

Beyond the face: how context modulates emotion processing in frontotemporal dementia subtypes

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The importance of assessing social cognition to characterize dementia syndromes is increasingly recognized, with lower social cognition capacity associated with reduced functional independence and greater carer burden. Emotion recognition is impaired in both behavioural-variant frontotemporal dementia and semantic dementia, yet the social and behavioural changes observed in these syndromes in everyday situations varies. To date, most studies have investigated isolated, context-free stimuli indexing recognition of facial emotions only. Here, we aimed to investigate how contextual information (i.e. emotional body language) influences emotion recognition, within the framework of the Social Context Network Model. Thirty-one patients with frontotemporal dementia (19 behavioural-variant frontotemporal dementia; 12 semantic dementia) and 20 healthy age- and education-matched controls were assessed on three tasks which varied contextual cues: (i) face alone; (ii) context alone; and (iii) face embedded in context. Voxel-based morphometry was used to identify neural correlates of task performance. Our results demonstrated that both behavioural-variant frontotemporal dementia and semantic dementia patients performed worse than controls in recognizing emotions from face alone and context alone. Importantly, performance differed when faces were presented in context. While both behavioural-variant frontotemporal dementia and semantic dementia patients performed similarly to controls on congruent items (i.e. face emotion and body emotion are the same) (P -values > 0.05), patients with behavioural-variant frontotemporal dementia performed worse than both controls ($P < 0.001$) and patients with semantic dementia ($P = 0.044$) for incongruent items (i.e. face emotion and body emotion are different). Neuroimaging analyses revealed that abnormal contextual influence was associated with lower integrity of the right parahippocampal gyrus/amygdala and left precentral gyrus. Together, these results indicate that patients with behavioural-variant frontotemporal dementia are over-reliant on external contextual information. Conversely, in semantic dementia and controls, contextual influence varies, with the degree of contextual influence appearing to be mediated, at least in part, by the facial expression depicted. The profile in behavioural-variant frontotemporal dementia is reminiscent of the 'environmental dependency syndrome' described in frontal lesion patients. It also converges with recent evidence of abnormal face perception in this group. From a theoretical perspective, our findings demonstrate that the capacity to incorporate contextual body language is dependent on the integrity of both contextual association brain regions (i.e. parahippocampal gyrus), as well as regions necessary for processing dynamic body movements. Clinically, these results open new avenues for rehabilitation of social impairments in dementia.

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Abbreviations: ACE = Addenbrooke's Cognitive Examination; bvFTD = behavioural-variant frontotemporal dementia; SCNM = Social Context Network Model

Introduction

Social cognition is increasingly recognized to play an important role in determining current and future functional capacity and independence of dementia patients, and their associated carer burden. Social cognition is a dynamic, multi-componential process that requires the simultaneous appraisal of multiple sources of information, including cognitive (insight, appraisal, self-regulation), internal (autonomic and physiological responses), social (e.g. type of interaction) and contextual. How we measure the integrity of social cognition therefore has an important place in the clinical investigation of dementia patients. Yet, tests of social cognition are usually devoid of contextual information that we rely on in day-to-day situations to make judgments about the emotional state of others. To date, the majority of research examining emotion perception has relied on isolated photographs of basic facial expressions. This long tradition, stemming from seminal work by Ekman and colleagues (Ekman *et al.*, 1969, 1972; Ekman and Friesen, 1976; Ekman, 1992) has proved invaluable towards understanding the cognitive and neurobiological bases of facial emotion perception in healthy and clinical populations, but fails to capture how emotions are perceived in day-to-day life. Indeed, we are rarely presented with a floating face devoid of contextual cues and information.

Of relevance here, recent work has revealed that contrary to previous accounts, context does substantially influence perception of emotional facial expressions (Aviezer *et al.*, 2012a, b). Context includes both 'internal' information (e.g. interoceptive awareness of one's own body signals such as heartrate, respiration rate) and 'external' information (e.g. body language, surrounding scene, vocal prosody), encompassing any cues external to the target facial expression (Barrett *et al.*, 2011; Hassin *et al.*, 2013). In healthy adults, provision of external contextual information, such as incongruent body and scene contexts, changes the categorization and interpretation of facial emotions (de Gelder, 2006; Van den Stock *et al.*, 2007, 2014; Aviezer *et al.*, 2012b; Hortensius *et al.*, 2016). Furthermore, this contextual information influences early perceptual processes, whereby patterns of eye fixations will vary depending on whether the contextual information is congruent, incongruent or neutral in relation to the information conveyed by the faces (Aviezer *et al.*, 2012b).

How external context influences emotion perception in clinical populations characterized by progressive brain diseases affecting regions known to participate in social cognition has been surprisingly understudied. Emerging evidence, however, suggests that how contextual information is processed may be the key to understanding the nature of social cognition deficits in some of these brain disorders (e.g. Huntington's disease; Aviezer *et al.*, 2009). One such brain disorder is the behavioural variant of frontotemporal dementia (bvFTD). BvFTD is characterized by marked changes in personality, behaviour and social graces associated with early atrophy in the ventromedial prefrontal cortex and insula (Seeley *et al.*, 2008). Patients with bvFTD become apathetic, socially disinhibited, less empathetic and show executive dysfunction (Rascovsky *et al.*, 2011). A second disorder, also part of the frontotemporal lobar degeneration family, is semantic dementia (also known as semantic-variant primary progressive aphasia). Patients with semantic dementia present with a global loss of conceptual/semantic knowledge (Hodges *et al.*, 1992; Gorno-Tempini *et al.*, 2011) arising from anterior temporal lobe atrophy (usually left > right), which becomes increasingly bilateral with disease progression (Kumfor *et al.*, 2016). Clinically, this loss manifests as speech that is fluent, but empty of content (Hodges *et al.*, 1992; Adlam *et al.*, 2006). In both bvFTD and semantic dementia, emotion processing deficits are well established, particularly regarding facial emotion recognition (Lavenu *et al.*, 1999; Rosen *et al.*, 2002; Kumfor and Piguet, 2012; Kumfor *et al.*, 2013). Interventions to address these impairments, however, are largely non-existent. Understanding of how context influences emotion recognition in these groups may therefore also provide insights into potential avenues for rehabilitation of social cognition impairment (e.g. by providing congruent contextual information to enhance understanding of social cues).

The neurobiological basis that governs the integration of contextual information and facial emotion perception is unclear. Perception of emotional body language alone is thought to be dependent on three brain systems that are responsible for visuomotor perception, body awareness and reflex-like information, and encompass anterior frontal, premotor and occipital cortices, as well as subcortical regions including the pulvinar, striatum, amygdala and superior colliculi (de Gelder, 2006). Further integration of contextual body language and facial emotional expression likely involves the parahippocampal and fusiform gyrus

specifically (Van den Stock *et al.*, 2014), as well as the amygdala (Hortensius *et al.*, 2016). The Social Context Network Model (SCNM) (Ibañez and Manes, 2012), has recently proposed that the integration of contextual information is underpinned by a network of brain regions including the frontopolar and dorsolateral-prefrontal cortices, insula cortex and temporal regions. In particular, the SCNM temporal hub (anterior temporal cortices, amygdala, parahippocampal gyrus, periaqueductal grey matter) is involved in context-target associative learning. Temporal regions receive polysensory and somatosensory information necessary for global contextual integrations. The anterior and medial temporal lobes contribute to the establishment of links between such contextual associations and incoming information from fronto-insular regions. Importantly, these brain regions overlap with the patterns of atrophy observed in bvFTD and semantic dementia.

