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COMMENTARY

Mild cognitive impairment: some steps forward

There is no doubt that the term mild cognitive impairment (MCI) has become popular in the last decades (Flicker *et al.*, 1991; Petersen *et al.*, 1997). A superficial quantification of the publications that include said term in the title in the Web of Science yields 9,334 citations, including 6,553 articles, 667 reviews, 187 editorials, 37 books, and 249 patents.

But the controversial nature of the concept becomes apparent from the titles of some of the oldest and more cited editorials: "Mild cognitive impairment as a clinical entity and treatment target" (Petersen and Morris, 2005); "Mild cognitive impairment is not a clinical entity and should not be treated" (Gauthier and Touchon, 2005).

A recent review of the concept of MCI states that "MCI is generally regarded as the borderland between the cognitive changes of aging and very early dementia, but while conceptually reasonable, the construct poses difficulties in clinical practice" (Petersen, 2016). The review recognizes the conceptual similarity of this construct and that of "mild neurodegenerative disorder," a pre-dementia phase in the general category neurocognitive disorders of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (American Psychiatric Association, 2013). Although recognizing its controversial nature, the expert concludes by recommending the usefulness of the concept for the clinician: "As treatable etiologies of MCI are identified (such as those due to psychiatric conditions, medications, or medical comorbidities), the cognitive deficits may be reversible. Biomarker development should provide the clinician with new tools to identify and hopefully treat MCI."

The advantages and disadvantages of the use of biomarkers for the diagnosis of Alzheimer's disease (AD) have led to discussions within the IPA, some published in *International Psychogeriatrics* (Chiu and Brodaty, 2013; Dubois *et al.* 2013; O'Brien, 2013a; 2013b).

Two recent editorials of IPG analyze the evolution of the MCI concept. The first of them points out among its limitations the absence of functional loss as a diagnostic criterion. It also mentions the lower variability shown by the incidence studies of the non-amnestic MCI variant with respect to the amnestic MCI variant, suggesting that there may be greater agreement in the definition of the former. In summary, "while MCI does not constitute a valid diagnostic entity, it is a useful label to describe persons who may benefit from early drug intervention for AD" (Ritchie and Ritchie, 2012).

The second editorial, after recalling that isolated and single biomarkers validity remains poor, that for diagnosis proposes these tests are much more useful in ruling out Alzheimer disease than ruling it in, predicts the probable evolution of the MCI concept, from its current binary conception, "have or not have MCI" to a conception of a multidimensional clinical spectrum. It recommends the need to carry out large longitudinal studies of young healthy populations, which include not only the study of biomarkers but also various risk factors and using new, sophisticated, and more complex statistical analysis tools that can disentangle the complexity of the variables involved.

We adhere to its conclusions: "If we can deliver on the promise of better characterizing the clinical spectrum of neurodegenerative disease that relies on (1) multi-domain biomarkers and more accurate neuroimaging techniques looking at a much more detailed part of the brain complemented with (2) more sensitive and psychometrically robust computerized neuropsychological testing, and (3) risk factors both fixed and modifiable with (4) good measures of change, then large categorical approaches will be replaced by accurate individualized predictions. This approach will not only identify the disease accurately to create an appropriately phenotyped sample for clinical trials but also better distinguish neurodegeneration from other neuropsychiatric conditions like anxiety and depression and help drive personalized therapeutic and prevention interventions….For now, the main reason for identifying MCI or any other prodromal phase of dementia could well be to help engage people in clinical research and offer pragmatic advice on life style and health modifications, which undoubtedly have a beneficial effect on brain health" (Saunders *et al.*, 2017).

In this context of expectation and continuous debate, we welcome in this issue of *International Psychogeriatrics* three papers that represent a step forward to improve the diagnostic accuracy and clinical utility of the MCI concept.

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The paper of Beer *et al.* (2018) assumes that semantic interference, conceptualized as a "cognitive stress test," can be a sensitive indicator of the onset of dementia. The authors study a new instrument, Semantic Interference Test (SIT), the result of an adaptation of a pre-existing instrument, which taps proactive and retroactive semantic interference, for predicting progression from MCI to dementia.

