



Published in final edited form as:

Int Rev Psychiatry. 2013 April ; 25(2): 178–196. doi:10.3109/09540261.2013.763340.

Language, Executive Function and Social Cognition in the Diagnosis of Frontotemporal Dementia Syndromes

Michał Harciarek¹ and Stephanie Cosentino^{2,*}

¹Division of Clinical Psychology and Neuropsychology, Institute of Psychology, University of Gdańsk, Gdańsk, Poland ²Cognitive Neuroscience Division, Gertrude H. Sergievsky Center, Taub Institute for Research on Alzheimer's Disease and the Aging Brain, and the Department of Neurology, Columbia University Medical Center, New York, USA

Abstract

Frontotemporal dementia (FTD) represents a spectrum of non-Alzheimer's degenerative conditions associated with focal atrophy of the frontal and/or temporal lobes. Frontal and temporal regions of the brain have been shown to be strongly involved in executive function, social cognition and language processing and, thus, deficits in these domains are frequently seen in patients with FTD or may even be hallmarks of a specific FTD subtype (i.e., relatively selective and progressive language impairment in primary progressive aphasia). In this review, we have attempted to delineate how language, executive function, and social cognition may contribute to the diagnosis of FTD syndromes, namely the behavioral variant FTD as well as the language variants of FTD including the three subtypes of primary progressive aphasia (PPA): non-fluent/agrammatic, semantic, and logopenic. This review also addresses the extent to which deficits in these cognitive areas contribute to the differential diagnosis of FTD versus AD. Finally, early clinical determinants of pathology are briefly discussed and contemporary challenges to the diagnosis of FTD are presented.

Keywords

frontotemporal dementia; primary progressive aphasia; executive function; language; social cognition

INTRODUCTION

More than a century ago, Arnold Pick first described patients presenting with gradual changes in behavior and personality accompanied by progressive aphasia due to frontotemporal lobar degeneration (Pick, 1892, 1904). Subsequently, cases with a similar clinical picture associated with frontal and/or temporal atrophy were reported and referred to as Pick's disease. In the early 1940's, however, Pick's disease began to be defined on the

Correspondence: Michał Harciarek, Ph.D., Institute of Psychology, University of Gdańsk, Bałtyckiego 4, 80-952 Gdańsk, Poland, psymh@univ.gda.pl, tel: (+ 48)-604-555-101, fax: (+ 48)-58-557-43-24.

*Both authors contributed equally to the preparation of this manuscript

basis of round silver staining inclusions, and it became evident that only a small number of subjects clinically diagnosed with Pick's disease met these neuropathological criteria. This lack of consistency between the clinical and the pathological presentations led to the conclusion that Pick's disease is a rare condition diagnosable only on autopsy. As a result, over the next few decades, the differential diagnosis of this unique clinical entity from other dementias received relatively little attention. In the 1970's and 1980's, however, interest in understanding progressive behavioral and language changes as a consequence of circumscribed atrophy was revived. While many labels for the clinical presentation have been proposed (e.g., see Brun, 1987; Brun et al., 1994; Neary et al., 1998), frontotemporal dementia (FTD) has become the preferred umbrella term used to describe a spectrum of non-Alzheimer's degenerative conditions associated with focal atrophy of the frontal lobes and/or temporal lobes (Hodges, 2007; Kertesz, 2008). Of note, this and other terms were initially applied mainly to the behavioral presentation, whereas the aphasic presentation was described as Primary Progressive Aphasia (PPA) (Mesulam, 1987).

Presently, FTD, an acronym recognized also as frontotemporal disease or frontotemporal degeneration (for discussion see Kertesz, 2011), is now considered the second most common cause of young onset dementia after AD (Ratnavalli et al., 2002; Rosso et al., 2003). Clinically, FTD can be divided into two variants: behavioral variant and the language variant, the latter also known as PPA (see Hodges, 2007). The behavioral variant is characterized by progressive deterioration in social function and personality that has been predominantly associated with increasing atrophy of the frontal lobes, and the mesial frontal surface in particular (Harciaiek & Jodzio, 2005; Rascovsky et al., 2011). By comparison, the language variant is suspected when there is a gradual language-speech and/or semantic impairment with relative sparing of other cognitive domains early in the disease course (Gorno-Tempini et al., 2011; Harciaiek & Kertesz, 2011; Mesulam et al., 2009). Based on the constellation of symptoms described later in this review, FTD-related PPA is typically classified into a nonfluent/agrammatic (nfvPPA) and semantic (svPPA) variant, the latter also referred to as semantic dementia. Although the neuroimaging findings in nfvPPA are heterogeneous, most of these cases are associated with progressive atrophy within the left inferior, opercular, and insular regions. In contrast, the clinical picture of svPPA is typically associated with bilateral atrophy of the anterior temporal lobes, more prominent on the left side. Of note, the most recent classification of PPA also encompasses the logopenic variant PPA (lvPPA), but its inclusion under the umbrella of the FTD syndromes is somewhat problematic. This is mainly due to the fact that most of these patients have atrophy extending beyond the fronto-temporal regions (e.g., parietal lobule), and about 60% of them have pathological changes characteristic of AD (see Gorno-Tempini et al., 2004, 2010; Grossman, 2010). Nonetheless, about one third of lvPPA cases share both clinical and pathological features of FTD, often making the differential diagnosis puzzling. Hence, we include details on lvPPA in the various sections below.

Establishing correlations between clinical phenotype and pathology in FTD is challenging, particularly because the clinical spectrum typically evolves as the disease progresses. Also, some patients commonly have mixed syndromes even at the initial presentation to the clinic. For example, patients with PPA have been shown to develop early behavioral features characteristic of bvFTD (Marczinski, 2004). Moreover, a relatively homogenous clinical

syndrome like bvFTD has been shown to be associated with different pathological entities (see Rohrer et al., 2011). To complicate things further, FTD syndromes overlap clinically, pathologically and biologically with motor neuron disease (MND; including amyotrophic lateral sclerosis - ALS), corticobasal degeneration (CBD) and progressive supranuclear palsy (PSP) (Biglo et al., 2003; Hodges, 2011; Kertesz et al., 2000, 2005, 2007; McMonagle et al., 2006; Neary et al., 1998; Seelaar et al., 2011; Snowden et al., 2006, 2007). For example, although PPA is considered when there is isolated progressive language impairment with a relative preservation of nonverbal cognition in the first two years of the disease (Mesulam et al., 2009; Gorno-Tempini et al., 2011), many cases with the nvPPA have extrapyramidal features of CBD and PSP, which appear within two years of the language symptoms (Kertesz et al. 2000, 2005, 2007; Rohrer et al. 2010a). Hence, although FTD remains the most widely applied term to denote both clinical and pathological changes associated with progressive frontal and/or temporal atrophy, taking into account the extensive overlap with MND, CBD and PSP, a new term of Pick Complex has been recently proposed and applied (see Kertesz, 2011; Kertesz et al., 1994). Others have used “frontotemporal lobar degeneration” (FTLD) (Snowden et al., 1996) but this term is typically used by pathologists with qualifier letters to denote the underlying proteinopathy (Cairns et al., 2007).

Nonetheless, a number of studies have shown that the clinical syndrome of bvFTD, although pathologically heterogeneous, is most often related to ubiquitinated frontotemporal lobar degeneration (FTLD-U) and frontotemporal lobar degeneration associated with tau (FTLD-T), excluding AD pathology (e.g., Hodges, 2011; Rohrer et al., 2011). Further, nvPPA has been predominantly associated with FTLD-T, whereas svPPA has been almost entirely related to FTLD-U. Also, as already mentioned, although about 40% of cases with lvPPA have FTLD-U pathology, in most cases the pathological changes are those of AD (e.g., Grossman, 2010). Thus, in this light, the early differential diagnosis of FTD syndromes seems to be particularly important, since it may strongly suggest the pathological basis of each syndrome. An accurate clinical diagnosis may then in turn significantly contribute to the choice of the most appropriate treatment method, if such a treatment is eventually discovered.

In this review, we have attempted to delineate how language, executive function, and social cognition may contribute to the diagnosis of FTD syndromes as well as to the differentiation of these syndromes from AD. The clinical determinants of pathology are problematic, and determining the primary cognitive deficit in some FTD syndromes remains a matter of debate. However, we believe that a comprehensive neuropsychological assessment with emphasis on language, social cognition and executive function, when combined with neuroimaging, will significantly increase the specificity of the early differential diagnosis of FTD. For the purpose of this study, we have discussed language, executive function and social cognition only in the two main FTD syndromes, namely bvFTD and PPA, although when appropriate we also refer to MND, CBD or PSP.

LANGUAGE IN THE DIAGNOSIS OF FTD SYNDROMES

One of the main goals of clinical neuroscience is to differentiate between the early stages of neurodegenerative conditions caused by different underlying pathologies. Although both FTD and AD may start with progressive aphasia, the language profile of FTD-related and AD-related PPA has often been shown to be dissociable. Therefore, a comprehensive language assessment may significantly contribute to the correct diagnosis of these two dementing diseases. Further, for natural reasons, language testing is crucial in the early differentiation between the behavioral and language variants of FTD, although at later stages of the disease some overlap may be present, especially between bvFTD and svPPA (see Kertesz et al., 2007).

PPA is characterized by isolated speech and language impairment during the first two years of the disease course (Gorno-Tempini et al., 2011; Mesulam, 2001, 2003). However, later in the disease, aphasia in FTD and AD is typically accompanied by a specific neuropsychological profile (for review see Harciarek & Jodzio, 2005). Thus, to diagnose PPA and its specific variant, a neuropsychological assessment should involve administration of a number of tests that, apart from examining patient's deficits within and across language domains, could help to characterize patient's behavior, overall cognitive status, as well as performance in specific non-language domains (e.g., memory, visuo-perceptual abilities). This could be best achieved by using a comprehensive language battery such as *the Western Aphasia Battery-Revised* (Kertesz, 2007) or *Boston Diagnostic Aphasia Examination* (Goodglass et al., 2001), together with some experimental tasks of speech processing. Once the diagnosis of PPA is established, a clinician should use the speech and language profile to identify a certain subtype of PPA that could potentially point to the underlying pathology of this syndrome (Hu et al., 2010; for review see Harciarek & Kertesz, 2011). Of note, there may be no clear cut between the progressive aphasia subtypes, as a subset of cases present with mixed or possible PPA (Kertesz et al., 2005, 2007, 2010; Mesulam et al., 2008).

Language profile of the behavioral variant FTD

Language in bvFTD is initially spared, with behavioral and personality changes being the diagnostic features (Rascovsky et al., 2011). While some patients with bvFTD demonstrate difficulty naming action words, this deficit has been shown to be associated with executive abilities, and may not reflect defective verb processing (i.e., retrieving the lexical features of verbs) per se (d'Honinckhun & Pillon, 2008; Rhee et al., 2001; Silveri et al., 2003). One possibility is that verb naming requires access to a more elaborate set of linguistic and semantic information than naming nouns, and thus places greater demands on executive resources including working memory and selective attention (Silveri et al., 2003). However, d'Honinckhun and Pillon (2008) have demonstrated that differential difficulty with action versus object words in an individual with bvFTD may be a product of the manner in which verb naming is assessed. Specifically, in a case study of bvFTD, a disproportionate verb naming deficit was seen only when static pictures were used to probe verb naming, and not when verbal descriptions of videotaped actions were used as probes. The authors argue that this dissociation reflects the greater demands on executive resources for naming verbs rather

than nouns based on static pictures, as such pictures are missing crucial temporal and spatial information inherent to verbs.

Nonetheless, as the disease progresses, many patients develop semantic problems typical for svPPA (Kertesz et al., 2007), reflecting the significant overlap in the distribution of neuropathology across these two FTD syndromes. Similarly to svPPA, subjects with bvFTD frequently present with severe pragmatic disturbance, disinhibited output, and stereotypic thematic perseverations. Alternatively, in relation to their frontal lesions and apathy, patients with bvFTD may not participate in communication and, thus, may be perceived as logopenic. Finally, due to an overlap with nvPPA, a subset of patients with bvFTD may become non-fluent or even mute, especially at the late stages of the disease.

Language profiles of the language variant FTD (PPA)

Non-fluent/agrammatic variant PPA—The earliest language problems seen in nvPPA encompass rather non-specific anomia and word finding difficulties (Ash et al., 2010; Blair et al., 2007; Clark et al., 2005; Harciaiek & Kertesz, 2009; Kertesz & Munoz, 2002; Kertesz et al., 2003a; Knibb et al., 2009). Initially, patients with nvPPA may still seem to have fluent speech, although their output typically becomes effortful and halting due to articulatory problems. Importantly, however, most subjects with nvPPA begin to experience progressive problems with sentence construction and syntax relatively early (Gorno-Tempini et al., 2011; Gunawardena et al., 2010; Kertesz, 2008; Mesulam et al., 2009; Rohrer et al., 2010a). Therefore, speech becomes agrammatic and difficult to comprehend, often due to a significant shortage of verbs and phonological errors in conversational speech (Hillis et al., 2002, 2004). Additionally, agrammatism in nvPPA may include omitting required determiners, and failure to produce appropriate subject-verb agreement (Ash et al., 2009). Moreover, *apraxia of speech*, a phenomenon characterized by impaired motor planning and sequencing of the movements required for correct speech production, is also among the initial signs of nvPPA (Gorno-Tempini et al., 2004; Josephs et al., 2006). These patients may predominantly present with stuttering, severe difficulties repeating strings of syllables, as well as defective prosody, slow rate and reduced complexity of speech (Budd et al., 2010; Ogar et al., 2005, 2006, 2007; Wilson et al., 2010). It is important to note that apraxia of speech is often present with CBD (Josephs & Duffy, 2008) and may be a good marker of tau pathology (Josephs et al., 2006). Individuals with progressive apraxia of speech may also sometimes present with dysarthria with systematic distortion of speech that mirrors articulatory problems seen MND (Duffy et al. 2007).

