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Research report

# Social influence on associative learning: Double dissociation in high-functioning autism, early-stage behavioural variant frontotemporal dementia and Alzheimer's disease

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## ARTICLE INFO

## ABSTRACT

*Introduction:* Most of our learning activity takes place in a social context. I examined how social interactions influence associative learning in neurodegenerative diseases and atypical neurodevelopmental conditions primarily characterised by social cognitive and memory dysfunctions.

*Methods:* Participants were individuals with high-functioning autism (HFA, $n = 18$), early-stage behavioural variant frontotemporal dementia (bvFTD, $n = 16$) and Alzheimer's disease (AD, $n = 20$). The leading symptoms in HFA and bvFTD were social and behavioural dysfunctions, whereas AD was characterised by memory deficits. Participants received three versions of a paired associates learning task. In the *game with boxes test*, objects were hidden in six candy boxes placed in different locations on the computer screen. In the *game with faces*, each box was labelled by a photo of a person. In the *real-life version* of the game, participants played with real persons.

*Results:* Individuals with HFA and bvFTD performed well in the computer games, but failed on the task including real persons. In contrast, in patients with early-stage AD, social interactions boosted paired associates learning up to the level of healthy control volunteers. Worse performance in the real life game was associated with less successful recognition of complex emotions and mental states in the Reading the Mind in the Eyes Test. Spatial span did not affect the results.

*Conclusions:* When social cognition is impaired, but memory systems are less compromised (HFA and bvFTD), real-life interactions disrupt associative learning; when disease process impairs memory systems but social cognition is relatively intact (early-stage AD), social interactions have a beneficial effect on learning and memory.

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## 1. Introduction

Researchers and clinicians routinely use laboratory tests to assess learning and memory in different patients with cognitive dysfunctions. Despite the widespread application of this approach, neuropsychological tests of learning and memory do not take into consideration the inherently social nature of knowledge acquisition, expression and transmission in humans and animals. Studies of social cognition emphasize notions such as attribution, attitudes, cultural symbols, recognition of complex emotions, and empathizing with the feelings and thoughts of others (Adolphs, 2009; Cacioppo & Decety, 2011; Fiske & Taylor, 2013; Frith & Frith, 2012), but rarely consider how episodic memory traces are recruited to maintain and promote interpersonal interactions and social bonds (e.g., who was cooperative and aggressive?, who owns behaviourally relevant objects?) (Brennan & Kendrick, 2006; Davidson, Drouin, Kwan, Moscovitch, & Rosenbaum, 2012; Emery & Clayton, 2004; review in Allen & Fortin, 2013).

The conceptual and philosophical difference between "learning and memory research" and "social cognitive research" has practical relevance: based on the clinical features, physicians differentiate diseases characterised by social dysfunctions and neuropsychiatric symptoms [e.g., behavioural variant frontotemporal dementia (bvFTD) and autism-spectrum disorders] and diseases characterised by cognitive deficits, for instance, the loss of episodic memory [e.g., early-stage Alzheimer's disease (AD)] (Frith, 2012; Hodges, 2013). New data from bvFTD, however, indicate that this dichotomy is much too simplistic, and clinically relevant memory deficits are present in bvFTD (Hornberger & Piguet, 2012).

The purpose of the work presented here was to address the interaction between these two domains. Specifically, I studied how real-life social interactions may affect object–place associative learning and short-term spatial memory in mostly "social" and "memory" disorders. To achieve this aim, I compared the performance of patients with early-stage bvFTD, AD and high-functioning autism (HFA) on a paired associates learning (PAL) task administered in a laboratory setting and a real-life setting with actors. In a classic PAL test, participants learn where objects are hidden via the acquisition of object–location associations. Extensive evidence suggests that laboratory PAL tests are sensitive to the pathology of the medial temporal lobe, including the hippocampal formation, which is a core structure in the pathophysiology of AD (Blackwell et al., 2004; O'Connell et al., 2004; Sahakian et al., 1988; Swainson et al., 2001). In contrast, the majority of studies reported normal PAL and other cue-induced recall performances in individuals with HFA (review in Boucher, Mayes, & Bigham, 2012). Considering bvFTD, recent results suggest that, contrary to the predominant clinical conceptualisation of the illness (Neary et al., 1998), episodic memory is impaired (Hornberger & Piguet, 2012). However, patients with early-stage bvFTD showed normal performances on PAL tasks, e.g., face–place associations (Clague, Dudas, Thompson, Graham, & Hodges, 2005), or their deficit was much less pronounced than that of patients with AD (Lee, Rahman, Hodges, Sahakian, & Graham, 2003). Overall, PAL is optimal to model and compare different laboratory tasks and real-life learning scenarios.

I had two main hypotheses. First, based on data from previous studies introduced above, I expected impaired laboratory PAL performance in AD and intact or less affected laboratory PAL performance in HFA and bvFTD. The second assumption was that when real persons sitting in different locations hid objects, that is, in a real-life version of the PAL task, individuals with social dysfunctions (HFA and bvFTD) would display an impoverished performance, whereas patients with AD would not show a further decline or improve performance relative to the laboratory PAL task. The basis of this assumption was that social functions, e.g., the representation of mental states of others, are implicated in real-life learning, and deficient social cognition might interfere with memory in bvFTD and HFA. If dysfunctional real-life PAL were due to altered social cognition in HFA and bvFTD, worse performance on advanced affective Theory of Mind (ToM) tests (e.g., the identification of complex social emotions and attribution of mental states) would be associated with poorer real-life PAL performance.

## 2. Materials and methods

### 2.1. Participants

Individuals with AD, bvFTD and HFA were enrolled at the National Institute of Psychiatry and Addictions, Budapest (North Hungary) and the University of Szeged, Faculty of Medicine, Szeged (South Hungary). Specialists referred patients to these centres from the whole country. We focused on recently diagnosed patients with bvFTD and AD (time since diagnosis less than 1 year) to avoid confounding effects due to generalized cognitive dysfunctions and chronic behavioural and psychological symptoms. Young and elderly control participants with negative history for neurological and psychiatric disorders were recruited via email advertisements and personal networks. Diagnoses were made according to established criteria: National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS–ADRDA) for probable AD (McKhann et al., 1984), Lund–Manchester criteria for bvFTD (Neary et al., 1998) and Autism Diagnostic Interview, Revised (Lord, Rutter, & Le Couteur, 1994) for HFA. Patients with bvFTD were also evaluated according to the International Consensus Criteria for bvFTD (Rascovsky et al., 2011). All patients met the criteria of probable bvFTD (at least three of six behavioural symptoms, significant functional decline, and neuroimaging evidence of frontal lobe atrophy). Frontal lobe atrophy was described by the Kipps index (Kipps et al., 2007). Medial temporal lobe atrophy was evaluated using the Scheltens scale (Scheltens et al., 1992). In addition to standard diagnostic tools, a cerebrospinal fluid biomarker was available, the phosphorylated tau/amyloid beta 42 (Aβ42) ratio, which distinguishes AD from bvFTD with high sensitivity and specificity (cut-off: .21) (de Souza et al., 2011). The following scales and tests were used to assess clinical symptoms and background cognitive status: Mini-Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975), Addenbrooke's Cognitive Evaluation (ACE)