



Abstracts

Functional markers of executive dysfunction in primary progressive aphasia: A systematic review

by Kristin Thomsen | Stefanie Keulen | Seçkin Arslan | Université Côte d'Azur, CNRS, BCL, 24 Avenue des Diables Bleus, 06357, Nice Cedex 4, France. | Brussels Centre for Language Studies (BCLS), Vrije Universiteit Brussel (VUB), Brussels, Belgium | Université Côte d'Azur, CNRS, BCL, 24 Avenue des Diables Bleus, 06357, Nice Cedex 4, France.

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Introduction and aims

Primary progressive aphasia (PPA) is a neurodegenerative focal dementia, predominantly characterised by language impairment and frontotemporal cortical atrophy (Mesulam, 2001). Non-linguistic cognitive domains have been assumed to remain intact in the initial phases of PPA resulting in these avenues often being disregarded in research and diagnostic procedures (Mesulam, 2001). However, research has also reported evidence for the deterioration of executive functions (EFs) in PPA patients (Coemans et al., 2022). The frontal and temporal lobes are commonly associated with higher level executive functioning, language processing and memory (Gorno-Tempini et al., 2011). Thus, atrophy in these areas may lead to executive dysfunction and language impairments, making it difficult to process language and perform day-to-day activities. EFs are essential mental processes in the brain and are commonly distinguished into three core components; 'inhibition,' which refers to the ability to override or ignore prepotent responses and regulate attentional demands by filtering out distracting stimuli; 'shifting,' which refers to the ability to rapidly adapt one's attention to new and changing task demands; and 'updating,' which refers to the ability to constantly monitor information in working memory to acquire new more relevant information for the task at hand (Miyake et al., 2000; Lehto et al., 2003, Diamond, 2012). Functional markers can provide insights into the mechanisms and atrophy underlying executive dysfunction in PPA; therefore, they provide a suitable model to examine the brain systems implicated in neurodegenerative brain disease and its significance for executive control deficits.

The objectives of this systematic review were

- to investigate and compare previous findings of functional markers linked to executive dysfunction in PPA and FTD.
- to examine what information distinctive functional markers can provide in the evaluation of executive function deficits in PPA and FTD, and to what effect executive function deficits can be assessed through the characteristics of functional markers.

Methods

This systematic review followed the PRISMA guidelines (Moher et al., 2009). Studies from the online publication databases PubMed and Web of Science were searched for literature relevant to the review. Only full-text articles published in peer-reviewed journals, in English were retained. Additionally, individual references were examined to obtain further relevant studies that were not accessible through the online search. Primary inclusion criteria for further analysis were (1) a PPA or an FTD diagnosis with mentioning of language deficits, (2) the inclusion of neuropsychological testing including the assessment of EF components or resting-state connectivity, (3) the reported use one of the following functional assessments: electroencephalography (EEG), magnetoencephalography (MEG), positron emission tomography (PET) or functional magnetic resonance imaging (fMRI).

Results

After application of the relevant criteria, a total of fourteen studies were included in this systematic review for qualitative analysis: two EEG studies, seven MEG studies and five fMRI studies. The systematic review search indicated no clear functional markers to diagnostically evaluate executive deficits in PPA. However, evidence from MEG imaging found EF deficit correlations to a reduction in functional connectivity in the left frontal cortex, indicating the possibility of using MEG resting-state functional connectivity changes as a way to detect early executive dysfunction in the Alzheimer's disease spectrum (Ranasinghe et al., 2014). Nevertheless, not all studies found severe executive function deficits in PPA patients. In an fMRI study, PPA patients with a severe decline in language related tasks were found to perform nearly equivalently to healthy subjects on a demanding control task (Sonty et al., 2003).

Discussion

Research on functional markers linked to executive dysfunction in PPA and FTD is scarce. This may explain why the majority of the present findings were not replicated across studies concerned with comparable functional assessments. Therefore, further research is still needed in the assessment of the underlying functional mechanisms related to executive dysfunction in focal dementias. However, existing research suggests that executive impairments in PPA may be related to atrophy in frontal brain regions (Rogalski et al., 2011). Reductions in functional connectivity may also indicate deficits in the neural network connected to cognitive functions. This way, functional markers offer valuable information of potential executive degeneration and thus prove relevant for future studies.

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