin et al., 2005), we examined associations between empathy and executive functions. Finally, we tested whether empathy distinguished between bvFTD and non-bvFTD better than a traditional measure of executive functioning.

Methods

The Alzheimer's Disease Center (ADC) program was created by the US National Institute on Aging to support large-scale research on Alzheimer's disease and related disorders, resulting in the National Alzheimer's Coordinating Center (NACC) database. ADCs located across the United States began collecting prospective and standardized longitudinal data in September 2005, compiled in the Uniform Data Set (UDS). An additional module, the NACC FTLD Behavior & Language Domains (NACC FTLD), was added in 2012 to collect clinical information specifically related to FTLD. Previous publications describe NACC data in detail (Beekly et al., 2007; Besser et al., 2018). As determined by the University of Washington Human Subjects Division, the NACC database itself is exempt from IRB review and approval because it does not involve human subjects, as defined by federal and state regulations. However, all contributing ADCs are required to obtain informed consent from their participants in accordance with the Helsinki Declaration and to maintain their own separate IRB review and approval from their institution prior to submitting data to NACC. Authors were granted access to a limited data set for use in this study by NACC (Proposal ID 1232).

Participants

The current clinical case series includes data from 791 UDS participants who completed UDS visits with an FTLD module between February 2012 and March 2019 at 25 ADCs. The sample was nearly evenly split by sex (56.9% male), and most had completed post-secondary education. A majority of participants identified as White (93.7%), followed by African American (2.7%), Asian (2.3%), and other/unknown (1.3%). The sample was separated into bvFTD ($n = 406$) and non-bvFTD ($n = 385$) based on clinical diagnosis, most often reached by consensus conference, according to formal criteria (i.e., Rascovsky et al., 2011 international consensus criteria for bvFTD). The non-bvFTD group was primarily composed of patients diagnosed with other forms of FTD ($n = 212$) but also included primary clinician diagnoses of Alzheimer's disease ($n = 58$), progressive supranuclear palsy ($n = 44$), corticobasal degeneration ($n = 32$), dementia with Lewy bodies ($n = 15$), posterior cortical atrophy ($n = 13$), and other/unspecified ($n = 11$). Descriptive characteristics of participants by group and corresponding references for diagnostic guidelines are provided in Table 1. Inclusion criteria required a diagnosis of dementia and the completion of all items on an empathy informant-report scale.

Procedures

Upon initial UDS visit, demographic, clinical, and neuropsychological data were collected using standardized UDS and NACC

https://doi.org/10.1017/S1355617722000704 Published online by Cambridge University Press

FTLD module protocols. Each participant was paired with a co-participant who knows them well (e.g., family member, caregiver, etc.) to complete informant-report measures. Only data from initial patient visits are included in the current study to minimize the impact of advanced disease state. For some participants, cognitive data were partially missing because a test was not administered or the patient was unable to provide a response because of a physical, cognitive, or behavioral problem.

In 2015, Version 2 of the standardized UDS neuropsychological battery was partially updated to include equivalent nonproprietary tests in Version 3 (Weintraub et al., 2018). Thus, participants assessed using UDS Version 3 were assessed with different, but similar, measures in some cognitive domains from those enrolled in the study prior to 2015. All updated measures showed strong correlations with corresponding tests in the previous version (Monsell et al., 2016). Raw score equivalents established by the Crosswalk study (Monsell et al., 2016) were used to equate like measures when relevant.

Measures

Empathy

The Interpersonal Reactivity Index (IRI) is an informant-report measure of the cognitive and emotional components of dispositional empathy (Davis, 1980, 1983). A 14-item, 5-point Likert scale short form with two main subscales was used. The Empathic Concern scale (IRI-EC), representing the original Emotional Empathy scale, is intended to capture reciprocal other-centered emotional responding. The Perspective Taking scale (IRI-PT), representing the original Cognitive Empathy scale, measures the tendency for spontaneously imagining others' cognitive perspective. Raw scores for each scale range from 7 to 35, with higher scores interpreted as reflecting a greater degree of empathy.

Cognition

Global cognitive functioning was assessed using the Montreal Cognitive Assessment (Nasreddine et al., 2005; UDS-V3) or the Mini-Mental State Exam (Folstein et al., 1975; UDS-V2). Naming ability was measured using a 30-item version of the Boston Naming Test (Kaplan et al., 1983; UDS-V2) or the Multilingual Naming Test (Ivanova et al., 2013; UDS-V3). Letter and semantic fluency were assessed with the total number of words that begin with the letter F and total number of animals generated in one minute, respectively (Weintraub et al., 2009). Visuomotor speed was measured with a version of Trail Making Test-Part A (TMT-A) that was customized for the UDS protocol (Weintraub et al., 2009). A version of Trail Making Test-Part B (TMT-B), also customized for the UDS protocol, was used to assess set-shifting skills and divided attention (Weintraub et al., 2009). Working memory was measured by the digit span backward length score from the Wechsler Memory Scale-Revised (Wechsler, 1987) or the Number Span Test (norms not yet published).

