Detecting dysexecutive syndrome in neurodegenerative diseases: Are we using an appropriate approach and effective diagnostic tools?

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Title

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Executive functions impairment and dysexecutive behaviors both contribute to dysexecutive syndrome in frontotemporal dementia and cortico-basal degeneration.

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Text

The term 'dysexecutive syndrome' refers to a dysregulation of executive functions domain, and is strictly associated to frontal lobe damage. Dysexecutive syndrome typically encompasses emotional, motivational and behavioral symptoms, as well as cognitive deficits[1]. This invalidating condition can be observed in various clinical domains, and above all characterizes degenerative diseases such as frontotemporal dementia (FTD), and - on a lesser degree - corticobasal degeneration (CBD).

In recent years, neuropsychological tools have been used to investigate dysexecutive syndrome[2]. However, to date this field of clinical research suffers from a significant paradox: while clinicians and caregivers perceive with ease the presence of the symptoms that characterize patients' clinical picture, surprisingly it has not yet been clearly understood as promptly and reliably detecting this cohort of symptoms with effective diagnostic tools.

The paper by Gansler *et al.*[3] has the merit to make a significant step further in this direction, by proposing the distinction but also the strict synergy between the realms of 'executive functions' (EF) and 'dysexecutive behaviors' (DB), and by supporting the utility to integrate EF and DB measures for diagnostic purposes. In detail, Gansler *et al*. included a large cohort of patients (N=243) affected by the behavioural variant of FTD (bvFTD, N=124), primary progressive aphasia (PPA, N=34), or CBD (N=85): for the majority of them, the authors collected patients' performance on an EF neuropsychological battery (the Delis-Kaplan Executive Function System), and caregivers' report of patients' behavior through the FrSBe (the Frontal Behavior Scale). As expected, bvFTD patients got significantly lower scores on EF tests and higher scores on the DB measure, compared to other sub-groups. Interestingly, factor analyses showed that EF and DB were distinct but overlapping constructs, and this was corroborated at a neuroimaging level too: the EF composite was uniquely associated with left lateral and dorsomedial prefrontal cortex, and with the middle temporal gyrus and temporo-parietal junction, while DB was uniquely associated with cingulate gyrus bilaterally, right sub-callosal gyrus, and right frontal anterior pole. The rostral part

of the lateral and dorsomedial prefrontal cortex was associated with both EF and DB. Lastly, authors' results showed that by considering EF and DB measures jointly, diagnostic precision increased significantly (even if this was more true for PPA and CDB, as for bvFTD cases DB measures alone already possessed good explanatory power).

In our view, Gansler *et al.*'s study takes into account seriously the need to improve an early and precise detection of neurodegenerative diseases symptoms by considering the interplay between neural, cognitive, and behavioral levels. To make another step further, we support the position that future studies in this field should also include an assessment of Theory of Mind (ToM) abilities, i.e. the capacity to explain and predict other people's behavior by attributing independent mental states to them. As recently shown[4,5], ToM is another domain significantly involved in dementias and CBD partially dissociated from EF impairment, and interestingly ToM tasks typically present a higher degree of "ecological" validity, compared to standard neuropsychological tests. Researchers and clinicians should therefore consider to include a careful ToM assessment to improve diagnostic procedures, with the ultimate goal to implement effective management strategies.

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