The Challenges of Young-Onset Dementia: A Case of Semantic Dementia

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Introduction

We present a case of a previously very high functioning middle-aged man who was referred for assessment and diagnosis of a probable Young-Onset Dementia (YOD). Although he had been showing symptoms for some years, his diagnosis was delayed because of his ability to compensate and 'cover-up' his deficits. The Neuropsychiatry Unit is a specialized tertiary diagnostic unit located at the Royal Melbourne Hospital in Parkville, Victoria, Australia. The unit specializes in the diagnosis and management of individuals with YOD and those who present with complex behavioral/psychiatric/neurological syndromes.

Clinical Case

The patient was a 53-year-old, right-handed, Caucasian man (A.H.) who presented to a tertiary diagnostic unit (Neuropsychiatry Unit) with a 2-3 year history of progressive cognitive decline, predominately affecting his language and ability to recognise people. In retrospect, his wife reported the onset of subtle word finding difficulties dating back approximately seven years; however, as he remained functional in his work as an engineer at a large automotive manufacturing company, these were dismissed. Approximately three years ago these difficulties had become much more noticeable, whereby; he was experiencing much more significant word finding difficulties and problems with recognising old friends. Around this time he was made redundant from his job, however, as this coincided with large-scale layoffs, it is unclear whether this was due to his emerging cognitive difficulties.

By way of his personal history, Mr. A.H. was born in country Victoria and performed well at school. He completed a Bachelor of Engineering and then completed an MBA. He was employed as an engineer and then as a manager for a large automotive manufacturing company. Since then he has not worked but does some 'odd jobs' around the house and for friends at a basic level. Mr. A.H. married in his 20s, and he and his wife have three children (aged 12 -16). He continues to drive and is independent with his personal ADL. Mr. A.H. experienced financial difficulties as he had fallen prey to 'phishing scams' due to his inability to interpret the errors in language and to 'read' the intentions of others.

Mr. A.H. was seen for neuropsychological assessment during his admission to the Neuropsychiatry Unit. During the interview, he stated that he was in the hospital to "help out." He went on to explain that he found the process "interesting" and that the investigations were all requiring him to do things that he had never done before. He was not explicitly questioned about his cognitive deficits at his wife's request as she was worried about him ruminating over errors and reacting negatively. Throughout the course of the assessment, Mr. A.H. was able to recognize when he was performing poorly (e.g., when not able to answer questions), but did not view these errors as reflective of a drop in performance, rather that they reflected skills he had never possessed.

His premorbid level of functioning was estimated to have been within at least the *high average to superior range* based on his educational and occupational history, as well as his performance on non-verbal hold tasks. His performance on non-verbal tasks (e.g., Matrix Reasoning SS=16) was consistent with this estimate. Traditional tests of premorbid function (e.g., TOPF) were not able to be used given his severe reading impairment. Mr. A.H. showed weaknesses in his verbal attention, verbal working memory, and inhibitory control. His verbal new learning and memory were affected

by his language difficulties; non-verbal memory was reasonably intact. Mr. A.H. was unable to identify various famous faces and did not benefit from semantic cues (e.g., “He is the current prime minister of Australia”). Assessment of social cognition showed that Mr. A.H. had difficulties with understanding and identifying basic emotions, particularly sarcasm.

His performance on language-based tasks was severely affected. On the Wechsler Test of Adult Reading he was unable to read even the high-frequency words aloud accurately (e.g., “know” was read as “now”), showing evidence of surface dyslexia. He was able to write wellknown information (e.g., address, family names); however, his writing to dictation was marked by spelling errors (e.g., “outside” was “at soud”) indicating surface dysgraphia. His conversational language was fluent but empty, with phonemic and semantic paraphasias as well as word finding difficulties.

The SYDBAT (Sydney Language Battery) was used to further assess his language (Savage et al., 2013). This measure comprises four subtests: confrontation naming, single word repetition, word comprehension and semantic association. The SYDBAT was designed to identify particular subtypes of Primary Progressive Aphasia (PPA) syndromes, and is often used in conjunction with other tests (e.g., Sentence Repetition Test; Cookie Theft Picture). A decision matrix is used to determine which variant of PPA is most likely; in Mr. A.H.’s case, his severe compromise in semantic association and confrontation naming made semantic dementia his most likely diagnosis. Further language assessment revealed that Mr. A.H. was unable to name objects when they were described to him verbally (e.g., “What is the name of the bird that flies at night and hoots?”) and did not benefit from multiple choice cueing.