As the disease progresses, language impairment becomes more prominent and speech fluency decreases. Further, many subjects experience reading and writing difficulties, although reading problems are typically mild and phonemic in nature (Graham et al., 2004; Patterson et al., 2006; Rohrer et al., 2010a). As a point of comparison, semantic deficits are not observed in nvPPA (Kertesz et al., 2005, 2007). Also, patients have preserved comprehension (Hodges et al., 2008; Kertesz et al., 2010; Weintraub et al., 1990), although agrammatism often impairs comprehension of sentences with complex syntactic constructions as well as multi-part sequential commands (Blair et al., 2007; Grossman et al., 1996; Hodges & Patterson, 1996; Peelle et al., 2008; Rohrer et al., 2010a).

Language profile of semantic variant PPA—The language profile of semantic variant PPA, also recognized as “fluent PPA” (Adlam et al., 2006; Clark et al., 2005), “temporal variant FTD” (Bozeat et al., 2000), “semantic dementia” (Hodges et al., 1992; Snowden et al., 1989) or, in Japanese literature, “Gogi (word meaning) aphasia” (Tanabe et al., 1992), is probably the most homogeneous among all PPA syndromes associated with FTLD. Overall, this variant of PPA is characterized by a progressive loss of semantic knowledge (Hodges et al., 1992; Julien et al., 2008; Kashibayashi et al., 2010; Mayberry et al., 2011; Snowden et al., 1989; see also Gorno-Tempini et al., 2011). Thus, patients with svPPA lose the meaning of words, seen particularly in the context of naming and single-word comprehension (Adlam et al., 2006; Hodges et al., 1992; Kertesz et al., 1998, 2010). Despite circumlocutions, and overuse of closed class words, pronouns, verbs, and high frequency nouns, however, the speech of patients with svPPA remains fluent, so they are typically able to carry out a conversation. As a result of well-preserved phonology, subjects with svPPA can also flawlessly repeat words, even when multisyllabic such as ‘hippopotamus’ (Hodges et al., 2008) Hence, svPPA somewhat resembles “transcortical sensory aphasia” in which articulation, phonology, and syntax are preserved but the patient does not comprehend well and has severe anomia.

As the disease progresses, the speech of patients with svPPA may still be considered fluent. Nonetheless, it becomes semantically jargonistic, frequently irrelevant to the questions being asked or the topic discussed (Kertesz et al., 1998, 2010). In fact, profound pragmatic disturbance, including garrulous, excessive, and frequently disinhibited output; stereotypic thematic perseverations; and not stopping to listen, are commonly considered the hallmark features of svPPA (Ash et al., 2006; Kertesz et al., 2010). Later, as a result of lexical-semantic impairment, the length of patients’ connected speech becomes constantly shorter, resulting in mutism. Importantly, as svPPA progresses, problems with single-word comprehension become evident also for more typical words, with patients themselves frequently asking the meaning of words, typically nouns. Importantly, the “What is...?” questioning in conversation and also while asked to define words, has recently been shown to be the primary diagnostic feature of svPPA (Kertesz et al., 2010).

Although naming and semantic fluency are impaired in AD, they are typically more severely impaired in svPPA (Blair et al., 2007; Marczyński & Kertesz, 2006). Moreover, patients with svPPA are unlikely to benefit from cuing to the same extent as AD patients (see Gregory & Hodges, 1996). This is because the brain networks that support word and object knowledge have been directly affected in svPPA, resulting in an entire loss of knowledge for a word, rather than difficulty accessing the word which we often see in AD. For example, when shown a picture of a comb, a patient with AD may describe it as something that is used to brush hair, and with phonemic cuing (the word begins with “co”) can often pull up the correct name. In contrast, a patient with svPPA may not recognize the picture, and may be unassisted by cuing.

Language profile of logopenic variant PPA—Logopenic variant PPA has only been recently described (see Gorno-Tempini et al., 2004, 2011). Similar to nfvPPA, its initial clinical picture encompasses slowed speech output with frequent word-finding pauses and phonemic paraphasias. Nonetheless, in lvPPA, there is no agrammatism, impaired motor

control of speech, or expressive aprosodia, although in lvPPA expressive aprosodia may be sometimes also present due to word-finding pauses that disrupt the rhythm and intonation of speech. Further, patients with lvPPA do not produce telegraphic speech with missing function words and morphemes (Wilson et al., 2010). Additionally, in contrast to svPPA, confrontation naming is typically only moderately affected and single word comprehension is preserved. However, patients with lvPPA usually have severe difficulty repeating and/or comprehending sentences and longer phrases, while reproduction of short, single words remains spared. Thus, a phonological short-term memory deficit has been suggested to be the core impairment that underlies most language deficits in lvPPA (Gorno-Tempini et al., 2008).

Nonetheless, since logopenia is also a feature of nfvPPA and deficits in single-word comprehension and sentence-level grammar emerge later in the course of lvPPA, individuals with lvPPA might sometimes be better referred to as “progressive mixed aphasia” (Grossman, 2010; Mesulam et al., 2008, 2009). Importantly, in addition to the defective phonological loop of working memory, subjects with lvPPA often present with episodic memory impairment (Mesulam et al., 2008) as well as acalculia (Rohrer et al., 2010b), bringing their clinical picture closer to AD rather than to FTD.

Contribution of cognitive assessment to the diagnosis of language impairment in FTD

Many widely used cognitive measures (e.g., memory tests) are language-based. Thus, individuals with PPA may obtain lower scores due to their language impairment. For example, patients with svPPA may fail on verbal memory tasks such as *the Ray Auditory Verbal Learning Test* or *the Hopkins Verbal Learning Test* because they may not understand the instructions or may try to remember a word by its phonology rather than its meaning. As a point of comparison, some subjects with logopenic or nonfluent variant PPA may have severe problems memorizing a list of words owing to defective phonological processing and/or may not be able to provide an answer due to distorted speech output or mutism. The same issue seems to also be true for the interpretation of scores obtained on general cognitive function scales such as *the Mini-Mental State Examination* (MMSE) (see Kertesz et al., 2003b). Hence, at least some patients with PPA could potentially be misdiagnosed as having a more generalized dementia. It is worth mentioning, however, that although a total score on such scales may be unreliable in many cases, the profile of the performance as well as the qualitative analysis of subscales may inform the diagnosis of PPA, or even its specific subtype. For example, since phonological, motor and visuo-perceptual abilities are generally preserved in svPPA, these subjects may be the only individuals with PPA who are able to accurately repeat words and sentences or copy a design. In contrast, such patients typically have severe anomia and may frequently ask the meaning of the ‘to be remembered’ words (Kertesz et al., 2010). Similar dissociations in performance may be seen on the *Clock Drawing Test*, a sensitive and multidimensional cognitive screen with a strong semantic component (see Blair et al., 2006; Cahn-Weiner et al., 1999). While patients with svPPA may obtain a perfect score in the copy condition, drawing to command might be severely impaired; e.g., they may not know what ‘a clock’ is.

Specific language assessment in the differential diagnosis of PPA subtypes

A problem with identifying a specific subtype of PPA is that a comprehensive neuropsychological assessment might be very time consuming and tiring for a patient as well as for a clinician, especially if the entire language battery is used. Some standardized, validated, and practical-length batteries such as the *Western Aphasia Battery (WAB)-Revised*, however, enable testing of both language and non-language cognitive domains. The WAB is composed of several subtests that assess different aspects of language, including spontaneous speech (information content and fluency), comprehension, repetition, and naming. Based on a specific combination of these features, the classification of aphasic subtypes can be accomplished. The supplementary measures consist of reading, writing, and nonverbal tests that include measures of praxis, drawing, block design, calculation, and *Raven's Progressive Matrices*. Importantly, although this battery was initially designed to diagnose and classify aphasia due to stroke, it has been subsequently shown to have a high accuracy in differentiating progressive aphasias (Blair et al., 2007; Kertesz et al., 2005, 2007, 2010). Also, significant differences across PPA subtypes may be seen even within some single subtests such as the Auditory Recognition subtest. For example, it has been shown that although correct auditory recognition depends on aphasia severity and might be modified by word frequency only patients with svPPA appear to develop impaired comprehension of words depicting body parts, and these deficits are seen relatively early in the course of the disease (Harciarek & Kertesz, 2009). In contrast, impaired repetition of single words and short sentences is typically only seen in nfvPPA (Hodges et al., 2008).

Despite the fact that all patients with PPA perform poorly on verbal fluency tasks, the profile of performance across phonemic (letter) and semantic (category) fluency tasks is often dissociable across PPA subtypes (Kertesz et al., 1998, 2010; see also Hodges & Pattersen, 2007). Category fluency (e.g. generating as many names of animals within 1 minute) is typically differentially impaired as compared to letter fluency (e.g., generating words beginning with F, A, or S) in svPPA, likely owing to lexico-semantic dysfunction, whereas the reverse pattern appears to characterize nfvPPA and lvPPA groups, likely due to impaired fluency and phonology (Laisney et al., 2009). Also, Ringman and coworkers (2010) have recently found that, while performing a phonemic fluency task, patients with FTD, regardless of its variant, tend to generate the word "f*ck" during the "F" trial, whereas such use of profanity is not seen in patients with AD.

Naming impairment is seen in all individuals with PPA, although it has been shown to be the most severely affected in the svPPA subtype. While phonological paraphasias and semantic impairment also develop in AD (Appell et al., 1982; Chertkow & Bub, 1990; Chertkow et al., 2008), these deficits are typically accompanied or preceded by a prominent episodic memory deficit. Single word comprehension problems characteristic of svPPA are less frequent in AD, where comprehension deficits are more likely to resemble Wernicke's aphasia (Kertesz et al., 2010). With regard to reading, patients with svPPA have preserved phonology and therefore correctly relate letters to sounds while reading regular words, unlike patients with nfvPPA. However, the sound of an irregular word is not related to its spelling, and must be learnt separately for each word. Patients with svPPA who have lost the lexical representation of this word read only by phonology and in turn, pronounce irregular

words as if they were regular (e.g. ‘yakt’ for “yacht”, ‘dufnut’ for ‘doughnut’); a phenomenon known as *surface dyslexia* (Fushimi et al., 2009; Jefferies et al., 2004; Kertesz et al., 1998, 2010; Wilson et al., 2009b). In svPPA patients, this may also apply to writing (*surface dysgraphia*) (Caine et al., 2009).

As a part of the diagnostic criteria, patients with nvPPA often present with agrammatism (see Gorno-Tempini et al., 2011). Thus, written production tests (such as a written description of a picture) or syntax comprehension tasks are useful in the differential diagnosis of PPA, since they can reveal even mild grammatical errors in nvPPA (Weintraub et al., 1990, 2009). Also, Mesulam and coworkers (2008) has recently indicated that the presence of syntactic impairment may reliably predict tauopathy at autopsy. However, whereas evaluating lexical-semantic processing may be relatively easily done with a combination of the measures described above plus some word-picture matching tests like *the Pyramids and Palm Trees Test* (Howard & Patterson, 1992), assessment of syntax seems to be much more challenging. To test grammatical comprehension, some experimental sentence-matching tasks are typically applied. Grammatical comprehension may also be tested by providing the patient with a sentence and asking questions that probe understanding of grammatical relations between sentence components (Grossman et al., 2005). Such tasks, however, require well-preserved single word comprehension and working memory and, thus, their diagnostic utility in PPA may be limited, especially at the later stages of the disease.

The ability to produce grammatically correct sentences has frequently been examined using picture description tasks as well as through linguistic analysis of spontaneous speech (Beeke et al., 2003; Gorno-Tempini et al., 2004; Kertesz, 2007). Such tasks provide a very rich source of data; however, it is very difficult to control the topic, the rate, and length of the interchange during testing. A recently developed test, *the Northwestern Anagram Test* (NAT) (Weintraub et al., 2009), addresses these limitations by evaluating the accuracy of word order under controlled sentence production conditions. In the NAT, a picture stimulus depicting two actors (e.g., ‘a man’ and ‘a woman’) and an action (e.g., ‘kiss’) is shown to a subject. Each drawing has printed words and arrows labeling each actor and action. The subject is provided with individual word cards presented in a scrambled order and is asked to assemble these cards into a meaningful sentence based on the picture. Additional advantages of this task include its utility in patients with word finding difficulties or working memory problems as well as in those who have speech production and word comprehension deficits. Also, in addition to providing few clues as to permissible word combinations, the NAT examines several canonical and non-canonical errors.

Although rarely done, the analysis of non-verbal sound processing may also be helpful in differentiating between PPA variants. Evidence for this comes from a study by Goll and colleagues (2010) who investigated the processing of complex non-verbal sounds in a consecutive series of 20 patients with PPA. Their results indicate that deficits of early auditory perceptual analysis may be characteristic for nvPPA, whereas deficits of representational processing may occur in both non-fluent and semantic variant PPA. Also, defective semantic processing tends to be modality specific in nvPPA, whereas this impairment is more severe and generic in svPPA. Importantly, in this study the diagnosis of

PPA was based on Neary's et al. criteria and, thus, at least a subset of the nonfluent patients could have potentially had lvPPA if the most recent criteria of PPA had been applied.

