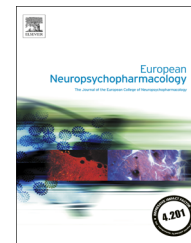




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Quantifying motivational deficits and apathy: A review of the literature

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Received 29 June 2014; accepted 23 August 2014

KEYWORDS

Alzheimer's disease;
Apathy;
Assessment tools;
Major depressive disorder;
Parkinson's disease;
Schizophrenia

Abstract

Varying definitions of apathy in the published literature and a lack of a consensus regarding diagnostic criteria make the identification and quantification of apathy difficult in both clinical trials and clinical practice. The Apathy Evaluation Scale was developed specifically to assess apathy, but variations in the threshold values defined for clinically significant apathy diminish its use as a screening tool in clinical trials, although it has demonstrated sensitivity to changes in treatment in a number of studies. The Neuropsychiatric Inventory contains an Apathy subscale, which has been used to identify clinical trial populations (with a consistent threshold value) and measure changes following treatment. Few of the other assessment tools currently used in patients with neuropsychiatric disorders are specific for apathy or explore it in any depth, most have not been validated in the general population, do not have cut-off points representing clinically significant apathy, and its changes over time and in response to treatment. Further research is required to address these issues in order to facilitate the quantification of apathy and its natural history. Such research should be conducted with the aim of developing new, specific tools for use across neuropsychiatric disorders.

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1. Introduction and rationale

Apathy, in the context of patients with neuropsychiatric disorders, is the focus of an increasing number of clinical and observational studies, due to its negative impact on functioning and quality of life (Leroi et al., 2011; Konstantakopoulos et al.,

2011; Benito-Leon et al., 2012; Kuhlmei et al., 2013). While a range of assessment scales exists for screening and measurement of apathy, none are currently considered the 'gold standard' tool. Some are apathy-specific, e.g. the Apathy Evaluation Scale (AES), while others contain subscales or components relating to apathy, e.g. the Neuropsychiatric Inventory (NPI). These are reviewed and summarised here in the context of individuals with Alzheimer's disease (AD), Parkinson's disease (PD), schizophrenia and major depressive disorder (MDD), and in the general population (as selected on the basis of the quantity of literature available). Recommendations based upon

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this review are made regarding applicability in both clinical practice and the clinical trial settings, and future research approaches are suggested.

2. Experimental procedures

MEDLINE[®] as accessed through PubMed[®] was the sole database used in this review. Initial search terms were the following: (Apathy OR motivation OR motivational deficit OR avolition OR lassitude OR loss of interest) AND (rating scale OR assessment); (apathy OR motivation OR motivational deficit OR avolition OR lassitude OR loss of interest) AND (depression OR psychosis OR schizophrenia OR Alzheimer's disease OR dementia OR Parkinson's disease); (apathy OR motivation OR motivational deficit OR avolition OR lassitude OR loss of interest) AND (antidepressant OR antipsychotic OR neuroleptic OR anticholinergic OR antiparkinsonian OR dopaminergic).

English language articles published up to September 2013 were selected, with no time limit for the earliest date of publication. Relevant citations within the publications identified via the searches were also reviewed. The full articles were analysed for the following information: (1) components relating to apathy/motivation; (2) validation and psychometric properties; (3) application in recent clinical studies (published 2011-2013). Secondly, the rating scales identified were themselves used as search terms to identify further relevant articles.

3. Apathy/motivation-focused assessment tools

3.1. Tools used in the general population

Assessment tools for the investigation of apathy in the general population have largely been based on an evaluation of motivation along a continuum, from high to low. In general, they do not contain any defined cut-off values for lack of motivation (Vallerand et al., 1992; Pelletier et al., 1995).