An MRI at the time of his admission revealed severe temporal lobe atrophy, more prominent on the left as is commonly observed in SD. The hippocampi were also atrophied in proportion to the temporal lobe atrophy. A SPECT study showed focal left anterior temporal hypoperfusion consistent with a left Broca’s area defect. The overall impression was consistent with SD.

In summary, the profile on neuropsychological testing showed profound impairment in aspects of language function, including confrontation naming, semantic comprehension, surface dyslexia, surface dysgraphia, and expressive language difficulties. There was evidence of impairments in verbal new learning and memory, impaired facial recognition, and emotional recognition. His non-verbal skills, including memory, were largely intact. This profile is prototypical of what one would expect from SD. Taken together with the imaging findings which were consistent with SD as well as the natural history of the illness (initial language changes progressing over time to produce functional impairment), a diagnosis of SD was given. Although Mr. A.H. was still able to attend to his personal ADL (e.g., dressing, grooming, eating), he was impaired in his ability to complete more complex community and domestic ADLs (e.g., banking, child rearing) because of his significant semantic loss. In people with YOD, often the impairments at work are the first clue that this is a dementia; at home and within their familiar environment, deficits are often able to be masked until later in the illness, especially if the individual is high functioning.

The issue of a possible genetic cause was discussed with his wife, and they were referred to a neurogenetic counseling service for follow up. His care was transferred over to the outpatient service at the Neuropsychiatry Unit for ongoing medical, and social work follow up.

Semantic Dementia

Semantic dementia (SD) is one of the clinical variants of frontotemporal dementia (FTD) and is a neurodegenerative condition characterized by progressive loss of language function, affecting

naming and understanding of semantics (Gorno-Tempini et al., 2011; Hodges & Patterson, 2007). Typically, onset is before the age of 65. Most individuals with SD have ubiquitin-positive, tau-negative intraneural inclusions upon autopsy (Hodges & Patterson, 2007; Hodges et al., 2010)). Neuroimaging studies have shown bilateral, normally asymmetrical, anterior temporal lobe atrophy in the early stages of the illness; as the disease progresses, this can involve either or both the posterior temporal lobes or inferior frontal lobes (Hodges & Patterson, 2007). In some cases, FTD can be familial and specific disease-causing genetic mutations have been identified (e.g., *MAPt*, progranulin, C9ORF); however, SD is not commonly related to a genetic cause (Hodges et al., 2010).

The earliest symptom of semantic dementia is usually a loss of expressive vocabulary (Hodges & Patterson, 2007). Individuals essentially lose their understanding of the link between a word and its meaning. This then leads to a loss of receptive language skills. These impairments form the core diagnostic features of SD as set out by Gorno-Tempini and colleagues in 2011. Often these symptoms can be covered up by the individual in the early stages of the illness as typically only lower frequency words are affected early on. Speech becomes noticeable for anomia but retains its grammatical structure. Over time, spontaneous speech often becomes restricted to stereotypical phrases and single words. Other associated clinical features, which strengthen the diagnosis, include surface dyslexia or surface dysgraphia; these are syndromes in which the ability to pronounce or write irregularly spelled words (e.g., bought; sew) is affected (Gorno-Tempini et al., 2011). Individuals attempt to "regularise" the word (Gorno-Tempini et al., 2011) in their pronunciation or spelling (e.g. "brite" for "bright"; "/su/" for "sew").

Behavioural changes may appear early in the course of the illness and can be similar to those observed in behavioural variant FTD. These are, however, much less prominent and are not likely to be the core feature of the initial presentation. Some commonalities between the two conditions include a reduction in social graces and altered social functioning (Hodges & Patterson, 2007). Clinically, it is typical to see reductions in the in the understanding of sarcasm and intent in speech; this appears to be related to the loss of semantic comprehension. Other, more striking behavioural changes appear to be relatively unique to SD and include obsessional clock watching and new interests in jigsaw puzzles or word search puzzles (Hodges & Patterson, 2007). Often individuals with SD develop problems with recognition of familiar faces later in the course of the illness (Hodges & Patterson, 2007)

Although amnesia is not a core feature of the clinical presentation on neuropsychological testing, individuals with SD often complain of memory problems, and they generally perform poorly on verbal episodic memory tasks. As a consequence of this, patients are often misdiagnosed with Alzheimer's dementia. Comprehensive neuropsychological assessment is crucial as it illustrates the pattern of language impairments across multiple domains (e.g., auditory, written). Further, the assessment can highlight the sparing of non-verbal intellectual and learning skills, which can help to rule out other differential diagnoses. Differential diagnosis between the three Primary Progressive Aphasias (PPA) in the moderate to late stages of the illness is challenging due to global cognitive decline affecting all language domains.

