

EDITORIAL

International Psychogeriatric Association (IPA) consensus for defining psychosis in major and mild neurocognitive disorders

The International Psychogeriatric Association (IPA) is an organization of health professionals committed to serving the mental health of older persons. The IPA has a long tradition of addressing the needs of those with cognitive impairment and behavioral symptoms. In 1996, IPA published proceedings of its consensus conference entitled Behavioral and Psychological Signs and Symptoms of Dementia: Implications for Research and Treatment (Finkel, 1996) with an update in 2000 (Finkel and Burns, 2000). The effort continued with its work on defining agitation in cognitive disorders (Cummings *et al.*, 2015), and the IPA has demonstrated an enduring commitment to identifying and treating the clinical problems that pose some of the greatest challenges to the quality of life of patients and their families. Most recently, such contributions have led to the publication of Consensus Criteria for Psychosis in Major and Mild Neurocognitive Disorders (NCDs) (Cummings *et al.*, 2020). This IPA effort synthesizes contemporary global perspectives on the nature of behavioral and psychiatric symptoms accompanying cognitive disorders. This definitional work is the culmination of a collaboration of a wide range of stakeholders involved in multiple aspects of clinical care delivery for older persons, including mental health professionals, regulatory experts, and advocates for patients and their family members. Furthermore, the project was developed and advanced with the participation of internationally representative dementia experts including members of the Alzheimer's Association International Society to Advance Alzheimer's Research and Treatment Professional Interest Area (ISTAART PIA) and the International Society for CNS Clinical Trials and Methodology (ISCTM).

This effort builds on the work from nearly two decades ago done by IPA leaders in this area (Jeste and Finkel, 2000). It utilizes current clinical diagnostic criteria for cognitive impairment from the latest version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (American Psychiatric Association, 2013) and is informed by an international group of practitioners, resulting in a definition that would have practical implications and

be applicable to clinicians who routinely address these problems in their everyday practice.

Why do we need a new definition?

Since the 2000 publication of criteria for psychosis in Alzheimer's disease (AD) (Jeste and Finkel, 2000), the awareness and understanding of cognitive impairment and dementia has advanced in several ways. AD, the most common form of dementia, has received considerable prominence, particularly with the updating of criteria by McKhann *et al.* (2011), with the focus on clinical features that could be accessible to many practitioners. Recent scientific advances have helped initiate a more molecular approach to the diagnosis of AD (Jack *et al.*, 2018), which may require diagnostic evaluations that are not available to many patients across settings, particularly in low- and middle-income countries. Additionally, there is a growing awareness of multiple pathologies that co-occur in dementia and milder forms of cognitive impairment, making it difficult to define a single mechanism responsible for the observed symptoms.

Contrary to this molecular emphasis in diagnosis described by Jack *et al.* (2018), the approach of the International Classification of Diseases (ICD-10: World Health Organization, 2004) and DSM-5 is to use the characterization of major and mild NCDs. These classifications apply clinical criteria that are readily available and understandable to a diverse community of dementia practitioners across the world. As the IPA employed its broad survey methodology to reach clinicians and researchers across the world, it became apparent that the respondents wanted additional clarity to identify and define the symptoms of psychosis. For example, nearly 79% of survey respondents agreed that it would be helpful to provide examples of dementia-related delusions and hallucinations; 76% endorsed the separation of criteria for duration and severity; and 80% endorsed adding to the definition, the impact of psychosis on "patient or others' functioning" (Cummings *et al.*, 2020). The symptoms of hallucinations and

delusions in the presence of the cognitive and functional impairment of dementia that occurs primarily in an aging population raise a number of questions. These include the nature of the symptoms, the temporal relationship to the onset of the dementia, and the impact of aging sensory and physical changes on behavioral manifestations. More than 70% of respondents acknowledged that the criteria must consider both cultural determinants and sensory impairment. The working premise in this effort established that an optimal definition must provide the opportunity to enhance the ability for all practitioners to more effectively diagnose and treat these problems.

The IPA process for revising definitional criteria

This new consensus emerged from a multipronged approach to inform the resultant criteria. A working group that included IPA leadership and association members created the survey to assess the existing criteria with a focus on identifying areas that could be improved upon. The IPA supported the distribution of the survey to members and affiliated member groups and later, provided them with a summary and analysis of the global survey results. A larger international, multi-stakeholder work group was then formed to review the relevant literature, share knowledge from their specific areas of expertise, and evaluate the survey responses. There was remarkable (but not total) consensus between the published literature and survey responses covering the areas of phenotypic definition, symptom overlap, shared biology, and therapeutic approaches. Where disagreements across sources existed, the multi-stakeholder group weighed the evidence and made final recommendations for criteria, which were then sent to the same broad IPA membership for review and comment.

