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Featured Article

Subjective cognitive decline in cognitively normal elders from the community or from a memory clinic: Differential affective and imaging correlates

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Abstract

Introduction: Subjective cognitive decline (SCD) could indicate preclinical Alzheimer's disease, but the existing literature is confounded by heterogeneous approaches to studying SCD. We assessed the differential cognitive, affective, and neuroimaging correlates of two aspects of SCD: reporting high cognitive difficulties on a self-rated questionnaire versus consulting at a memory clinic.
Methods: We compared 28 patients from a memory clinic with isolated SCD, 35 community-recruited elders with similarly high levels of self-reported cognitive difficulties, and 35 community-recruited controls with low self-reported cognitive difficulties.
Results: Increased anxiety and amyloid β deposition were observed in both groups with high self-reported difficulties, whereas subclinical depression and (hippocampal) atrophy were specifically associated with medical help seeking. Cognitive tests showed no group differences.
Discussion: These results further validate the concept of SCD in both community- and clinic-based groups. Yet, recruitment methods influence associated biomarkers and affective symptomatology, highlighting the heterogeneous nature of SCD depending on study characteristics.

Keywords: Alzheimer's disease; Subjective cognitive decline; Cognitive complaint; Preclinical; Amyloid β; Florbetapir-PET; MRI; Atrophy; Hippocampus; Anxiety; Depression

1. Introduction

Some elder individuals experience subjective cognitive decline (SCD) while showing normal "objective" cognitive performances (i.e., scores within the normal range on standardized neuropsychological tests). Although these individuals have been described for decades [1], they have received increasing attention over the past few years, with the growing interest in characterizing preclinical stages of Alzheimer's disease (AD) [2,3]. Indeed, several epidemiologic studies have shown that, in elders without identifiable cognitive deficits, SCD is associated with a higher risk to develop mild cognitive impairment or AD dementia [4–8].

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Recent research has also shown that, at the group level, SCD is associated with neuroimaging biomarkers suggestive of AD (atrophy and/or hypometabolism in temporoparietal regions [9–21] and amyloid β (Aβ) deposition [18,22–26]), although negative findings have also been reported [27–31] (see Table 1 for review).

This converging evidence suggests that SCD could be among the first clinically observable signs of AD. However, individuals with SCD constitute a heterogeneous population [32]: in a considerable proportion of cases, SCD is likely due to non-AD etiologies including poor general health, sleep disorders, medication, or personality traits [33]. The current challenge is thus to identify the specific characteristics of SCD that are associated with an increased likelihood of AD etiology.

The SCD-Initiative working group recently published a conceptual framework for research on SCD in the context of preclinical AD; this initiative is meant to propose SCD criteria and encourage standardized research to refine our understanding of SCD [34]. Indeed, comparison between existing studies is currently hampered by the wide variability in the definition and criteria used to study SCD (aka "subjective cognitive/memory impairment," "cognitive/memory complaint," etc [34]). As recently highlighted [35,36], the recruitment procedure is an important source of variability among studies (see Table 1). SCD has been studied in volunteers from the community [18,22,23,25] or more rarely from population-based samples [14,26]; in these cases, diverse questions or questionnaires were used to quantify SCD [37]. Other studies have used a different approach, specifically assessing patients recruited from a memory clinic [9–11,13,17,24,38–41], that is, patients who sought help because of SCD. In the latter case, it could be hypothesized that the active process of seeking medical help is motivated by more important subjective cognitive difficulties and/or associated concern, which might have clinical relevance [42,43]. Previous studies generally reported AD-like brain alterations in clinical SCD individuals compared with community-recruited controls (see Table 1). However, groups are generally not matched on the level of self-reported cognitive difficulties: when documented, clinical SCD patients report more subjective difficulties than controls [11,24]. Then, it is not clear whether the presence of abnormal AD biomarkers is mainly associated with higher subjective difficulties or with the medical help-seeking behavior per se. Clarifying this point is crucial to determine whether selecting medical help seekers has actual added value to studying SCD and potentially to screen participants in the context of enrichment strategies for clinical trials in clinically normal individuals [3,26,44].

In addition, most studies have shown that SCD is more associated with subclinical anxiety and depression than to actual cognitive performances [9–16,33,45–47]. Interestingly, evidence also suggests that the psychoaffective symptomatology usually increases in early or preclinical stages of cognitive decline [48,49] and/or that it could even constitute a risk factor for subsequent cognitive decline [50,51] (for review and discussion, see the articles by Marchant and Howard [52] and Ismail et al [53]). Overall, the relationship between SCD and affective factors needs to be further refined, notably as anxiety and depression seem to parallel self-reported cognitive difficulties and could be associated with (and maybe trigger) medical help-seeking behavior.

Keeping with the aims of the SCD-Initiative and aforementioned caveats in the literature, the objective of the present study was to assess the relevance of recruitment setting in selecting SCD individuals to identify those with preclinical AD. For this purpose, we compared SCD patients recruited from a memory clinic (SCDclinic group) with individuals recruited from a pool of community-recruited volunteers who scored high on a self-rating cognitive difficulty scale (SCDcommunity group). We assessed the relevance of this feature with regard to neuropsychological performances, affective measures, and neuroimaging biomarkers (gray matter atrophy and Aβ deposition). We hypothesized that SCD individuals who seek help in a memory clinic would be more likely to have indicators of preclinical AD than those recruited from the general community.

2. Methods

2.1. Participants

A total of 100 cognitively normal individuals were included in the present study. They were all right handed, aged 54 years or older, and included in the multimodal neuroimaging study of early AD (IMAP+) in Caen, France. Participants were recruited from two main sources (see Fig. 1).

Twenty-eight patients were recruited from the local memory clinic (SCDclinic), which they attended because of self-reported cognitive concerns. During the interview, the clinician ensured that the complaint was not related to current medication taking, major psychiatric or neurologic conditions (including major depressive disorder or generalized anxiety disorder), or other medical conditions. Patients underwent standardized neuropsychological testing which did not identify any objective cognitive impairment (scores were in the normal range for each neuropsychological test). Patients were then offered to participate in the IMAP+ study to undergo additional cognitive and neuroimaging examinations.

Seventy-two participants were recruited from the community through public advertising, as they volunteered to participate in the IMAP+ study. They had no history of major medical condition, had never consulted a memory clinic, and performed in the normal range on a standardized neuropsychological examination. This group was further divided into two groups depending on their self-reported cognitive difficulties (see section 2.2.1 below). Using a median split, 35 individuals with low scores were used as a control group and the 35 individuals with the highest scores were considered as the SCDcommunity group; note that two individuals