CORTEX 49 (2013) 1844–1855

Available online at www.sciencedirect.com

SciVerse ScienceDirect

Journal homepage: www.elsevier.com/locate/cortex

Research report

Mentalising music in frontotemporal dementia

*Laura E. Downey, Alice Blezat, Jennifer Nicholas, Rohani Omar, Hannah L. Golden, Colin J. Mahoney, Sebastian J. Crutch and Jason D. Warren**

Dementia Research Centre, UCL Institute of Neurology, University College London, London, United Kingdom

ARTICLE INFO

Article history:
Received 1 June 2012
Reviewed 24 July 2012
Revised 1 August 2012
Accepted 10 September 2012
Action editor Daniel Tranel
Published online 5 October 2012

Keywords:
Mentalising
Theory of mind
Music
Frontotemporal dementia

ABSTRACT

Despite considerable recent interest, the biological basis and clinical diagnosis of behavioural variant frontotemporal dementia (bvFTD) pose unresolved problems. Mentalising (the cognitive capacity to interpret the behaviour of oneself and others in terms of mental states) is impaired as a prominent feature of bvFTD, consistent with involvement of brain regions including ventro-medial prefrontal cortex (PFC), orbitofrontal cortex and anterior temporal lobes. Here, we investigated mentalising ability in a cohort of patients with bvFTD using a novel modality: music. We constructed a novel neuropsychological battery requiring attribution of affective mental or non-mental associations to musical stimuli. Mentalising performance of patients with bvFTD ($n = 20$) was assessed in relation to matched healthy control subjects ($n = 20$); patients also had a comprehensive assessment of behaviour and general neuropsychological functions. Neuroanatomical correlates of performance on the experimental tasks were investigated using voxel-based morphometry of patients' brain magnetic resonance imaging (MRI) scans. Compared to healthy control subjects, patients showed impaired ability to attribute mental states but not non-mental characteristics to music, and this deficit correlated with performance on a standard test of social inference and with carer ratings of patients' empathic capacity, but not with other potentially relevant measures of general neuropsychological function. Mentalising performance in the bvFTD group was associated with grey matter changes in anterior temporal lobe and ventro-medial PFC. These findings suggest that music can represent surrogate mental states and the ability to construct such mental representations is impaired in bvFTD, with potential implications for our understanding of the biology of bvFTD and human social cognition more broadly.

1. Introduction

Frontotemporal lobar degeneration (FTLD) refers to a group of diseases collectively characterised by atrophy of the frontal and temporal lobes. The most common syndrome of FTLD, behavioural variant frontotemporal dementia (bvFTD), manifests as progressive behavioural decline leading to severe social dysfunction, as reflected in recent consensus diagnostic criteria (Rascovsky et al., 2011). The bvFTD syndrome presents important neurobiological and clinical problems. The neurobiological basis for the selective erosion of neural circuitry mediating complex behaviours in bvFTD remains poorly

* *Corresponding author*. Dementia Research Centre, UCL Institute of Neurology, University College London, 8–11 Queen Square, London WC1N 3BG, United Kingdom.
E-mail address: jason.warren@ucl.ac.uk (J.D. Warren).
0010-9452
http://dx.doi.org/10.1016/j.cortex.2012.09.011

understood, while early diagnosis is often difficult due to the insidious nature of behavioural decline, potential confusion with primary psychiatric illness and phenotypic overlap with other dementia diseases (Gregory et al., 2002; Snowden et al., 2003; Balsis et al., 2005). Accordingly, there is considerable interest in identifying novel metrics of bvFTD that might illuminate underlying mechanisms and potentially facilitate diagnosis. An important emerging theme in the neurobiology of bvFTD is the concept of a selectively vulnerable, large-scale brain network including prefrontal cortex (PFC), orbitofrontal cortex (OFC), anterior cingulate, insula and their projections: this network is likely to be fundamentally concerned with social cognitive processing and the signature of network involvement may separate bvFTD from other neurodegenerative disorders (Seeley et al., 2007, 2012; Zhou et al., 2010, 2012; Raj et al., 2012). This evidence suggests that biomarkers that can capture network characteristics might be diagnostically useful, and that network function in bvFTD might be best assessed using indices of complex social behaviours.