In addition to the changes endorsed in the survey described above, several other revisions were made in the new criteria and they are listed in Table 1. In particular, the new criteria facilitate the diagnosis of psychosis in the mild NCD/mild cognitive impairment phase of neurodegenerative disorders. The new criteria also overtly broaden the criteria to include all non-AD NCDs too. The separation of duration and severity and the expansion of each provided additional descriptive information addressed some uncertainty from the initial survey about symptom duration. The follow-up survey found 72% endorsement of the 1-month interval for duration and 88% endorsement of definitions of severity (Cummings *et al.*, 2020). In the initial survey, there was mixed enthusiasm with fewer than 50% endorsing the continued use of the

term “negative symptoms” as an associated feature and 59% endorsing its replacement with “apathy,” which has recently been recognized as a separate syndrome (Robert *et al.*, 2018). There was high agreement for specifically excluding delirium from the definitional text and acknowledging the exclusion for shared cultural beliefs. Overall, 90% of respondents found the new definition provided to be an improvement over previous versions.

Strengths and limitations of the IPA process

The IPA process was designed to maximize input to the criteria from a broad group of stakeholders with an emphasis on the clinicians serving the patient population. While it includes many stakeholders, the framework remains in a traditional model of psychiatric symptom evaluation, with major changes reflected in how we categorize and define the cognitive impairment. The approach has served the IPA well and is consistent with how the field defines psychiatric conditions in general. A limitation of this approach is that there is minimal information available on the validation of instruments that could independently identify symptom clusters and syndromes within dementia populations. Additionally, the condition is not readily associated with a single biology that could be used to target interventions. However, as the science and biology of psychosis grows, these criteria can be re-evaluated just as they have been now, to integrate this information. The criteria require prospective assessment and research in this area will be guided by them while identifying their strengths and weaknesses.

Work for the future

The process of building this consensus highlighted the need for better tools to identify and measure psychotic symptoms. Some have observed the breadth of tools that exist with overlapping items, including some with apparent convergent validity, and have suggested that item analysis and more standardized administration techniques may be a valuable future contribution. Of particular note is the observation that antecedent events and analysis of causes and consequences of specific behaviors and symptoms are critical steps to identifying appropriate psychosocial and other nonpharmacological interventions. The work of the consensus team acknowledges the need to demonstrate clinical meaningfulness, the value of the definition to enhance clinical decision-making, and to create evidenced-based clinical care pathways. Prospective validation of the criteria is a critical next step in

Table 1. Comparison of criteria (adapted with permission; The American Journal of Geriatric Psychiatry)

CRITERIA/CHANGE	JESTE AND FINKEL (2000)	CUMMINGS <i>ET AL.</i> (2020)
Symptoms/ADDITION of definitions and descriptions	Visual or auditory hallucinations Delusions	Visual or auditory hallucinations (e.g. seeing silent individuals standing in the room, seeing children in the yard, or seeing animals in the house) Delusions (fixed false beliefs that the patient believes to be true, e.g. that the spouse is unfaithful, that possessions are being stolen, or that one is not who one claims to be)
Primary diagnosis/UPDATED	All the criteria for dementia of the Alzheimer type are met	All the criteria for any major and mild neurocognitive disorder are met, with the etiologic diagnoses specified (e.g. major neurocognitive disorder (Alzheimer's disease)). Specific diagnoses include Alzheimer's disease, dementia with Lewy bodies, vascular dementia, Parkinson disease dementia, frontotemporal dementia, progressive supranuclear palsy, mild cognitive impairment, traumatic brain injury, and corticobasal degeneration. Other rarer causes of major and mild neurocognitive disorder are also appropriate when diagnosed as a cause of psychosis
Chronology/UNCHANGED	There is evidence from the history that the symptoms in Criterion A have not been present continuously since prior to the onset of the symptoms of dementia	The symptom(s) in Criterion A have been present, at least intermittently, for 1 month or longer.
Duration/SEPARATION OF severity	The symptom(s) in Criterion A have been present, at least intermittently, for 1 month or longer. Symptoms are severe enough to cause some disruption in patients' and/or others' functioning	The symptom(s) in Criterion A have been present, at least intermittently, for 1 month or longer.
Severity/ADDITION of description of disruption		"Symptoms are severe enough to cause some disruption in patients' and/or others' functioning or pose a threat to the safety of self or others. Disruption" is defined as interfering with the patient's or others' ability to accomplish activities of daily living or interact as usual socially; "patient's functioning" is defined as being able to interact with family members and others, not being preoccupied with hallucinations, etc.; "other's functioning" is defined as interfering with the ability of others to care for or interact with the patient or causing distress to the partner.
Exclusion/ADDED more detail; delirium, other medical problems, sensory and cultural origins of symptoms	Criteria for schizophrenia, schizoaffective disorder, delusional disorder, or mood disorder with psychotic features have never been met	A diagnosis of psychosis in major or mild neurocognitive disorder should be excluded in the following patients: 1. Patients who have met the criteria for schizophrenia, schizoaffective disorder, delusional disorder, mood disorder with psychotic features, or depression with psychotic features. 2. When the psychosis occurs exclusively during the course of a delirium. 3. When the psychosis is solely attributable to another general-medical