To date, how contextual cues influence emotion perception in bvFTD and semantic dementia has been relatively unexplored. In bvFTD, deficits in understanding sarcasm are well recognized (Kipps *et al.*, 2009; Rankin *et al.*, 2009; Kumfor *et al.*, 2017). This impairment in bvFTD has been interpreted as difficulty in integrating contextual information to inform the interpretation of subtle vocal and facial paralinguistic cues (Ibañez and Manes, 2012). Other studies have attempted to use more ecologically valid stimuli that provide additional contextual information (short film stimuli), and found that reduced capacity to dynamically interpret someone's emotional state in people with dementia, is associated with right orbitofrontal integrity (Goodkind *et al.*, 2011). The potential influence of context in semantic dementia has been unexplored. Historically, evidence suggests that patients with frontal lesions rely on environmental contextual cues to a non-adaptive extent (Lhermitte, 1986). These findings, combined with the patterns of atrophy in bvFTD and semantic dementia, suggest that contextual integration may be disrupted in these syndromes. In addition to the potential clinical implications, investigations of patient groups with relatively circumscribed brain atrophy offer a unique opportunity to test the SCNM, and determine the relative contributions of frontal and temporal regions for integration of contextual information to inform social behaviour.

Here, we aimed to: (i) determine how contextual cues (emotional body language) influence facial emotion recognition in bvFTD and semantic dementia compared to healthy controls; and (ii) establish the neural correlates associated with social context integration. We predicted that both bvFTD and semantic dementia would show less contextual influence on emotion perception than healthy controls and that this effect would be dependent on degeneration of brain regions supporting context-target associations recognized by the SCNM, including temporal regions (hippocampus, parahippocampus, amygdala) and anterior connections with frontal regions (Ibañez and Manes, 2012). Thus, we hypothesized that bvFTD patients would fail to appreciate how context *alters* the meaning of

facial expressions, responding in a concrete manner reflecting increased dependence on superficial, environmental cues. In semantic dementia, we hypothesized that patients' impaired performance would be predominantly due to neurocognitive deficits related to emotion processing. Irrespective of diagnosis, we predicted that contextual influences would be associated with both the specific context-target association areas (i.e. temporal regions, body language areas) as well as with frontal regions involved in contextual updates, prediction and integration.

Materials and methods

Thirty-one FTD patients (19 bvFTD; 12 semantic dementia) were recruited from FRONTIER, the younger-onset dementia research clinic based in Sydney, Australia. All patients underwent comprehensive neuropsychological assessment, were assessed by an experienced behavioural neurologist and had a structural brain MRI. Diagnosis of bvFTD and semantic dementia was determined by a multi-disciplinary team including a behavioural neurologist, neuropsychologist and occupational therapist according to current consensus criteria (Gorno-Tempini *et al.*, 2011; Rascovsky *et al.*, 2011). Patients who presented with right-lateralized anterior temporal lobe atrophy and behavioural change/prosopagnosia, consistent with right semantic dementia were excluded (Chan *et al.*, 2009; Kumfor *et al.*, 2016). One patient who showed right-sided atrophy, but was left-handed and presented with predominant language impairment and met criteria for semantic dementia was included (re-running the relevant analyses on the main experimental variables of interest after excluding this individual did not change the pattern of results). In addition, 20 healthy controls were recruited from the FRONTIER volunteer database. Exclusion criteria for patients and controls included: concurrent psychiatric diagnosis, presence of other dementia or neurological syndrome, and/or history of alcohol or substance abuse. In addition, all controls were required to score $\geq 88/100$ on the Addenbrooke's Cognitive Examination-Revised (ACE-R) or the recently revised ACE-III to ensure they did not have any significant cognitive impairments (Mioshi *et al.*, 2006; Hsieh *et al.*, 2013). All patients scored $>40/100$ on the ACE.

The South Eastern Sydney Local Health District and the University of New South Wales ethics committees approved the study. Participants or their Person Responsible provided informed consent in accordance with the Declaration of Helsinki. Participants volunteered their time and were reimbursed for travel costs.

Background neuropsychological assessment

All participants completed the ACE (Revised or ACE-III) as a general screener of cognitive function (Mioshi *et al.*, 2006; Hsieh *et al.*, 2013). In addition, a comprehensive neuropsychological assessment was conducted to assess attention, working memory and processing speed [Digit Span (Wechsler, 1997); Trail Making Test (Tombaugh, 2004)], language [Sydney Language Battery (Savage *et al.*, 2013)], visuospatial

functioning and episodic memory [Rey Complex Figure (Rey, 1941)] and verbal fluency (Spreen and Strauss, 1998).

Emotion processing tasks

All participants completed Tasks A–C (see below) as part of their clinical assessment. Task B was always completed immediately after Task C, to avoid any potential for perseveration. Task A was typically completed in a different testing session on the same day. See Fig. 1 for example stimuli of each of the tasks.

Task A: Recognition of isolated facial expressions (face only)

To assess the ability to identify facial emotional expressions in isolation, we used the Facial Affect Selection Test (Miller *et al.*, 2012; Kumfor *et al.*, 2014) (Fig. 1, Task A). Here, participants view an array of seven faces, each expressing a different emotion (anger, disgust, fear, sadness, surprise, happiness or neutral) across 42 trials and are asked to ‘Point to the...face’. Responses are untimed and no feedback is provided. Images were selected from the NimStim database (www.mac-brain.org), were cropped to remove non-facial information (e.g. hair) and were converted to greyscale. Here, we focused only on performance for the emotions anger, disgust, fear and sadness, to enable comparisons with Tasks B and C.

Task B: Recognition of context only (body only)

Tasks B and C were adapted from existing stimuli (Aviezer *et al.*, 2012b) (Fig. 1, Task B). For Task B, participants viewed four contexts (anger, disgust, fear, sadness) with a grey circle covering the face and were asked to select the emotional label (anger, disgust, fear, sadness, surprise, happiness) that best described the emotion of the context as expressed by the body language. Images were presented one at a time with the emotional labels at the bottom of the screen (Aviezer *et al.*,

2009). Responding was untimed and no feedback was provided.

Task C: Contextual effects

For Task C, images of five individuals each posing prototypical facial expressions (anger, disgust, fear, sadness) were obtained from the Ekman and Friesen (1976) series (Fig. 1, Task C). Each of the 20 faces were combined with four pictures of emotional bodies conveying prototypical emotions (anger, disgust, fear, sadness). The emotional bodies and faces were converted to greyscale and appeared on a light grey background. A fully crossed design was employed such that each of the 20 facial expressions were paired with the four body expressions, resulting in 80 trials. As for Task B, participants selected the label that best matched the facial expression (anger, disgust, fear, sadness, surprise, happiness) (Aviezer *et al.*, 2009). Responding was untimed and no feedback was provided.

