Christopher Kipps - selected references

1 Kipps, C. M., Hodges, J. R., & Hornberger, M. (2010). Nonprogressive behavioural frontotemporal dementia: recent developments and clinical implications of the 'bvFTD phenocopy syndrome'. *Current Opinion in Neurology, 23,* 628-632.
Notes: PURPOSE OF REVIEW: The clinical features of behavioural variant frontotemporal dementia (bvFTD) are well established; however, recent work has identified patients fulfilling diagnostic criteria for the disease who do not appear to progress clinically. This review describes means of distinguishing this group at an early stage from patients who are likely to deteriorate. RECENT FINDINGS: Despite indistinguishable clinical profiles, studies in a cohort of bvFTD patients showed a particularly good prognosis in a subgroup of predominantly male patients in whom initial structural imaging was normal. This could not be explained by differences in disease duration, and was confirmed by subsequent PET studies. Retrospective review of clinical data in these groups verified that the current clinical diagnostic criteria are both insensitive to true progressive bvFTD, particularly in the early stages, and also poorly specific. In contrast, measures of activity of daily living performance, executive function and tests of social cognition appear to have better discriminatory value for patients who show clear clinical progression, with many individual diagnoses verified by post mortem examination in this group. SUMMARY: It remains doubtful that the nonprogressive group have a neurodegenerative disease. The implication for the current clinical diagnostic criteria and their proposed revision is discussed
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2 Kipps, C. M., Hodges, J. R., Fryer, T. D., & Nestor, P. J. (2009). Combined magnetic resonance imaging and positron emission tomography brain imaging in behavioural variant frontotemporal degeneration: refining the clinical phenotype. *Brain, 132,* 2566-2578.
Notes: In patients with the behavioural variant of frontotemporal dementia, prognosis is often surprisingly good when there is normal structural imaging at presentation. Imaging abnormalities are not, however, mandatory for diagnosis, which in the absence of suitable biomarkers, remains entirely clinical. We aimed to test whether cases with normal structural imaging have hypometabolism suggestive of underlying neurodegeneration, or whether it is likely that such patients are false positive diagnoses of behavioural variant frontotemporal dementia. Patients with this disease (n = 24) and age-matched controls (n = 12) underwent both magnetic resonance imaging (MRI) and quantitative fluorodeoxyglucose-positron emission tomography (FDG-PET) scanning, together with clinical and behavioural assessments. Regions of interest were used to calculate metabolic rate in frontotemporal and control regions. Using a semi-quantitative visual rating scale, patients were divided into MRI-abnormal (n = 15) and MRI-normal groups (n = 9). There was definite frontotemporal hypometabolism in the MRI-abnormal group (particularly in the mesial and orbitofrontal regions) even after accounting for brain volume loss, whereas the MRI-normal group was similar to controls in all regions. In contrast, cognitive and behavioural indices did not separate the two behavioural variant frontotemporal dementia patient groups. The results suggest that the clinical syndrome of the behavioural variant of frontotemporal dementia may not be specific for a neurodegenerative disease, and we hypothesize the existence of a phenocopy. A number of alternative neuropsychiatric and developmental explanations are discussed. We advise caution in diagnosing the illness in patients without imaging abnormalities, and propose that imaging findings are included in criteria for diagnosis
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3 Kipps, C. M., Nestor, P. J., Acosta-Cabronero, J., Arnold, R., & Hodges, J. R. (2009). Understanding social dysfunction in the behavioural variant of frontotemporal dementia: the role of emotion and sarcasm processing. *Brain, 132,* 592-603.
Notes: Social interaction is profoundly affected in the behavioural form of frontotemporal dementia (bvFTD) yet there are few means of objectively assessing this. Diagnosis of bvFTD is based on informant report, however a number of individuals with a clinical profile consistent