EXECUTIVE FUNCTIONING IN THE DIAGNOSIS OF FTD SYNDROMES

The executive abilities, such as abstract reasoning, concept formation, mental set shifting, problem solving, working memory, and inhibition of a prepotent response, are a group of high level cognitive functions united by their role in the control and direction of lower level functions (Stuss & Levine, 2002). An in depth discussion of executive abilities is beyond the scope of this review; however, it should be noted that these heterogeneous abilities appear to share an underlying commonality as well as to separate into discrete processes. For example, while mental set-shifting, monitoring / updating, and inhibiting a prepotent response are correlated, they can also be distinguished from each other on the basis of latent variable analysis, and contribute differentially to performance on specific neuropsychological tasks (Miyake et al., 2000). The majority of work in FTD, and thus this review, will evaluate the integrity of executive functioning via standard neuropsychological tests that generally place demands on a combination of more specific executive abilities.

Executive dysfunction is often assumed to be a hallmark feature of FTD given the well established and robust association between executive abilities and frontal lobe integrity (Gazzaley et al., 2007; Royall et al., 2002). Indeed, executive deficits are often present in bvFTD, can be seen in the language variants of FTD, and have even been detected as early features of FTD in "pre-symptomatic" tau mutation carriers (Alberici et al., 2004; Ferman et al., 2003). Interestingly, however, executive deficits are not necessarily the primary features of FTD and may even be absent on formal neuropsychological testing, particularly when examining total quantitative score rather than using a qualitative approach to examine errors. As we have seen above, the PPA variants of FTD are characterized predominantly by language symptoms and, as we will see in the following section, social cognitive deficits may be more salient than executive dysfunction in the behavioral variant of FTD. In this section, we review the literature on executive disturbances in FTD, and highlight results that have been produced from autopsy-proven studies.

Executive profile of the behavioral variant FTD (bvFTD)

As the primary neuropathologic changes in bvFTD occur in the prefrontal cortex, it is to be expected that executive deficits would be a major component of the clinical presentation. In fact, a full range of executive deficits has been reported in clinically defined bvFTD (Carlin et al., 2000; Cosentino, et al., 2006; Huey et al., 2009; Johns et al., 2009; Krueger et al., 2007; Strenziok et al., 2011) as well as pathologically confirmed bvFTD (Grossman et al., 2007; Rascovsky et al., 2008; Rascovsky et al., 2002). For example, Johns and colleagues (2009) reported deficits in bvFTD across four domains of executive functioning including working memory; (e.g., Brown-Peterson dual task paradigm), inhibitory control (e.g., Stroop Test), planning (e.g., Tower of London), and generative behaviors (e.g., verbal fluency). Huey and colleagues (2009) also demonstrated a range of executive deficits in bvFTD on subtests of the Delis-Kaplan Executive Function Systems battery (DKEF-S) including sorting, verbal fluency, and abstract reasoning, the latter of which was severe enough to distinguish bvFTD patients from a group with CBD. Deficits have been reported not just for

total score, but for numerous subscores within a task, such as time to completion, number of moves, and total rule violations on tasks such as the Tower of London. Moreover, studies using experimental tasks to isolate specific elements of executive functioning including planning and decision making support the idea that fundamental deficits in these abilities are present in bvFTD (Krueger et al., 2007; Strenziok et al., 2011).

Although executive dysfunction is not specific to bvFTD, studies based on both clinical diagnoses (Hodges et al., 1999; Libon et al., 2007; Lindau et al., 2000; Mathuranath et al., 2000; Walker et al., 2005) and pathological confirmation (Grossman et al., 2007; Rascovsky et al., 2002; Rascovsky et al., 2008) have generally reported it to be more pronounced than in AD. Performance on tasks of verbal fluency is one of the most frequently noted means of discriminating between AD and FTD clinically, and even among FTD subtypes as discussed earlier (Marczinski & Kertesz, 2006). Imaging and autopsy confirmed studies have reported distinct patterns of performance across phonemic versus semantic fluency tasks that are characteristic of bvFTD, svPPA, and AD. Identifiable patterns of performance across these groups derive from the differential demands of each type of fluency task on frontal versus temporal regions (Harciarek et al., 2012; Laisney et al., 2009). While both tasks require executive resources for the efficient organization and production of novel information, semantic tasks such as animal naming also rely heavily on access to temporal lobe networks that support categorical knowledge. Thus, a significant advantage of phonemic over category fluency is thought to reflect relatively preserved prefrontal versus temporal networks (Baldo et al., 2006; Lopez et al., 2000), and is considered to be a characteristic (but not universal) feature of the early AD cognitive profile. The reverse pattern has been reported secondary to primarily prefrontal compromise in bvFTD and equally impaired performance has been shown in svFTD (Laisney et al., 2009). Rascovsky and colleagues (2007) calculated a semantic index representing the relative integrity of semantic fluency in relation to overall fluency in pathologically confirmed cases of AD and FTD. Scores on this index discriminated between AD and bvFTD with 90% correct classification. As may have been expected, the svFTD cases performed more comparably to patients with AD.

Importantly, however, measures of executive functioning do not always distinguish between bvFTD and AD (Collette et al., 2007; Diehl & Kurz, 2002; Kertesz et al., 2003; Piquard et al., 2004; Wicklund et al., 2004), and this is particularly the case when groups are compared on overall accuracy scores rather than on qualitative aspects of performance. For example, Kertesz and colleagues (2003) found that a behavioral measure (i.e., the Frontal Behavior Inventory) was more accurate in cognitive measures for discriminating between 52 individuals with bvFTD (a portion of which were autopsy confirmed) and 52 individuals with AD. Frequently comparable performance across these groups reflects not only the fact that areas of the prefrontal cortex are compromised in AD, but the fact that complex executive tasks place demands on working memory capacity supported by posterior regions of the brain (Stopford, et al., 2012). However, there is growing recognition that differences in executive abilities across bvFTD and AD may be evident in qualitative aspects of performance rather than the overall quantitative scores. Possin and colleagues (2012) recently examined the neuroanatomic basis of repetitions versus total correct on a design fluency task in patients with various forms of dementia. While overall number of correct designs was associated with the integrity of frontal, parietal, and temporal regions

bilaterally, repetitions were uniquely predicted by right and left lateral PFC volumes. Accordingly, patients with bvFTD made significantly more design repetitions than the other dementia groups despite comparable scores for overall number of designs correct. Similarly, Thompson and colleagues (2005) found that characterizing errors across a range of cognitive tests to capture the presence of concrete thought, perseveration, organizational approach, and confabulation was more useful in distinguishing between AD and FTD than the traditional scores on the individual tests, and increased classification accuracy from 71% to 96% (J. C. Thompson et al., 2005). Carey and colleagues (2008) explored rule violation errors on a tower task that required complex planning in patients with AD and FTD (Carey et al., 2008). They hypothesized that such errors would be more specific to the FTD group than the overall accuracy scores which likely reflect a multitude of cognitive processes including processing speed and spatial organization. Indeed, while the two groups were similarly impaired for the overall accuracy score, the FTD group was more likely to violate task rules either by moving two disks at once or by placing a large disk on top of a small disk. Such rule violations in FTD or the tendency to make „out of set” errors is characteristic of prefrontal compromise seen in other degenerative diseases (Giovannetti et al., 2001; Lamar et al., 2010a). For example, when compared to patients with AD, patients with VaD compromising frontal subcortical networks make more out of set errors when asked to identify similarities between two things (e.g. a dog and a lion). An out of set error would be „a lion can eat a dog”, whereas an in-set error would be „they both have legs”. That is, prefrontal compromise appears to influence the extent to which an individual can maintain the appropriate mental set, or operate within the specified parameters of the task (Lamar, et al., 2010b). Indeed, imaging work examining the neuroanatomic basis of rule violations has confirmed that the integrity of bilateral PFC regions, rather than posterior regions of the cortex, contributes to the frequency of rule violations (Possin et al., 2009). Qualitative error analysis is critical in identifying these informative errors.

It should be noted that several studies have reported certain executive abilities in the normal range in patients with FTD (C. A. Gregory & Hodges, 1996; Lough, et al., 2001; Rahman et al., 1999). This likely reflects the early compromise of orbitofrontal, ventromedial PFC and anterior temporal lobe areas as opposed to regions in the dorsolateral PFC (Seeley et al., 2008), resulting in relatively preserved executive abilities in the context of impaired behavior and social cognition (discussed later in this review). In general, however, performance is generally impaired in patients with bvFTD on at least one measure of executive functioning. For example, Lough and colleagues (2001) described the case of an individual with bvFTD who had significant personality and behavioral changes as well as impaired performance on a task of verbal fluency, yet intact performance on the Wisconsin Card Sorting Test. The authors demonstrated that the most notable deficit on formal testing was evident on an experimental Theory of Mind task which examined the patient’s ability to take the perspective of another person, a skill which falls into the increasingly recognized and researched domain of social cognition that will be discussed in the next section. Rahman and colleagues (1999) also found a dissociation in executive abilities among patients with mild bvFTD such that performance on spatial working memory and planning tasks was preserved, whereas a decision-making task revealed risk-taking behavior and increased deliberation time.

In summary, the majority of studies demonstrate at least some disruption of executive abilities in bvFTD, but it appears to be critical to assess a range of executive abilities, with particular attention paid to the qualitative aspects of performance than the total scores. Individuals who do not present with any executive dysfunction may either have relatively circumscribed atrophy, or may be part of a non-progressive FTD phenocopy group (Hornberger et al., 2008). Hornberger and colleagues (2008) studied a group of individuals longitudinally to determine the features which best discriminated between individuals who progressed over time (i.e., true FTD) versus those whose clinical symptoms remained stable (i.e., phenocopy group)(Hornberger et al., 2008). While both groups shared similar behavioral features at baseline, individuals who progressed over time typically demonstrated executive deficits on tests including Digit Span, Verbal Fluency, Trail Making, and the Hayling Test of Inhibitory Control.

Executive profiles of the language variant FTD (PPA)

As would be expected, executive dysfunction has been documented as the various PPAs progress and pathological changes become more widespread (Hsiung et al., 2012; Mesulam, 2003; Wicklund et al., 2007). The extent to which executive dysfunction is present early in the course of PPA is less clear, however. By definition, the language variants of FTD present with disproportionate and relatively isolated deficits in the expression and/or comprehension of language as discussed earlier. As such, deficits on executive and other verbally mediated cognitive measures early in the disease course may simply reflect these language deficits. Indeed, in a recent study examining cognitive predictors of spontaneous speech, executive abilities predicted words per minute in bvFTD, whereas grammatic measures predicted this ability in patients with nfvPPA (Gunawardena et al., 2010).

It is therefore not surprising that studies applying language based measures such as letter fluency report executive deficits in nfvPPA and svPPA. Interestingly, an early meta-analysis showed that executive measures such as FAS and Similarities that are heavily mediated by verbal functions tended to be impaired, whereas cognitive flexibility as measured by the Wisconsin Card Sort Test (WCST) was comparable across nfvPPA and healthy controls (Zakzanis, 1999). The integrity of nonverbal executive abilities was supported in the first relatively large study of PPA (primarily nfvPPA) versus bvFTD and AD in which subjects with PPA performed comparably to healthy controls and better than patients with AD or bvFTD on a nonverbal test of sorting and shifting (Wicklund et al., 2004). In contrast, a number of other studies have reported severe executive deficits in nfvPPA as measured by the WCST or Trail Making Test Part B (Knibb et al., 2009; Nestor et al., 2003). Further, the executive problems in subjects with nfvPPA have been sometimes shown to be of a greater magnitude than in bvFTD (Heidler-Gary et al., 2007). Variable disease severity is certain to contribute to the discrepancy across studies, and it is also likely that cognitive profiles differ on a case by case basis.

While many studies have examined neuropsychological functioning (Hodges et al., 1999) and correlates of executive abilities in svPPA, (Kramer et al., 2007; Marra et al., 2007), very few studies have directly examined executive functioning in svPPA compared to healthy controls using nonverbal tasks, and those that have demonstrate mixed results. For example,

patients with svPPA have been shown to have normal performance on multiple measures of executive functioning including the WCST and tasks of divided attention, whereas Stroop interference has been shown to be impaired (Perry & Hodges, 2000). Separate work has documented that all PPA subtypes are impaired in comparison to healthy controls as measured by number of lines per minute on a modified Trail Making Test (Gorno-Tempini et al., 2004).

To our knowledge, executive function has not been studied specifically in lvPPA given its relatively recent categorization as a PPA subtype. However, as a phonological short-term memory deficit has been suggested to be the core impairment that underlies most language deficits in lvPPA (Gorno-Tempini et al., 2008), this group may be expected to perform poorly on higher-level executive tasks that place demands on verbal working memory. In contrast, nonverbal executive tasks such as design fluency or tests of concept formation might be expected to be relatively preserved. Future work in this area is needed to address these diagnostic issues.

SOCIAL COGNITION IN THE DIAGNOSIS OF FTD SYNDROMES

Impairment in social cognition is a hallmark feature of bvFTD. Consider the pathologically confirmed case of Dr. A, described by Narvid and colleagues (2009), who began to evidence remarkable changes in interpersonal conduct and personality around the age of 62 in the context of relatively preserved performance on classic tests of executive functioning (Narvid et al., 2009). Once a successful surgeon, Dr. A was forced to retire due to a lack of responsiveness to the requests of colleagues in his practice. He became more aloof in his personal life, and demonstrated strange behaviors such as leaving his three year old grandchildren unattended at night, walking out of his son's wedding without clear reason or explanation, and making inappropriate sexual advances to women on multiple occasions. These changes in interpersonal behavior and personality are a core aspect of bvFTD, are commonly seen in svPPA, and have come to be conceptualized as fundamental deficits in social cognition.