This task was designed to assess the extent to which external contextual information (body posture) influences target emotional information (facial expression). The incongruent condition is designed to examine whether the participant is responding based on the target emotional information or based on the context. Two indices were calculated to determine the effect of context on categorization of facial expressions according to diagnosis: (i) ‘categorization accuracy’, which was defined as the percentage of times the facial expression was labelled correctly; and (ii) ‘contextual influence’, which was defined as the percentage of times the face was labelled as expressing the contextual emotion (i.e. emotion conveyed by the body expression), as opposed to any other emotion. For both categorization accuracy and contextual influence, scores were calculated for the congruent and incongruent trials separately.

Statistical analyses

Data were analysed using IBM SPSS (Version 23). Categorical variables were analysed using chi-square. Demographic variables and neuropsychological tests were analysed using univariate ANOVA. Univariate ANOVAs were also used to compare performance across groups on the Face alone task and on the Body alone task. To examine contextual effects (accuracy, contextual influence), we conducted separate repeated measures ANOVAs with congruency (congruent, incongruent) as the within-subjects factor and group (bvFTD, semantic dementia, controls) as the between-subjects factor. Sidak *post hoc* tests were conducted to investigate differences between groups while correcting for multiple comparisons. Linear regression analyses were carried out to identify whether performance on Tasks A and B, and/or diagnosis predicted categorization accuracy and contextual influence on Task C. We used multiple regression to determine the extent that each of these variables additionally predicted performance on the variables of interest. For all analyses, statistical significance was set at $P < 0.05$ unless otherwise stated.

Neuroimaging analyses

MRI acquisition

Participants underwent whole-brain structural MRI with a 3 T Phillips scanner. High resolution T_1 images were obtained

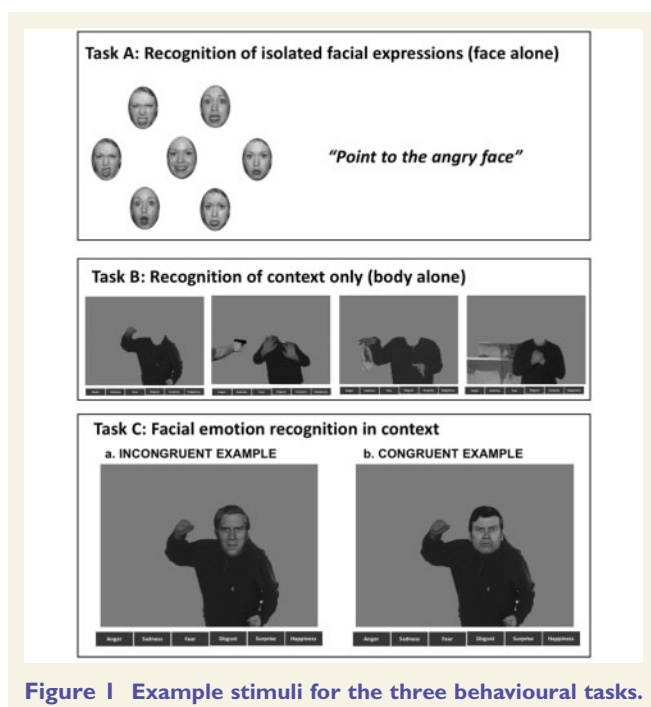


Figure 1 Example stimuli for the three behavioural tasks.

using the following protocol: 256×256 , 200 slices, 1 mm^2 in-plane resolution, 1 mm slice thickness, echo time/repetition time = 2.6/5.8 ms, flip angle = 8° . Brain scans were available for 16 bvFTD, 11 semantic dementia and 20 control participants.

Data preprocessing

FSL voxel-based morphometry (VBM), part of the FMRIB software library package <http://www.fmrib.ox.ac.uk/fsl/fslvbm/index.html> (Smith *et al.*, 2004) was used to analyse the MRI data (Ashburner and Friston, 2000; Mechelli *et al.*, 2005; Woolrich *et al.*, 2009). First, structural images were brain-extracted using BET and tissue segmentation was undertaken using automatic segmentation (FAST) (Zhang *et al.*, 2001). Then, grey matter partial volume maps were aligned to Montreal Neurological Institute standard space (MNI152) using non-linear registration (FNIRT), which uses a *b*-spline representation of the registration warp field (Rueckert *et al.*, 1999). A study-specific template was created and the native grey matter images were non-linearly re-registered. Modulation of the registered partial volume maps was carried out, by dividing them by the Jacobian of the warp field. The modulated, segmented images were smoothed with an isotropic Gaussian kernel (sigma = 3 mm, full-width at half-maximum = 8 mm).

Voxel-based morphometry analyses

A voxel-wise general linear model (GLM) was applied to investigate grey matter intensity differences using permutation-based, non-parametric statistics with 5000 permutations per contrast (Nichols and Holmes, 2002). In the first set of analyses, differences in grey matter integrity between patient groups and controls were investigated using *t*-tests.

To examine the neural correlates of task performance, categorization accuracy scores (i.e. correct facial emotion recognition in context) were entered into two separate GLMs to determine the regions associated with accuracy performance in each patient group (bvFTD, semantic dementia) combined with controls. This approach has been shown to achieve greater variance in scores, increasing the statistical power to detect behavioural correlations (Sollberger *et al.*, 2009). Then, to identify regions where reduced integrity correlated with greater contextual influence, we created two separate GLMs for each patient group (bvFTD, semantic dementia) combined with controls, with contextual influence included as the variable of interest. Finally, we conducted overlap and exclusive mask analyses to identify common and divergent regions in bvFTD and semantic dementia across analyses. Here, the statistical maps generated by the two contrasts were scaled using a threshold of $P < 0.001$, following which, the two contrasts were multiplied to create an inclusive, or overlap, mask across groups. For the exclusive analysis, again the contrasts were scaled using a threshold of $P < 0.001$, and these were subsequently divided by each other to identify regions specific to each contrast (Hornberger *et al.*, 2011; Irish *et al.*, 2014). For all analyses, a cluster extent threshold of > 100 voxels was applied. VBM analyses in all participants combined are reported in Supplementary Tables 5 and 6.

Results

Demographics and cognitive profiles

As reported in Table 1, no group differences were found in sex ($P = 0.590$), age ($P = 0.357$) or education ($P = 0.122$). In patient groups, no significant differences were found in disease duration, although bvFTD had greater functional severity than semantic dementia ($P = 0.002$). Neuropsychological performance in bvFTD and semantic dementia compared with controls is reported in Table 1. In brief, both groups showed impaired general cognition on the ACE (P -values < 0.001), with semantic dementia also performing lower than bvFTD ($P = 0.009$), likely reflecting the language demands of the task. The bvFTD group showed impaired performance across the range of neuropsychological tasks, compared with controls. In contrast, semantic dementia showed impaired naming and fluency performance, with attention, working memory and non-verbal episodic memory relatively well preserved.

