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The relationship between affective decision-making and theory of mind in the frontal variant of fronto-temporal dementia

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Abstract

Structural brain imaging and neuropsychological data implicate the orbital aspects of prefrontal cortex in the developing neuropathology of fvFTD. Damage to this region is associated with deficient performance on laboratory tasks assessing theory of mind (ToM) and affective decision-making (DM), but the relationship between these two capacities in patients with prefrontal cortex dysfunction is unclear. We studied a group of patients with early/mild fvFTD ($n = 20$) and a group of matched normal controls ($n = 10$) on the Iowa gambling task (IGT) of affective decision-making, and the "reading the mind in the eyes" (MIE) and "faux pas" (FP) tests of ToM. The fvFTD group was impaired in both ToM tasks and the IGT. While performance measures from the two ToM tasks were significantly correlated, they were not associated with IGT performance. This suggests that whilst similar prefrontal circuitry is implicated in ToM and DM tasks, these cognitive domains may be independent. In clinical settings, the IGT may be useful as a complementary tool to the frontal test battery for patients with early/mild fvFTD. Deficits in decision-making and ToM observed in this study have distinct but additive effects upon the development of social behaviour in patients with prefrontal dysfunction.

Keywords: Decision-making; Theory of mind; Fronto-temporal dementia

1. Introduction

The frontal variant of fronto-temporal dementia (fvFTD) is a prevalent form of early onset dementia with limited techniques available for detection and treatment (Ratnavalli, Brayne, Dawson, & Hodges, 2002). Patients with fvFTD present with profound changes in aspects of social cognition that are present from early in the illness course. Common behavioural symptoms include impulsivity and socially inappropriate behaviour, lack of empathy for others, lack of insight, and impaired decision-making in daily activities. Many of these features are also seen in patients with damage to the orbital aspect of the prefrontal cortex (Damasio, 1994; Malloy, Bihrle, Duffy, & Cimino, 1993) and recent brain imaging data indicate consistent anatomical and functional abnormalities in the orbito-frontal cortex (OFC) in fvFTD patients (Diehl et al., 2004; Ibach et al., 2004; Salmon et al., 2003).

Two capacities that are critical for healthy social behaviour, theory of mind (TOM; the capacity to infer the likely thoughts and intentions of others) and decision-making, are characteristically impaired in fvFTD (Gregory et al., 2002; Lough & Hodges, 2002; Lough et al., 2006). In a similar vein, patients with orbito-frontal lesions are also bad at ToM tasks including detection of deception (Stuss, Gallup, & Alexander, 2001), faux pas (Stone, Baron-Cohen, & Knight, 1998) and cheating (Stone, Cosmides, Tooby, Kroll, & Knight, 2002). Both groups appear to lack empathy (Lough et al., 2006; Rankin, Kramer, & Miller, 2005; Shamay-Tsoory, Tomer, Berger, & Aharon-Peretz, 2003).

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Decision-making associated with differing probabilities of reward and punishment has been termed 'affective' decision-making. In fvFTD, Rahman and co-workers (Rahman, Sahakian, Hodges, Rogers, and Robbins (1999) demonstrated abnormal betting behaviour using the Cambridge gambling task in patients with fvFTD compared to age-matched controls. In the Iowa gambling task (IGT), a classic test of decision-making ability, OFC lesion patients persist in making choices associated with high immediate rewards but greater long-term punishments (Bechara, Damasio, Damasio, & Anderson, 1994). Their performance has been explained on the basis of impaired somatic markers as an 'insensitivity to future rewards' (Bechara, Damasio, & Damasio, 2000). Briefly, the somatic marker hypothesis suggests that bodily states (somatic markers), induced by emotions, come to be associated with positive or negative outcomes, and in turn influence future decision-making by reinvoking the state via the somatosensory cortex (Damasio, 1996). This is believed to increase the efficiency of decision-making by biasing the individual (overtly or covertly) toward particular outcomes.

Thus both ToM and decision-making are linked to the integrity of the orbito-frontal cortex (Bechara et al., 1994; Berthoz, Armony, Blair, & Dolan, 2002; Gregory et al., 2002; Sabbagh, Moulson, & Harkness, 2004; Stone et al., 1998). Since this region is believed to be one of the earliest sites of pathology in fvFTD (Kril & Halliday, 2004), sensitive neuropsychological measures of affective decision-making and social cognition could have clinical utility in the early detection of cognitive dysfunction in fvFTD patients.