Analyses

SPSS version 25.0 was used for all statistical analyses. Chi-square and t-tests were used to examine group differences in demographic variables. Kolmogorov-Smirnov and Shapiro-Wilk tests were used to determine normality of data from the IRI and cognitive tests, and based on findings, nonparametric tests were used for group comparisons. Mann-Whitney U tests with Bonferroni correction for multiple comparisons were conducted to determine differences between bvFTD and non-bvFTD groups on the IRI-PT and IRI-EC empathy subscales, as well as for each cognitive measure. Additional analyses were conducted to determine difference on the same measures between the bvFTD group and subsets of the non-bvFTD group. Partial correlations controlling for age were used to examine associations between empathy subscales and selected neuropsychological measures. Area under receiver operating characteristic (ROC) curves were generated to examine the ability of the IRI subscales and a commonly used executive functioning measure (Trails B) to differentiate participants with bvFTD from the non-bvFTD group and two subgroups (AD and svPPA).

Table 2. Cognitive test scores by diagnostic group

	bvFTD ($n = 406$)			Non-bvFTD ($n = 385$)		
	n	Mean	*SD*	*n*	Mean	*SD*
Global Cognition**	385	23.06	5.77	356	21.66	6.57
Naming	376	20.34	8.52	343	19.48	9.20
Phonemic Fluency	227	6.99	4.88	211	7.02	4.29
Semantic Fluency	376	10.41	6.76	346	9.69	5.49
Trails A (seconds)***	351	58.35	33.28	326	71.19	42.02
Trails B (seconds)	267	167.36	92.45	248	188.65	91.58
Longest Digit Backward	378	3.40	1.63	352	3.18	1.54

Note. bvFTD, behavioral-variant frontotemporal dementia. Groups differences are significant at $^{**}p < .006$, $^{***}p < .001$.

Results

Participants in the bvFTD group were significantly younger than those in the non-bvFTD group, and the bvFTD group had a greater proportion of males than the non-bvFTD group. No statistically significant differences between groups were found for race or education (see Table 1).

Mann-Whitney U tests with Bonferroni correction ($\alpha = 0.0055$) showed that empathic concern [$U(N_{bvFTD} = 406, N_{non\text{-}bvFTD} = 385) = 45{,}437.50$, $z = -10.20$, $p < .001$, $r = -0.36$] and perspective taking [$U(N_{bvFTD} = 406, N_{non\text{-}bvFTD} = 385) = 41{,}604.00$, $z = -11.40$, $p < .001$, $r = -0.41$] scores were significantly lower for the bvFTD group ($Mdn_{IRI\text{-}EC} = 20$, $IQR = 10$ and $Mdn_{IRI\text{-}PT} = 13$, $IQR = 7$) than the non-bvFTD group ($Mdn_{IRI\text{-}EC} = 25$, $IQR = 10$ and $Mdn_{IRI\text{-}PT} = 19$, $IQR = 9$). Importantly, MMSE/MoCA scores were significantly better [$U(N_{bvFTD} = 385, N_{non\text{-}bvFTD} = 356) = 60{,}214.50$, $z = -2.86$, $p = .004$, $r = -0.11$] in the bvFTD group ($Mdn = 25$, $IQR = 8$) than in the non-bvFTD group ($Mdn = 23$, $IQR = 9$), suggesting that lower IRI scores in the bvFTD group are likely not attributable to lower global cognitive functioning (see Table 2). Review of cognitive test performances found only one additional significant difference between groups for Trails A scores [$U(N_{bvFTD} = 351, N_{non\text{-}bvFTD} = 326) = 48{,}010.00$, $z = -3.62$, $p < .001$, $r = -0.14$], with slower visuomotor speed demonstrated in the non-bvFTD group ($Mdn = 56$, $IQR = 196$) as compared to the bvFTD group ($Mdn = 49$, $IQR = 34$).

Further analyses were conducted to determine whether group differences on empathy and cognitive measures were present between the bvFTD group and subsets of the non-bvFTD group (AD and svPPA), which revealed similar findings to overall group analyses. Specifically, Mann-Whitney U tests with Bonferroni correction ($\alpha = 0.0055$) again showed that empathic concern [$U(N_{bvFTD} = 406, N_{AD} = 58) = 6494.50$, $z = -5.53$, $p < .001$, $r = -0.26$; $U(N_{bvFTD} = 406, N_{svPPA} = 61) = 8433.50$, $z = -4.02$, $p < .001$, $r = -0.19$], and perspective taking [$U(N_{bvFTD} = 406, N_{AD} = 58) = 6369.50$, $z = -5.67$, $p < .001$, $r = -0.26$; $U(N_{bvFTD} = 406, N_{svPPA} = 61) = 9119.00$, $z = -3.32$, $p < .001$, $r = -0.15$] scores were significantly lower for the bvFTD group compared to the AD group ($Mdn_{IRI\text{-}EC} = 27$,

https://doi.org/10.1017/S1355617722000704 Published online by Cambridge University Press

Table 3. Partial correlation matrix of bvFTD group IRI empathy subscales and cognitive scores, controlling for age

	IRI PT	IRI EC	Global cognition	Naming	Letter fluency	Category fluency	Trails A seconds	Trails B seconds	Digits backward
IRI-PT	–								
IRI-EC	0.56***	–							
Global cognition	0.05	0.02	–						
Naming	0.05	−0.12	0.64***	–					
Letter fluency	0.01	−0.04	0.46***	0.35***	–				
Category fluency	−0.03	−0.14	0.59***	0.53***	0.74***	–			
Trails A seconds	0.15	0.1	−0.33***	−0.06	−0.41***	−0.37***	–		
Trails B seconds	0.03	0.09	−0.40***	−0.06	−0.47***	−0.43***	0.60***	–	
Digits backward	0.02	−0.05	0.32***	0.09	0.48***	0.40***	−0.40***	−0.52***	–

Note. IRI, interpersonal reactivity index; PT, perspective taking; EC, emotional control; bvFTD, behavioral-variant frontotemporal dementia. ***$p < .001$.