Emotion processing results

Task A: Recognition of isolated facial emotional expressions

Performance on the three emotion processing tasks is depicted in Fig. 2. For recognition of faces alone, an overall effect of group was observed [$F(2,48) = 22.467$, $P < 0.001$], with both bvFTD and semantic dementia performing worse than controls in recognizing isolated facial expressions averaged across emotions (both P -values < 0.001) (Fig. 2A). No difference between patient groups was observed ($P > 0.999$).

Task B: Context alone

Examination of the ability to recognize contextual information (i.e. emotional body language scenes) with facial information removed, revealed an overall effect of group [$F(2,50) = 8.792$, $P = 0.001$], with both bvFTD ($P = 0.005$) and semantic dementia ($P = 0.002$) performing lower than controls (Fig. 2B). No difference between patient groups was observed ($P = 0.808$).

Task C: Contextual effects

For categorization accuracy, a significant group \times congruency interaction was observed [$F(2,48) = 4.180$, $P = 0.021$], as well as main effects of group [$F(2,48) = 10.261$, $P < 0.001$] and congruency [$F(1,48) = 146.844$, $P < 0.001$] (Fig. 2C). *Post hoc* comparisons of the above interaction revealed that irrespective of congruency, bvFTD patients performed worse than controls ($P < 0.001$), with a similar trend in semantic dementia ($P = 0.079$), but no difference between the bvFTD and semantic dementia groups ($P = 0.277$). Importantly, the profiles of performance between bvFTD and semantic dementia differed, depending

Table 1 Demographic variables and cognitive profile according to group

	BvFTD (n = 19)	SD (n = 12)	Controls (n = 20)	Statistic	P	
Sex (M:F)	13:6	6:6	12:8	1.056	0.590	
Age (y)	62.7 ± 8.7	64.9 ± 8.3	66.3 ± 6.1	1.054	0.357	
Education (y)	12.6 ± 2.7	13.9 ± 2.7	14.2 ± 1.9	2.194	0.122	
Disease duration (y)	6.4 ± 3.2	5.7 ± 2.8	-	0.351	0.558	
FRS Score	-0.7 ± 1.0	0.8 ± 1.1	-	12.506	0.002	
ACE (/100)	77.5 ± 12.0	65.7 ± 12.0	96.3 ± 2.9	36.312	<0.001	Patients < controls; SD < bvFTD
Digits-F	6.1 ± 1.2	6.7 ± 1.5	7.7 ± 1.1	8.430	<0.001	BvFTD < controls
Digits-B	3.7 ± 1.0	4.7 ± 1.7	5.7 ± 1.4	10.272	<0.001	BvFTD < controls
Trails A (s)	48.8 ± 19.9	44.1 ± 21.0	29.2 ± 7.3	7.021	0.002	BvFTD > controls
Trails B (s)	140.7 ± 77.4	130.4 ± 131.2	67.2 ± 21.6	4.109	0.023	BvFTD > controls
RCF Copy (/36)	27.3 ± 5.7	32.8 ± 1.7	32.6 ± 3.0	10.001	<0.001	bvFTD < controls; SD
RCF Recall (/36)	10.1 ± 6.9	15.0 ± 4.2	18.5 ± 6.5	8.006	0.001	bvFTD < controls
Naming (30)	20.1 ± 4.6	8.4 ± 5.2	28.1 ± 1.7	109.134	<0.001	Patients < controls; SD < bvFTD
Letter Fluency	26.6 ± 14.2	25.4 ± 6.8	53.3 ± 15.7	21.491	<0.001	Patients < controls

Values are mean ± standard deviation. FRS = Functional Rating Scale. Higher scores denote higher functioning. FRS score missing for two patients with bvFTD and two patients with semantic dementia (SD). Where relevant, maximum scores are provided in parentheses. ACE = Addenbrooke's Cognitive Examination; RCF = Rey Complex Figure.

Missing Scores: Digit span: one control; Trails A: one bvFTD, one Control; Trails B: one bvFTD (and discontinued: three bvFTD), one Control; RCF Copy: one bvFTD, one semantic dementia, two controls; RCF Recall: one bvFTD, one semantic dementia, three controls; SYDBAT naming: 12 bvFTD; Letter Fluency: five bvFTD, two semantic dementia.

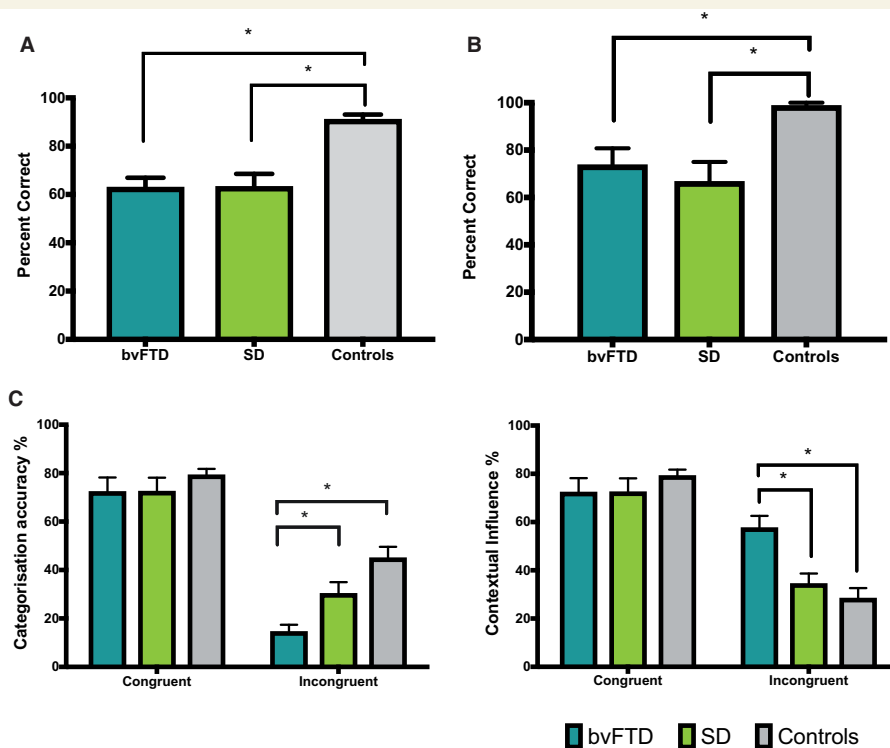


Figure 2 Behavioural performance on the emotion processing tasks. (A) Recognition of isolated facial expressions in bvFTD and semantic dementia (SD) compared to controls. Bars are group means with error bars depicting standard error of the mean (SEM). Face alone scores missing for one patient with bvFTD and one patient with semantic dementia. (B) Recognition of context only according to group. (C) Contextual effects (i) Categorization accuracy; and (ii) Contextual influence (categorization as context) in bvFTD and semantic dementia compared with controls. Bars represent mean and SEM. * $P < 0.05$ compared to controls, Sidak adjusted for multiple comparisons.

on the congruency of the context. While both bvFTD and semantic dementia performed similarly to controls on congruent items (bvFTD versus controls $P = 0.620$; semantic dementia versus controls $P = 0.722$), bvFTD performed

worse than both controls ($P < 0.001$) and semantic dementia ($P = 0.044$) for incongruent items. Semantic dementia performed lower than controls for incongruent items, although this was marginal ($P = 0.061$).

