Journal Watch

Fiona Kumfor^{*1,2,3} & Olivier Piguet^{1,2,3}

Lee SE, Khazenzon AM, Trujillo AJ et al. Altered network connectivity in frontotemporal dementia with *C9orf72* hexanucleotide repeat expansion. *Brain* 137(pt 11), 3047–3060 (2014).

The identification of the *C9orf72* repeat expansion has represented an important step in understanding the etiology of frontotemporal dementia (FTD) and motor neurone disease. Clinically, individuals with the *C9orf72* repeat expansion usually meet criteria for behavioral-variant FTD (bvFTD), motor neurone disease or both. Psychosis and episodic memory deficits, however, appear more prevalent in carriers than noncarriers. Neuroimaging findings are remarkably heterogeneous, with some *C9orf72* carriers showing minimal atrophy, even late in the disease course. Group analyses, however, typically reveal atrophy in the thalamus and cerebellum, and in the frontal, temporal and parietal regions.

In this study, Lee *et al.* sought to investigate large-scale neuronal network connectivity in 28 bvFTD patients (14 *C9orf72* carriers, 14 *C9orf72* noncarriers) and 14 healthy controls. The results revealed similar reductions in connectivity within the Salience Network in carriers and noncarriers, despite different patterns of structural atrophy. Interestingly, Salience Network changes in *C9orf72* carriers were associated with medial pulvinar thalamic atrophy. Importantly, single-subject analyses revealed network connectivity changes in individuals where limited structural atrophy was present.

The Salience Network is recruited during attention-demanding tasks, and is proposed to convey the emotional significance of stimuli.

Thus, alterations in Salience Network connectivity, rather than structural changes *per se*, may give rise to the clinical manifestation of bvFTD. These results go some way to reconciling the degree of clinical overlap in *C9orf72* carriers and noncarriers, despite heterogeneous atrophy patterns. Further, the findings indicate that functional abnormalities precede observable structural atrophy and may therefore offer potential as a preclinical biomarker.

– Written by Fiona Kumfor

Sturm VE, Yokoyama JS, Eckart JA et al. Damage to left frontal regulatory circuits produces greater positive emotional reactivity in frontotemporal dementia. *Cortex* 64C, 56–77 (2014).

Emotion processing disturbance is common in FTD, although research has focused predominantly on negative emotions. Lesions to the left prefrontal cortex decrease positive emotions but it is unknown whether such lesions could also result in an increase (i.e., dysregulation) in positive emotions. Dysregulation of positive emotions may give rise to inappropriate social interactions and behavior (e.g., disinhibition, risk taking), which are also found in FTD. In this study published in *Cortex*, Sturm *et al.* examined changes in processing positive emotions in 96 patients diagnosed with one of the three subtypes of FTD, compared with 36 healthy controls. Participants watched short movies designed to elicit either happiness or sadness while their facial and physiological responses to the movies were recorded.

The authors found that facial responses to the movies did not differ between controls and

¹Neuroscience Research Australia, Sydney, Australia

²School of Medical Sciences, the University of New South Wales, Sydney, Australia

³ARC Centre of Excellence in Cognition & Its Disorders, Sydney, Australia

*Author for correspondence: Tel.: +61 2 9399 1025; Fax: +61 2 9399 1047; f.kumfor@neura.edu.au

patients, even when considering the different subtypes of FTD separately. Notably, however, twice as many patients diagnosed with the behavioral, or the semantic variants of FTD showed reduced facial expression to the happy movie compared with the control and nonfluent variant of FTD participants. Voxel-based morphometry analyses conducted in the patient group revealed that reduced gray matter integrity in a network involving the left orbitofrontal, striatum and anterior cingulate cortices was associated with an increase in happiness-related facial mimicry and indices of physiological reactivity (i.e., increased heart rate and blood pressure). The authors propose that atrophy of this

left-hemisphere network impacts on the emotion regulation system and on the ability to suppress positive emotions.

– Written by Olivier Piguet

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