Social cognition has been described as the means by which we make sense of ourselves in relation to others and the environment in which we live (Fiske, 1993), or more broadly, as any cognitive process that is engaged to understand or interpret the self in relation to others (Forbes & Grafman, 2010). While an in-depth discussion of the construct of social cognition (Sollberger et al., 2010) is beyond the scope of this paper, it is important to note that social cognitive abilities consist of a number of converging implicit and explicit processes that form the basis of the complex and dynamic set of behaviors and mutually shared expectations that enable individuals to successfully interact with one another across a range of different scenarios and environments. Social cognition is thus generally studied in terms of a number of component processes that are associated with each other and in some cases influence one another (Eslinger et al., 2011). These processes can be broken down and conceptualized as functions pertaining to the perception of social and emotional signals (e.g., emotion recognition through facial and vocal stimuli, comprehension of sarcasm), the evaluation of personal relevance of social and emotional signals (e.g., sensitivity to negative consequences of social decisions), social knowledge awareness (e.g., semantic knowledge

for social norms), behavior / personality (e.g., empathy), and higher order social information processing (e.g., Theory of Mind; TOM, moral reasoning) (Shany-Ur & Rankin, 2012). TOM, the ability to attribute independent mental and emotional states to another individual, is perhaps the social cognitive ability examined most frequently through formal testing, and can be broken down into cognitive and affective components (Baron-Cohen et al., 1999). Cognitive TOM, assessed with false belief tasks, examines one's ability to appreciate the difference between his or her knowledge and the knowledge of another individual. This form of cognitive understanding is thought to be a prerequisite for affective TOM, or the ability to empathize with another's mental state, typically measured with a faux pas task.

Compromise to any number of component abilities may alter the way in which an individual perceives or engages in social interactions, producing behavior that is judged to be abnormal, eccentric, inappropriate, or offensive. BvFTD is characterized by early and pervasive changes in brain regions that have been shown to be critical for social cognitive processes including the orbitofrontal cortex (Forbes & Grafman, 2010), ventromedial PFC (Lewis et al., 2011), insular cortex (Bernhardt & Singer, 2012) and anterior temporal lobes (Ross & Olson, 2010; Wong et al., 2012; Zahn et al., 2007). Right-sided networks that are especially vulnerable in bvFTD, appear to be particularly important for social cognition (Eslinger et al., 2011). Moreover, it has been suggested that von Economo neurons, specific neurons that are over-represented in the right anterior cingulate and fronto-insular cortex, and that are severely and selectively damaged in FTD, may be specialized for social cognition (Seeley et al., 2005). These morphologically unique and phylogenetically recent neurons offer an explanation as to why highly evolved capacities such as self-awareness and social cognition deteriorate early in FTD with the compromise of brain regions traditionally considered to be more primitive (Seeley et al., 2012).

Social cognitive profile of the behavioral variant FTD (bvFTD)

Dozens of case studies and between group comparisons have provided empirical support for the clinically described social cognitive deficits in bvFTD including impaired ability to process facial emotions (Cavallo et al., 2011; Gleichgerrcht et al., 2002; Miller et al., 2012; Torralva et al., 2009), detect socially inappropriate speech (Gleichgerrcht et al., 2010; C. Gregory et al., 2002; Torralva et al., 2009), adopt the perspective of another person (Adenzato et al., 2010; Eslinger et al., 2011; C. Gregory et al., 2002; Lough et al., 2001; Lough & Hodges, 2002), solve social dilemmas (Eslinger et al., 2007), perceive sarcasm (Kosmidis et al., 2008), or react to fearful or sad stimuli (Sturm et al., 2006; Werner et al., 2007).

There is some evidence that social cognitive deficits may in part reflect executive dysfunction more generally (Eslinger et al., 2011; Ybarra & Winkielman, 2012). For example, Eslinger and colleagues (2011) examined several aspects of social cognition in bvFTD including the ability to solve social dilemmas by completing a cartoon story with a socially appropriate ending, as well as empathy, TOM, and mental flexibility. The latter construct, conceived of as a classic executive function, has been posited to be an important component of the "social executor framework" model of social cognition. Indeed, the ability

to solve social dilemmas, while correlated with empathy and TOM, was best predicted by cognitive flexibility.

However, there is also evidence that changes in social cognition precede and outweigh executive dysfunction (Eslinger et al., 2007; Libon, et al., 2007) corresponding to the early compromise of orbitofrontal, ventromedial PFC and anterior temporal lobe areas prior to changes in dorsolateral PFC (Seeley et al., 2008). This dissociation has been highlighted in multiple case studies (Lough et al., 2001; Lough & Hodges, 2002) in which cognitive deficits appear to be subtle on intellectual testing and classic executive measures, yet severely impaired performance arises on tests of social cognition such as TOM and detection of faux-pas arguing for inclusion of such measures in a diagnostic assessment of bvFTD. In fact, recent recommendations for diagnostic batteries emphasize formal evaluation of social cognition via brief batteries that include assessment of abilities such as emotion recognition and TOM (Sarazin et al., 2012). For example, the Social Cognition and Emotional Assessment (SEA) and the mini-SEA have been shown to have good discriminability between bvFTD and other conditions such as AD and Major Depressive Disorder (Bertoux et al., 2011), and the Executive and Social Cognition Battery detected early deficits in mild bvFTD as compared to healthy controls when performance on classic executive tests was normal (ESCB; Gleichgerrcht et al., 2010; Torralva et al., 2009). Thus, while correlated with executive deficits, social cognitive impairments appear to be independent of executive deficits to some extent (Torralva et al., 2007), and frequent in the early stages of bvFTD.

Like deficits in executive functioning, social cognitive impairment is not specific to bvFTD, however. Multiple studies have demonstrated impaired social cognition in AD, including deficits in moral judgments and decision making (Torralva et al., 2000) and deficient reasoning regarding psychological versus physical causation (Verdon et al., 2007). Additionally, other patient populations including PSP, VaD and PD have been reported to have social cognitive changes to varying degrees (Allain et al., 2011; Bodden et al., 2010; Ghosh et al., 2012; Kawamura et al., 2007; Roca et al., 2010; Yu et al., 2012). However, a recent study directly comparing dementia groups revealed more severe social cognitive deficits in bvFTD as compared to non-FTD groups. Specifically, while individuals with PSP and VaD evidenced TOM deficits comparable to those with bvFTD, the latter group had greater difficulty detecting insincere speech (Shany-Ur et al., 2012).

Moreover, studies of emotion recognition, an ability that has been posited to contribute to social cognition more broadly (Petroni et al., 2011; Rosen et al., 2002; Rosen et al., 2004) have generally, but not always, supported a distinction between AD and bvFTD in this regard. While patients with bvFTD have intact recognition of familiar faces and preserved ability to match unfamiliar faces, they have been reported to be more impaired than patients with AD in detecting emotions through both facial expressions and voices (Keane et al., 2002; Kipps et al., 2009; Lavenu et al., 1999;), with some evidence that recognition of negative emotions is most impaired (Kumfor et al., 2011; Werner et al., 2007).

Case studies underscore the presence of deficits in bvFTD and a relative preservation of social functioning into the moderate stages of the AD (Lough et al., 2001; Sabat & Gladstone, 2010; Sabat & Lee, 2010). Most studies that have documented similar social

cognitive abilities in FTD and AD, including facial emotion processing (Bediou et al., 2009; Cavallo et al., 2011), down-regulating emotion following exposure to an aversive acoustic stimulus (Goodkind et al., 2010), and completion of stories that have socially dependent endings (Cavallo et al., 2011) have included multiple FTD subtypes in the sample and/or have had very small sample sizes, limiting their ability to detect differences between these groups. Moreover, social cognitive deficits in AD are generally accounted for by global cognitive decline (Shany-Ur & Rankin, 2012).

However, recent work continues to challenge the idea that specific aspects of social cognition are impaired in bvFTD as opposed to AD (Freedman et al., 2012; Miller et al., 2012), and has raised the possibility that non-social processes underlie social cognitive deficits (Fernandez-Duque et al., 2009). Moreover, it is important to emphasize that few if any autopsy confirmed studies have directly compared social cognitive abilities in bvFTD versus AD. Thus, individuals with relatively intact social cognition may have been misdiagnosed as AD and vice versa. While the majority of cases with early social cognitive deficits are likely to have bvFTD given the selective vulnerability of the OFC, vmPFC, and anterior temporal lobes in this disease and their importance for social cognition, individual cases of atypical AD can certainly present in this fashion, and even cases of typical AD may perform poorly on social cognitive tasks secondary to more global cognitive deficits.

Social cognitive profile of the language variant FTD (PPAs)

Although social cognitive features are the core of the bvFTD presentation, there is growing evidence that certain aspects of social cognition, emotional functioning, and behavior are quite frequently impaired early in the course of the svPPA (Kumfor & Piguet, 2012). In fact, similar deficits in social awareness have been reported across bvFTD and svPPA with regard to empathy, social withdrawal, and interest in family that set these groups apart from patients with AD (Bozeat et al., 2000). Even if such symptoms are not part of the initial presentation in PPA, they often arise over time. For example, in a group of individuals with mixed PPA subtypes, scores on the Frontal Behavior Inventory were in the normal range at baseline evaluation, but were comparable to a group of bvFTD after three years. Among other symptoms, there was an increase in socially undesirable behaviors including personal neglect, inappropriateness, and aggression (Marczinski et al., 2004).

While few studies have formally evaluated social cognition through experimental paradigms in PPA, a series of case studies exist and several larger studies based on retrospective chart reviews document notable early deficits in social cognition in svPPA, particularly in cases with primarily right hemisphere atrophy (Edwards-Lee et al., 1997; Gorno-Tempini et al., 2004; Perry et al., 2001; Sollberger et al., 2010; S. A. Thompson et al., 2003). For example, Sollberger et al. (2010) described a case of right-sided temporal lobe atrophy who presented with changes in interpersonal behaviors including reduced eye contact and poor respect for personal boundaries that occurred at approximately the same time as changes in nonverbal semantic knowledge. Similarly, Gorno-Tempini and colleagues (2004) described another case with markedly decreased empathy and a loss of social graces. Formal testing demonstrated mildly impaired ability to recognize negative emotions with preserved recognition of happiness; and severely impaired perspective taking and empathic concern.

These reports are consistent with that of Perry and colleagues (2001) who demonstrated severely impaired recognition of emotions based on facial expression and voices, and reduced empathy and interpersonal skills in another case of primarily right-sided temporal lobe atrophy. Moreover, in a retrospective review of 47 patients, 11 with right-sided temporal atrophy and 36 with left-sided atrophy, Thompson and colleagues (2003) found that change in social behavior was the most common behavioral symptom at presentation in the right-sided group, with 64% of patients displaying instances of rude, tactless, awkward, uncomfortable, or disinhibited behavior. In contrast, depression was the most common affective or social symptom in patients with left sided temporal atrophy, or svPPA. However, it has also been shown that after approximately 3–4 years, individuals with left-sided atrophy develop social and behavioral abnormalities that are comparable to those seen early in right-sided cases (Seeley et al., 2005).

Several studies have directly examined social cognitive abilities in PPA (Eslinger et al., 2007; Rosen et al., 2002; Rosen et al., 2004). Eslinger and colleagues (2007) found mild social cognitive deficits in a mixed group of aphasia cases in areas including empathy based on informant report, as well as TOM, and the ability to resolve social dilemmas in a series of cartoon stories. While these abilities were impaired in comparison to healthy controls, they were less impaired than in the bvFTD group however. Rosen and colleagues (2002) have shown in two separate studies that both bvFTD and svPPA are impaired at recognizing facial emotions, with the svPPA group displaying difficulty with negative emotions including sadness, anger, and fear in contrast to the bvFTD group who had difficulty with both negative and positive emotions. Primary deficits in emotion processing in svPPA have been supported by recent work that accounts for language and perceptual impairments (Miller et al., 2012) and other work that has documented deficits in the perception of emotion in unfamiliar music (Hsieh et al., 2012). Moreover, while both bvFTD and svPPA demonstrate more severe personality changes than patients with AD, svPPA has been associated with a marked increase in coldness with loss of social affiliation and nurturance as compared to bvFTD which has been associated with an increase in submissiveness (Rankin et al., 2003). This discrepancy was interpreted to be consistent with patterns of animal behavior in lesion based studies ablating frontal versus anterior temporal regions, with the former lesions resulting in passive behavior and the latter in more forceful rejection of maternal roles and sometimes aggressive behavior (Franzen & Myers, 1973).

While nvPPA and lvPPA may be accompanied by behavioral symptoms such as apathy, agitation, depression, or anxiety (Rohrer & Warren, 2010), individuals with these forms of PPA have been reported to have fewer socioemotional symptoms than those with svPPA (Rosen et al., 2006). However, the literature on social cognitive changes in nvPPA and lvPPA subtypes is scarce (Kumfor & Piguet, 2012). Recently, Kumfor and colleagues (2011) conducted the first study of facial emotion processing specifically in individuals with nvPPA, finding that this group along with bvFTD and svFTD had deficits in identifying negative emotions. However, both the bvFTD and nvFTD groups improved performance when the intensity of emotional expression was increased suggesting that inattention may underlie deficits in emotion recognition. No such improvement was seen in svPPA, again suggesting a primary deficit in emotion processing. Additional work using nonverbal

methodologies is required to more fully characterize the integrity of social cognition in nvPPA and lvPPA.