Focusing on contextual influence, again a significant group \times congruency interaction was observed [$F(2,48) = 14.432, P < 0.001$] and a main effect of congruency [$F(1,48) = 129.130, P < 0.001$], but not of group [$F(2,48) = 2.926, P = 0.063$] (Fig. 2C). Here, for the incongruent items, bvFTD patients were significantly more likely to label the facial emotion as that displayed by the context than both control ($P < 0.001$) and semantic dementia ($P = 0.006$) groups, whereas semantic dementia performed similarly to controls ($P = 0.775$). No difference in performance according to group was observed on congruent items (bvFTD versus controls $P = 0.620$; semantic dementia versus controls $P = 0.722$; bvFTD versus semantic dementia $P > 0.999$; Fig. 2C). Together, these results indicate that bvFTD patients are more likely to respond according to the emotion portrayed by the context, whereas in semantic dementia and controls, the response patterns vary depending on the perceptual similarity of the target emotional face and the emotion expressed by the context.

To examine whether differential language demands accounted for group differences in performance across Tasks A, B and C, we conducted correlational analyses on measures of receptive (SYDBAT comprehension) and expressive (SYDBAT naming) language and the three experimental tasks, in each group (Supplementary Table 1). No correlation reached significance and no clear pattern was evident across the different tasks, suggesting language impairment does not solely predict differences in task performance. Furthermore, to account for the possible role of attention on Task C specifically, we conducted correlational analyses between neuropsychological measures of attention (Digit Span Forward, Trial Making Test A) and contextual influence on the incongruent trials in each diagnostic group (Supplementary Table 2). Again, no correlation reached significance, suggesting that changes in attention alone does not account for group differences in the influence of contextual information.

Finally, to explore these divergent profiles further, we examined categorization accuracy and contextual influence as a function of emotion. Full details of analyses are provided in Supplementary Fig. 1. According to Aviezer *et al.* (2008), in healthy adults the degree of contextual influence varies according to the amount of similarity between the target facial expression and the facial expression usually associated with the context. For example, contextual effects are more likely to be seen when a disgust face is paired with an angry body than when paired with a fearful body, because of the perceptual similarity of angry and disgusted facial emotional expressions. Thus, if patients are influenced by the perceptual similarity of the facial expression, a gradient of contextual influence according to the perceptual similarity of the target emotion and context emotion would be observed, whereas if perceptual similarity does not play a role, a similar profile irrespective of emotion would be expected. In brief, bvFTD showed consistently worse accuracy and significantly greater contextual influence when emotional faces were presented in incongruent

contexts. Moreover, this pattern was not sensitive to the degree of perceptual similarity. In contrast, in controls, the degree of contextual sensitivity was modulated by the perceptual similarity of the congruent emotional face, in keeping with previous findings. In semantic dementia, the degree of contextual sensitivity differed from bvFTD, and tended to depend on the emotional face and emotional context.

Multiple regression

Next, we explored how performance on the Face alone and Body alone tasks predicted categorization accuracy and degree of contextual influence (Table 2). For categorization accuracy, Model 1, which included Face alone performance as the sole predictor explained 46.8% of the variance in emotion accuracy on Task C, with individuals who had better Face alone performance also showing higher categorization accuracy. While the inclusion of Body alone performance did not improve the model ($\Delta R^2 = 0.003$; $P = 0.588$), inclusion of diagnosis marginally improved

Table 2 Multiple regression examining how face alone accuracy, body alone accuracy and diagnosis determines categorization (target) accuracy and contextual influence

	B	SE B	β	P
Categorization accuracy				
Model 1				
Constant	-1.785	7.126		
Face alone	0.595	0.093	0.684	<0.001
Model 2				
Constant	-1.033	7.311		
Face alone	0.645	0.130	0.741	<0.001
Body alone	-0.054	0.098	-0.082	0.588
Model 3				
Constant	9.924	11.795		
Face alone	0.495	0.153	0.569	0.002
Body alone	-0.008	0.096	-0.013	0.932
Control versus bvFTD	-10.122	5.298	-0.287	0.063
Control versus SD	0.662	5.783	0.016	0.909
Contextual influence				
Model 1				
Constant	68.720	12.934		
Face alone	-0.363	0.168	-0.303	0.036
Model 2				
Constant	62.754	12.478		
Face alone	-0.753	0.223	-0.629	0.001
Body alone	0.422	0.168	0.466	0.016
Model 3				
Constant	15.853	18.667		
Face alone	-0.236	0.237	-0.197	0.325
Body alone	0.345	0.149	0.381	0.026
Control versus bvFTD	32.390	8.247	0.664	<0.001
Control versus SD	13.051	9.469	0.224	0.175

Categorization accuracy: $R^2 = 0.468$ for Model 1, $\Delta R^2 = 0.003$ for Model 2 $P = 0.588$; $\Delta R^2 = 0.069$ for Model 3, $P = 0.047$. Contextual Influence: $R^2 = 0.092$ for Model 1, $\Delta R^2 = 0.111$ for Model 2, $P = 0.016$; $\Delta R^2 = 0.231$ for Model 3, $P = 0.001$. SD = semantic dementia.

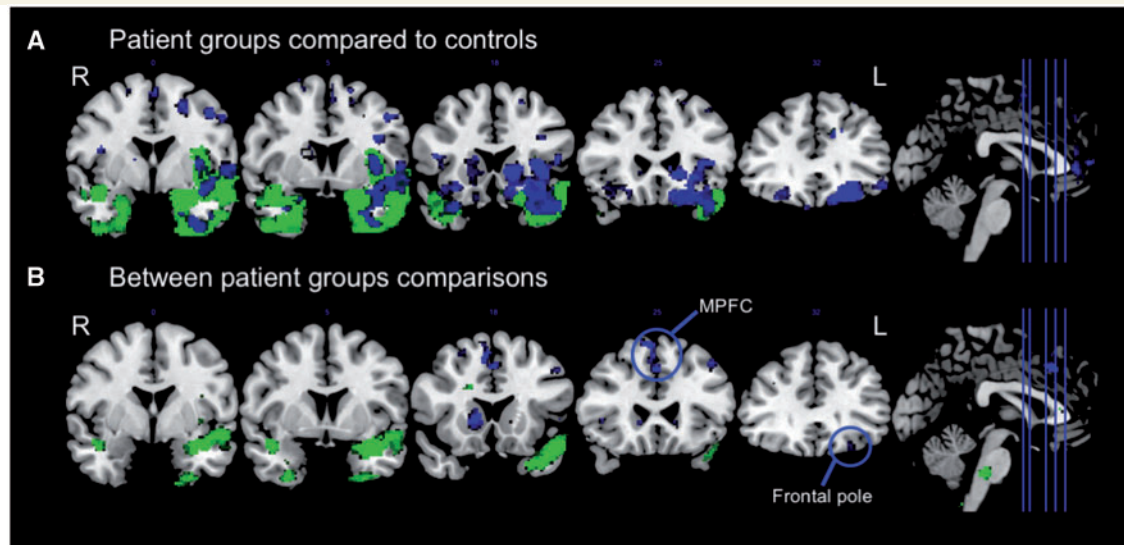


Figure 3 Neuroimaging patterns of atrophy. (A) Group differences between bvFTD and controls (blue) and semantic dementia and controls (green) and (B) group differences where bvFTD show lower intensity than semantic dementia (blue) and where semantic dementia show lower intensity than bvFTD (green). Note: All analyses reported at $P < 0.001$, voxelwise, uncorrected for multiple comparisons. MNI coordinates: $x = 0$; $y = 0, 5, 18, 25, 32$. L = left; R = right; MPFC = medial prefrontal cortex.