Table 4. Partial correlation matrix of non-bvFTD group IRI empathy subscales and cognitive scores, controlling for age

	IRI PT	IRI EC	Global cognition	Naming	Letter fluency	Category fluency	Trails A seconds	Trails B seconds	Digits backward
IRI-PT	–								
IRI-EC	0.68***	–							
Global cognition	0.02	0.06	–						
Naming	0.17	0.02	0.54***	–					
Letter fluency	−0.06	0.08	0.27**	0.05	–				
Category fluency	0.15	0.14	0.56***	0.56***	0.41***	–			
Trails A seconds	0.13	0	0.01	0.26**	−0.28**	−0.15	–		
Trails B seconds	0.17	0.05	−0.31**	0.21*	−0.35***	−0.22*	0.70***	–	
Digits backward	−0.08	0.09	0.27**	−0.12	0.46***	0.26**	−0.46***	−0.58***	–

Note. IRI, interpersonal reactivity index; PT, perspective taking; EC, emotional control; bvFTD, behavioral-variant frontotemporal dementia. *$p < .05$, **$p < .01$, ***$p < .001$.

$IQR = 11$ and $Mdn_{\text{IRI-PT}} = 18$, $IQR = 27$) and the svPPA group ($Mdn_{\text{IRI-EC}} = 24$, $IQR = 9$ and $Mdn_{\text{IRI-PT}} = 16$, $IQR = 10$). Global cognition was significantly lower [$U(N_{\text{bvFTD}} = 385, N_{\text{AD}} = 55) = 7946.50$, $z = -3.00$, $p = .003$, $r = -0.14$] in the AD group ($Mdn = 22$, $IQR = 8$) than in the bvFTD group and did not significantly differ between the svPPA and bvFTD groups. Further, a significant difference [$U(N_{\text{bvFTD}} = 267, N_{\text{AD}} = 36) = 3407.00$, $z = -2.86$, $p = .004$, $r = -0.16$] in visuomotor set-shifting scores on Trails B was found between the bvFTD group ($Mdn = 134$, $IQR = 273$) and the AD group ($Mdn = 239$, $IQR = 227$), with greater impairment demonstrated in the latter group. In the svPPA subgroup analyses, significant differences were also found for naming scores [$U(N_{\text{bvFTD}} = 376, N_{\text{svPPA}} = 48) = 2850.50$, $z = -7.73$, $p < .001$, $r = -0.38$] and longest digit span backward [$U(N_{\text{bvFTD}} = 378, N_{\text{svPPA}} = 57) = 8090.00$, $z = -3.10$, $p < .002$, $r = -0.15$], with comparatively superior naming skills in the bvFTD group ($Mdn_{\text{bvFTD}} = 24$, $IQR = 30$ and $Mdn_{\text{svPPA}} = 6$, $IQR = 27$) and longer digit span backward length in the svPPA group ($Mdn_{\text{bvFTD}} = 3$, $IQR = 1$ and $Mdn_{\text{svPPA}} = 4$, $IQR = 2$). No other significant differences were found on cognitive tests when comparing the bvFTD group with AD or svPPA subgroups.

Partial correlations examining whether a portion of the variance in empathy could be accounted for by cognitive performance did not yield significant associations of IRI scores with any neuropsychological measure in either group, contrary to expectations (see Tables 3 and 4). Most neuropsychological measures were moderately intercorrelated for the bvFTD and non-bvFTD groups.

Figure 1 shows ROC curves depicting the ability of the IRI subscales to differentiate the bvFTD group from the non-bvFTD group, as compared to the predictive value of a classical measure of executive functioning. When examining the two main groups, the IRI-PT scale showed the greatest clinical utility, with fair to good diagnostic accuracy for classifying bvFTD versus non-bvFTD participants (areas under the curve (AUC) = 0.76; SE = 0.02; 95% CI = 0.71, 0.80; $p < .05$). A cutoff score of less than or equal to 16.5 on the IRI-PT short-form scale produced a sensitivity of 75% and specificity of 64%. Similarly, the IRI-EC scale showed fair diagnostic accuracy in differentiating groups (AUC = 0.73; SE = 0.02; 95% CI = 0.68, 0.77; $p < .05$). A cutoff score of less than or equal to 23.5 on the IRI-EC short-form scale produced a sensitivity of 72% and a specificity of 63%. In contrast, Trails B failed to demonstrate clinical utility in differentiating groups, with diagnostic accuracy reaching poor levels at best at the upper end of the confidence interval (AUC = 0.57; SE = 0.03; 95% CI = 0.52, 0.62; $p < .05$).