Mentalising can be broadly defined as the cognitive capacity by which we interpret the behaviour of oneself and others in terms of mental states (Frith and Frith, 2003). The term 'theory of mind' (ToM) is often used interchangeably with mentalising, but can be defined more precisely as a crucial component of the mentalising process whereby mental states are explicitly attributed to others (Robbins, 2004). ToM and mentalising in the broader sense together constitute a key capacity within the wider domain of social cognition. These complex cognitive functions require the representation, analysis and integration of a variety of social signals. ToM capacity can be further subclassified as ToM for the attribution of beliefs and intentions ('cognitive' ToM) and ToM for the attribution of feeling states ('affective' ToM), though these separable capacities frequently interact in everyday life (Poletti et al., 2012). Widely used tests of ToM such as the 'Mind in the Eyes' task (Baron-Cohen et al., 2001) largely index affective ToM using stimuli derived from other humans, however it has been repeatedly shown that intentionality can be attributed even to abstract, inanimate stimuli (e.g., cartoon shapes: Heider and Simmel, 1944; Berry and Springer, 1993; Castelli et al., 2000; Blakemore et al., 2003). Neuroimaging studies in healthy individuals have linked the ability to mentalise with a network of brain regions, in particular ventro-medial PFC and frontal pole, OFC (Gallagher and Frith, 2003; Carrington and Bailey, 2009; Moll et al., 2011; Abu-Akel and Shamay-Tsoory, 2011) and the anterior temporal lobes (Fumagalli and Priori, 2012). The study of disease states potentially allows identification of brain areas critical for ToM. Impaired ToM occurs on a developmental basis as a hallmark of autism (Baron-Cohen et al., 1985, 1999) and may also develop in association with a variety of focal brain lesions (Martin-Rodriguez and Leon-Carrion, 2010). Deficits of ToM in neurodegenerative disease have attracted much recent attention and on clinical and neuroanatomical grounds may be particularly relevant to bvFTD (Schroeter, 2012; Poletti et al., 2012). Patients with bvFTD frequently have difficulty with aspects of social cognition that are likely to be relevant to ToM, including emotion recognition (Rosen et al., 2005; Kipps et al., 2009b; Omar et al., 2011), empathic concern and perspective taking (Lough et al., 2006; Rankin et al., 2006; Eslinger et al., 2011), and perception of humour and sarcasm (Snowden et al., 2003; Kosmidis et al., 2008; Kipps et al., 2009b). A specific mentalising deficit may be an early feature of bvFTD (Gregory et al., 2002; Adenzato et al., 2010) and neuroanatomical substrates for this deficit have been proposed. The distributed neural network that is damaged in bvFTD (Seeley et al., 2007; Zhou et al., 2010, 2012; Raj et al., 2012) overlaps brain areas previously implicated in ToM (Gallagher and Frith, 2003; Carrington and Bailey, 2009). Impaired ability to experience social emotions has been linked to frontopolar damage in bvFTD (Moll et al., 2011). In addition, bvFTD is often associated with damage involving anterior temporal lobe regions that represent social concepts underpinning normal mentalising (Zahn et al., 2009): these anterior temporal areas interact with medial PFC during moral reasoning (Fumagalli and Priori, 2012), while anterior temporal lobe damage has been implicated in the pathogenesis of cognitive and affective ToM deficits in another FTLD syndrome, semantic dementia (Duval et al., 2012).

Relations between mentalising, ToM and music processing have not been widely studied; however, music is likely a priori to engage brain processes relevant to ToM and it is an attractive candidate stimulus for probing such processes in bvFTD. Music typically entails decoding of an emotional 'message' and music-making generally has a strong social context across human societies (Mithen, 2005; Levitin, 2007). Music has been shown to modulate semantic information in other cognitive systems, such as language (Koelsch et al., 2004). Deficits in processing emotion information in music have been demonstrated in various disease states, notably the frontotemporal dementias, and are dissociable from the processing of other kinds of musical perceptual information (Stewart et al., 2006; Omar et al., 2010, 2011; Johnson et al., 2011; Hsieh et al., 2012). The brain mechanisms of music processing in health and disease and the brain substrates for processing emotional information in music have received considerable attention (Blood et al., 1999; Blood and Zatorre, 2001; Griffiths et al., 2004; Gosselin et al., 2006; Koelsch et al., 2006; Mitterschiffthaler et al., 2007; Mizuno and Sugishita, 2007; Caria et al., 2011; Brattico et al., 2011). Previous work has implicated a distributed network of cortical and subcortical (in particular, limbic) areas in mediating the emotional response to music, suggesting that music processing unites cognitive representational and evaluative mechanisms with the more 'primitive' neural mechanisms of reward and biological drives (Blood and Zatorre, 2001; Salimpoor et al., 2011; Omar et al., 2011). From this perspective, music might therefore be regarded as a comprehensive and biologically relevant model stimulus for assessing human frontal lobe functions.

More specifically, recognition of emotion in music engages prefrontal and anterior temporal components of the brain network previously implicated in ToM processing (Blood et al., 1999; Rankin et al., 2006; Mizuno and Sugishita, 2007; Zahn et al., 2007, 2009; Brattico et al., 2011; Eslinger et al., 2011) and damage involving this network has been linked specifically to deficits of music emotion recognition as well as ToM in bvFTD (Omar et al., 2011; Hsieh et al., 2012; Poletti et al., 2012). Most previous studies of music emotion processing in the normal brain and in disease states have assessed the processing of elementary or canonical emotions (e.g.,