the model ($\Delta R^2 = 0.069$; $P = 0.047$). Here, being diagnosed as bvFTD also tended to predict worse categorization accuracy performance compared with controls ($P = 0.063$).

For contextual influence, Face alone performance was also a significant predictor of contextual influence ($P = 0.036$), with greater Face alone scores predictive of lower contextual influence. Importantly, inclusion of Body alone scores also improved the model ($\Delta R^2 = 0.111$; $P = 0.016$), with higher Body alone scores predictive of greater contextual influence. Finally, inclusion of diagnosis as a dummy variable further improved the model ($\Delta R^2 = 0.231$; $P = 0.001$). Here, a diagnosis of bvFTD was predictive of greater contextual influence, over and above that explained by Face alone and Body alone performance ($P < 0.001$) but not with a diagnosis of semantic dementia ($P = 0.175$).

Neuroimaging results

Group comparisons: patterns of atrophy

Figure 3 displays the regional changes in brain integrity in patient groups compared to controls (Fig. 3A) and between patient groups (Fig. 3B; see also Supplementary Tables 3 and 4). BvFTD patients showed lower intensity in the frontal cortices, particularly the orbitofrontal and ventromedial prefrontal cortices, together with the insula, as well as the bilateral fusiform gyri. Direct comparisons with semantic dementia revealed that bvFTD patients had lower integrity than semantic dementia in the ventromedial prefrontal cortex, right caudate and right frontal pole. In contrast, compared to controls, semantic dementia showed bilateral temporal lobe atrophy, which was greater on the left, and extended into the amygdala, hippocampus, orbitofrontal

cortex and insula. Compared with bvFTD, semantic dementia had lower integrity in the left temporal fusiform cortex, and bilateral temporal pole, although this was greater on the left.

Neural correlates of categorization accuracy and contextual influence

First, categorization accuracy scores (i.e. correct facial emotion recognition in context) were entered into two separate whole brain GLMs to determine the regions associated with accuracy performance in each patient group (bvFTD, semantic dementia) combined with controls. In bvFTD, categorization accuracy was associated with integrity of the bilateral fusiform cortex, together with the medial and superior frontal gyrus, and right insula. In semantic dementia, categorization accuracy was associated with the left parahippocampal gyrus, extending into the amygdala and fusiform cortex, together with the right fusiform cortex and left superior temporal gyrus. Notably, an overlap analysis to identify regions that were commonly implicated in both bvFTD and semantic dementia identified the right parahippocampal gyrus/amygdala and left precentral gyrus (Table 3 and Fig. 4).

To identify regions that correlated with the degree of contextual influence, we created two separate GLMs for each patient group (bvFTD, semantic dementia) combined with controls (Table 4 and Fig. 4). Here, we found that in bvFTD, integrity of the bilateral fusiform cortex was associated with the degree of contextual influence (i.e. the tendency to respond to the emotion portrayed by the body rather than the face). In semantic dementia, contextual influence was associated with integrity of the right parahippocampal gyrus, right precentral gyrus and cerebellum.

Notably, the overlap analysis again revealed that in both bvFTD and semantic dementia, integrity of the right parahippocampal gyrus/amygdala was associated with the degree of contextual influence, with lower integrity of this region associated with a higher degree of contextual influence.

Finally, we conducted an overlap analysis to identify common regions implicated in both accuracy and categorization influence in both bvFTD and semantic dementia (Supplementary Table 7). Here, the only significant regions to emerge were the right parahippocampal gyrus/amygdala and the left precentral gyrus. Given the differential profile of performance between bvFTD and semantic dementia for contextual influence, we conducted an exclusive masking analysis to identify regions that correlated with contextual influence in bvFTD but not semantic dementia. In bvFTD, contextual influence was exclusively associated with lower integrity of the bilateral temporal fusiform cortex, parahippocampal gyrus, amygdala and orbitofrontal cortex (Supplementary Table 8 and Supplementary Fig. 2).

Discussion

Here, we aimed to examine how contextual information modulates emotion recognition in two dementia syndromes characterized by deficits in emotion processing—bvFTD and semantic dementia—and the neural correlates of this effect. Our results revealed that while bvFTD and semantic dementia show similar profiles when facial expressions are presented in isolation or when congruent contextual information is provided, divergent profiles emerge when facial expressions are presented in incongruent contexts. Specifically, bvFTD showed worse categorization accuracy and greater contextual influence than both semantic dementia and controls. Examination of the relationship between face alone, body alone and contextual effects, together with profiles of errors, demonstrated a consistent profile revealing that reduction in accuracy in bvFTD is due to an increased bias towards an over-reliance on external contextual information. Conversely, in semantic dementia, the profile appeared to reflect a more generalized loss of emotion knowledge, irrespective of

Table 3 Voxel-based morphometry results showing regions of significant grey matter intensity, which correlate with categorization accuracy according to group

Regions	Side	MNI			Voxels
		x	y	z	
BvFTD combined with controls					
Temporal fusiform gyrus, anterior division extending into inferior temporal gyrus,	L	-30	-10	-50	5203
Temporal fusiform gyrus, posterior division	R	32	-10	-38	2295
Precentral gyrus	L	-48	-4	22	1502
Superior temporal gyrus	L	-48	-38	2	1322
Medial frontal cortex	R	12	40	-12	963
Superior frontal gyrus	R	41	74	61	662
Cerebellum	R	20	-72	-40	427
Lateral occipital cortex, superior division	R	24	-84	18	326
Cerebellum	L	-20	-68	-34	322
Posterior cingulate	L	-14	-40	40	269
Central opercular cortex, insula	R	44	-10	16	235
Supramarginal gyrus, posterior division	L	-62	-46	42	212
Middle frontal gyrus	L	-26	2	44	181
Posterior cingulate	R	8	-20	44	169
Precuneus	R	6	-72	48	152
Postcentral gyrus	R	36	-32	36	133
Semantic dementia combined with controls					
Parahippocampal gyrus, extending into temporal fusiform cortex and amygdala	L	-28	0	-36	1305
Temporal fusiform cortex, posterior division	R	38	-12	-44	1100
Superior temporal gyrus, posterior division	L	-64	-24	6	1071
Parietal operculum cortex	R	54	-28	22	146
Middle temporal gyrus, anterior division	L	-58	-8	-30	135
Regions of overlap					
Temporal fusiform cortex, posterior division, extending into amygdala	R	36	-10	-38	556
Precentral gyrus	L	67	59	48	371
Parahippocampal gyrus, anterior division, extending into amygdala	L	-28	0	-38	301
Insular cortex	L	-32	-24	6	242
Parahippocampal gyrus	L	-30	-24	-24	239
Temporal pole	L	-44	18	-32	236

All analyses reported at $P < 0.001$, voxelwise, uncorrected for multiple comparisons. Clusters reported if > 100 contiguous voxels.

