

Beyond Frailty in Alzheimer's Disease: Should We Move to the Concept of Intrinsic Capacity?

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Dear Editor,

Frailty, a state of increased vulnerability to poor resolution of homeostasis following a stress (1), is of increased interest in the field of Alzheimer's disease (AD) and related diseases. The two dominant models of frailty, the phenotype model (2) and the cumulative deficit model (3), were first described in 2001. Twenty years later, the International Working Group added frailty in their recommendation for clinical diagnosis of AD as a "factor that can increase the risk of progression to Alzheimer's disease" (4). Indeed, there is emerging literature showing relationships between frailty and clinical AD (5, 6), independently from neuropathology (7). Recently, Canevelli et al. hypothesized that frailty could explain the discrepancy between lesions and symptoms of AD (8).

Beyond the model of frailty, the World Health Organization introduced the new concept of intrinsic capacity (IC), defined as "the composite of all the physical and mental capacities of an individual" in the context of healthy ageing, including five key domains: locomotion, vitality, cognitive, psychological, and sensory functions (9). In this regard, higher IC has been associated with a lower risk of frailty onset; conversely, decline in IC has been already associated to neurocognitive disorders. Indeed, beyond cognition, which is intrinsically affected in AD, other components of IC, such as vitality (or nutrition) (10), locomotion (11), mood (12) or sensory loss (13), were previously associated with worse cognition or increased dementia risk in older adults. Thus, we assume that, beyond frailty, a capacity-centred model, with detection and management of IC declines in older adults with AD, will be an important step toward a better global and integrative approach to AD.

From a deficit-centred model to a capacity-centred model

Fan and Cheong recently described frailty as "the clinical viewpoint of a glass half empty, where it highlights functional deficits accumulated with aging and existing comorbidities, while IC represents a glass half

full, accounting for the functional reserves of the patient" (14). A positive and integrated vision may lead to a better involvement of participants and healthcare professionals. Notably, even if frailty has not been conceived as a condition for excluding patients from interventions (15), it is usually viewed by clinicians in a negative, potentially exclusionary way. Moreover, to provide a comprehensive global and integrative approach to older adults beyond the "perimeter of geriatric medicine", IC appears to be an important step forward in the field of AD (15).

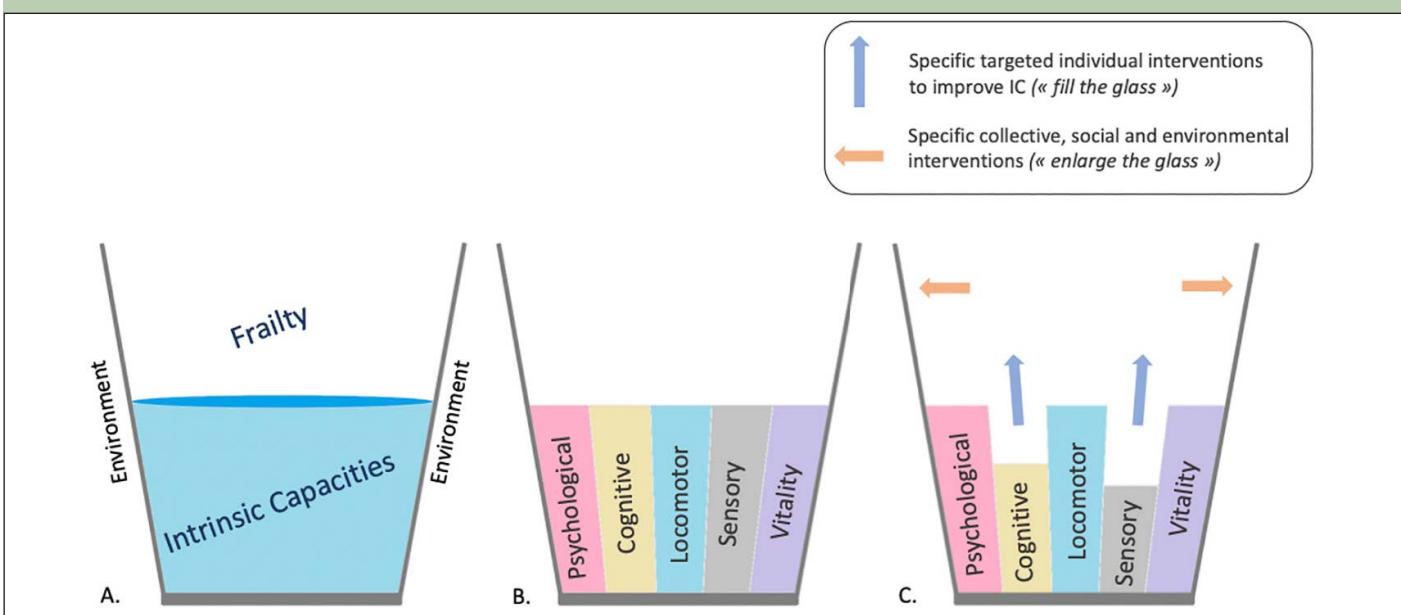
An opportunity to promote the integrated care program in older adults, including those with AD