Subgroup ROC curve analyses comparing classification of bvFTD and AD participants again found fair to good diagnostic accuracy of the IRI-PT scale (AUC = 0.76; SE = 0.04; 95% CI = 0.68, 0.84; $p < .001$) and the IRI-EC scale (AUC = 0.73; SE = 0.05; 95% CI = 0.64, 0.82; $p < .001$), with poor diagnostic accuracy of Trails B (AUC = 0.64; SE = 0.05; 95% CI = 0.56, 0.73; $p = .005$). Optimal cutoff scores were again identified as 16.5 on the IRI-PT scale (sensitivity = 75%, specificity = 61%) and 23.5 on the IRI-EC scale (sensitivity = 72%, specificity = 63%). When comparing classifications of the bvFTD and svPPA participants, a similar but less robust pattern of fair diagnostic utility was found for the IRI-PT (AUC = 0.66; SE = 0.04; 95% CI = 0.58, 0.73; $p < .001$) and the IRI-EC (AUC = 0.68; SE = 0.04; 95% CI = 0.60, 0.76; $p < .001$); Trails B again failed to demonstrate clinical utility in differentiating groups (AUC = 0.38; SE = 0.04; 95% CI = 0.30, 0.46; $p = .006$). Cutoff scores were identified as 14.5 on the IRI-PT (sensitivity = 64%, specificity = 64%) and 22.5 on the IRI-EC (sensitivity = 66%, specificity = 64%).

Discussion

The results of the current study indicate that informant-reported cognitive and emotional empathy was significantly lower in the bvFTD group than the non-bvFTD group. This finding is consistent with existing literature and the primary diagnostic features of

https://doi.org/10.1017/S1355617722000704 Published online by Cambridge University Press

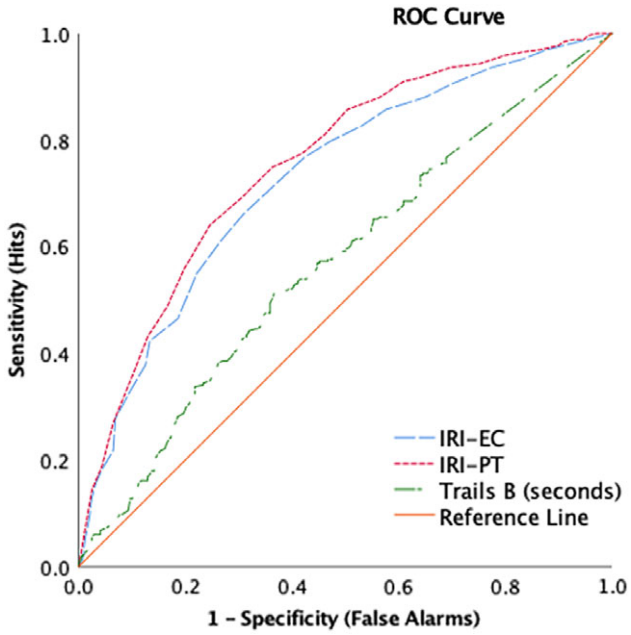

Figure 1. Receiver operating characteristic (ROC) curves comparing sensitivity and specificity of the Interpersonal reactivity index (IRI) emotional control (EC) and perspective taking (PT) scales with that of Trails B performance in seconds for the purpose of differentiating the bvFTD group ($n = 267$) from the non-bvFTD group ($n = 248$). Cases with missing Trails B data were excluded.

bvFTD (i.e., changes in social and emotional functioning), as opposed to the primary diagnostic features of primary progressive aphasias (i.e., language deficits) or FTD with motor neuron disease (i.e., motor decline). These findings remained true in subgroup comparisons of AD and svPPA, selected because of a greater likelihood of behavioral disturbance in these syndromes compared to other subgroups. Importantly, the non-bvFTD group demonstrated significantly worse performances on measures of global cognitive functioning and visuomotor processing speed than the bvFTD group, indicating that the lower ratings on measures of informant-reported empathy in the bvFTD group cannot be explained by lower overall cognitive functioning. Similarly, the AD group demonstrated lower global cognitive functioning and visuomotor set-shifting than the bvFTD group; the svPPA group showed no difference in global cognition but worse naming skills and longer digit span backward performances than the bvFTD group, which again are consistent with expectations and would not account for difference in empathy findings. Further, the IRI scales showed significantly better clinical utility in differentiating groups than a commonly used measure of executive functioning, the Trailmaking Test, Part B on all group and subgroup comparisons. The current investigation highlights the potential importance of including social-emotional symptoms of bvFTD as a significant element in neuropsychological evaluations for which a progressive dementia is in the differential diagnosis, as neuropsychological evaluations often under-emphasize these areas of functioning. While many neuropsychologists may ask about changes in social and emotional functioning during the neurobehavioral interview, typically little objective data are gathered via performance-based neuropsychological tests or informant- or self-report measures in these domains.

No associations were found between measures of neurocognitive functioning and informant-reported empathy, indicating that neuropsychological measures of language and executive functioning that tend to target higher-level cognitive processes may not adequately capture the skills necessary for perspective taking and inference of emotional state. Thus, the executive functioning measures may have targeted the functional capacity of certain regions of the prefrontal cortex (i.e., the dorsolateral prefrontal cortex) but did not identify deficits in social and emotional functioning that have been linked to degeneration in the orbitofrontal cortex (Beer et al., 2006). However, this finding contrasts with that of Rankin et al. (2005), who also evaluated neurocognitive correlates of the IRI in patients with various dementias, including bvFTD. Their study reported significant correlations between cognitive and emotional aspects of empathy and measures of nonverbal generation, letter and semantic fluency, and abstract reasoning, with nearly a third of variance on the Perspective Taking scale attributable to semantic fluency performance. These disparate findings are unlikely to be attributable to sample characteristics such as age, education, or global cognition, which appear to be similar across samples. Factors that may explain this discrepancy include the substantially larger sample size in the current study and inclusion of non-bvFTD participants in correlational analyses in the Rankin et al. (2005) study.