From a neuropsychological, and indeed, anatomical perspective, the relationship between the theory of mind and decision-making remains unclear. Successful performance on the Iowa gambling task does not seem to place any demands on the ability to infer others' beliefs and intentions. Conversely, even difficult ToM tasks may load only negligibly on decision-making systems. Nonetheless, the prefrontal mechanisms of these sets of processes appear to overlap (Bechara et al., 1994; Berthoz et al., 2002; Gregory et al., 2002; Sabbagh et al., 2004; Stone et al., 1998). One possibility is that the spatial resolution of group lesion studies is insufficient to detect anatomical dissociations between decision-making and ToM processes *within* the orbito-frontal region, an area of the brain with documented functional heterogeneity (O'Doherty, Kringelbach, Rolls, Hornak, & Andrews, 2001; Ongur, Ferry, & Price, 2003). Another explanation is that the extended neural circuitry involved in decision-making and ToM are distinct, and the orbito-frontal cortex simply represents the one area of convergence in two independent circuits. A further possibility is that a higher-order mechanism may regulate both affective decision-making and ToM via a common resource (Adolphs, 2003).

There were two main objectives in the present study. The first was to investigate the sensitivity of the Iowa gambling task in patients with early/mild stages of fvFTD, which has not been done previously. The second objective was to examine the relationship between deficits in affective decision-making and ToM in the same group of patients with frontal lobe degeneration. We hypothesized that performance on the decision-making and theory of mind tasks would correlate based on a shared neural substrate in the orbito-frontal cortex.

2. Methods

2.1. Subjects

Twenty fvFTD patients were recruited as part of a broader ongoing study on fronto-temporal dementia currently being conducted at the Cognitive Neurology Division Raul Carrea Institute for Neurological Research. The present study only included patients with early/mild stages of fvFTD. All presented with prominent changes in personality plus social behaviour verified by a caregiver. They showed frontal atrophy on MRI or hypoperfusion on SPECT and there were variable deficits on tests of frontal executive function. These were compared to a group of healthy controls ($n = 10$), recruited within the same geographical area as the study patients and matched for age and level of education. FTD diagnosis was made applying Lund and Manchester criteria (Neary et al., 1998), although in keeping with studies from Cambridge we prefer the label fvFTD (Gregory et al., 2002; Rahman et al., 1999). Dementia severity was assessed using the clinical dementia severity rating scale (CDR) (Hughes, Berg, Danziger, Coben, & Martin, 1982). All patients underwent a standard examination battery including neurological, neuropsychiatric and neuropsychological examinations and a MRI-SPECT.

2.2. Assessment of atrophy on MRI

To assess frontal atrophy in the fvFTD group, we used a visual rating scale developed by the Cambridge group (Galton et al., 2001; Gregory et al., 2002). The frontal ratings were undertaken using T_1 coronal images through the frontal and anterior temporal lobes. The frontal lobes were assessed, using a four-point scale (0 = no atrophy; 1 = mild atrophy; 2 = moderate; 3 = marked). Patient scans were anonymized and assessed blinded, together with scans from 10 normal age-matched control subjects by one highly experienced rater (F.M.) on two separate occasions.

2.3. General neuropsychological battery

Cognitive status was measured using the Addenbrooke's cognitive examination (ACE) (Mathuranath, Nestor, Berrios, Rakowicz, & Hodges, 2000) and the mini-mental state exam (Folstein, Folstein, & McHugh, 1975). Subjects were also administered a standard neuropsychological battery, in order to characterise background cognitive functioning. Premorbid IQ was assessed using the WAT-BA (word accentuation test-Buenos Aires) (Burin, Jorge, Arizaga, & Paulsen, 2000). Attention and concentration were assessed with forward digit span (Wechsler & Stone, 1987) and the trail making test (part A). Memory was assessed using the logical memory (story recall) subtest from the Wechsler memory scale-revised (Wechsler & Stone, 1987). Semantic function was assessed by the pyramid and palm trees test of associative semantic memory (Howard & Patterson, 1992), naming using the Boston naming test (adapted version) (Goodglass & Kaplan, 1983) and comprehension with the token test (adapted version) (Spreen & Benton, 1977). Verbal fluency was tested using timed generation of words starting with the letter "*P*". Executive or frontal function was evaluated by the Raven colored progressive matrices (Raven, 1995), digit span backwards (Wechsler & Stone, 1987), the trail making test (part B) (Partington & Leiter, 1949), the letters and numbers ordering subtest from the WAIS (Wechsler & Stone, 1987) and the Wisconsin card sorting test (WCST), modified version (Nelson, 1976) and the frontal assessment battery (Dubois, Slachevsky, Litvan, & Pillon, 2000).

2.4. Decision-making task

2.4.1. Iowa gambling task

The computerised version of the Iowa gambling task involves continuous card selection from four separate decks (A, B, C and D) using a mouse, and is completed after 100 selections. Each card choice is awarded a number of points (either $50 or $100) but occasional choices yield an additional penalty. Card choices from decks A and B generate large wins ($100) but occasional