The challenges of Young-Onset Dementia (YOD)

The stereotype of dementia being a condition that affects only the elderly continues to be pervasive within our society. Furthermore, dementia awareness campaigns, research studies, and the media perpetuate the notion that this is a singular disease which affects the elderly. These attitudes raise significant challenges for those who find their cognitive capacity changing at a much younger age – often when they are at their peak earning capacity, with families and financial obligations. The

challenges of diagnosis and the years it sometimes takes to arrive at an accurate diagnosis require a comprehensive multidisciplinary approach in which neuropsychological assessment is an integral part.

In our experience at the Neuropsychiatry Unit, people with YOD delay seeking medical assessment for their cognitive inefficiencies. This is usually because symptoms are ascribed to stress or mood disorders, caused for example by workplace stress, work/life balances or other psychosocial factors. The view that "this can't be dementia" is also highly prevalent; the exception to this is in families with a history of YOD. Once medical attention is sought, the actual process of diagnosis is often challenging because of the heterogeneity of the disorders which can result in YOD, including metabolic, genetic, infectious, and inflammatory processes. There seems to be a reluctance by primary care physicians to diagnose YOD in the absence of a clear genetic cause (e.g., Huntington's disease), and often multiple specialist opinions are sought. The lack of clarity around diagnosis, as well as misdiagnosis further adds to the stress experienced by the person and their family.

Although the needs of people with YOD can be similar to those with a later onset of dementia, some are vastly different. This is due to the challenges presented by their age, physical health, fitness and various socioeconomic factors. Residential care facilities are not equipped to manage younger, fit, people with dementia. For caretakers, there is the challenge of combining the emotional needs of their partner as well as that of a family, together with the social and economic challenges of loss of income, social status and supports. The lack of YOD appropriate services can contribute to increased caregiver burden.

In Mr. A.H.'s case, his behavioral changes and rigidity had a great impact on his wife and children. His wife reported that he would become 'locked' in arguments with their youngest son who did not understand his father's responses and actions; he has also become increasingly embarrassed by his father's behavior at school events and having friends over to the house. Ongoing social support and counseling were set up for the family as well as several psychoeducational sessions to assist the children with their understanding of Mr. A.H.'s dementia, which may be critical in keeping Mr. A.H. at home for as long as possible.

Given Mr. A.H.'s lack of insight into his symptoms, speech therapy intervention was declined. Ordinarily, ongoing speech therapy would be of importance in clients with PPAs for two reasons. The first is to assist the person with PPA to communicate more effectively and to train them to use communication aids where possible. There has been some evidence within the literature regarding successes in anomia therapy in people in the early stages of SD (e.g., Jokel & Anderson, 2012) but these have been mainly done within a research context. The second reason for ongoing speech therapy is to train the person's communication partners in how to prompt and assist with expressive communication.

Select references and recommended reading

Gorno-Tempini, M.L., Hillis, A.E., Weintraub, A., Kertesz, A., Mendez, M., Cappa, S.F., …. & Grossman, M. (2011). Classification of Primary Progressive Aphasia and its variants. *Neurology, 76:1*, 1-9.

