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Perspective

Alzheimer's Disease and Mild Cognitive Impairment: A Public Health Perspective

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Abstract

In the context of international concern about the problem of dementia and, specifically, of Alzheimer's disease, AD, we focus our interest in the subject of mild cognitive impairment, MCI, from the public health perspective. We review relevant literature and find evidence supporting the notion that MCI has specific interest for the early diagnosis and secondary prevention of AD, although discrepancies in the prevalence reported internationally and, more importantly, discrepancies shown in the conversion rate into AD, suggest that efforts should be done to better characterize the MCI syndrome. We also review literature supporting an optimistic perspective for primary prevention in dementia and AD, in view of the recent identification of potentially modifiable risk factors. Should a well characterized MCI construct be confirmed as preclinical dementia, the research agenda might be aimed at the identification of risk and protective factors associated with MCI, so that intervention studies aiming at the most promising targets for preventive potential might be implemented.

Keywords: Alzheimer's disease; Mild Cognitive Impairment; Prevention

Mild Cognitive Impairment and Secondary Prevention of Dementia and Alzheimer's Disease

Dementia and more specifically the most common of them, Alzheimer's disease (AD) is a source of increasing, international concern, as shown by the World Dementia Council meeting at the G8 dementia summit in December 2013 [1]. It is also apparent the relevance of the problem of dementia for the public health and, in this context, the preclinical diagnosis may be crucial for secondary prevention, since early interventions could be eventually implemented. For an early diagnosis, the so called 'mild cognitive impairment', MCI [2] has attracted a great deal of interest ever since different authors have suggested that this construct is a gray, transitional state between aging and dementia, particularly dementia caused by AD [3]. However, we have some concerns in relation to MCI, as presently characterized. We first suggest that the wide differences in the prevalence of MCI reported to date [4] might be due to methodological differences in studies, but also to factors such as the heterogeneity or the disparity in characterization of the syndrome [5]. Specifically, we have recently reported in the baseline of the longitudinal, Zaragoza Dementia and Depression (ZARADEMP) Study [6], that the weighted prevalence of MCI diagnosed according to the classical Petersen's criteria [2] was 7.9% for the aged 65+ years, but it was approximately half (3.7%) when using the new criteria in DSM-5-MCI [7]. Therefore, initiatives such as the international efforts to better characterize and homogenize the MCI construct, such as the COSMIC project seem to be well justified [8].

A second, and probably more relevant concern relates to the fact that some population studies have shown that a considerable proportion of individuals with MCI do not progress to dementia, even after 10 years of follow-up [9]. We argue that, if MCI cases are sought

as examples of preclinical dementia, then the MCI construct needs better characterization to increase its power to predict subsequent onset of fully expressed dementia, in particular AD. We have suggested that the new DSM-5 category called "Mild Neurocognitive Disorder" might be a better predictor, since the diagnostic criteria appear to be more stringent than the widely used previous conception of MCI as described originally by Petersen (P-MCI) [2,7]. Moreover, we have also shown that non-cognitive, negative-type symptoms were more typically found in DSM5-MCI when compared with P-MCI [7], and this type of negative symptoms have been found to be associated with dementia and AD in the community, and to be good discriminators of non-cases [10].

Primary Prevention of Dementia and Alzheimer's Disease?

Some optimism has recently been observed surrounding the public health perspective in the field of dementia and AD, because of the proposed potential of primary prevention. Some authorized researchers suggest that approximately one third of Alzheimer's disease burden worldwide might be attributed to potentially modifiable risk factors [11], specifically to the following seven factors: diabetes, midlife hypertension, midlife obesity, physical inactivity, depression, smoking, and low educational attainment. We have some data consistent with this research, since we found that the life-time risk of AD is almost double among the illiterate [12]; and that major depression increases four times the risk of AD [13]. If MCI is an example of preclinical dementia and AD, it would be worth testing hypotheses related to the causal association of the suggested risk factors with MCI. We are also encouraged to search environmental risk factors or protectors of dementia and MCI, based on findings suggesting that the prevalence and/or incidence of these conditions may be lower in the Southern European city of Zaragoza when compared with cities in Northern and Western Europe [7,12,14]; and

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on findings implying that the prevalence of dementia in the same city has decreased in men in the last decade [15].

A Research Agenda on Mild Cognitive Impairment

The research agenda, therefore, may include the testing of the predictive power of well characterized MCI constructs in longitudinal studies such as the ZARADEMP project [6], although we, as other authors, have argued that the incorporation of biomarker assessments would provide additional power to the constructs based on clinical criteria [7,16]. The agenda may also include the testing of hypotheses about the associations with MCI, not only of the seven risk factors related to AD, but also of new risk factors such as behavioral features, including health behaviors and lifestyles; biomedical factors, including multimorbidity and access to care; or testing the potential protective effects of factors such as the Mediterranean diet. Ideally, the associations should be quantified and interactions of risk factors should be explored. Large community samples are desirable for this kind of investigation, and the new European initiatives for trans-national research are promising. The identification of risk and protective factors would pave the way for the design of intervention studies aiming at the most promising targets for preventive potential, and the findings could eventually lead to inform existing and future prevention policy.

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