CHALLENGES TO THE DIAGNOSIS OF FTD

FTD and other degenerative diseases such as AD are characterized by progressive cognitive and behavioral changes that begin relatively focally and eventually become more global in nature. As such, individuals who present in the moderate stages of disease are often difficult to differentially diagnose. Moreover, despite the prototypical presentations of these diseases, there are atypical presentations of each disease that can obscure differential diagnosis. Performance profiles, rather than absolute levels of performance, provide information regarding the underlying distribution of neuropathology, and thus the likely etiology of cognitive and functional changes (Libon, et al., 2007; Pachana et al., 1996).

Moreover, pathologically or genetically confirmed cases of FTD and AD are critical in determining the extent to which specific cognitive profiles are characteristic or predictive of a specific disease. For example, we know that there is a subset of patients with pathologically verified AD who present primarily with behavioral changes and/or a pattern of executive dysfunction on neuropsychological testing (Johnson et al., 1999; Mez et al., in press; Woodward et al., 2010). An early study by Johnson and colleagues demonstrated that this subgroup has disproportionate involvement of the prefrontal cortex at autopsy as compared to patients presenting with the classic amnesic profile (Johnson et al., 1999). Such cases of “frontal variant” AD can be difficult to distinguish from FTD (Woodward et al., 2010). Conversely, individuals with the progranulin (PGRN) mutation for FTD can present with early memory problems, extrapyramidal signs, or visual hallucinations that point clinicians to diagnoses of AD or other degenerative diseases such as dementia with Lewy Bodies (Le Ber et al., 2008). Thus, although we have traditionally ruled out FTD based on the presence of an amnesic syndrome, it is becoming increasingly apparent that an “AD-like” profile is not incompatible with FTD pathology (Hornberger et al., 2010). As such, one must use caution when relying on clinically defined groups to determine differential patterns of cognitive functioning across dementia syndromes. Ideally, autopsy-proven studies are required to avoid circular reasoning, and to comprehensively characterize the cognitive profiles of various diseases.

Acknowledgments

While preparing this manuscript, MH was receiving a scholarship from the Polish Ministry of Science and Higher Education. SC is supported by a Paul B. Beeson Career Development Award through NIA and the American Federation of Aging Research.

REFERENCES

- Adenzato M, Cavallo M, Enrici I. Theory of mind ability in the behavioural variant of frontotemporal dementia: an analysis of the neural, cognitive, and social levels. *Neuropsychologia*. 2010; 48(1):2–12. [PubMed: 19666039]
- Adlam AL, Patterson K, Rogers TT, Nestor PJ, Salmon CH, Acosta-Cabrero J, Hodges JR. Semantic dementia and fluent primary progressive aphasia: two sides of the same coin? *Brain*. 2006; 129:3066–3080. [PubMed: 17071925]

- Appell J, Kertesz A, Fisman M. A study of language functioning in Alzheimer patients. *Brain and Language*. 1982; 17:73–91. [PubMed: 7139272]
- Alberici A, Gobbo C, Panzacchi A, Nicosia F, Ghidoni R, Benussi L, Binetti G. Frontotemporal dementia: impact of P301L tau mutation on a healthy carrier. *Journal of Neurology, Neurosurgery & Psychiatry*. 2004; 75:1607–1610.
- Allain P, Havet-Thomassin V, Verny C, Gohier B, Lancelot C, Besnard J, Le Gal D. Evidence for deficits on different components of theory of mind in Huntington's disease. *Neuropsychology*. 2011; 25:741–751. [PubMed: 21728429]
- Ash S, McMillan C, Gunawardena D, Avants B, Morgan B, Khan A, Grossman M. Speech errors in progressive non-fluent aphasia. *Brain and Language*. 2010; 113:13–20. [PubMed: 20074786]
- Ash S, Moore P, Antani S, McCawley G, Work M, Grossman M. Trying to tell a tale: discourse impairments in progressive aphasia and frontotemporal dementia. *Neurology*. 2006; 66:1405–1413. [PubMed: 16682675]
- Baldo JV, Schwartz S, Wilkins D, Dronkers NF. Role of frontal versus temporal cortex in verbal fluency as revealed by voxel-based lesion symptom mapping. *Journal of the International Neuropsychological Society*. 2006; 12:896–900. [PubMed: 17064451]
- Baron-Cohen S, Ring HA, Wheelwright S, Bullmore ET, Brammer MJ, Simmons A, Williams S. Social intelligence in the normal and autistic brain: an fMRI study. *European Journal of Neuroscience*. 1999; 11:1891–1898. [PubMed: 10336657]
- Bediou B, Ryff I, Mercier B, Millierey M, Henaff MA, D'Amato T, Calder A. Impaired social cognition in mild Alzheimer disease. *Journal of Geriatric Psychiatry and Neurology*. 2009; 22:130–140. [PubMed: 19321881]
- Beeke S, Wilkinson R, Maxim J. Exploring aphasic grammar. 2: Do language testing and conversation tell a similar story? *Clinical Linguistics and Phonetics*. 2003; 17:109–134. [PubMed: 12762207]
- Bernhardt BC, Singer T. The neural basis of empathy. *Annual Review of Neuroscience*. 2012; 35:1–23.
- Bertoux M, Delavest M, de Souza LC, Funkiewiez A, Lepine JP, Fossati P, Sarazin M. Social Cognition and Emotional Assessment differentiates frontotemporal dementia from depression. *Journal of Neurology, Neurosurgery & Psychiatry*. 2011; 83:411–416.
- Bigio EH, Lipton AM, White CL 3rd, Dickson DW, Hirano A. Frontotemporal and motor neurone degeneration with neurofilament inclusion bodies: additional evidence for overlap between FTD and ALS. *Neuropathology and Applied Neurobiology*. 2003; 29:239–253. [PubMed: 12787321]
- Bodden ME, Mollenhauer B, Trenkwalder C, Cabanel N, Eggert KM, Unger MM, Kalbe E. Affective and cognitive Theory of Mind in patients with parkinson's disease. *Parkinsonism and Related Disorders*. 2010; 16:466–470. [PubMed: 20538499]
- Blair M, Kertesz A, McMonagle P, Davidson W, Bodi N. Quantitative and qualitative analyses of clock drawing in frontotemporal dementia and Alzheimer's disease. *Journal of the International Neuropsychological Society*. 2006; 12:159–165. [PubMed: 16573849]
- Blair M, Marczyński CA, Davis-Faroque N, Kertesz A. A longitudinal study of language decline in Alzheimer's disease and frontotemporal dementia. *Journal of the International Neuropsychological Society*. 2007; 13:237–245. [PubMed: 17286881]
- Bozeat S, Gregory CA, Ralph MA, Hodges JR. Which neuropsychiatric and behavioural features distinguish frontal and temporal variants of frontotemporal dementia from Alzheimer's disease? *Journal of Neurology, Neurosurgery & Psychiatry*. 2000; 69:178–186.
- Brun A. Frontal lobe degeneration of non-Alzheimer type. I. *Neuropathology*. *Archives of Gerontology & Geriatrics*. 1987; 6:193–208.
- Brun A, Englund E, Gustafson L, Passant U, Mann DMA, Neary D, Snowden JS. Clinical and neuropathological criteria for frontotemporal dementia. The Lund and Manchester Groups. *Journal of Neurology, Neurosurgery & Psychiatry*. 1994; 57:416–418.
- Budd MA, Kortte K, Cloutman L, Newhart M, Gottesman RF, Davis C, Hillis AE. The nature of naming errors in primary progressive aphasia versus acute post-stroke aphasia. *Neuropsychology*. 2010; 24:581–589. [PubMed: 20804246]

- Cahn-Weiner DA, Sullivan EV, Shear PK, Fama R, Lim KO, Yesavage JA, Pfefferbaum A. Brain structural and cognitive correlates of clock drawing performance in Alzheimer's disease. *Journal of the International Neuropsychological Society*. 1999; 5:502–509. [PubMed: 10561930]
- Caine D, Breen N, Patterson K. Emergence and progression of 'non-semantic' deficits in semantic dementia. *Cortex*. 2009; 45:483–494. [PubMed: 19231477]
- Cairns NJ, Bigio EH, Mackenzie IR, Neumann M, Lee VM, Hatanpaa KJ, Mann DM. Neuropathologic diagnostic and nosologic criteria for frontotemporal lobar degeneration: consensus of the Consortium for Frontotemporal Lobar Degeneration. *Acta Neuropathologica (Berlin)*. 2007; 114:5–22. [PubMed: 17579875]
- Carey CL, Woods SP, Damon J, Halabi C, Dean D, Delis DC, Kramer JH. Discriminant validity and neuroanatomical correlates of rule monitoring in frontotemporal dementia and Alzheimer's disease. *Neuropsychologia*. 2008; 46:1081–1087. [PubMed: 18093623]
- Carlin D, Bonerba J, Phipps M, Alexander G, Shapiro M, Grafman J. Planning impairments in frontal lobe dementia and frontal lobe lesion patients. *Neuropsychologia*. 2000; 38:655–665. [PubMed: 10689042]
- Cavallo M, Enrici I, Adenzato M. The comprehension of social situations in a small group of patients with frontotemporal dementia and Alzheimer's disease. *Acta Neuropsychologica*. 2011; 9:167–176.
- Chertkow H, Bub D. Semantic memory loss in dementia of Alzheimer's type. What do various measures measure? *Brain*. 1990; 113:397–417. [PubMed: 2328410]
- Chertkow H, Whatmough C, Saumier D, Duong A. Cognitive neuroscience studies of semantic memory in Alzheimer's disease. *Progress in Brain Research*. 2008; 169:393–407. [PubMed: 18394489]
- Clark DG, Charuvastra A, Miller BL, Shapira JS, Mendez MF. Fluent versus nonfluent primary progressive aphasia: a comparison of clinical and functional neuroimaging features. *Brain and Language*. 2005; 94:54–60. [PubMed: 15896383]
- Collette F, Amieva H, Adam S, Hogge M, Van der Linden M, Fabrigoule C, Salmon E. Comparison of inhibitory functioning in mild Alzheimer's disease and frontotemporal dementia. *Cortex*. 2007; 43:866–874. [PubMed: 17941345]
- Cosentino S, Chute D, Libon D, Moore P, Grossman M. How does the brain support script comprehension?. A study of executive processes and semantic knowledge in dementia. *Neuropsychology*. 2006; 20:307–318. [PubMed: 16719624]
- d'Honinchtun P, Pillon A. Verb comprehension and naming in frontotemporal degeneration: the role of the static depiction of actions. *Cortex*. 2008; 44:834–847. [PubMed: 18489963]
- Diehl J, Kurz A. Frontotemporal dementia: patient characteristics, cognition, and behaviour. *International Journal of Geriatric Psychiatry*. 2002; 17(10):914–918. [PubMed: 12325050]
- Duffy JR, Peach RK, Strand EA. Progressive apraxia of speech as a sign of motor neuron disease. *American Journal Speech-Language Pathology*. 2007; 16:198–208.
- Edwards-Lee T, Miller BL, Benson DF, Cummings JL, Russell GL, Boone K, Mena I. The temporal variant of frontotemporal dementia. *Brain*. 1997; 120:1027–1040. [PubMed: 9217686]
- Eslinger PJ, Moore P, Anderson C, Grossman M. Social cognition, executive functioning, and neuroimaging correlates of empathic deficits in frontotemporal dementia. *Journal of Neuropsychiatry and Clinical Neuroscience*. 2011; 23:74–82.
- Eslinger PJ, Moore P, Troiani V, Antani S, Cross K, Kwok S, Grossman M. Oops! Resolving social dilemmas in frontotemporal dementia. *Journal of Neurology, Neurosurgery & Psychiatry*. 2007; 78:457–460.
- Ferman TJ, McRae CA, Arvanitakis Z, Tsuboi Y, Vo A, Wszolek ZK. Early and pre-symptomatic neuropsychological dysfunction in the PPND family with the N279K tau mutation. *Parkinsonism and Related Disorders*. 2003; 9:265–270. [PubMed: 12781592]
- Fernandez-Duque D, Baird JA, Black SE. False-belief understanding in frontotemporal dementia and Alzheimer's disease. *Journal of Clinical and Experimental Neuropsychology*. 2009; 31:489–497. [PubMed: 18686116]
- Forbes CE, Grafman J. The role of the human prefrontal cortex in social cognition and moral judgment. *Annu Rev Neurosci*. 2010; 33:299–324. [PubMed: 20350167]

