

COMMENTARY

Toward international consensus on the definition of agitation in cognitive disorders

Commentary on “Agitation in cognitive disorders: Progress in the International Psychogeriatric Association consensus clinical and research definition” by Sano *et al.*

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Agitation is frequent in clinical practice

Agitation is a common condition in many cognitive disorders, including Alzheimer’s disease, Parkinson’s disease, various types of dementia, and mild cognitive impairment (Panca *et al.*, 2019; Van der Mussele *et al.*, 2015). Causes of agitation in cognitive disorders are not fully understood but may be related to a combination of factors capable of inducing or exacerbating a dysfunctional person–environment interaction. These can be internal to the person (changes in brain structure and function, physical discomfort, confusion, pain, fear, communication difficulties, sleep/wake rhythm alterations, and repetitive behaviors) or come from outside (excess or lack of stimuli in the environment, too complex communications, behavior inappropriate to the context, difficulty recognizing objects that were familiar, and inability to recognize family and friends).

Although some studies have examined the phenomenon with a view to promoting greater understanding and awareness, there is currently no definitive definition that takes into account the multicomponent dimension of agitation. As pointed out by Cummings *et al.* (2015), a shared definition of agitation, applicable in conditions of cognitive impairment, would facilitate a broad spectrum of research, including pharmacological and nonpharmacological intervention studies, epidemiological investigations, clinical studies, and research on the neurobiological correlates of agitation. A definition would also provide a framework for diagnostic nomenclatures such as the International Statistical Classification of Diseases and Related Health Problems (ICD-11) (World Health Organization, 2019) and the Diagnostic and Statistical Manual

of Mental Disorders – Text Revised (DSM-5 TR) (American Psychiatric Association, 2022).

IPA’s provisional definition of agitation

In 2014–2015, the International Psychogeriatric Association (IPA) convened a group of international experts on dementia and agitation who, through the conduct of some surveys, engaged in an iterative process that led to the publication of a provisional definition of agitation in cognitive disorders (Cummings *et al.*, 2015). This work increased awareness and attention both on the clinical condition and on the need to use clear and shared criteria to facilitate timely diagnosis and identify suitable treatments. The consensus based the definition of the following four criteria: 1) patients meet the criteria for cognitive impairment or dementia syndrome; 2) patients exhibited persistent or frequently recurring (i.e. over a period of 2 weeks or longer) verbal or motor behaviors that were distressing; 3) the behaviors produced an excess of disability, and 4) the behaviors were not solely attributable to another psychiatric, medical, or environmental condition. These criteria reflect the contribution of clinicians and researchers who, through a rigorous and transparent consensus process, hypothesized a definition of agitation that was easily recognizable and standardized with the available clinical skills and assessment tools (Cummings *et al.*, 2015).

Rating scales such as the Cohen-Mansfield Agitation Inventory (CMAI) (Cohen-Mansfield *et al.*, 1989), the Neuropsychiatric Inventory (NPI) (Cummings *et al.*, 1994), or the Behavioral Pathology in Alzheimer’s

Disease (BEHAVE-AD) (De Deyn and Wirshing, 2001; Reisberg *et al.*, 1987) are often used to identify patients for clinical trials of anti-agitation agents and to measure clinical symptoms in descriptive and intervention studies. Rating scales, however, are not definitions; rather, they are means of measuring the frequency or severity of symptoms. Furthermore, most doctors do not use them in clinical practice with patients. Therefore, to promote an improvement in the quality of clinical care and research, a definition that does not depend on a particular rating scale is needed (Cummings *et al.*, 2015).

The survey conducted by Sano *et al.* (2023)

The results presented by Sano *et al.* (2023) in this issue of *International Psychogeriatrics* are significant as they offer an exhaustive account of the feedback accrued over several years, following the dissemination of a provisional definition of agitation, both in terms of acceptance and recognition by the scientific community of the same, and validation and application of that definition in clinical and research populations. Aiming to advocate for the removal of the term “provisional,” Sano *et al.* (2023) first provided an overview of the current state of knowledge on agitation in cognitive disorders in terms of prevalence, cost, and underlying neurobiology and then traced the development of the IPA temporary criteria. Subsequently, they described the amount of work supporting the relevance of the definition developed by IPA, up to the finalization of the aforementioned criteria. Finally, some clinical circumstances in which agitation is observed in cognitive disorders were exposed, involving patients and caregivers in the process of developing a shared vocabulary, useful to describe those behaviors considered as main components of agitation. In agitated patients, in fact, the diagnosis is of a clinical nature and is based on an accurate anamnesis, on the observation of the behavior and on the cognitive assessment, which involves multidisciplinary teams, and formal and informal caregivers. The latter must detect changes in patients’ cognitive state, within their daily actions, behaviors, and mood changes based on usual everyday observations.