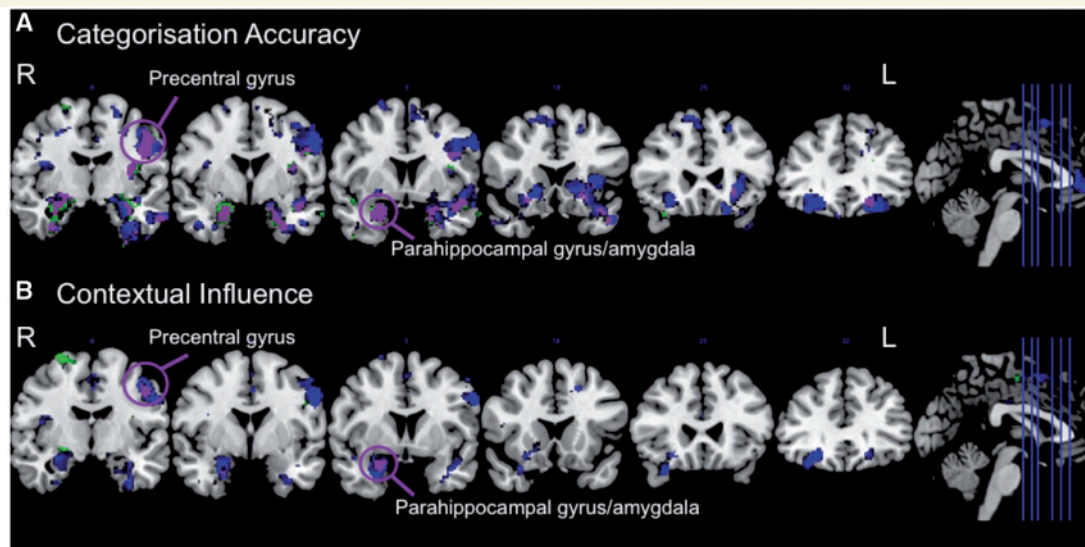


Figure 4 Neural correlations of categorization accuracy and contextual influence. Regions that correlate with (A) categorization accuracy and (B) contextual influence in bvFTD and controls (blue) and semantic dementia and controls (green). Regions of overlap in bvFTD and semantic dementia are shown in purple. The only common regions to emerge across all analyses were the right parahippocampal gyrus/amygdala and the left precentral gyrus. Note: All analyses reported at $P < 0.001$, voxelwise, uncorrected for multiple comparisons. MNI coordinates: $x = 0$; $y = -8, 0, 5, 18, 25, 32$. L = left; R = right.

Table 4 Voxel-based morphometry results showing regions of significant grey matter intensity that correlate with contextual influence according to group

Regions	Side	MNI			Voxels
		x	y	z	
BvFTD combined with controls					
Temporal fusiform cortex, extending into amygdala, orbitofrontal cortex, parahippocampal gyrus	R	34	-6	-38	1322
Precentral gyrus	L	-48	-4	28	820
Temporal fusiform cortex, extending into parahippocampal gyrus and hippocampus	L	-32	-10	-44	790
Planum temporale	L	-46	-32	6	391
Posterior cingulate	R	14	-22	40	336
Posterior cingulate	L	-10	-34	44	106
Semantic dementia combined with controls					
Cerebellum	R	36	24	16	220
Precentral gyrus, extending into superior frontal gyrus	R	20	-18	62	169
Temporal pole, extending into parahippocampal gyrus, orbitofrontal cortex	R	24	6	-24	133
Planum temporale	L	-38	-34	14	132
Lateral occipital cortex, superior division	R	30	-86	24	107
Regions of overlap					
Parahippocampal gyrus, amygdala	R	24	0	-30	98 ^a

All analyses reported at $P < 0.001$, voxelwise, uncorrected for multiple comparisons. Clusters reported if > 100 contiguous voxels, ^awith the exception of the overlap analysis where the largest cluster is reported. L = left; R = right.

whether this information was presented via the face or via contextual cues. In both groups, contextual influence was related to integrity of the right parahippocampal gyrus/amygdala and the left precentral gyrus. Here, we discuss how our findings inform knowledge of the nature of social impairments in bvFTD and semantic dementia, and how they shed light on the neural basis of integration of social context.

Two complementary processes explain the over-reliance on contextual information observed in bvFTD. First, our findings demonstrate that presence of facial information

does not alter interpretation of contextual information. This is further supported by evidence that integrity of the anterior bilateral temporal fusiform is associated with degree of contextual influence in bvFTD, regions that have been previously implicated in face processing. While previously, early face processing was assumed to be intact in bvFTD, recent reports suggest that at least some aspects of face processing are indeed impaired in this syndrome (Kumfor et al., 2011, 2015; De Winter et al., 2016; Hutchings et al., 2017), which aligns with the current findings.

Second, patients with bvFTD appear to experience difficulty in integrating and/or modulating contextual information, resulting in inappropriate behaviour. This is akin to the 'environmental dependency syndrome' (also known as utilization/imitation behaviour) described in frontal lesion patients (Lhermitte, 1983, 1986; Lhermitte *et al.*, 1986) whereby individuals produced inappropriate behaviours, which were externally induced by contextual social and physical information, irrespective of the intended goals, expected intentions, appropriateness, social norms or emotional consequences (see also Mesulam, 1986; Burgess *et al.*, 2009). This behaviour is remarkably consistent with the response pattern observed here in bvFTD. Interestingly, a recent study that used the Multifaceted Empathy Task in bvFTD reported that ratings for context-only stimuli appeared to account for ratings when viewing people embedded in contexts (Oliver *et al.*, 2015). While this previous study did not explicitly set out to explore contextual influences of emotion processing, their pattern of results accords well with the current findings. According to these accounts, and postulated by the SCNM, damage to the frontal lobes results in a 'slaving of the frontal lobe' such that external contextual cues (as in the case of emotional body language) trigger automatic reliance on the emotional context that is no longer modulated by other sources of information. This breakdown becomes particularly acute when understanding of other sources of information is also impaired (i.e. here, core facial information).