Executive functioning is a complex construct, and the ecological validity of executive functioning measures is variable, making it difficult to measure comprehensively and coherently (Burgess et al., 1998; Odhuba et al., 2005). More specifically, many neuropsychological measures of executive functioning target higher order reasoning abilities that heavily implicate the dorsolateral prefrontal cortex (Possin et al., 2014). However, these tests are less effective at measuring subtle changes in personality and social behavior caused by damage to the orbitofrontal cortex or deficits in drive and motivation caused by damage to the cingulate cortex. This is problematic for the diagnosis of bvFTD, as degeneration tends to begin in the anterior cingulate cortex and lateral orbitofrontal cortex (Ravdin & Katzen, 2013; Seeley et al., 2008). Thus, family and friends may notice differences in the way that patients function interpersonally before neuropsychological test data identify a clear pattern of cognitive deficits typically associated with frontal and temporal lobe functions, especially early in the disease process. This may be especially true for individuals with a high cognitive reserve, relevant to the current study given the high educational attainment in this sample (Placek et al., 2016; Maiovis et al., 2018). Perspective-taking and empathic concern represent unique aspects of empathy, yet we found similar results in these two scales in this study. While cognitive aspects of empathy, such as perspective taking, may be impaired in other neurodegenerative etiologies such as Alzheimer's disease, this is most likely due to widespread atrophy and global cognitive decline (Dermody et al., 2016). In bvFTD, early neurodegeneration is selective for fronto-insular and temporal networks that are critical for social cognition (Dermody et al., 2016), thus likely to impact both dissociable aspects of empathy.

The current study was limited by the lack of a control group with no diagnosis and participants with dementias outside of the FTD syndromes. Further, though attempts were made to minimize the impact of advanced disease duration on these findings by comparing global cognition between groups and limiting data to that collected during the initial UDS visit, participants were permitted to enroll at any stage of cognitive impairment and this study did not directly control for disease duration. Additionally, the high education level of our sample may limit generalizability to patients with lower educational attainment, as the presence of increased cognitive reserve could have buffered the association between neurocognitive performance and empathy ratings. The neurocognitive

https://doi.org/10.1017/S1355617722000704 Published online by Cambridge University Press

measures available in the data set were restricted by nature of the UDS and FTLD module protocols, which limited the ability of constructs to be optimally represented in this study's analyses. For example, a wider range of executive tests that are less impacted by other domains (e.g., impact of motor speed on TMT-B), such as measures of abstraction and mental set-shifting, may be more useful in distinguishing bvFTD from other dementia presentations; additionally, scores on a word reading test would have been preferable to years of education in efforts to accurately control for premorbid ability, but such data was unavailable. Finally, while it is possible that informant ratings on the IRI implicitly factored into the overall conceptualization of the patient presentation, clinician diagnoses were ultimately based on formal diagnostic criteria; thus, we believe that these results provide valuable information about effective means of quantifying loss of empathy and its usefulness in diagnosing a condition that is often misdiagnosed. Future research should examine the neuroanatomical correlates of neurocognitive measures (particularly executive functioning), their ecological validity, and their sensitivity in identifying underlying neuropathology, especially as it relates to social cognition. Of particular interest might be performance-based measures that assess empathy or similar constructs more objectively for use in FTD evaluations (e.g., affect recognition tasks, social problem-solving tasks), as recent literature suggests a scarcity of such measures specifically validated for neurocognitive disorders (Wright et al., 2021). Furthermore, a multimodal approach to assessing empathy that includes performance-based measures, informant-report, and self-report, as opposed to any singular method in isolation, is recommended as best practice (Wright et al., 2021).

Overall, results indicate that informant ratings of empathy offer a unique source of clinical information that could have utility in detecting neurobehavioral changes specific to bvFTD before a clear neurocognitive pattern emerges on testing. In particular, these findings support the usefulness of obtaining information about changes in empathy using a readily available and standardized method that takes little time to administer. Given lack of convergence of performance on traditional neurocognitive measures with early neurobehavioral changes in bvFTD, it could prove beneficial to use informant-report measures of empathy in evaluations for which this disorder is included in the differential diagnosis.

Conflicts of Interest. None.

