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Apraxia profiles—A single cognitive marker to discriminate all variants of frontotemporal lobar degeneration and Alzheimer's disease

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Abstract

Introduction: Apraxia is common in neurodegenerative dementias but underrepresented in clinical workup for differential diagnoses.

Methods: Praxis-profiles were assessed with the Dementia Apraxia Test in 93 patients with early stages of biologically supported Alzheimer's disease or frontotemporal lobar degeneration: semantic primary-progressive aphasia, nonfluent primary-progressive aphasia, and behavioral variant frontotemporal dementia. Associations with core cognitive deficits of the dementia subtypes (i.e., visuospatial, sociocognitive, and semantic-linguistic) were explored.

Results: Patients showed significant apraxia compared with healthy controls but also disease-specific praxis-profiles. Using only the Dementia Apraxia Test, all four dementia subtypes could be correctly discriminated in 64.4% of cases, and in 78.2% when only distinguishing Alzheimer's disease versus frontotemporal lobar degeneration. Praxis-profiles showed consistent associations with core cognitive impairments of the different dementia subtypes.

Discussion: The Dementia Apraxia Test is a valid, time-efficient and versatile cognitive marker to delineate variants of frontotemporal lobar degeneration and Alzheimer's disease in clinical routine, facilitating differential diagnoses of dementia subtypes in early disease stages.

Keywords: Apraxia; Primary-progressive aphasia; Frontotemporal dementia; Semantic dementia; Frontotemporal lobar degeneration; Alzheimer's disease; Differential diagnosis; neuropsychology

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1. Background

Apraxia relates to a neuropsychological deficit regarding imitation or pantomiming of limb or face postures despite intact sensorimotor skills and task comprehension [1,2]. Impairments in praxis may occur early in a range of neurocognitive disorders and can be used as a cognitive marker for early neurodegenerative dementias [3–5]. Despite its recent inclusion as a basic cognitive domain in the DSM-5, praxis assessment is underrepresented in both routine neuropsychological workup and current diagnostic criteria for neurocognitive disorders [6,7].

Disease progression, rate of functional decline, caregiver burden, and therapeutic approaches differ profoundly between neurodegenerative dementia subtypes [8,9]. A correct differential diagnosis in early disease stages is thus essential for patients, caregivers, and health practitioners.

In the absence of ready-to-use biomarkers for frontotemporal lobar degeneration (FTLD), clinical criteria for the behavioral variant frontotemporal dementia (bvFTD) and the two language variants, nonfluent primary progressive aphasia (nfPPA) and semantic variant primary progressive aphasia (svPPA), have been consecutively refined, improving their diagnostic accuracy [10,11]. Nevertheless, neither unambiguous operationalizations of diagnostic core features (e.g., "loss of empathy" for bvFTD; "semantic memory dysfunction" for svPPA) nor straightforward and brief clinical tests with sufficient differential value to discriminate between these dementia subtypes simultaneously are available. The correct application of the clinical criteria and a clinical differentiation of the FTLD variants from each other and from Alzheimer's dementia (AD) thus remains challenging, particularly in nonexpert settings and for patients in early disease stages [12–14].

Although standardized neuropsychological testing is recommended to differentiate between the different dementia types in early disease stages, a range of former neuropsychological principles have recently been questioned or shown to be invalid for a reliable differentiation between FTLD and early stage AD: Impairments in verbal memory tests may occur to similar degrees in patients with bvFTD and AD either due to confounding executive influences or due to AD-like hippocampal atrophy in subsamples of patients with bvFTD [15,16]. Similarly, cognitive domains that place high demands on language (including verbal memory tests) are frequently confounded with deficits in task comprehension and/or semantic memory in patient with PPA [17,18]. Taken together, a considerable overlap regarding performance in standard neuropsychological domains exists between patients with different underlying neurodegenerative etiologies, particularly when only time-efficient screening tests are available [9,19,20].

Standardized assessment of praxis-profiles is time efficient, reliable, and places comparatively little demands on potentially confounding cognitive influences such as working memory or language comprehension. It may thus serve as a versatile neuropsychological tool to differentiate clinically heterogeneous dementia subtypes in early disease stages. However, although mentioned as a basic cognitive domain, apraxia is largely neglected in clinical or neuropsychological routine examinations. Here, we explored patterns of praxis disturbances and tested the clinical feasibility of a single praxis screening for the differential diagnosis between early stages of AD and the three most frequent clinical variants of FTLD (bvFTD, svPPA, and nfPPA). We hypothesized that specific praxis-profiles (operationalized by divergent performance in different praxis domains) are associated with core cognitive deficits of the different dementia syndromes (i.e., visuospatial deficits in AD, linguistic-semantic deficits in PPA, and social cognitive impairment in bvFTD).

2. Methods

2.1. Participants

A total of 93 patients with early (<3 years after the first symptom-onset) neurodegenerative diseases were enrolled in the memory disorder unit at the Department of Neurology at the University Hospital Münster, Germany. The initial diagnostic workup was conducted at our inpatient clinic and included neurological examination, history taking with patients and caregivers, consultation of medical records, comprehensive neuropsychological testing as presented in detail elsewhere [19], motor and speech assessment, and analysis of cerebrospinal fluid (CSF) for dementia biomarkers. Structural T1- and FLAIR-magnetic resonance imaging images of the brain were available from all patients. In addition, 18-Fluorodeoxyglucose Positron Emission Tomography scans were available in 70% (46/66) of patients with suspected FTLD. All recruited patients matched the current criteria for probable AD, probable bvFTD, or imaging-supported PPA evaluated by a multidisciplinary team of senior neurologists and neuropsychologists [10,11,21]. Briefly, patients with probable AD (N = 27) presented with memory decline objectified in episodic memory tests and had high or at least intermediate evidence for the pathophysiological process of AD based on neuroimaging and biomarker constellation [21]. Patients with probable bvFTD (N = 31) presented with symptom constellations of social conduct decline, apathy, loss of empathy, and/or executive dysfunction in neuropsychological assessment as well as a consistent frontal and/or anterior temporal atrophy or hypometabolism [10]. Patients with svPPA (N = 21) showed prominent naming and fluency deficits but circumlocutory speech as initial symptoms, whereas patients with nfPPA (N = 14) initially presented with effortful, halting speech either with or without agrammatism. All patients with PPA showed signs of either brain atrophy or hypometabolism consistent