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Perspective

Implementation of subjective cognitive decline criteria in research studies

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Abstract

Introduction: Subjective cognitive decline (SCD) manifesting before clinical impairment could serve as a target population for early intervention trials in Alzheimer's disease (AD). A working group, the Subjective Cognitive Decline Initiative (SCD-I), published SCD research criteria in the context of preclinical AD. To successfully apply them, a number of issues regarding assessment and implementation of SCD needed to be addressed.

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Methods: Members of the SCD-I met to identify and agree on topics relevant to SCD criteria operationalization in research settings. Initial ideas and recommendations were discussed with other SCD-I working group members and modified accordingly.
Results: Topics included SCD inclusion and exclusion criteria, together with the informant's role in defining SCD presence and the impact of demographic factors.
Discussion: Recommendations for the operationalization of SCD in differing research settings, with the aim of harmonization of SCD measurement across studies are proposed, to enhance comparability and generalizability across studies.

Keywords: Subjective cognitive decline (SDC); Alzheimer's disease; SCD-I; Preclinical; Operationalization; Harmonization

1. Introduction

Subjective cognitive decline (SCD) is receiving increasing attention as a risk factor for incident dementia because of Alzheimer's disease (AD) [1]. SCD manifests before the onset of clinical impairment [2] and as such could serve as a potential target population for early intervention trials [3]. Recently, an international working group, the Subjective Cognitive Decline Initiative (SCD-I), published research criteria for SCD in the context of preclinical AD [4]. To successfully apply these criteria, several issues with regard to assessment and implementation of SCD need to be addressed.

The categorization of SCD is largely based on self-report not only by an individual but also potentially by an informant and by the interpretation of this report by the investigator. Currently, there is neither a neuropsychological test score nor any accepted self- or observer/informant scale to classify an individual with SCD. SCD assessment also varies by research setting, that is, epidemiological [5–11] versus memory clinic [12–16]. In memory clinics, the mere fact that an individual was referred may serve to define the existence of decline. Moreover, a detailed clinical history is often obtained in addition to neuropsychological testing, similar to the clinical diagnosis of mild cognitive impairment (MCI) [17–19] and dementia [20]. This is in contrast to epidemiologic studies that typically comprised volunteer-based samples, where the meaning and significance of decline may differ. For multicenter research trials and for comparability across studies, however, it is crucial to define research criteria for SCD that promote consistency across sites [4]. This implies that subjective clinical judgment has to be reduced, and objective scales and tests with defined cutoffs are needed to provide an operationalized diagnosis [21]. This permits a transparent understanding and potential replication of the definition of SCD across studies. At the same time, it is evident that different studies have different objectives, participant populations, and available methods and measures [21–23]. Therefore, flexibility of SCD operationalization is required to serve the aim of each respective study. The need for flexibility precludes one general SCD operationalization for identical application across studies. Furthermore, a single approach would limit research because, currently, variability of SCD operationalization continues to increase scientific understanding of SCD. Finally, a single approach would not be practical with regard to ongoing studies and may not be feasible when considering effects of culture and language on SCD reporting.

The aim of this opinion article is to address core issues in SCD research in more depth and to provide recommendations on how to begin operationalizing and implementing SCD criteria with the long-term goal of fostering comparability and harmonization of criteria for future clinical trial enrollment.

2. Methods

To achieve the study goals, a writing group was established, comprising 10 members of the SCD-I working group. The writing group met at the 2015 Alzheimer's Association International Conference in Washington, DC, to identify and agree on topics relevant to the operationalization of SCD criteria in research settings [4]. Selected topics included those related to SCD inclusion and exclusion criteria, together with the role of the informant in defining the presence of SCD and the impact of key demographic factors.

Members of the writing group drafted individual sections of this article. The manuscript was then discussed with other members of the SCD-I working group and modified accordingly. Recommendations on the operationalization of SCD in research settings were formulated based on theoretical considerations, the existing literature, and expert opinion.

3. Results

In the following sections, components of the SCD criteria are discussed in detail with regard to their use in research studies.

3.1. Operationalization of the SCD inclusion criteria

3.1.1. Self-experienced persistent decline in cognitive capacity in comparison with a previously normal status and not related to an acute event

SCD in the context of preclinical AD refers to the self-perception of a decline in cognitive performance in daily