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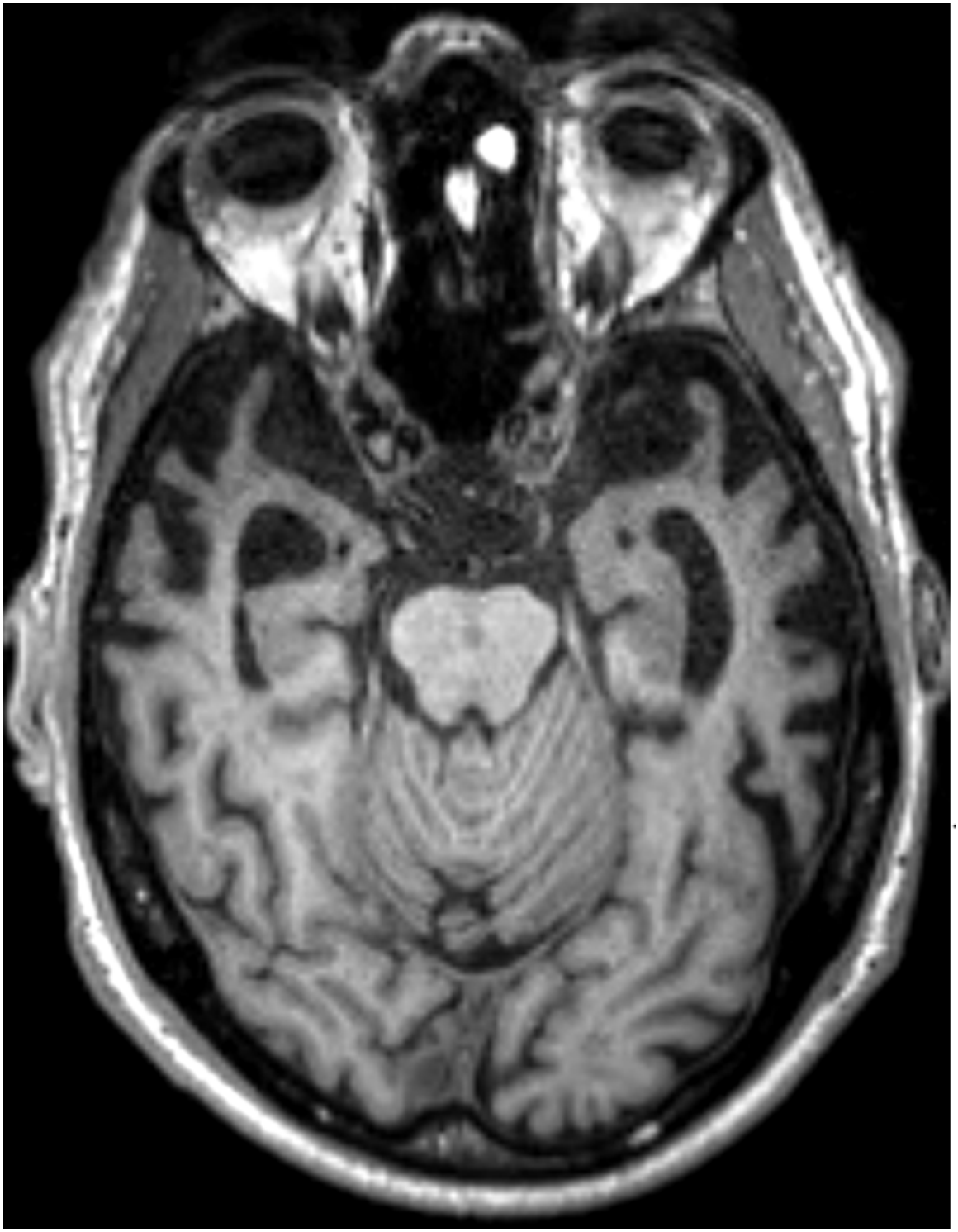
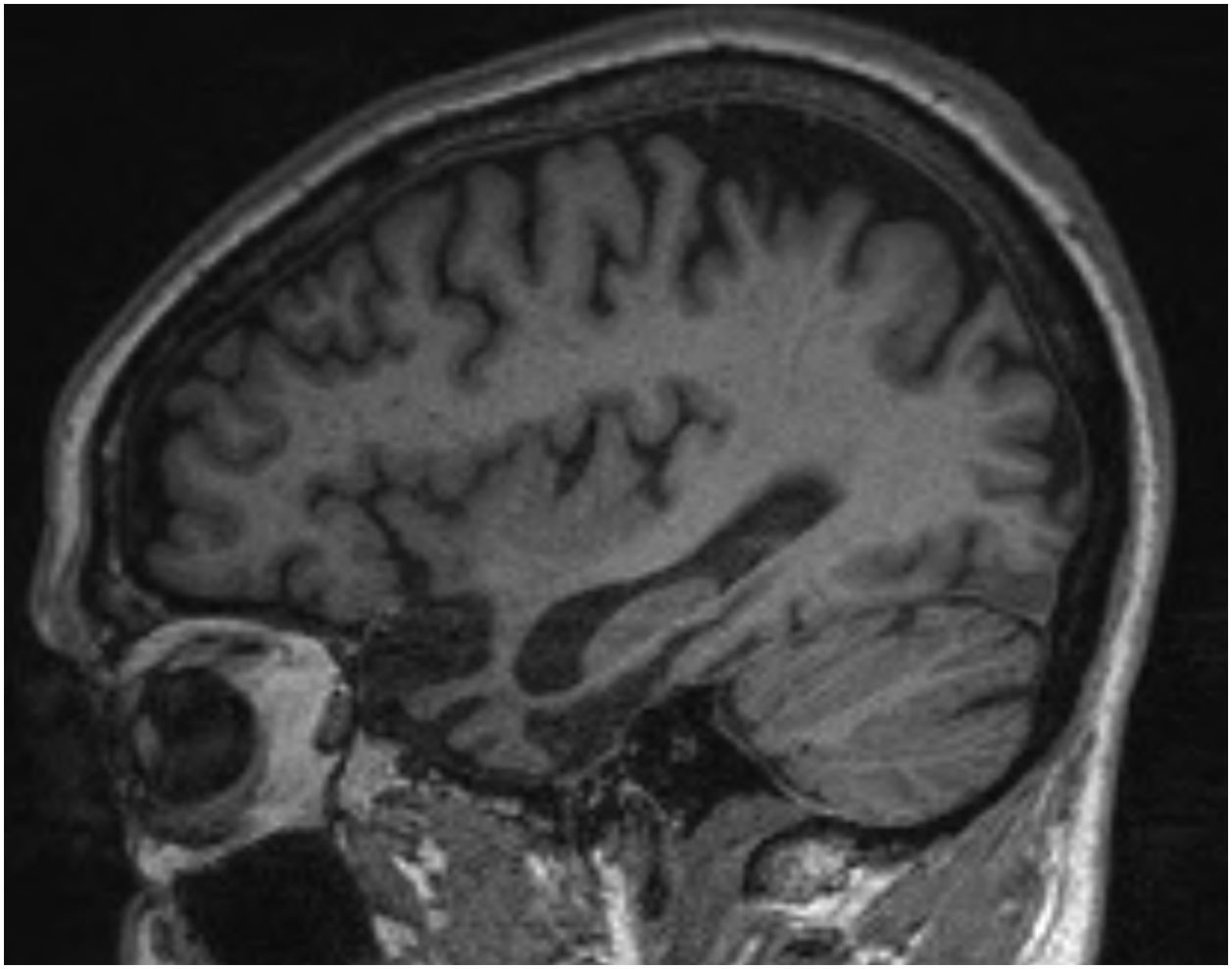
Savage, S., Hseih, S., Leslie, F., Foxe, D., Piguet, O., & Hodges, J.R. (2013). Distinguishing subtypes in Primary Progressive Aphasia: application of the Sydney Language Battery. *Dementia and Geriatric Cognitive Disorders*, *35 (3-4)*, 208-218