Table 1. Continued

CRITERIA/CHANGE	JESTE AND FINKEL (2000)	CUMMINGS <i>ET AL.</i> (2020)
Associated features/REMOVAL of negative symptoms Clarification of mood disorder with psychotic features	<p>With agitation: when there is evidence, from history or examination, of prominent agitation with or without physical or verbal aggression</p> <p>With negative symptoms: when prominent negative symptoms, such as apathy, affective flattening, avolition, or motor retardation, are present</p> <p>With depression: when prominent depressive symptoms, such as depressed mood, insomnia or hypersomnia, feelings of worthlessness or excessive or inappropriate guilt, or recurrent thoughts of death, are present</p>	<p>condition (e.g. hypothyroidism) or direct physiological effects of a substance (e.g. a drug of abuse, a medication).</p> <p>4. When the symptoms are culturally appropriate (e.g. ancestor hallucinations in some cultures).</p> <p>5. When the hallucinations are more readily attributable to conditions known to cause hallucinations such as epilepsy, migraine, disease of the sensory organs, or stroke.</p> <p>With agitation: when there is evidence, from history or examination, of prominent agitation with or without physical or verbal aggression.</p> <p>With depression: when prominent depressive symptoms, such as depressed mood, insomnia or hypersomnia, feelings of worthlessness or excessive or inappropriate guilt, or recurrent thoughts of death are present (note that mood disorder with psychotic features is an exclusion for the diagnosis of psychosis with major or mild neurocognitive disorders)</p>

demonstrating the validity, reliability, and utility of the criteria. IPA will promote these activities through its unyielding commitment to serving its multidisciplinary members and to advancing knowledge in our field. All of these efforts are devoted to improving the lives of older adults at risk for, or living with mental and cognitive disorders.

The IPA is proud to have had the opportunity to support this effort using its established methodologies and engaging its global multidisciplinary community. This consensus definition for psychosis in major and mild NCD will help advance the goals of detection and recognition of these conditions, providing a common ground for creating pathways of care that include both nonpharmacological and pharmacological interventions. Regulatory issues exist across multiple agencies, including those that oversee care delivery in different settings as well as those that regulate pharmaceutical development. Criteria for training of care providers, establishing optimal staff-to-patient ratios, and identifying environmental requirements to serve persons with specific neuropsychiatric symptoms to optimize their care are as critical as criteria for demonstrating pharmaceutical efficacy in clinical trials. The proposed definition provides a common ground for better characterizing populations to engage in research, clinical protocols for the evaluation of interventions, and development of standards of

care for these vexing problems. Always ready for future discovery, the IPA supports this work as the “next step” in addressing a serious public health problem. We are hopeful that this effort will promote future novel and even more valuable perspectives, into these vitally important features of the dementia syndrome. We are excited that new research efforts may now be catalyzed leading to innovations in dementia care practices and service delivery that demonstrably improve the lives of older adults across the globe.

Conflicts of interest

Mary Sano, PhD, is the Immediate Past President of International Psychogeriatric Association. She has been a paid consultant to the following companies: Avenir, Biogen, BioXcel, F. Hoffman LaRoche, NovoNordisk, and vTv Therapeutics.

Dr. Cummings has provided consultation to Acadia, Actinogen, Acumen, Alektor, Alkahest, Alzheon, AriBio, Avanir, Axsome, Behren Therapeutics, Biogen, Cassava, Cerecin, Cerevel, Cortexyme, Cytox, EIP Pharma, Eisai, Foresight, GemVax, Genentech, Green Valley, Grifols, Janssen, Jazz, Karuna, Merck, Novo Nordisk, Otsuka, ReMYND, Resverlogix, Roche, Samumed, Samus, Signant Health, Sunovion, Suven, United Neuroscience,

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MARY SANO,¹ JEFFREY CUMMINGS,²
DILIP V. JESTE,^{3,4,5} SANFORD FINKEL⁶ AND
WILLIAM REICHMAN⁷

¹Department of Psychiatry, Icahn School of Medicine at Mount Sinai, NYC and the James J Peters VAMC, Bronx, NY, USA

²Chambers-Grundy Center for Transformative Neuroscience, Department of Brain Health, School of Integrated Health Science, University of Nevada Las Vegas (UNLV), Las Vegas, NV, USA

³Department of Psychiatry, University of California San Diego, La Jolla, CA, USA

⁴Sam and Rose Stein Institute for Research on Aging, University of California San Diego, La Jolla, CA, USA

⁵Department of Neurosciences, University of California San Diego, La Jolla, CA, USA

⁶Department of Psychiatry, University of Chicago Medical School, Chicago, IL, USA

⁷Baycrest Health Sciences and the Department of Psychiatry, Temerty School of Medicine, University of Toronto, Toronto, Canada

Email: mary.sano@mssm.edu

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