Integrated Care for Older PEople (ICOPE) corresponds to person-centred and integrated guidelines at the community-level to manage declines in IC (16, 17). ICOPE notably recommends to use tools (including self-administered tools) to screen for loss in IC in primary care. This also aims to support the "self-empowerment of each individual for his/her health status" (15). In the future, if ICOPE is developed on a large scale in older adults, cognition-specialized physicians (e.g., neurologists, geriatricians or psychiatrists) will see patients with a cognitive complaint, but perhaps also with declines in IC in other domains (i.e., sensory, psychological, vitality or locomotion), screened with ICOPE tools. As clinicians, it will be important to understand the relationships between these declines in IC and to propose personalized and tailored interventions in order to improve IC and functional abilities.

Decline in specific IC will lead to specific targeted interventions, centred on the individual's values and priorities

A decline in IC will lead to targeted interventions; for example, a sensory loss could be managed, which could lead to improve the functional abilities. IC being independently associated with incident frailty (18), screening and management of IC loss (19) may lead to

Figure 1. Intrinsic capacities (i.e., psychological, cognitive, locomotor, sensory and vitality) as the “glass half full” and opportunity for individual and collective interventions



The more the glass is filled (i.e., individual with high intrinsic capacities) the more the frailty decreases (A. and B.). In addition, the size of the glass may correspond to the individual's environment. This approach may open window to develop specific targeted interventions to improve functional abilities in AD at the individual level (“fill the glass”, blue arrows) and at the collective level (“enlarge the glass”, orange arrows) (C.). This schematic representation highlights the individual heterogeneity in IC and environmental characteristics, that could lead to personalized interventions.

reduce frailty occurrence, and then improve functional abilities and prevent negative events in patients with AD. Therapeutic and preventive approaches based on IC by using competences of the people rather than their deficits (comparable to the neurocognitive rehabilitation approach in AD) may be proposed.

Interventions should not only focus on the individuals, but also focus on the environmental characteristics, and actions are needed against the social determinants of frailty and IC declines (20). The World Health Organization defines healthy ageing as “the process of developing and maintaining the functional ability that enables well-being in older age” (9), encompassing the relationships between IC and environmental characteristics. Environment comprises “all the factors in the extrinsic world that form the context of an individual’s life”, including factors from the micro level to the macro-level (home, communities and the broader society) (9). Thus, contrary to the concept of frailty, the concept of functional abilities has been developed in a more global and less individual way: functional abilities are made up of the IC (at the individual level) and relevant environmental characteristics (at the collective level) (9). This approach may lead to specific interventions at the individual and the collective level (Figure).

To conclude, if the concept of IC has been developed in the context of healthy ageing, we assume that it may be a major advance in the field of AD and related diseases. IC is not the opposite of frailty, which corresponds to a clinically relevant reduction of IC (15) previously associated with AD (4–7). The monitoring of IC in older

adults, including those with AD will help to detect patient’s “fragilization” (15), to adapt the personalized care, to better motivate the people regarding therapeutic approaches and finally to delay cognitive and functional decline, with specific cognitive (21) and non-cognitive (19) interventions. Future research is needed to confirm that IC could represent prognostic factors in AD, to better understand the inter-relationship between cognition and other IC declines, as well as to confirm that the IC monitoring in AD is efficient to improve clinical outcomes.

Conflict of interests: None.

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