Snowden, J.S., Bathgate, D., Varma, A., Blackshaw, A., Gibbons, Z.C., & Neary, D. (2001). Distinct behavioural profiles in frontotemporal dementia and semantic dementia. *J Neurol Neurosurg Psychiatry, 70,* 323-332

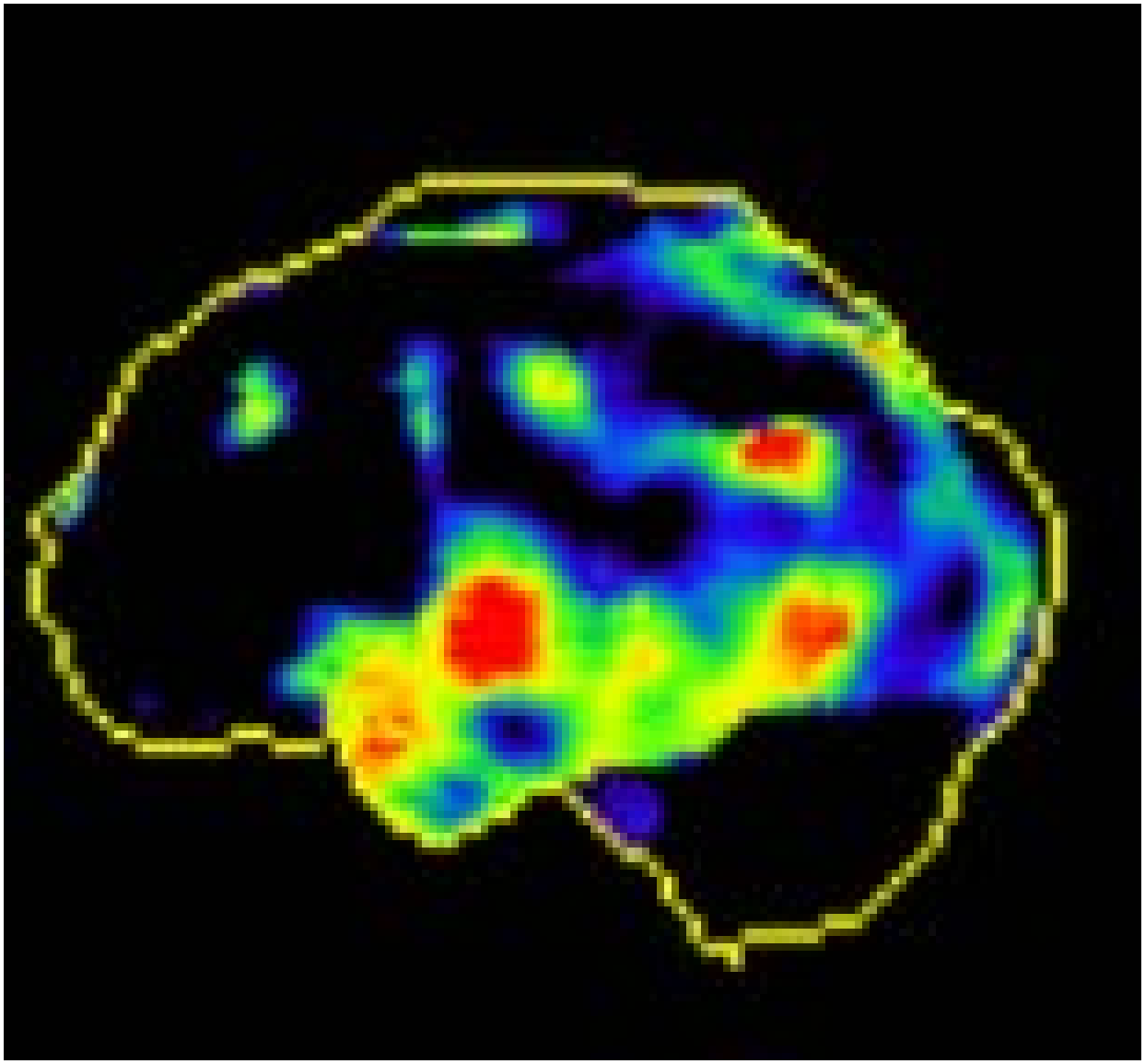
Walterfang, M., Sui, R., & Velakoulis, D. (2006). The NuCOG: validity and reliability of a brief cognitive screening tool in neuropsychiatric patients. *Australian and New Zealand Journal of Psychiatry, 40 (11-12)*, 995-1002.



Axial T1 image at level of pons: Significant generalised temporal lobe atrophy, greater on the left.

