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Social cognition in Alzheimer's disease: A separate construct contributing to dependence

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Abstract The extent to which social cognitive changes reflect a discrete constellation of symptoms dissociable from general cognitive changes in Alzheimer's disease (AD) is unclear. Moreover, whether social cognitive symptoms contribute to disease severity and progression is unknown. The current multicenter study investigated cross-sectional and longitudinal associations between social cognition measured with six items from the Blessed Dementia Rating Scale, general cognition, and dependence in 517 participants with probable AD. Participants were monitored every 6 months for 5.5 years. Results from multivariate latent growth curve models adjusted for sex, age, education, depression, and recruitment site revealed that social cognition and general cognition were unrelated cross-sectionally and throughout time. However, baseline levels of each were related independently to dependence, and change values of each were related independently to change in dependence. These findings highlight the separability of social and general cognition in AD. Results underscore the relevance of considering social cognition when modeling disease and estimating clinical outcomes related to patient disability.

Keywords: Alzheimer's disease; Social cognition; Cognition; Dependence

1. Introduction

Social cognition has been described as a set of converging implicit and explicit processes that are engaged to understand or interpret the self in relation to others [1,2]. This set of processes forms the basis of the complex set of behaviors and mutually shared expectations that enable individuals to interact successfully with one another across a range of situations [3]. In contrast to certain presentations of frontotemporal dementia (FTD), early Alzheimer's disease (AD) is characterized frequently by preserved social cognition [4]. In fact, social cognition often remains intact into the moderate stages of the disease [5,6]. However, a small subset of individuals with AD evidence marked changes in social cognition early during the disease that is sometimes severe enough to elicit misdiagnoses of FTD. Even in cases that fit the typical AD profile, with amnestic deficits being prominent, individuals have been shown to demonstrate impairment on objective social cognitive tests including Theory of Mind (ToM) and emotion recognition [7,8], and in some cases these impairments can be commensurate with those in FTD. See Harciarek and Cosentino [9] for a review.

The extent to which social cognitive deficits represent a component of the disease that is separable from general

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cognitive deficits in AD has not been examined formally. Existing work has demonstrated that functional deficits and psychiatric symptoms (i.e., depression, psychosis, agitation), although related to general cognitive impairment in AD, are separable elements of the disease [10–12]. Social cognitive symptoms may represent yet another specific manifestation of disease pathology that is distinct anatomically and/or behaviorally from general cognitive impairment. For example, social behaviors have been shown to have distinct neural circuitry originating in the orbitofrontal regions of the prefrontal cortex (PFC) and mapping onto specific regions (e.g., ventral vs. dorsal) of subcortical structures, including the striatum, globus pallidus, and thalamus [13,14]. Behavioral evidence for the dissociation between this circuitry and other circuits originating in the PFC can be seen, for example, in the frequent dissociation between social cognition and executive abilities in behavioral variant FTD [15–19]. It has also been suggested that social cognitive deficits may reflect compromise within a network including the PFC, insula, and temporal lobe that is critical for updating and processing contextual cues [20]. This social context network model has been proposed recently as a possible basis for the social cognitive changes in behavioral variant FTD.

Alternatively, it is possible that social cognitive deficits in AD stem from more general cognitive deficits. For example, it has been suggested that impairment on objective tests of emotion recognition and ToM may reflect deficits in visuoperception or executive functioning, for example [21]. The first aim of this study was to examine the cross-sectional and longitudinal associations between subjectively rated social cognitive symptoms assessed with a six-item subscale from the Blessed Dementia Rating Scale (BDRS) and general cognition for the first time in a large cohort of individuals with AD. A second, related aim was to clarify the extent to which subjectively rated social cognitive symptoms, although potentially unrelated to general cognitive symptoms, have relevance to disease severity and course assessed with the Dependence Scale (DS) [22], a measure that has been recommended for modeling AD progression [23]. The DS accounts for more variance in clinical outcomes than cognitive scores alone [23]. Indeed, when compared with other markers of disease including the Mini-Mental State Examination (MMSE), Disability Assessment in Dementia, and Clinical Dementia Rating, the DS accounted for the greatest amount of variance in a variety of economic (e.g., direct medical costs) and quality-of-life outcomes for patients and caregivers. It has thus been recommended for use in models of long-term disease progression in AD.

2. Material and methods

2.1. Participants and procedures

The current sample included 517 patients diagnosed with probable AD and enrolled in the Multicenter Study of Predictors of Disease Course in Alzheimer's Disease. Local institutional review boards at all participating sites approved the study. Full study procedures are described elsewhere [24,25]. In brief, patients were recruited in two waves at outpatient clinics and clinical research centers at four sites in the United States and Europe: Columbia University Medical Center (n = 208), John Hopkins School of Medicine (n = 147), Massachusetts General Hospital (n = 124), and the Hôpital de la Salpêtrière in Paris, France (n = 38). Diagnoses of probable AD were made using National Institute of Neurological and Communicable Diseases and Stroke–Alzheimer's Disease and Related Disorders Association criteria [2] at consensus conferences attended by at least two physicians specializing in dementia and one neuropsychologist. Complete inclusion and exclusion criteria for the study have been described previously [24,25]. All patients were required to have mild dementia defined by a Modified Mini-Mental State Examination (mMMSE) score of 30 points or more (described later), which is approximately equivalent to a Folstein MMSE score of 16 points or more. Exclusion criteria were evidence for a cause of dementia other than AD, parkinsonism, stroke, alcoholism, schizophrenia, schizoaffective disorder, and electroconvulsive therapy within 2 years preceding study enrollment or a history of 10 or more electroconvulsive treatments in a single course.

2.2. Measures

Social cognitive symptoms were assessed at each occasion on a scale from 0 to 6 points based on a subset of informant-rated items from the BDRS [26] that query whether the patient is (*i*) more stubborn than before and less able to adapt to change, (*ii*) more self-centered than before; (*iii*) unconcerned about others' feelings, (*iv*) unable to control emotions, (*v*) easily angered, and (*vi*) likely to make strange jokes or laugh at things that are not funny. These items were shown previously to load together on a single factor that was independent from three other factors assessing symptoms related to general cognitive symptoms (e.g., remembering short lists, finding the way around the house), apathy (e.g., less interest in starting new things, less likely to participate in hobbies, decreased emotional reactions), and basic self-care (e.g., eating, dressing, and bladder control) [27].

Global cognitive status was evaluated at each occasion with the mMMSE [28]. In addition to items from the MMSE [29], the mMMSE includes items that allow for more comprehensive assessment of working memory, calculation, recall of the current and four previous presidents of the United States, confrontation naming, repetition, and visuoconstruction. The scale was translated and modified for assessments at the Paris site. Scores range from 0 to 57 points, with higher scores indicating better cognitive functioning.

Depressive symptoms were assessed at baseline with the Columbia University Scale for Psychopathology in AD [30],