Funding Statement. The NACC database is funded by NIA/NIH Grant U24 AG072122. NACC data are contributed by the NIA-funded ADCs: P50 AG005131 (PI James Brewer, MD, PhD), P50 AG005133 (PI Oscar Lopez, MD), P50 AG005134 (PI Bradley Hyman, MD, PhD), P50 AG005136 (PI Thomas Grabowski, MD), P50 AG005138 (PI Mary Sano, PhD), P50 AG005142 (PI Helena Chui, MD), P50 AG005146 (PI Marilyn Albert, PhD), P50 AG005681 (PI John Morris, MD), P30 AG008017 (PI Jeffrey Kaye, MD), P30 AG008051 (PI Thomas Wisniewski, MD), P50 AG008702 (PI Scott Small, MD), P30 AG010124 (PI John Trojanowski, MD, PhD), P30 AG010129 (PI Charles DeCarli, MD), P30 AG010133 (PI Andrew Saykin, PsyD), P30 AG010161 (PI David Bennett, MD), P30 AG012300 (PI Roger Rosenberg, MD), P30 AG013846 (PI Neil Kowall, MD), P30 AG013854 (PI Robert Vassar, PhD), P50 AG016573 (PI Frank LaFerla, PhD), P50 AG016574 (PI Ronald Petersen, MD, PhD), P30 AG019610 (PI Eric Reiman, MD), P50 AG023501 (PI Bruce Miller, MD), P50 AG025688 (PI Allan Levey, MD, PhD), P30 AG028383 (PI Linda Van Eldik, PhD), P50 AG033514 (PI Sanjay Asthana, MD, FRCP), P30 AG035982 (PI Russell Swerdlow, MD), P50 AG047266 (PI Todd Golde, MD, PhD), P50 AG047270 (PI Stephen Strittmatter, MD, PhD), P50 AG047366 (PI Victor Henderson, MD, MS), P30 AG049638 (PI Suzanne Craft, PhD), P30 AG053760 (PI Henry Paulson, MD, PhD), P30 AG066546 (PI Sudha Seshadri, MD), P20 AG068024 (PI Erik Roberson, MD, PhD), P20 AG068053 (PI Marwan Sabbagh, MD), P20 AG068077 (PI Gary Rosenberg, MD), P20 AG068082 (PI Angela Jefferson, PhD), P30 AG072958 (PI Heather Whitson, MD), P30 AG072959 (PI James Leverenz, MD).

References

Armstrong, M. J., Litvan, I., Lang, A. E., Bak, T. H., Bhatia, K. P., Borroni, B., Boxer, A. L., Dickson, D. W., Grossman, M., Hallett, M., Josephs, K. A., Kertesz, A., Lee, S. E., Miller, B. L., Reich, S. G., Riley, D. E., Tolosa, E., Troster, A. I., Vidailhet, M., & Weiner, W. J. (2013). Criteria for the diagnosis of corticobasal degeneration. *Neurology*, *80*(5), 496–503.

Bang, J., Spina, S., & Miller, B. L. (2015). Non-Alzheimer's dementia. *Lancet (London, England)*, *386*(10004), 1672–1682.

Beekly, D. L., Ramos, E. M., Lee, W. W., Deitrich, W. D., Jacka, M. E., Wu, J., Kukull, W. A., & NIA Alzheimer's Disease Centers (2007). The National Alzheimer's Coordinating Center (NACC) database: The Uniform Data Set. *Alzheimer Disease and Associated Disorders*, *21*(3), 249–258.

Beer, J. S., John, O. P., Scabini, D., & Knight, R. T. (2006). Orbitofrontal Cortex and social behavior: Integrating self-monitoring and emotion-cognition interactions. *Journal of Cognitive Neuroscience*, *18*(6), 871–879.

Bensimon, G., Ludolph, A., Agid, Y., Vidailhet, M., Payan, C., Leigh, P. N., & NNIPPS Study Group (2009). Riluzole treatment, survival and diagnostic criteria in Parkinson plus disorders: The NNIPPS study. *Brain: A Journal of Neurology*, *132*(1), 156–171.

Besser, L., Kukull, W., Knopman, D. S., Chui, H., Galasko, D., Weintraub, S., Jicha, G., Carlsson, C., Burns, J., Quinn, J., Sweet, R. A., Rascovsky, K., Teylan, M., Beekly, D., Thomas, G., Bollenbeck, M., Monsell, S., Mock, C., Zhou, X. H., ... Morris, J. C. (2018). Version 3 of the National Alzheimer's Coordinating Center's Uniform Data Set. *Alzheimer Disease and Associated Ddisorders*, *3*(4), 351–358.

Brooks, B. R., Miller, R. G., Swash, M., Munsat, T. L., & World Federation of Neurology Research Group on Motor Neuron Diseases (2000). El Escorial revisited: Revised criteria for the diagnosis of amyotrophic lateral sclerosis. Amyotrophic lateral sclerosis and other motor neuron disorders: Official publication of the World Federation of Neurology. *Research Group on Motor Neuron Diseases*, *1*(5), 293–299.

Burgess, P., Alderman, N., Evans, J., Emslie, H., & Wilson, B. (1998). The ecological validity of tests of executive function. *Journal of the International Neuropsychological Society*, *4*(6), 547–558.

Cairns, N. J., Bigio, E. H., Mackenzie, I. R. A., Neumann, M., Lee, V. M.-Y., Hatanpaa, K. J., White, C. L. III, Schneider, J. A., Grinberg, L. T., Halliday, D., Duyckaerts, C., Lowes, J. S., Holm, I. E., Tolnay, M., Okamoto, K., Yokoo, H., Murayama, S., Woulfe, J., Munoz, D. G., ... Mann, D. M. A. (2007). Neuropathologic diagnostic and nosologic criteria for frontotemporal lobar degeneration: Consensus of the Consortium for Frontotemporal Lobar Degeneration. *Acta Neuropathologica*, *114*(1), 5–22.