- Franzen EA, Myers RE. Neural control of social behavior: prefrontal and anterior temporal cortex. *Neuropsychologia*. 1973; 11:141–157. [PubMed: 4197348]
- Freedman M, Binns MA, Black SE, Murphy C, Stuss DT. Theory of Mind and Recognition of Facial Emotion in Dementia: Challenge to Current Concepts. *Alzheimer Disease and Associated Disorders*. 2012 Mar 8. [Epub ahead of print].
- Fushimi T, Komori K, Ikeda M, Lambon Ralph MA, Patterson K. The association between semantic dementia and surface dyslexia in Japanese. *Neuropsychologia*. 2009; 47:1061–1068. [PubMed: 19162051]
- Gazzaley A, Sheridan MA, Cooney JW, D’Esposito M. Age-related deficits in component processes of working memory. *Neuropsychology*. 2007; 21:532–539. [PubMed: 17784801]
- Ghosh BC, Calder AJ, Peers PV, Lawrence AD, Acosta-Cabronero J, Pereira JM, Rowe JB. Social cognitive deficits and their neural correlates in progressive supranuclear palsy. *Brain*. 2012; 135:2089–2102. [PubMed: 22637582]
- Giovannetti T, Lamar M, Cloud BS, Swenson R, Fein D, Kaplan E, Libon DJ. Different underlying mechanisms for deficits in concept formation in dementia. *Archives of Clinical Neuropsychology*. 2001; 16:547–560. [PubMed: 14590153]
- Gleichgerrcht E, Torralva T, Roca M, Manes F. Utility of an abbreviated version of the executive and social cognition battery in the detection of executive deficits in early behavioral variant frontotemporal dementia patients. *Journal of the International Neuropsychological Society*. 2010; 16:687–694. [PubMed: 20398437]
- Goll JC, Crutch SJ, Loo JH, Rohrer JD, Frost C, Bamiou DE, Warren JD. Non-verbal sound processing in the primary progressive aphasia. *Brain*. 2010; 133:272–285. [PubMed: 19797352]
- Goodglass, H.; Kaplan, E.; Barresi, B. *Boston Diagnostic Aphasia Examination*. 3rd edition. Lutz, Florida: PAR; 2001.
- Goodkind MS, Gyurak A, McCarthy M, Miller BL, Levenson RW. Emotion regulation deficits in frontotemporal lobar degeneration and Alzheimer’s disease. *Psychology and Aging*. 2010; 25:30–37. [PubMed: 20230125]
- Gorno-Tempini ML, Brambati SM, Ginex V, Ogar J, Dronkers NF, Marcone A, Miller BL. The logopenic/phonological variant of primary progressive aphasia. *Neurology*. 2008; 71:1227–1234. [PubMed: 18633132]
- Gorno-Tempini ML, Dronkers NF, Rankin KP, Ogar JM, Phengrasamy L, Rosen HJ, Miller BL. Cognition and anatomy in three variants of primary progressive aphasia. *Annals of Neurology*. 2004; 55:335–346. [PubMed: 14991811]
- Gorno-Tempini ML, Hillis AE, Weintraub S, Kertesz A, Mendez M, Cappa SF, Grossman M. Classification of primary progressive aphasia and its variants. *Neurology*. 2011; 76:1006–1014. [PubMed: 21325651]
- Graham NL, Patterson K, Hodges JR. When more yields less: speaking and writing deficits in nonfluent progressive aphasia. *Neurocase*. 2004; 10:141–155. [PubMed: 15788253]
- Gregory C, Lough S, Stone V, Erzincinoglu S, Martin L, Baron-Cohen S, Hodges JR. Theory of mind in patients with frontal variant frontotemporal dementia and Alzheimer’s disease: theoretical and practical implications. *Brain*. 2002; 125:752–764. [PubMed: 11912109]
- Gregory CA, Hodges JR. Clinical features of frontal lobe dementia in comparison to Alzheimer’s disease. *Journal of Neural Transmission. Supplementum*. 1996; 47:103–123.
- Grossman M. Primary progressive aphasia: clinicopathological correlations. *Nature Review. Neurology*. 2010; 6:88–97.
- Grossman M, Libon DJ, Forman MS, Massimo L, Wood E, Moore P, Trojanowski JQ. Distinct antemortem profiles in patients with pathologically defined frontotemporal dementia. *Archives of Neurology*. 2007; 64:1601–1609. [PubMed: 17998442]
- Grossman M, Mickanin J, Onishi K, Hughes E, D’Esposito M, Ding XS, Reivich M. Progressive non-fluent aphasia: Language, cognitive and PET measures contrasted with probable Alzheimer’s disease. *Journal of Cognitive Neuroscience*. 1996; 8:135–154. [PubMed: 23971420]
- Grossman M, Rhee J, Moore P. Sentence processing in frontotemporal dementia. *Cortex*. 2005; 41:764–777. [PubMed: 16353366]

- Gunawardena D, Ash S, McMillan C, Avants B, Gee J, Grossman M. Why are patients with progressive nonfluent aphasia nonfluent? *Neurology*. 2010; 75:588–594. [PubMed: 20713947]
- Harciaiek M, Jodzio K. Neuropsychological differences between frontotemporal dementia and Alzheimer's disease. *Neuropsychology Review*. 2005; 3:131–145. [PubMed: 16328732]
- Harciaiek M, Kertesz A. Longitudinal study of single-word comprehension in semantic dementia: a comparison with primary progressive aphasia and Alzheimer's disease. *Aphasiology*. 2009; 23:606–626.
- Harciaiek M, Kertesz A. Primary progressive aphasias and their contribution to the contemporary knowledge about the brain-language relationship. *Neuropsychology Review*. 2011; 21:271–287. [PubMed: 21809067]
- Harciaiek M, Williamson JB, Biedunkiewicz B, Lichodziejewska-Niemierko M, Debska-Slizien A, Rutkowski B. Risk factors for selective cognitive decline in dialyzed patients with end-stage renal disease: evidence from verbal fluency analysis. *Journal of the International Neuropsychological Society*. 2012; 18:162–167. [PubMed: 22088797]
- Heidler-Gary J, Gottesman R, Newhart M, Chang S, Ken L, Hillis AE. Utility of behavioral versus cognitive measures in differentiating between subtypes of frontotemporal lobar degeneration and Alzheimer's disease. *Dementia and Geriatric Cognitive Disorders*. 2007; 23:184–193. [PubMed: 17220629]
- Hillis AE, Oh S, Ken L. Deterioration of naming nouns versus verbs in primary progressive aphasia. *Annals of Neurology*. 2004; 55:268–275. [PubMed: 14755731]
- Hillis AE, Tuffiash E, Caramazza A. Modality-specific deterioration in naming verbs in nonfluent primary progressive aphasia. *Journal of Cognitive Neuroscience*. 2002; 14:1099–1108. [PubMed: 12419132]
- Hodges, JR. Frontotemporal dementia syndromes. New York: Cambridge University Press; 2007.
- Hodges JR. Clinico-pathological correlations in Frontotemporal dementia: an update on the Cambridge series and review of the literature. *Acta Neuropsychologica*. 2011; 9:177–192.
- Hodges JR, Martinos M, Woollams AM, Patterson K, Adlam AL. Repeat and Point: differentiating semantic dementia from progressive non-fluent aphasia. *Cortex*. 2008; 44:1265–1270. [PubMed: 18761140]
- Hodges JR, Patterson K. Nonfluent progressive aphasia and semantic dementia: a comparative neuropsychological study. *Journal of the International Neuropsychological Society*. 1996; 2:511–524. [PubMed: 9375155]
- Hodges JR, Patterson K. Semantic dementia: a unique clinicopathological syndrome. *Lancet Neurology*. 2007; 6:1004–1014.
- Hodges JR, Patterson K, Oxbury S, Funnell E. Semantic dementia. Progressive fluent aphasia with temporal lobe atrophy. *Brain*. 1992; 115:1783–806. [PubMed: 1486461]
- Hodges JR, Patterson K, Ward R, Garrard P, Bak T, Perry R, Gregory C. The differentiation of semantic dementia and frontal lobe dementia (temporal and frontal variants of frontotemporal dementia) from early Alzheimer's disease: a comparative neuropsychological study. *Neuropsychology*. 1999; 13:31–40. [PubMed: 10067773]
- 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. [PubMed: 20142613]
- Hornberger M, Piguet O, Kipps C, Hodges JR. Executive function in progressive and nonprogressive behavioral variant frontotemporal dementia. *Neurology*. 2008; 71:1481–1488. [PubMed: 18981369]
- Howard, D.; Patterson, K. *Pyramids and palm trees: a test of semantic access from pictures and words*. Bury, St. Edmunds: Thames Valley Test Company; 1992.
- Hsieh S, Hornberger M, Piguet O, Hodges JR. Brain correlates of musical and facial emotion recognition: evidence from the dementias. *Neuropsychologia*. 2012; 50:1814–1822. [PubMed: 22579645]
- Hsiung GY, DeJesus-Hernandez M, Feldman HH, Sengdy P, Bouchard-Kerr P, Dwosh E, Mackenzie IR. Clinical and pathological features of familial frontotemporal dementia caused by C9ORF72 mutation on chromosome 9p. *Brain*. 2012; 135:709–722. [PubMed: 22344582]

- Hu WT, McMillan C, Libon D, Leight S, Forman M, Lee VM, Grossman M. Multimodal predictors for Alzheimer disease in nonfluent primary progressive aphasia. *Neurology*. 2010; 75:595–602. [PubMed: 20713948]
- Huey ED, Goveia EN, Paviol S, Pardini M, Krueger F, Zamboni G, Grafman J. Executive dysfunction in frontotemporal dementia and corticobasal syndrome. *Neurology*. 2009; 72:453–459. [PubMed: 19188577]
- Jefferies E, Lambon Ralph MA, Jones R, Bateman D, Patterson K. Surface dyslexia in semantic dementia: a comparison of the influence of consistency and regularity. *Neurocase*. 2004; 10:290–299. [PubMed: 15788266]
- Johns EK, Phillips NA, Belleville S, Goupil D, Babins L, Kelner N, Chertkow H. Executive functions in frontotemporal dementia and Lewy body dementia. *Neuropsychology*. 2009; 23:765–777. [PubMed: 19899835]
- Johnson JK, Head E, Kim R, Starr A, Cotman CW. Clinical and pathological evidence for a frontal variant of Alzheimer disease. *Archives of Neurology*. 1999; 56:1233–1239. [PubMed: 10520939]
- Josephs KA, Duffy JR. Apraxia of speech and nonfluent aphasia: a new clinical marker for corticobasal degeneration and progressive supranuclear palsy. *Current Opinions in Neurology*. 2008; 21:688–692.
- Josephs KA, Duffy JR, Strand EA, Whitwell JL, Layton KF, Parisi JE, Petersen RC. Clinicopathological and imaging correlates of progressive aphasia and apraxia of speech. *Brain*. 2006; 129:1385–1398. [PubMed: 16613895]
- Julien CL, Thompson JC, Neary D, Snowden JS. Arithmetic knowledge in semantic dementia: is it invariably preserved? *Neuropsychologia*. 2008; 46:2732–2744. [PubMed: 18586284]
- Kashibayashi T, Ikeda M, Komori K, Shinagawa S, Shimizu H, Toyota Y, Tanimukai S. Transition of distinctive symptoms of semantic dementia during longitudinal clinical observation. *Dementia and Geriatric Cognitive Disorders*. 2010; 29:224–232. [PubMed: 20375502]
- Kawamura M, Ichikawa H, Koyama S, Ishihara K. [Amyotrophic lateral sclerosis with dementia-neuropsychological aspect]. *Brain Nerve*. 2007; 59:1083–1091. [PubMed: 17969348]
- Keane J, Calder AJ, Hodges JR, Young AW. Face and emotion processing in frontal variant frontotemporal dementia. *Neuropsychologia*. 2002; 40:655–665. [PubMed: 11792405]
- Kertesz A, Davidson W, McCabe P, Munoz D. Behavioral quantitation is more sensitive than cognitive testing in frontotemporal dementia. *Alzheimer Disease and Associated Disorders*. 2003; 17:223–229. [PubMed: 14657786]
- Kertesz A. *The Western Aphasia Battery-Revised*. New York: Grune & Stratton; 2007.
- Kertesz A. Frontotemporal dementia: a topical review. *Cognitive and Behavioral Neurology*. 2008; 21:127–133. [PubMed: 18797253]
- Kertesz A. Frontotemporal Dementia (FTD) 2011. *Acta Neuropsychologica*. 2011; 9:103–114.
- Kertesz A, Blair M, McMonagle P, Munoz D. The diagnosis and course of frontotemporal dementia. *Alzheimer Disease and Associated Disorders*. 2007; 21:155–163. [PubMed: 17545742]
- Kertesz A, Davidson W, McCabe P. Primary progressive semantic aphasia: a case study. *Journal of the International Neuropsychological Society*. 1998; 4:388–398. [PubMed: 9656612]
- Kertesz A, Davidson W, McCabe P, Munoz D. Behavioral quantitation is more sensitive than cognitive testing in frontotemporal dementia. *Alzheimer Disease and Associated Disorders*. 2003b; 17:223–239. [PubMed: 14657786]
- Kertesz A, Davidson W, McCabe P, Takagi K, Munoz D. Primary progressive aphasia: diagnosis, varieties, evolution. *Journal of the International Neuropsychological Society*. 2003a; 9:710–719. [PubMed: 12901777]
- Kertesz A, Hudson L, Mackenzie IR, Munoz DG. The pathology and nosology of primary progressive aphasia. *Neurology*. 1994; 44:2065–2072. [PubMed: 7969961]
- Kertesz A, Jesso S, Harciaiek M, Blair M, McMonagle P. What is semantic dementia?: a cohort study of diagnostic features and clinical boundaries. *Archives of Neurology*. 2010; 67:483–489. [PubMed: 20385916]
- Kertesz A, Martinez-Lage P, Davidson W, Munoz DG. The corticobasal degeneration syndrome overlaps progressive aphasia and frontotemporal dementia. *Neurology*. 2000; 55:1368–1375. [PubMed: 11087783]

