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Review

Self-awareness in Mild Cognitive Impairment: Quantitative evidence from systematic review and meta-analysis

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ABSTRACT

Here we quantitatively summarized evidence of impaired awareness in Mild Cognitive Impairment (MCI) and meta-analytically explored the relationship between Subjective Cognitive Complaints (SCC) and actual cognitive impairment. Twenty-three studies were included, 14 comparing awareness measures in MCI and healthy elderly subjects, and 16 also exploring the neuropsychological underpinnings of impaired awareness. Moderator analyses were conducted to determine whether self-awareness varied according to patient group, the particular state in relation to which insight was assessed, or the approach to measuring awareness. The meta-analysis shows that MCI patients have knowledge of their neuropsychological deficits and that level of awareness varies according to cognitive status, language and memory abilities. The assessment technique employed impacted on the insight phenomena. Specifically, MCI patients seem particularly accurate in evaluating the current state of their performance during an ongoing task and this could be essential in regulating their behavior so that compensative strategies are practiced and greater cognitive independence is achieved. Thus, assessment technique and cognitive status are crucial factors that influence level of awareness and should be taken into consideration in awareness evaluation and rehabilitation.

Contents

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"*Everyone complains of his memory, and no one complains of his judgment*." François de La Rochefoucauld, 17th century writer

1. Introduction

Although Mild Cognitive Impairment (MCI) is a remarkably controversial entity (Stewart, 2012), it remains a central construct given the importance of achieving an early diagnosis of neurodegenerative disorders. The most controversial aspect in diagnosing MCI is the relevance of subjective cognitive complaints (SCC), and there has been a long-running debate about the predictive validity of self-reported concerns about cognitive impairment and dementia. Indeed, the importance of early diagnosis depends on the degree to which likelihood and speed of progression can be accurately predicted (Stewart, 2012). Although numerous longitudinal studies have shown that subjective complaints of cognitive loss are predictive of future cognitive impairment and dementia even in pre-MCI samples (e.g.: Jessen et al., 2011) and in individuals with normal cognitive test performance (non-MCI, Jessen et al., 2014), findings are conflicting (e.g.: Reid and MacLullich, 2006).

Unawareness of cognitive decline is frequently observed in patients with Alzheimer's Disease (AD) (e.g.: Vogel et al., 2004), which is destined to occur in many persons with MCI given that they are at risk for developing the disease (Roberts et al., 2014). Indeed, the concept of MCI assumes that a cognitive continuum exists between normality and AD, i.e., the main cause of dementia. The criteria for MCI, as originally defined by Petersen et al. (1997), include: (1) memory problems, (2) objective memory disorder, (3) absence of other cognitive disorders or repercussions on daily life, (4) normal general cognitive functioning and (5) absence of dementia. Given the diverse presentation of patients' symptoms in the clinical context (due to heterogeneity in etiological factors such as type of degenerative lesions, vascular factors, psychiatric disorders and non-neurological concomitant diseases), the concept was extended (Petersen et al., 2001) and more homogenous MCI subtypes were delineated. Considering the high conversion rate from MCI to AD, which is characterized by the presence of anosognosia (i.e. lack of knowledge of disease, Prigatano and Schacter, 1991) for impairments in activities of daily living, cognitive dysfunctions and behavioral changes (Orfei et al., 2010; Starkstein et al., 2006), MCI patients also might be expected to be less than fully aware of their symptoms. In fact, reduced self-awareness is also observed in MCI patients (Galeone et al., 2011; Vogel et al., 2004, 2005) even though levels of awareness are heterogeneous among samples (Kalbe et al., 2005; Vogel et al., 2004, 2005), and this might contribute to the fact that SCC are not consistently present in MCI patients.

The neuropsychological model of unawareness in MCI and AD (Hannesdottir and Morris, 2007) distinguishes between unawareness *secondary* to memory or executive dysfunction, which may disturb the immediate ability to judge cognitive performance, and *primary* unawareness, which directly affects the long-term and enduring self-awareness system based on one's set of beliefs of his own capacities, attitudes and traits in relation to those of others (Agnew and Morris, 1998; Kaszniak and Edmonds, 2010). According to the model, the likelihood of unawareness in MCI expands with increasing cognitive impairment (Wolfsgruber et al., 2014) and may differ according to MCI subtype (as lack of insight is supposed to be especially present in the frontal/disexecutive form of MCI) and consequent to impairments in specific aspects of memory function (e.g.: consolidation processes, Morris and Mograbi, 2013) in the amnestic type. An additional source of heterogeneity in levels of awareness might derive from the research methods employed (Clare et al., 2013) as for example, different methods of assessing memory awareness elicit different types of awareness phenomena, not necessarily interchangeable or directly comparable (Hannesdottir and Morris, 2007; Marková, 2005).

In recent years, different techniques for measuring impaired awareness in AD and MCI have allowed for the quantification of severity levels. There is, however, no "gold standard" among different methods and self-awareness can be either rated by a competent clinician or self-appraised using questionnaires or structured interviews in which the person rates everyday abilities or symptoms ('off line assessment', Bunnell et al., 1999). Then, personal beliefs about illness status or cognitive/functional/behavioral/affective changes are compared to informant ratings (subjective rating discrepancy, Reisberg et al., 1985) to quantify the extent of unawareness. Nevertheless, the type of insight elicited varies greatly depending on the particular mental or physical state in relation to which is assessed, because awareness is a relational concept that can only be expressed in relation to something to be aware of (i.e. the 'object' of insight, Marková and Berrios, 2001). Alternatively, some authors have used objective measures of memory-monitoring abilities by modifying meta-cognitive paradigms in which participants are asked to make predictions about their performance on a particular memory task ('online' error detection). Unawareness of deficit can be evaluated in terms of prediction accuracy (objective-judgement discrepancy, Hannesdottir and Morris, 2007), which reflects generalized self-efficacy beliefs about cognitive and functional abilities and requires self-monitoring (Kaszniak and Edmonds, 2010), control (Cosentino et al., 2007) and decision making abilities (Agnew and Morris, 1998).

In view of the above and to clarify the potential sources of heterogeneity in MCI self-awareness, we considered timely to systematically review the current literature on awareness in MCI and to quantify the extent of impaired awareness in the targeted population. Meta-analytical techniques were also applied to investigate the magnitude of the supposed association between awareness and neurocognition. Certainly, the question about whether SCC have a role in detecting MCI and dementia is clinically relevant and can be considered a vital public health issue because persons with cognitive disorders come to the attention of the health care system only when symptoms are recognized. If subjective complaint is more sensitive than objective testing in predicting subsequent progression to organic dementia, then general physicians should routinely question patients and family members about cognition and quantitative measures of SCC should be habitually introduced in MCI testing.

2. Material and methods

2.1. Review questions and objectives

Although we did not follow a published pre-specified protocol during our systematic review, the inclusion/exclusion criteria, search strategy and primary assessed variables of the papers were defined a-priori according to the guidelines proposed in the PRISMA statement (Moher et al., 2009). Our main aim was to quantify the extent of impaired self-awareness in MCI and the magnitude of the awareness-cognition relationship. These main issues were further refined by addressing four related but more specific objectives. Specifically, we evaluated whether self-awareness differs according to: (a) recruitment source (through physician referral or announcement and advertising); (b) MCI subtype (i.e. amnestic, non-amnestic, multiple or single-domain), and ($b_{ancillary}$) whether it is affected by degree of memory impairment; (c) we verified whether the particular physical/mental state in relation to which awareness is assessed can influence its clinical manifestation; and (d) we determined the potential impact of the assessment technique employed on the phenomenon of awareness elicited.