Carr, A. R., & Mendez, M. F. (2018). Affective empathy in behavioral variant frontotemporal dementia: A meta-analysis. *Frontiers in Neurology*, *9*, 2456.

Crutch, S. J., Schott, J. M., Rabinovici, G. D., Boeve, B. F., Cappa, S. F., Dickerson, B. C., Dubois, B., Graff-Radford, N. R., Krolak-Salmon, P., Lehmann, M., Mendez, M. F., Pijnenburg, Y., Ryan, N. S., Scheltens, P., Shakespeare, T., Tang-Wai, D. F., Filer, W. M., Bain, L., Carrillo, M. C., & Fox, N. C. (2013). Shining a light on posterior cortical atrophy. *Alzheimer's & Dementia*, *9*(4), 463–465.

Davis, M. H. (1980). A multidimensional approach to individual differences in empathy. *JSAS Catalog of Selected Documents in Psychology*, *10*, 85.

Davis, M. H. (1983). Measuring individual differences in empathy: Evidence for a multidimensional approach. *Journal of Personality and Social Psychology*, *44*(1), 113–126.

Dermody, N., Wong, S., Ahmed, R., Piguet, O., Hodges, J. R., & Irish, M. (2016). Uncovering the neural bases of cognitive and affective empathy deficits in Alzheimer's disease and the behavioral-variant of frontotemporal dementia. *Journal of Alzheimer's Disease: JAD*, *53*(3), 801–816.

Desmarais, P., Lanctôt, K. L., Masellis, M., Black, S. E., & Herrmann, N. (2018). Social inappropriateness in neurodegenerative disorders. *International Psychogeriatrics*, *30*(2), 197–207.

https://doi.org/10.1017/S1355617722000704 Published online by Cambridge University Press

Eslinger, P. J. (1998). Neurological and neuropsychological bases of empathy. *European Neurology*, *39*(4), 193–199.

Eslinger, P. J., Moore, P., Anderson, C., & Grossman, M. (2011). Social cognition, executive functioning, and neuroimaging correlates of empathic deficits in frontotemporal dementia. *The Journal of Neuropsychiatry and Clinical Neurosciences*, *23*(1), 74–82.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, *12*(3), 189–198.

Gorno-Tempini, M. L., Hillis, A. E., Weintraub, S., Kertesz, A., Mendez, M., Cappa, S. F., Ogar, J. M., Rohrer, J., Black, S., Boeve, B. F., Manes, F., Dronkers, N. F., Vandenberghe, R., Rascovsky, K., Patterson, K., Miller, B., Knopman, D. S., Hodges, J. R., Mesulam, M. M., & Grossman, M. (2011). Classification of primary progressive aphasia and its variants. *Neurology*, *76*(11), 1006–1014.

Ivanova, I., Salmon, D. P., & Gollan, T. H. (2013). The multilingual naming test in Alzheimer's disease: Clues to the origin of naming impairments. *Journal of the International Neuropsychological Society: JINS*, *19*(3), 272–283.

Kaplan, E., Goodglass, H., Weintraub, S., & Goodglass, H. (1983). *Boston naming test*. Lea & Febiger.

Litvan, I., Bhatia, K. P., Burn, D. J., Goetz, C. G., Lang, A. E., McKeith, I., Quinn, N., Sethi, K. D., Shults, C., Wenning, G. K., & Movement Disorders Society Scientific Issues Committee (2003). Movement Disorders Society Scientific Issues Committee report: SIC Task Force appraisal of clinical diagnostic criteria for Parkinsonian disorders. *Movement Disorders: Official Journal of the Movement Disorder Society*, *18*(5), 467–486.

Mackenzie, I. R. A., Neumann, M., Bigio, E. H., Cairns, N. J., Alafuzoff, I., Kril, J., Kovacs, G. G., Ghetti, B., Halliday, G., Holm, I. E., Ince, P. G., Kamphorst, W., Revesz, T., Rozemuller, A. J. M., Kumar-Singh, S., Akiyama, H., Baborie, A., Spina, S., Dickson, D. W., … Mann, D. M. A. (2010). Nomenclature and nosology for neuropathologic subtypes of frontotemporal lobar degeneration: An update. *Acta Neuropathologica*, *119*(1), 1–4.

Maiovis, P., Ioannidis, P., Gerasimou, G., Gotzamani-Psarrakou, A., & Karacostas, D. (2018). Cognitive reserve hypothesis in frontotemporal dementia: Evidence from a brain spect study in a series of greek frontotemporal dementia patients. *Neuro-Degenerative Diseases*, *18*(2-3), 69–73.

McKhann, G. M., Knopman, D. S., Chertkow, H., Hyman, B. T., Jack, C. R. Jr, Kawas, C. H., Klunk, W. E., Koroshetz, W. J., Manly, J. J., Mayeux, R., Mohs, R. C., Morris, J. C., Rossor, M. N., Scheltens, P., Carrillo, M. C., Thies, B., Weintraub, S., & Phelps, C. H. (2011). The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*, *7*(3), 263–269.

McKeith, I. G., Boeve, B. F., Dickson, D. W., Halliday, G., Taylor, J. P., Weintraub, D., Aarsland, D., Galvin, J., Attems, J., Ballard, C. G., Bayston, A., Beach, T. G., Blanc, F., Bohnen, N., Bonanni, L., Bras, J., Brundin, P., Burn, D., Chen-Plotkin, A., … Kosaka, K. (2017). Diagnosis and management of dementia with Lewy bodies: Fourth consensus report of the DLB Consortium. *Neurology*, *89*(1), 88–100.