- Kertesz A, McMonagle P, Blair M, Davidson W, Munoz DG. The evolution and pathology of frontotemporal dementia. *Brain*. 2005; 128:1996–2005. [PubMed: 16033782]
- Kertesz A, Munoz DG. Primary progressive aphasia: a review of the neurobiology of a common presentation of Pick complex. *American Journal of Alzheimers Disease and Other Dementias*. 2002; 17:30–36.
- Kipps CM, Mioshi E, Hodges JR. Emotion, social functioning and activities of daily living in frontotemporal dementia. *Neurocase*. 2009; 15:182–189. [PubMed: 19172432]
- Knibb JA, Woollams AM, Hodges JR, Patterson K. Making sense of progressive non-fluent aphasia: an analysis of conversational speech. *Brain*. 2009; 132:2734–2746. [PubMed: 19696033]
- Kosmidis MH, Aretouli E, Bozikas VP, Giannakou M, Ioannidis P. Studying social cognition in patients with schizophrenia and patients with frontotemporal dementia: theory of mind and the perception of sarcasm. *Behavioural Neurology*. 2008; 19:65–69. [PubMed: 18413920]
- Kramer JH, Quitania L, Dean D, Neuhaus J, Rosen HJ, Halabi C, Miller BL. Magnetic resonance imaging correlates of set shifting. *Journal of the International Neuropsychological Society*. 2007; 13:386–392. [PubMed: 17445286]
- Krueger F, Rostami E, Huey ED, Snyder A, Grafman J. Evidence of an inferior total-order planning strategy in patients with frontotemporal dementia. *Neurocase*. 2007; 13:426–437. [PubMed: 18781442]
- Kumfor F, Miller L, Lah S, Hsieh S, Savage S, Hodges JR, Piguet O. Are you really angry? The effect of intensity on facial emotion recognition in frontotemporal dementia. *Social Neuroscience*. 2011; 6:502–514. [PubMed: 21957889]
- Kumfor F, Piguet O. Disturbance of emotion processing in frontotemporal dementia: a synthesis of cognitive and neuroimaging findings. *Neuropsychology Review*. 2012; 22:280–297. [PubMed: 22577002]
- Laisney M, Matuszewski V, Mezenge F, Belliard S, de la Sayette V, Eustache F, Desgranges B. The underlying mechanisms of verbal fluency deficit in frontotemporal dementia and semantic dementia. *Journal of Neurology*. 2009; 256:1083–1094. [PubMed: 19363702]
- Lamar M, Libon DJ, Ashley AV, Lah JJ, Levey AI, Goldstein FC. The impact of vascular comorbidities on qualitative error analysis of executive impairment in Alzheimer's disease. *Journal of the International Neuropsychological Society*. 2010a; 16:77–83. [PubMed: 19835657]
- Lamar M, Price CC, Giovannetti T, Swenson R, Libon DJ. The dysexecutive syndrome associated with ischaemic vascular disease and related subcortical neuropathology: a Boston process approach. *Behavioural Neurology*. 2010b; 22:53–62. [PubMed: 20543459]
- Lavenu I, Pasquier F, Lebert F, Petit H, Van der Linden M. Perception of emotion in frontotemporal dementia and Alzheimer disease. *Alzheimer Dis Assoc Disord*. 1999; 13(2):96–101. [PubMed: 10372953]
- Le Ber I, Camuzat A, Hannequin D, Pasquier F, Guedj E, Rovelet-Lecrux A, Brice A. Phenotype variability in progranulin mutation carriers: a clinical, neuropsychological, imaging and genetic study. *Brain*. 2008; 131:732–746. [PubMed: 18245784]
- Lewis PA, Rezaie R, Brown R, Roberts N, Dunbar RI. Ventromedial prefrontal volume predicts understanding of others and social network size. *Neuroimage*. 2011; 57:1624–1629. [PubMed: 21616156]
- Libon DJ, Massimo L, Moore P, Coslett HB, Chatterjee A, Aguirre GK, Grossman M. Screening for frontotemporal dementias and Alzheimer's disease with the Philadelphia Brief Assessment of Cognition: a preliminary analysis. *Dementia and Geriatric Cognitive Disorders*. 2007; 24:441–447. [PubMed: 17971665]
- Libon DJ, Xie SX, Moore P, Farmer J, Antani S, McCawley G, Grossman M. Patterns of neuropsychological impairment in frontotemporal dementia. *Neurology*. 2007; 68:369–375. [PubMed: 17261685]
- Lindau M, Almkvist O, Kushi J, Boone K, Johansson SE, Wahlund LO, Miller BL. First symptoms--frontotemporal dementia versus Alzheimer's disease. *Dementia and Geriatric Cognitive Disorders*. 2000; 11:286–293. [PubMed: 10940680]

- Lopez OL, Hamilton RL, Becker JT, Wisniewski S, Kaufer DI, DeKosky ST. Severity of cognitive impairment and the clinical diagnosis of AD with Lewy bodies. *Neurology*. 2000; 54:1780–1787. [PubMed: 10802784]
- Lough S, Gregory C, Hodges JR. Dissociation of social cognition and executive function in frontal variant frontotemporal dementia. *Neurocase*. 2001; 7:123–130. [PubMed: 11320160]
- Lough S, Hodges JR. Measuring and modifying abnormal social cognition in frontal variant frontotemporal dementia. *Journal of Psychosomatic Research*. 2002; 53:639–646. [PubMed: 12169338]
- Marczinski CA, Davidson W, Kertesz A. A longitudinal study of behavior in frontotemporal dementia and primary progressive aphasia. *Cognitive and Behavioural Neurology*. 2004; 17:185–190.
- Marczinski CA, Kertesz A. Category and letter fluency in semantic dementia, primary progressive aphasia, and Alzheimer's disease. *Brain and Language*. 2006; 97:258–265. [PubMed: 16325251]
- Marra C, Quaranta D, Zinno M, Misciagna S, Bizzarro A, Masullo C, Gainotti G. Clusters of cognitive and behavioral disorders clearly distinguish primary progressive aphasia from frontal lobe dementia, and Alzheimer's disease. *Dementia and Geriatric Cognitive Disorders*. 2007; 24:317–326. [PubMed: 17851236]
- Mathuranath PS, Nestor PJ, Berrios GE, Rakowicz W, Hodges JR. A brief cognitive test battery to differentiate Alzheimer's disease and frontotemporal dementia. *Neurology*. 2000; 55:1613–1620. [PubMed: 11113213]
- Mayberry EJ, Sage K, Lambon Ralph MA. At the edge of semantic space: The breakdown of coherent concepts in semantic dementia is constrained by typicality and severity but not modality. *Journal of Cognitive Neuroscience*. 2011; 23:2240–2251. [PubMed: 21126159]
- McMonagle P, Blair M, Kertesz A. Corticobasal degeneration and progressive aphasia. *Neurology*. 2006; 67:1444–1451. [PubMed: 17060571]
- Mesulam MM. Primary progressive aphasia - differentiation from Alzheimer's disease. *Annals of Neurology*. 1987; 22:533–534. [PubMed: 3324947]
- Mesulam MM. Primary progressive aphasia. *Annals of Neurology*. 2001; 49:425–432. [PubMed: 11310619]
- Mesulam M, Weineke C, Rogalski E, Cobia D, Thompson C, Weintraub S. Quantitative template for subtyping primary progressive aphasia. *Archives of Neurology*. 2009; 66:1545–1551.
- Mesulam M, Wicklund A, Johnson N, Rogalski E, Leger GC, Rademaker A, Bigio EH. Alzheimer and frontotemporal pathology in subsets of primary progressive aphasia. *Annals of Neurology*. 2008; 63:709–719. [PubMed: 18412267]
- Mesulam MM. Primary progressive aphasia--a language-based dementia. *New England Journal of Medicine*. 2003; 349:1535–1542. [PubMed: 14561797]
- Mez J, Cosentino S, Brickman A, Huey E, Manly J, Mayeux R. Dysexecutive versus amnesic Alzheimer's disease subgroups: An analysis of demographic, genetic, and vascular factors in the National Alzheimer's Coordinating Center database. *Alzheimer's disease and Associated Disorders*. (in press).
- Miller LA, Hsieh S, Lah S, Savage S, Hodges JR, Piguet O. One size does not fit all: face emotion processing impairments in semantic dementia, behavioural-variant frontotemporal dementia and Alzheimer's disease are mediated by distinct cognitive deficits. *Behavioural Neurology*. 2012; 25:53–60. [PubMed: 22207423]
- Miyake A, Friedman NP, Emerson MJ, Witzki AH, Howerter A, Wager TD. The unity and diversity of executive functions and their contributions to complex "Frontal Lobe" tasks: a latent variable analysis. *Cognitive Psychology*. 2000; 41:49–100. [PubMed: 10945922]
- Narvid J, Gorno-Tempini ML, Slavotinek A, Dearmond SJ, Cha YH, Miller BL, Rankin K. Of brain and bone: the unusual case of Dr. A. *Neurocase*. 2009; 15:190–205. [PubMed: 20183548]
- Neary D, Snowden JS, Gustafson L, Passant U, Stuss D, Black S, Benson DF. Frontotemporal lobar degeneration: a consensus on clinical diagnostic criteria. *Neurology*. 1998; 51:1546–1554. [PubMed: 9855500]
- Nestor PJ, Graham NL, Fryer TD, Williams GB, Patterson K, Hodges JR. Progressive non-fluent aphasia is associated with hypometabolism centred on the left anterior insula. *Brain*. 2003; 126:2406–2418. [PubMed: 12902311]

- Ogar JM, Dronkers NF, Brambati SM, Miller BL, Gorno-Tempini ML. Progressive nonfluent aphasia and its characteristic motor speech deficits. *Alzheimer Disease and Associated Disorders*. 2007; 21:23–30.
- Ogar J, Slama H, Dronkers N, Amici S, Gorno-Tempini ML. Apraxia of speech: an overview. *Neurocase*. 2005; 11:427–432. [PubMed: 16393756]
- Ogar J, Willock S, Baldo J, Wilkins D, Ludy C, Dronkers N. Clinical and anatomical correlates of apraxia of speech. *Brain and Language*. 2006; 97:343–350. [PubMed: 16516956]
- Pachana NA, Boone KB, Miller BL, Cummings JL, Berman N. Comparison of neuropsychological functioning in Alzheimer's disease and frontotemporal dementia. *Journal of the International Neuropsychological Society*. 1996; 2:505–510. [PubMed: 9375154]
- Patterson K, Graham NL, Lambon-Ralph MA, Hodges JR. Progressive non-fluent aphasia is not a progressive form of non-fluent (post-stroke) aphasia. *Aphasiology*. 2006; 20:1018–1034.
- Peelle JE, Troiani V, Gee J, Moore P, McMillan C, Vesely L, Grossman M. Sentence comprehension and voxel-based morphometry in progressive nonfluent aphasia, semantic dementia, and nonaphasic frontotemporal dementia. *Journal of Neurolinguistics*. 2008; 21:418–432. [PubMed: 19727332]
- Perry RJ, Hodges JR. Differentiating frontal and temporal variant frontotemporal dementia from Alzheimer's disease. *Neurology*. 2000; 54:2277–2284. [PubMed: 10881252]
- Perry RJ, Rosen HR, Kramer JH, Beer JS, Levenson RL, Miller BL. Hemispheric dominance for emotions, empathy and social behaviour: evidence from right and left handers with frontotemporal dementia. *Neurocase*. 2001; 7:145–160. [PubMed: 11320162]
- Petroni A, Canales-Johnson A, Urquina H, Guex R, Hurtado E, Blenkman A, Ibanez A. The cortical processing of facial emotional expression is associated with social cognition skills and executive functioning: a preliminary study. *Neuroscience Letters*. 2011; 505:41–46. [PubMed: 22001365]
- Pick A. Über die Beziehung der senilen Hirnatrophie zur Aphasie. *Pragischer Medizinischer Wochenschrift*. 1892; 17:165–167.
- Pick A. Über primäre progressive Demenz bei Erwachsenen. *Pragischer Medizinischer Wochenschrift*. 1904; 29:417–420.
- Possin K, Brambati SM, Rosen H, Johnson JK, Pa J, Weiner MW, Kramer JK. Rule violation errors are associated with right lateral prefrontal cortex atrophy in neurodegenerative disease. *Journal of the International Neuropsychological Society*. 2009; 15:354–364. [PubMed: 19402921]
- Possin K, Chester SK, Laluz V, Bostrom A, Rosen H, Miller BL, Kramer JK. The frontal-anatomic specificity of design fluency repetitions and their diagnostic relevance for behavioral variant frontotemporal dementia. *Journal of the International Neuropsychological Society*. 2012; 18:834–844. [PubMed: 22835330]
- Piquard A, Derouesne C, Lacomblez L, Sieroff E. [Planning and activities of daily living in Alzheimer's disease and frontotemporal dementia]. *Psychologie & Neuropsychiatrie um Vieillissement*. 2004; 2:147–156.
- Rahman S, Sahakian BJ, Hodges JR, Rogers RD, Robbins TW. Specific cognitive deficits in mild frontal variant frontotemporal dementia. *Brain*. 1999; 122:1469–1493. [PubMed: 10430832]
- Rankin KP, Kramer JH, Mychack P, Miller BL. Double dissociation of social functioning in frontotemporal dementia. *Neurology*. 2003; 60:266–271. [PubMed: 12552042]
- Rascovsky K, Salmon DP, Hansen LA, Galasko D. Distinct cognitive profiles and rates of decline on the Mattis Dementia Rating Scale in autopsy-confirmed frontotemporal dementia and Alzheimer's disease. *Journal of the International Neuropsychological Society*. 2008; 14:373–383. [PubMed: 18419836]
- Rascovsky K, Salmon DP, Ho GJ, Galasko D, Peavy GM, Hansen LA, Thal LJ. Cognitive profiles differ in autopsy-confirmed frontotemporal dementia and AD. *Neurology*. 2002; 58:1801–1808. [PubMed: 12084880]
- Rascovsky K, Hodges JR, Knopman D, Mendez MF, Kramer JH, Neuhaus J, Miller BL. Sensitivity of revised diagnostic criteria for the behavioural variant of frontotemporal dementia. *Brain*. 2011; 134:2456–2477. [PubMed: 21810890]
- Ratnavalli E, Brayne C, Dawson K, Hodges JR. The prevalence of frontotemporal dementia. *Neurology*. 2002; 58:1615–1621. [PubMed: 12058088]