The Academic Motivation Scale (AMS) consists of seven subscales, covering intrinsic motivation, extrinsic motivation, and amotivation; each of which contain four items that the individual self-rates using a seven-point scale (Vallerand et al., 1992). The AMS was validated in university students, and showed adequate levels of internal consistency and test-retest reliability. The Sports Motivation Scale (SMS) is a comparable tool, with the exception that it focuses on students undertaking sporting activities (Pelletier et al., 1995). The 16-item Academic Amotivation Inventory (AAI) also rates the presence of motivation (Legault et al., 2006) and has been applied to school children. The AAI showed strong correlations with academic self-esteem, lack of academic interest, academic anxiety and indifference regarding academic achievement.

The Intrinsic Motivation Inventory (IMI) is a comprehensive, self-rated, 54-item, six-subscale tool (Ryan, 1982; Choi et al., 2009). It focuses on the degree of motivation present in an individual, with 'amotivation' at the low end of the scale. It has demonstrated good psychometric properties.

3.2. Tools used in patients with neuropsychiatric disorders

Some rating scales for use in neuropsychiatric disorders are available in alternative versions, for the clinician's objective assessment, the patient's subjective assessment and the caregiver's assessment. While the patient has the greatest experience of her/his emotional state, apathy may be associated with lack of insight, so a clinician's objective evaluation may be more valid than a patient's self-rating (Starkstein et al., 2001; Njomboro and Deb, 2012). A caregiver may also be able to provide a more accurate record of the frequency and duration of symptoms than the individual concerned. Interview of the patient by the clinician provides an opportunity to compare the caregiver's insights with the patient's perceptions (de Medeiros et al., 2010).

The AES was specifically designed to provide a detailed exploration of the behavioural, cognitive and emotional aspects of apathy (Table 1) (Marin et al., 1991). Versions for the ratings of clinicians (AES-C), caregivers (AES-I) and patients (AES-S) are available, and a 10-item short version of the AES (AES-10) has been created specifically for use among nursing-home residents (Lueken et al., 2007).

The AES was initially validated in individuals with AD, stroke, MDD and healthy elderly subjects (Marin et al., 1991). It demonstrated high inter-rater reliability and test-retest reliability; there was also a clear discrimination between apathy and depression, and apathy and anxiety on the AES-C and AES-S. Mean AES scores were also significantly higher for stroke, AD and MDD patients relative to control subjects. In another sample of patients with dementia, AES-S and AES-I total scores were weakly correlated with the depression subscale of the NPI, while AES-C total score was not correlated with NPI-Depression score (Clarke et al., 2007). The internal consistencies of the apathy factors in each scale were high.

Threshold values of the AES total score have been proposed as indicators of clinically significant apathy. However, these have differed across studies, ranging from ≥ 30 to ≥ 41.5 (Marangell et al., 2002; Marin et al., 1991; Clarke et al., 2007; Cramer et al., 2010; Varanese et al., 2011; Raskin et al., 2012; Lenze et al., 2012; Clarke et al., 2008). To date no studies have reported discrete ranges for different severities of apathy or the determination of a minimal clinically important difference (MCID) in AES score, although changes in mean scores have indicated a sensitivity to treatment effects in AD, PD and MDD patients (Padala et al., 2010; Lam et al., 2012; Drapier et al., 2008; Marangell et al., 2002; Ravindran et al., 2008; Raskin et al., 2012; Lenze et al., 2012).

Several factor analyses of the AES-C, AES-I and AES-S have been conducted in individuals with AD and other types of dementia, PD, MDD, stroke and subarachnoid haemorrhage, and psychosis. These studies identified two or three factors in the AES with varying terminologies, including interest; cognitive-behavioural; social indifference; insight and social contacts (Marin et al., 1991; Hsieh et al., 2012; Clarke et al., 2007; Ahearn et al., 2012; Faerden et al., 2008). One study has described an AES-apathy subscale, comprising 12 items from the original scale that all relate to interests, motivation and initiative, with clinically significant apathy defined as a score of ≥ 27 (Faerden et al., 2008, 2009).

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