



Clinical Postcard

“Everything hurts!” Distress in semantic variant primary progressive aphasia



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Semantic variant primary progressive aphasia (svPPA; or semantic dementia), is a language-predominant subtype of frontotemporal dementia (FTD) (Gorno-Tempini et al., 2011). Like behavioral variant FTD (bvFTD), svPPA is associated with behavioral changes (e.g., obsessions, compulsions) (O'Connor et al., 2016). However, a small number of studies have reported that there are more depressive symptoms (Bozeat, Gregory, Lambon Ralph, & Hodges, 2000), compulsions (Seeley et al., 2005) and exaggerated emotional displays (Snowden et al., 2001) in patients with svPPA compared to bvFTD. We suggest that emotional distress is an important aspect of the svPPA

neuropsychiatric profile, representing a mirror contrast to the emotional blunting observed in bvFTD. Here we evaluate these observations in 9 svPPA patients, with 10 bvFTD patients included as a contrast group. These patients represent a random sample for whom we have collected extensive research data, although we developed these observations from the clinical treatment of many more patients.

Repetitive behaviors are common in both bvFTD and svPPA (Seeley et al., 2005). However, we find that: 1) repetitive behaviors (“compulsions”) in svPPA are more often driven by repetitive thoughts (“obsessions”) than in bvFTD, and 2) these

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thoughts and behaviors are associated with greater dysphoria and distress in svPPA than bvFTD. We commonly observe dysphoric rumination in svPPA (Cases S2, S3, S5, S6), including obsessive focus on traumatic events (Case S1), as well as obsession-driven behaviors (6/9 svPPA; Table 1). For example Case S2 was obsessed with fears of contamination, covered his living room with paper towels, and became extremely upset if he was touched. By contrast, while patients with bvFTD frequently perform repetitive behaviors, they are not usually associated with dysphoric rumination and tend to be more stimulus-bound, or sometimes linked to specific delusions. For example, Case B4 would frequently pace, but the pacing was not linked to any obsessive thoughts or distress. Even when behaviors in bvFTD are linked to repetitive

thoughts (2/10 bvFTD; Table 1), they still tend not to be characterized by distress. Case B9 had a fixed delusion that a tree would fall on her bedroom, but if she slept somewhere other than her bedroom she was fine. Arguably, this delusional obsession should be associated with *more* distress than this bvFTD patient displayed; she was in fact “under concerned”.

Eating changes in svPPA patients may also be characterized by distress. While bvFTD is usually associated with hyperphagia and weight gain (Ahmed et al., 2016), we note that restricted eating and weight loss are more common in svPPA (8/9 svPPA, 0/10 bvFTD; Table 1). For example, Case S2 would only eat hamburgers, Case S5 would only eat plain yogurt and sweet potatoes, Case S3 asked every day for a Wendy’s \$5 meal, and all expressed intense dysphoria if forced to eat other foods.

Table 1 – Demographics and distress-related symptoms for svPPA (S) and bvFTD (B) patients.

	Age	Sex	CDR	Global Cognition (MMSE/30)	Obsessions/Repetitive Thoughts	Restrictive Eating	Somatic distress	Mood Lability	Suicidality
<i>svPPA Patients</i>									
Case S1	72	F	1	27	+	+	+	+	–
Case S2	63	M	1	29	+	+	+	+	+
Case S3	57	M	2	12	+	+	+	+	+
Case S4	56	F	1	14†	–	–	–	+	+
Case S5	54	F	1	30	+	+	+	+	+
Case S6	60	F	1	10†	+	+	+	+	+
Case S7	69	M	1	30	–	+	–	+	+
Case S8	63	F	nc	131‡	+	+	– ^a	–	–
Case S9	65	F	nc	117‡	–	+	–	–	+
<i>bvFTD Patients</i>									
Case B1	49	F	2	13	–	– ^b	–	–	–
Case B2	56	M	1	24	–	–	–	–	–
Case B3	65	F	1	27	–	– ^b	–	–	–
Case B4	49	F	2	18	–	– ^b	–	–	–
Case B5	51	F	2	23	+	– ^b	–	–	–
Case B6	71	F	1	24	–	–	–	–	– ^c
Case B7	54	F	1	29	–	– ^b	–	–	–
Case B8	68	M	1	22	–	– ^b	–	–	–
Case B9	59	F	1	25	+	– ^b	–	–	–
Case B10	61	M	1	28	–	–	–	–	–

Note. + = Yes, symptom present; – = No, symptom absent. CDR = Clinical Dementia Rating 0–3, 1:mild 2:moderate 3:severe (Hughes, Berg, Danziger, Coben, & Martin, 1982). nc = not completed. MMSE = Mini Mental State Exam. Global Cognition: † = Montreal Cognitive Assessment (MoCA)/30; ‡ = Dementia Rating Scale (DRS-2)/144. ^a complains of toe/thumb cramps and pain in neck/head, but it was unclear whether these met criteria for true somatic complaints. ^b = hyperphagia present. ^c = a couple of incidents of unprovoked anger toward husband, but no sign of true mood lability.

Somatic complaints are another source of distress in svPPA patients (5/9 svPPA, 0/10 bvFTD; Table 1). Relatedly, we note increased pain/tactile sensitivity in svPPA, while the pain threshold in bvFTD is likely higher than normal (Snowden et al., 2001). This sensitivity has manifested as svPPA patients wincing or crying during routine clinical procedures such as ECG and blood draw (Cases S2, S3, S5). Case S5 avoided wearing certain clothes and sitting in chairs due to physical discomfort. Case S2 kicked or hit strangers whom he perceived to be in his personal space. We have heard patients describe near constant states of physical discomfort, stating that “everything hurts”.

Finally, we find patients with svPPA often present with mood lability intermixed with irritability or hypomanic affect (7/9 svPPA, 0/10 bvFTD; Table 1). For example, Case S2 came in with elevated and expansive mood, describing his new business idea as “like Edison coming up with the lightbulb”, but at a subsequent visit he was depressed and suicidal. In our experience, many patients with svPPA endorse suicidal ideation (7/9 svPPA, 0/10 bvFTD; Table 1). For instance, Case S5 would say that she “could not wait” to kill herself, Case S6 would repeatedly say “I’ll kill myself if... [e.g., someone takes away my license]”. Case S2 obsessively attempted to steal and collect needles, explaining that he needed them to kill himself.

Overall, we assert that the neuropsychiatric profile of svPPA is characterized by significant distress and dysphoria, while bvFTD is associated with emotional blunting (Neary et al., 1998). This may not be captured in the literature because standardized measures do not always include the direction/valence of the change (e.g., eating changes – Neuropsychiatric Inventory). It is possible that neuroanatomical differences between svPPA and bvFTD may explain their distress symptom profiles; for example, early ventromedial prefrontal cortex (VMPFC) compromise in bvFTD may contribute to emotional blunting, while degeneration of other limbic regions with reciprocal VMPFC connections, such as the anterior temporal lobes, may result in increased emotional reactivity and distress (Koenigs et al., 2008; Snowden et al., 2001). One major challenge in distinguishing the bvFTD and svPPA phenotypes is that both VMPFC and anterior temporal disruption is present in both disorders, albeit to varying degrees, resulting in mixed phenotypes. In addition, the neuroanatomical distribution and the symptom profiles can change over the disease course.

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Declaration of Competing Interest

The authors report no conflicts of interest.

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