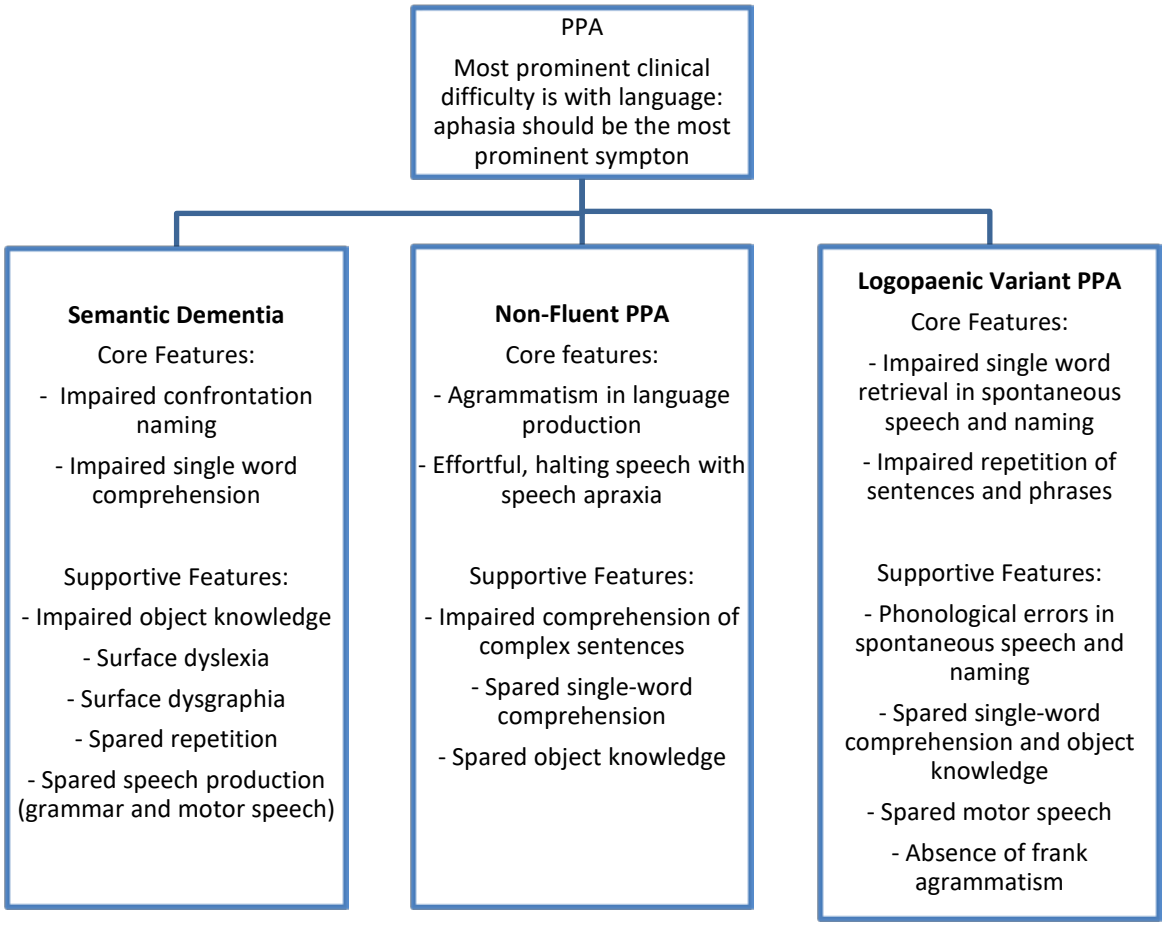


Sagital T1 slice at the left hippocampal body: Significant temporal lobe and hippocampal atrophy



Technetium-99m SPECT imaging at the left lateral aspect (sagittal slice) demonstrating hypoactivity of temporal lobe and to lesser extent, the inferior parietal lobe.

Differential diagnosis of the three sub-types of PPA (adapted from Gorno-Tempini et al, 2011)



Differential diagnosis of SD from other common forms of YOD

	Core Symptoms at onset	Core features on NP Ax at onset	Symptoms less consistent with diagnosis at onset	Features on NP ax less consistent with diagnosis at onset
SD	• Object naming difficulties • Loss of semantic knowledge	• Severely impaired confrontation naming • Impaired semantic knowledge • Impaired verbal learning and memory	• Early change in personality • Topographic disorientation • Early changes in behaviour	• Non-verbal memory impairments
AD	• Episodic memory loss • Topographic disorientation	• Severely impaired memory and new learning • Visuospatial impairment (e.g. clock) • Impaired semantic fluency	• Early change in personality • Changes in basic language structure • Changes in reading ability	• Severe executive impairment • Impairment in basic attention • Impairment in basic language skills
bvFTD	• Behaviour change • Personality change • Apathy and amotivation • Lack of social graces	• Severely impaired executive function • Impairment in higher order attention • Impairment on social cognition	• Change in communication • Preserved behaviour • Preserved social graces	• Rapid forgetting • Visuospatial impairment • Language impairment
VaD	• Depression and apathy • Step-wise decline • Everyday memory problems	• Severely impaired attention • Severely impaired processing speed • Memory secondarily affected	• Impaired social graces • Early changes in speech and language skills • Loss of autobiographical memory	• Very severe rapid forgetting • Early changes in verbal skills