The SIT had already demonstrated good discriminative capacity between cognitively normal adults and adults' cases with amnestic MCI (in samples with high probability of presenting AD). The objective of the present study is to define the ideal cut-off points to determine the progression from MCI to Dementia. In an elegant design, the authors study two well-characterized samples along four years, one clinic and the other a community research cohort, to verify their hypotheses: (1) optimal thresholds predicting MCI progression to dementia would be lower (i.e. worse or more impaired) than optimal clinical thresholds previously established for distinguishing MCI from normal cognition; (2) optimal thresholds would more clearly differentiate MCI progressors to dementia from non-progressors in the clinical than in the population-based cohort in which the underlying prevalence of AD and other dementia are likely to be lower.

Authors should be more than happy with the results. Throughout the four years of follow-up, 22.8% of participants in the clinical sample and 10.3% participants in the community sample progressed to dementia. SIT performed reasonable well and similarly for predicting progression from MCI to dementia in both samples; and research hypothesis were confirmed.

Nevertheless, the authors prefer to be cautions on their conclusions. They, of course, underline the apparent positive qualities of the SIT, including its minimal education and cultural bias; but they also recommend the use of other neuropsychological instruments, classical and novel, to study MCI and its progression to dementia. They take this opportunity to remind us the varied uses of neuropsychological assessment: (a) differentiating normal from abnormal performance; (b) differentiating between different diagnostic groups; and (c) delineating those individuals at most risk for disease progression.

Another paper (Park *et al.*, 2018) consists in the validation of a computerized screening test system for MCI. Authors describes the limitations of well-known screening instruments such us MoCa have to detect MCI and the convenience of using computerized cognitive tests, that facilitates the standardization of the administration of the test and that also makes possible to measure reaction time. Considering that the existing instruments do not give enough weight to memory scores and may not reflect the characteristics of older adults with MCI, authors developed a novel instrument, the mobile cognitive function test system for screening MCI (mSTS–MCI). It consists of eight items of memory, one item for attention and four items for executive function (score from 0 to 28).

The validation sample was recruited from communities and welfare centers in South Korea. While the new instrument scores are highly correlated with the MoCA-K scores, it shows extraordinary ROC curves (for total score and reaction time). Coherently, its Predictive Positive Value and Negative Predictive Value are much better than those presented by MoCA-K. These promising results should be revalidated in future studies with bigger and more heterogeneous samples, in particular, regarding the level of education.

The third paper addresses the evaluation of the MCI by means of a functional measure. The objective of the paper by Hedman *et al.* (2018) is to explore if the changes in the perceived challenge of certain everyday technologies (ETs) can be used to detect signs of functional change in MCI.

Authors argue that cognitive ability affects how many types of ETs people use and how efficient this use is. A declining pattern regarding the ability to use ETs might predict future dementia.

The paper provides several examples of how various ETs that are common in the lives of older people (coffee maker, washing machine, mobile phone ...) can challenge their cognitive abilities.

A sample of people with MCI was recruited from a memory clinic in Stockholm and was followed for five years. These people described their difficulties with respect to 92 ETs throughout the five years of follow-up. A Rasch model was used to transform the ordinal ETUQ scores into relative linear measures expressed in log odds probability units (logists). The derived model includes *person measures* that reflect the perceived ability in ET, and *item measures* that reflect the relative challenge of each ET. The model analyzes the Differential Item Functioning, that is, the increasing challenge of every ET after five years.

Results are shown for the most reported items, a list of 46 ETs. Interestingly, five items considered at baseline as "relatively more easy" became more challenging five years later: washing machine, TV with remote control, hand-held mixer, internet interaction, and cash machine (ATM). As conclusions of this study, the change of perceived challenges of ETs may indicate functional change in persons with cognitive decline, and

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both easy and more challenging ETs need to be addressed in future studies.

These three papers illustrate the need for a multidimensional approach to the evaluation of MCI. The first two advocate a refinement of the neuropsychological evaluation of the MCI. The last one suggests the possibility of creating new instruments based on the complaints of deterioration of the functional capacity that the subjects formulate and pays value to the individual as the reference of its own impairment.

No doubt that MCI researchers will be very busy in the coming years. Clinicians just have to wait . . . for the results of international trials using robust multidimensional measures of MCI, carried out in large heterogeneous samples, with subjects followed along enough number of years. . . .

Conflict of interest

None.

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