Specifically, the study by Sano *et al.* (2023) highlights how the behavioral symptoms of dementia commonly recognized in the moderate and severe stages of the disease can actually occur in all stages of cognitive impairment, with an increasing prevalence with the worsening of the disease. In addition, Sano and coworkers emphasize the importance of recognizing the economic consequences of agitation. For example, a study on individuals diagnosed with Alzheimer’s disease and treated by mental health

services in the South East London catchment area reported that agitation was associated with a higher risk of hospitalization and days spent in nursing homes, mental health departments, and general hospitals and further costs associated with any institutional admission in the subsequent 6 months (Knapp *et al.*, 2016).

The paper by Sano *et al.* (2023) stands out from the literature; in that, it provides a cutting-edge perspective, arguing in favor of deleting the word “provisional” from the definition of agitation in cognitive disorders, given its current acceptance and widespread use in the field. Those scholars argue that the criteria identified by the IPA are now standard in many types of research, and that they can be considered as widely accepted rather than still provisional. In fact, international researchers seem to be aware of the definition proposed by the IPA and commonly include it in the methods section of their papers; the criteria have also been used in observational studies and in pharmacological and nonpharmacological intervention studies, as well as in the guidelines of professional societies and government agencies, with a view to improving awareness of the phenomenon and the quality of the research (Cummings *et al.*, 2015). As evidence of this, the large clinical trials database maintained by the US National Library of Medicine at the National Institutes of Health (NIH), available to the public since February 2000, was searched for studies using the IPA criteria published between 01/01/2015 and 07/01/2021. The search identified 55 intervention trials. Of the 55 studies, 31 evaluated the efficacy and tolerability or safety of treatments for agitation in dementia, while 24 did not treat agitation and were therefore excluded from the analysis. Of the 31 agitation studies, 25 used specific criteria to define agitation in the study method section, while 6 did not. The criteria used included the IPA’s provisional agitation criteria (16 of the 25 studies: 64%) or criteria defined by scales such as the NPI (7 studies: 28%) and the CMAI (2 studies, 8%).

IPA’s criteria for agitation are now widely shared

Overall, the study by Sano *et al.* (2023) aimed to reconsider the definition of agitation promoted by the IPA, retracing the same process used for the provisional definition, trying to keep the criteria unchanged as much as possible, with the view of ensuring continuity with past, ongoing, and planned studies, while incorporating advances that underline the no longer provisional nature of the criteria. To this end, a survey was sent to members of the IPA and its

affiliated organizations, asking for their opinion on the criteria as a whole. The survey was circulated three times in a 6-week period, from January 10, 2020 to February 5, 2020, to 5233 email addresses. There were 192 respondents, with 169 complete answers (88.0%) and 23 partial ones (12.0%), representing people from 40 countries. The majority of respondents (62.4%) had been in the psychogeriatric field for 16 years or more. The adaptation of the criteria title with the elimination of the term “provisional” met with broad consensus (90.1% of participants). Finally, Sano’s team members highlighted the importance of making further modifications by integrating some special contexts and circumstances (terminal agitation, acute agitation, agitation in the emergency department, and agitation in specific conditions of cognitive impairment) that went beyond those considered at the time of the criteria conceptualization.

Conclusion

The study by Sano *et al.* (2023) highlights the progress that has been made in defining agitation in cognitive disorders, a phenomenon whose management typically involves a multifaceted approach, including environmental modifications, behavioral interventions, and medications, where adequate. The dissemination of shared and standardized criteria and education on the phenomenon of agitation (families and operators) is promoted so that the linguistic gap between the two parties involved can gradually be reduced and thus favor the progress of research and the improvement of clinical practice. In fact, available data suggest that families tend to use a different vocabulary to describe agitation and to attribute it to causes other than those identified by clinicians (Gilmore-Bykovskiy *et al.*, 2020; Polenick *et al.*, 2018). Adequate and specific training could improve care for patients with agitation and cognitive impairment. The wide range of contexts in which agitation occurs – home, hospital wards, emergency departments, nursing homes, and intensive care units – suggests that an educational effort able to reach many settings of care is widely needed. Finally, a further challenge concerns the possibility of creating appropriate tools for measuring and evaluating agitation, in line with the criteria proposed by the IPA.

Conflict of interest

None.

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