- Rhee J, Antiquena P, Grossman M. Verb comprehension in frontotemporal degeneration: the role of grammatical, semantic, and executive components. *Neurocase*. 2001; 7:173–184. [PubMed: 11320164]
- Ringman JM, Kwon E, Flores DL, Rotko C, Mendez MF, Lu P. The use of profanity during letter fluency tasks in frontotemporal dementia and Alzheimer disease. *Cognitive and Behavioral Neurology*. 2010; 23:159–164. [PubMed: 20829665]
- Roca M, Torralva T, Gleichgerrcht E, Chade A, Arevalo GG, Gershanik O, Manes F. Impairments in social cognition in early medicated and unmedicated Parkinson disease. *Cognitive and Behavioural Neurology*. 2010; 23:152–158.
- Rohrer JD, Warren JD. Phenomenology and anatomy of abnormal behaviours in primary progressive aphasia. *Journal of the Neurological Sciences*. 2010; 293(1–2):35–38. [PubMed: 20400120]
- Rohrer JD, Lashley T, Schott JM, Warren JE, Mead S, Isaacs AM, Warren JD. Clinical and neuroanatomical signatures of tissue pathology in frontotemporal lobar degeneration. *Brain*. 2011; 134:2565–2581. [PubMed: 21908872]
- Rohrer JD, Ridgway GR, Crutch SJ, Hailstone J, Goll JC, Clarkson MJ, Warren JD. Progressive logopenic/phonological aphasia: erosion of the language network. *Neuroimage*. 2010b; 49:984–993. [PubMed: 19679189]
- Rohrer JD, Rossor MN, Warren JD. Syndromes of nonfluent primary progressive aphasia: a clinical and neurolinguistic analysis. *Neurology*. 2010a; 75:603–610. [PubMed: 20713949]
- Rohrer JD, Rossor MN, Warren JD. Alzheimer's pathology in primary progressive aphasia. *Neurobiology of Aging*. 2012; 33:744–752. [PubMed: 20580129]
- Rosen HJ, Allison SC, Ogar JM, Amici S, Rose K, Dronkers N, Gorno-Tempini. Behavioral features in semantic dementia vs other forms of progressive aphasias. *Neurology*. 2006; 67(10):1752–1756. [PubMed: 17130406]
- Rosen HJ, Pace-Savitsky K, Perry RJ, Kramer JH, Miller BL, Levenson RW. Recognition of emotion in the frontal and temporal variants of frontotemporal dementia. *Dementia and Geriatric Cognitive Disorders*. 2004; 17:277–281. [PubMed: 15178936]
- Rosen HJ, Perry RJ, Murphy J, Kramer JH, Mychack P, Schuff N, Miller BL. Emotion comprehension in the temporal variant of frontotemporal dementia. *Brain*. 2002; 125:2286–2295. [PubMed: 12244085]
- Ross LA, Olson IR. Social cognition and the anterior temporal lobes. *Neuroimage*. 2010; 49:3452–3462. [PubMed: 19931397]
- Rosso SM, Donker Kaat L, Baks T, Jooze M, de Koning I, Pijnenburg Y, van Swieten JC. Frontotemporal dementia in The Netherlands: patient characteristics and prevalence estimates from a population-based study. *Brain*. 2003; 126:2016–2022. [PubMed: 12876142]
- Royall DR, Lauterbach EC, Cummings JL, Reeve A, Rummans TA, Kaufer DI, Coffey CE. Executive control function: a review of its promise and challenges for clinical research. A report from the Committee on Research of the American Neuropsychiatric Association. *Journal of Neuropsychiatry and Clinical Neurosciences*. 2002; 14:377–405. [PubMed: 12426407]
- Sabat S, Gladstone C. What intact social cognition and social behavior reveal about cognition in the moderate stage of Alzheimer's disease: A case study. *Dementia*. 2010; 9:61–78.
- Sabat S, Lee J. Relatedness among people diagnosed with dementia: Social cognition and the possibility of friendship. *Dementia*. 2010; 11:315–327.
- Sarazin M, Dubois B, de Souza LC, Bertoux M. Should the Social Cognition and Emotional Assessment replace standard neuropsychological tests for frontotemporal dementia? *Expert Review of Neurotherapeutics*. 2012; 12:633–635. [PubMed: 22650163]
- Seelaar H, Rohrer JD, Pijnenburg YA, Fox NC, van Swieten JC. Clinical, genetic and pathological heterogeneity of frontotemporal dementia: a review. *Journal of Neurology, Neurosurgery and Psychiatry*. 2011; 82:476–486.
- Seeley WW, Bauer AM, Miller BL, Gorno-Tempini ML, Kramer JH, Weiner M, Rosen HJ. The natural history of temporal variant frontotemporal dementia. *Neurology*. 2005; 64:1384–1390. [PubMed: 15851728]

- Seeley WW, Crawford R, Rascofsky K, Kramer JH, Weiner M, Miller BL, Gorno-Tempini ML. Frontal paralimbic network atrophy in very mild behavioral variant frontotemporal dementia. *Archives of Neurology*. 2008; 65:249–255. [PubMed: 18268196]
- Seeley WW, Merkle FT, Gaus SE, Craig AD, Allman JM, Hof PR, Economo CV. Distinctive neurons of the anterior cingulate and fronto-insular cortex: a historical perspective. *Cerebral Cortex*. 2012; 22:245–250. [PubMed: 21653703]
- Shany-Ur T, Rankin KP. Personality and social cognition in neurodegenerative disease. *Current Opinion in Neurology*. 2011; 24:550–555. [PubMed: 22002077]
- Silveri MC, Salvigni BL, Cappa A, Della Vedova C, Puopolo M. Impairment of verb processing in frontal variant-frontotemporal dementia: a dysexecutive symptom. *Dementia & Geriatric Cognitive Disorders*. 2003; 16:296–300. [PubMed: 14512727]
- Snowden JS, Goulding PJ, Neary D. Semantic dementia: a form of circumscribed cerebral atrophy. *Behavioural Neurology*. 1989; 2:167–182.
- Snowden J, Neary D, Mann D. Frontotemporal lobar degeneration: clinical and pathological relationships. *Acta Neuropathologica*. 2007; 114:31–38. [PubMed: 17569065]
- Snowden, JS.; Neary, D.; Mann, DMA. *Fronto-Temporal Lobar Degeneration: Fronto-temporal Dementia, Progressive Aphasia, Semantic Dementia*. London: Churchill Livingstone; 1996.
- Snowden JS, Pickering-Brown SM, Mackenzie IR, Richardson AM, Varma A, Neary D, Mann DM. Progranulin gene mutations associated with frontotemporal dementia and progressive non-fluent aphasia. *Brain*. 2006; 129:3091–3102. [PubMed: 17003069]
- Sollberger M, Rankin KP, Miller BL. Social cognition. *Continuum (Minneapolis, Minn)*. Behavioral Neurology. 2010; 16:69–85.
- Stopford CL, Thompson JC, Neary D, Richardson AM, Snowden JS. Working memory, attention, and executive function in Alzheimer's disease and frontotemporal dementia. *Cortex*. 2012; 48:429–446. [PubMed: 21237452]
- Strenziok M, Pulaski S, Krueger F, Zamboni G, Clawson D, Grafman J. Regional brain atrophy and impaired decision making on the balloon analog risk task in behavioral variant frontotemporal dementia. *Cognitive and Behavioural Neurology*. 2011; 24:59–67.
- Sturm VE, Rosen HJ, Allison S, Miller BL, Levenson RW. Self-conscious emotion deficits in frontotemporal lobar degeneration. *Brain*. 2006; 129:2508–2516. [PubMed: 16844714]
- Stuss DT, Levine B. Adult clinical neuropsychology: lessons from studies of the frontal lobes. *Annual Review of Psychology*. 2002; 53:401–433.
- Tanabe H, Ikeda M, Nakagawa Y, Yamamoto H, Ikejiri Y, Kazui H. Gogi (worn meaning) aphasia and semantic memory for words. *Higher Brain in Functional Research*. 1992; 12:153–167.
- Thompson JC, Stopford CL, Snowden JS, Neary D. Qualitative neuropsychological performance characteristics in frontotemporal dementia and Alzheimer's disease. *Journal of Neurology, Neurosurgery & Psychiatry*. 2005; 76:920–927.
- Thompson SA, Patterson K, Hodges JR. Left/right asymmetry of atrophy in semantic dementia: behavioral-cognitive implications. *Neurology*. 2003; 61:1196–1203. [PubMed: 14610120]
- Torralva T, Dorrego F, Sabe L, Chemerinski E, Starkstein SE. Impairments of social cognition and decision making in Alzheimer's disease. *International Psychogeriatrics*. 2000; 12:359–368. [PubMed: 11081956]
- Torralva T, Kipps CM, Hodges JR, Clark L, Bekinschtein T, Roca M, Manes F. The relationship between affective decision-making and theory of mind in the frontal variant of fronto-temporal dementia. *Neuropsychologia*. 2007; 45:342–349. [PubMed: 16893555]
- Torralva T, Roca M, Gleichgerrcht E, Bekinschtein T, Manes F. A neuropsychological battery to detect specific executive and social cognitive impairments in early frontotemporal dementia. *Brain*. 2009; 132:1299–1309. [PubMed: 19336463]
- Verdon CM, Fossati P, Verny M, Dieudonne B, Teillet L, Nadel J. Social cognition: an early impairment in dementia of the Alzheimer type. *Alzheimer Disease and Associated Disorders*. 2007; 21:25–30. [PubMed: 17334269]
- Walker AJ, Meares S, Sachdev PS, Brodaty H. The differentiation of mild frontotemporal dementia from Alzheimer's disease and healthy aging by neuropsychological tests. *International Psychogeriatrics*. 2005; 17:57–68. [PubMed: 15945591]

- Weintraub S, Mesulam MM, Wieneke C, Rademaker A, Rogalski EJ, Thompson CK. The northwestern anagram test: measuring sentence production in primary progressive aphasia. *American Journal of Alzheimers Disease and Other Dementias*. 2009; 24:408–416.
- Weintraub S, Rubin NP, Mesulam MM. Primary progressive aphasia. Longitudinal course, neuropsychological profile, and language features. *Archives of Neurology*. 1990; 47:1329–1335. [PubMed: 2252450]
- Werner KH, Roberts NA, Rosen HJ, Dean DL, Kramer JH, Weiner MW, Levenson RW. Emotional reactivity and emotion recognition in frontotemporal lobar degeneration. *Neurology*. 2007; 69:148–155. [PubMed: 17620547]
- Wicklund AH, Johnson N, Weintraub S. Preservation of reasoning in primary progressive aphasia: further differentiation from Alzheimer's disease and the behavioral presentation of frontotemporal dementia. *Journal of Clinical and Experimental Neuropsychology*. 2004; 26:347–355. [PubMed: 15512925]
- Wicklund AH, Rademaker A, Johnson N, Weitner BB, Weintraub S. Rate of cognitive change measured by neuropsychologic test performance in 3 distinct dementia syndromes. *Alzheimer Disease and Associated Disorders*. 2007; 21:S70–S78. [PubMed: 18090428]
- Wilson SM, Brambati SM, Henry RG, Handwerker DA, Agosta F, Miller BL, Gorno-Tempini ML. The neural basis of surface dyslexia in semantic dementia. *Brain*. 2009; 132:71–86. [PubMed: 19022856]
- Wilson SM, Henry ML, Besbris M, Ogar JM, Dronkers NF, Jarrold W, Gorno-Tempini ML. Connected speech production in three variants of primary progressive aphasia. *Brain*. 2010; 133:2069–2088. [PubMed: 20542982]
- Wong CL, Harris JA, Gallate JE. Evidence for a social function of the anterior temporal lobes: low-frequency rTMS reduces implicit gender stereotypes. *Soc Neurosci*. 2012; 7(1):90–104. [PubMed: 21954929]
- Woodward M, Jacova C, Black SE, Kertesz A, Mackenzie IR, Feldman H. Differentiating the frontal variant of Alzheimer's disease. *International Journal of Geriatric Psychiatry*. 2010; 25:732–738. [PubMed: 19823987]
- Ybarra O, Winkelman P. On-line social interactions and executive functions. *Frontiers in Human Neuroscience*. 2012; 6:75. [PubMed: 22509160]
- Yu RL, Wu RM, Chiu MJ, Tai CH, Lin CH, Hua MS. Advanced Theory of Mind in patients at early stage of Parkinson's disease. *Parkinsonism and Related Disorders*. 2012; 18:21–24. [PubMed: 21868278]
- Zahn R, Moll J, Krueger F, Huey ED, Garrido G, Grafman J. Social concepts are represented in the superior anterior temporal cortex. *Proceedings of the National Academy of Sciences of the U S A*. 2007; 104:6430–6435.
- Zakzanis KK. The neuropsychological signature of primary progressive aphasia. *Brain and Language*. 1999; 70:70–85. [PubMed: 10534372]