with the disease have no imaging abnormality and seem to remain stable, with doubt about the presence of underlying neurodegenerative pathology. We aimed to quantify aspects of the behavioural disorder and link it to the underlying level of atrophy in socially relevant brain regions. We tested individuals with either bvFTD (N = 26) or Alzheimer's disease (N = 9) and 16 controls using The Awareness of Social Inference Test (TASIT) to assess their ability to identify emotion and sarcasm in video vignettes. A subset of bvFTD patients (N = 21) and controls (N = 12) were scanned using MRI within 6 months of assessment. There was marked impairment in the ability of bvFTD patients whose scans showed abnormalities to recognize sarcastic, but not sincere statements. Their capacity to interpret negative emotion was also impaired, and this appeared to be a major factor underlying the deficit in sarcasm recognition. Clinically diagnosed bvFTD patients whose scans were normal, Alzheimer's disease patients and controls had no difficulty in appreciating both types of statement. In a multivariate imaging analysis it was shown that the sarcasm (and emotion recognition) deficit was dependent on a circuit involving the lateral orbitofrontal cortex, insula, amygdala and temporal pole, particularly on the right. Performance on a more global test of cognitive function, the Addenbrooke's Cognitive Examination did not have a unique association with these regions. The TASIT is an objective test of social dysfunction in bvFTD which indexes the frontotemporal volume loss in bvFTD patients and provides an objective measure for separating behavioural patients who are likely to decline from those who may remain stable. These results provide additional evidence for the role of the orbitofrontal cortex and related structures in the processing of socially relevant signals, particularly those where negative emotion recognition is important
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4 Kipps, C. M., Mioshi, E., & Hodges, J. R. (2009). Emotion, social functioning and activities of daily living in frontotemporal dementia. *Neurocase, 15,* 182-189.
Notes: Social functioning in FTD is profoundly affected, and forms the basis for the clinical diagnosis of the behavioural variant of the disease (bv-FTD). In particular, there are deficits in emotional processing, but the inter-relationship of such deficits to other aspects of social functioning remains unclear. We studied patients with bv-FTD (n = 14) and AD (n = 14), and compared their performance on a test of emotion recognition with their scores on two carer-based assessments: the Disability Assessment for Dementia (DAD) of activities in daily living (ADL), and the Cambridge Behavioural Inventory (CBI). The bv-FTD group had significantly greater impairments in ADLs, and had higher scores on the CBI, compared to the AD group. Despite a deficit in emotion recognition, particularly involving negative emotions, in the FTD group relative to AD and controls, performance on this task did not correlate with ADL ratings which instead, correlated highly with carer-rated apathy levels on the CBI. The study highlights the multifactorial nature of social dysfunction in FTD which is important in the management of these patients and in designing effective behavioural and therapeutic interventions. The relationship of emotional processing to other aspects of social cognition in FTD is reviewed
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5 Kipps, C. M., Knibb, J. A., Patterson, K., & Hodges, J. R. (2008). Neuropsychology of frontotemporal dementia. In *Handbook of Clinical Neurolog, Vol. 88*, Ed.by P.J.Vinken & G.W.Bruyn.Amsterdam:Elsevier.(Chapter 28, pp. 527-548).

6 Kipps, C. M., Knibb, J. A., & Hodges, J. R. (2007). Clinical presentation of frontotemporal dementia. In J.R.Hodges (Ed.), *Frontotemporal dementia syndromes* (pp. 38-79). Cambridge: Cambridge University Press.

7 Kipps, C. M. & Hodges, J. R. (2006). Theory of mind in frontotemporal dementia. *Social neuroscience, 1,* 235-244.
Notes: Patients with frontotemporal dementia (FTD) exhibit marked chages in social and emotional functioning including lack of empathy, disinhibition, altered emotional reactivity, apathy and lack of insight. These changes are believed to be dependent on progressive frontal

and temporal lobe degeneration. In this review, we discuss the nature of defective theory of mind and empathy in this group and relate it to regional dysfunction in the orbitofrontal and medial prefrontal cortex, based on evidence from several recent studies. The role of executive ability and co-existing emotional deficits are also considered.

8 Kipps, C. M. & Hodges, J. R. (2005). Cognitive assessment for clinicians. *Journal of Neurology, Neurosurgery and Psychiatry, 76 Suppl 1,* i22-i30.
Notes: MRC Cognition and Brain Sciences Unit, 15 Chaucer Road, Cambridge CB2 2EF, UK.