Monsell, S. E., Dodge, H. H., Zhou, X-H., Bu, Y., Besser, L. M., Mock, C., Hawes, S. E., Kukull, W. A., & Weintraub, S. (2016). Results from the NACC Uniform Data Set Neuropsychological Battery Crosswalk Study. *Alzheimer Disease & Associated Disorders*, *30*(2), 134–139.

Nasreddine Z. S., Phillips N. A., Bédirian V., Charbonneau S., Whitehead V., Collin I., Cummings J. L., & Chertkow H. (2005). The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society*, *53*(4), 695–699.

Odhuba, R., van den Broek, M., & Johns, L. (2005). Ecological validity of measures of executive functioning. *The British Journal of Clinical Psychology*, *44*(2), 269–278.

Perry, D. C., Brown, J. A., Possin, K. L., Datta, S., Trujillo, A., Radke, A., Karydas, A., Kornak, J., Sias, A. C., Rabinovici, G. D., Gorno-Tempini, M. L., Boxer, A. L., De May, M., Rankin, K., Sturm, V. E., Lee, S. E., Matthews, B. R., Kao, A. W., Vossel, K. A., … Seeley, W. W. (2017). Clinicopathological correlations in behavioural variant frontotemporal dementia. *Brain*, *140*(12), 3329–3345.

Placek, K., Massimo, L., Olm, C., Ternes, K., Firn, K., Van Deerlin, V., Lee, E. B., Trojanowski, J. Q., Lee, V. M.-Y., Irwin, D., Grossman, M., & McMillan, C. T. (2016). Cognitive reserve in frontotemporal degeneration: Neuroanatomic and neuropsychological evidence. *Neurology*, *87*(17), 1813–1819.

Possin, K. L., LaMarre, A. K., Wood, K. A., Mungas, D. M., & Kramer, J. H. (2014). Ecological validity and neuroanatomical correlates of the NIH EXAMINER executive composite score. *Journal of the International Neuropsychological Society : JINS*, *20*(1), 20–28.

Rankin, K. P., Kramer, J. H., & Miller, B. L. (2005). Patterns of cognitive and emotional empathy in frontotemporal lobar degeneration. *Cognitive and Behavioral Neurology*, *18*(1), 28–36.

Rankin, K. P., Gorno-Tempini, M. L., Allison, S. C., Stanley, C. M., Glenn, S., Weiner, M. W., & Miller, B. L. (2006). Structural anatomy of empathy in neurodegenerative disease. *Brain: A Journal of Neurology*, *129*(Pt 11), 2945–2956.

Rascovsky, K., Hodges, J. R., Knopman, D., Mendez, M. F., Kramer, J. H., Neuhaus, J., van Swieten, J. C., Seelaar, H., Dopper, E. G. P., Onyike, C. U., Hillis, A. E., Josephs, K. A., Boeve, B. F., Kertesz, A., Seeley, W. W., Rankin, K. P., Johnson, J. K., Gorno-Tempini, M.-L., Rosen, H., … Miller, B. L. (2011). Sensitivity of revised diagnostic criteria for the behavioural variant of frontotemporal dementia. *Brain*, *134*(9), 2456–2477.

Ravdin, L., & Katzen, H. (2013). *Handbook on the neuropsychology of aging and dementia (Clinical handbooks in neuropsychology)*. Springer.

Seeley, W. W., Crawford, R., Rascovsky, K., Kramer, J. H., Weiner, M., Miller, B. L., & Gorno Tempini, M. L. (2008). Frontal paralimbic network atrophy in very mild behavioral variant frontotemporal dementia. *Archives of Neurology*, *65*(2), 249–255.

Wechsler, D. (1987). *Manual for the Wechsler Memory Scale-Revised*. The Psychological Corporation.

Weintraub, S., Besser, L., Dodge, H. H., Teylan, M., Ferris, S., Goldstein, F. C., Giordani, B., Kramer, J., Loewenstein, D., Marson, D., Mungas, D., Salmon, D., Welsh-Bohmer, K., Zhou, X.-H., Shirk, S. D., Atri, A., Kukull, W. A., Phelps, C., & Morris, J. C. (2018). Version 3 of the Alzheimer Disease Centers' Neuropsychological Test Battery in the Uniform Data Set (UDS). *Alzheimer Disease and Associated Disorders*, *32*(1), 10–17.

Weintraub, S., Salmon, D., Mercaldo, N., Ferris, S., Graff-Radford, N. R., Chui, H., Cummings, J., DeCarli, C., Foster, N. L., Galasko, D., Peskind, E., Dietrich, W., Beekly, D. L., Kukull, W. A., & Morris, J. C. (2009). The Alzheimer's Disease Centers' Uniform Data Set (UDS). *Alzheimer Disease & Associated Disorders*, *23*(2), 11.

Wright, J. K. X., Grainger, S. A., Coundouris, S. P., & Henry, J. D. (2021). Affective empathy in neurodegenerative disorders: The importance of measurement type. *Neuroscience and Biobehavioral Reviews*, *127*(5), 808–819.

https://doi.org/10.1017/S1355617722000704 Published online by Cambridge University Press