In our experience, spontaneous utilization or imitation behaviours are rarely seen in bvFTD patients in the clinic, but can be provoked frequently (Ghosh and Dutt, 2010). Lower spontaneous behaviours may reflect improved diagnostic accuracy, meaning patients are assessed earlier in the disease course and/or reflect the constrained testing environment, which minimizes these behaviours (Mesulam, 1986). Notably, some researchers have also suggested that the lack of abnormal testing results in patients with frontal lesions is due to inadequacy in neuropsychological assessments targeting frontal brain regions (Burgess *et al.*, 2009). Our results indicate that contextual influence is sensitive to social cognition impairment and appears specific to bvFTD. While we did not set out to assess utilization behaviour/environmental dependency, it would be interesting to examine whether the degree of contextual influence is associated with day-to-day manifestations of these behaviours.

Patients with semantic dementia showed marginally lower categorization accuracy than healthy older controls. Unlike bvFTD, however, semantic dementia performance was modulated by context, at least in part. This profile suggests that in semantic dementia, an overall decline in the capacity to decode both facial and body expressions accounts for their lower performance, and may reflect an ongoing degradation of social conceptual knowledge (Kumfor *et al.*, 2016), irrespective of task demands. Interestingly, both controls and semantic dementia patients showed response patterns that varied according to the degree of similarity between the emotion of the context and the face (i.e.

more likely to interpret a disgust face as anger, when presented in an angry context), indicating a degree of contextual integration. The SCNM proposes that the ability to form context-target associations is dependent on temporal regions, via basic associative processes that require activity in the hippocampus, amygdala and perirhinal cortex; this converges with our neuroimaging findings. It is therefore somewhat surprising that in semantic dementia, a degree of contextual influence was maintained, given their widespread temporal lobe atrophy, which includes the perirhinal cortex and to some degree the hippocampus and lateral temporal lobe (Davies *et al.*, 2005). While the SCNM does not make specific predictions about laterality of regions involved, the current findings suggest that contextual integration of social information is lateralized to the right hemisphere and thus, is likely to be more pronounced in semantic dementia patients with predominant right-lateralized temporal lobe atrophy. This hypothesis would converge with the known greater behavioural changes in this group compared to typical left-lateralized semantic dementia patients (Kumfor *et al.*, 2016). Our results in semantic dementia should also be interpreted with the caveat that our sample size in this group was 12. While this sample size is in line with other studies in these relatively rare clinical populations, it is possible that the power achieved was insufficient to detect smaller effects. Thus, replication studies will be important to confirm the contextual influences on emotion processing in this population. Future studies should examine the performance of right-lateralized semantic dementia patients on emotion recognition tasks that involve integration of context. Here, our results demonstrate that, at the behavioural level, divergent profiles of performance are present in bvFTD and semantic dementia, which may account for the differences in the nature of behavioural and social changes observed in these syndromes.

Our neuroimaging analyses uncovered two key brain regions that were implicated in categorization accuracy and contextual influence in both patient groups: the right parahippocampal gyrus/amygdala and the left precentral gyrus. The parahippocampal cortex is necessary for mediating global contextual associations (Bar, 2004) and in particular, the capacity to link visual objects with their typical context (Bar and Aminoff, 2003; Aminoff *et al.*, 2013). Here, we saw consistent associations with the parahippocampal gyrus as well as the anterior temporal fusiform, amygdala, orbitofrontal cortex and insula, which converges with previous findings investigating sarcasm detection (Rankin *et al.*, 2009). In healthy adults, both the parahippocampal gyrus, fusiform and amygdala are differentially activated in response to faces in context, while amygdala lesions moderate this effect (Van den Stock *et al.*, 2014; Hortensius *et al.*, 2016). Thus, our results provide convergent support that the parahippocampal gyrus, particularly on the right, plays an important role in forming context-target associations between facial expressions and their observed context.

The second structure that was reliably identified in our neuroimaging analyses was the left precentral gyrus. While

not typically implicated in facial expressions of emotion, the precentral gyrus shows increased activation when individuals passively view still body images, which has been interpreted as the brain ‘filling in’ expected dynamic information (Kourtzi and Kanwisher, 2000; de Gelder, 2006). Thus, it is possible that in order to interpret gestures/emotional body language accurately, a basic motor resonance mechanism that engages the left precentral gyrus may be necessary. Indeed, activation of this region is seen across a range of tasks including observing meaningless gestures, observing others’ actions and viewing emotion and implied motion (Straube *et al.*, 2012; Saggat *et al.*, 2014; Kolesar *et al.*, 2017). Our results suggest that in line with the SCNM, impaired automatic resonance (a motor forward mechanism) induces inadequate anticipatory signals (i.e. signal lacking implicit integration of gesture and facial information, or prediction error account), thus leading to inadequate categorization of the emotion (Ibañez and Manes, 2012). To summarize, the key manipulation of including body language here, has demonstrated the likely need to integrate signals from regions that were typically considered as involved in movement only, to support interpretation of emotional contexts, specifically body language.

Importantly, the regions identified here did not extend to the insula, a region which is affected early in bvFTD. According to the SCNM, the frontal, temporal and insula cortices are involved in different aspects of social context integration. While the temporal cortices are necessary for forming associations between the context and the target stimuli, the insula forms a hub to integrate internal and external signals. That is, the insula is necessary for detecting changes in internal body states and coordinating this information with external social contextual cues. How this ability is affected in bvFTD is only beginning to be explored, however, a recent study demonstrated that aspects of interoception are abnormal in this syndrome (García-Cordero *et al.*, 2016). Given that no attention to internal or interoceptive processing of these emotional signals was induced by the tasks in this study, it is not entirely surprising that associations with the insula were not observed. Future studies that explore the relationship between interoception, emotion processing and social cognition will help to further our understanding of how social context is integrated in neurodegenerative disorders, and also refine the SCNM (Van den Stock and Kumfor, 2017).

This study represents the first attempt to examine contextual influences of emotion perception in frontotemporal dementia, and our results raise some interesting new issues, which warrant further examination. The current findings in bvFTD suggest an over-reliance on external contextual cues. A direct prediction of this profile is that implicit presentation of contextual cues (e.g. via priming or subliminal stimulus presentation times) would significantly reduce (or even invert) the contextual effect in bvFTD. This hypothesis has direct implications for our clinical and theoretical understanding of context effects. In addition, close examination of lateralization effects, and how this can be integrated into the

SCNM deserves attention. Finally, it should be noted that our experimental tasks were not entirely matched for task demands. While Task A used a selection paradigm, Tasks B and C used a labelling paradigm. Importantly, we were interested in comparing performance between groups and between conditions within tasks. Thus, potential variabilities in task demands are of less direct relevance to the interpretation of the results. Furthermore, correlations with performance on neuropsychological measures assessing receptive and expressive language did not reveal clear relations between task design and language impairments (Supplementary material). Similarly, no clear relationship between impaired attention and over-reliance on contextual cues were observed. Nevertheless, future studies that use tasks with identical demands will help to rule out any potential influence other aspects of cognitive impairment may have in these patient populations.

From a clinical perspective, our results have a number of potential implications. First, as alluded to earlier, tests that examine the relative influence of external contextual cues appear sensitive to a diagnosis of bvFTD, and may also provide insight into some of the ‘behavioural dependency’ that is reported by carers, but difficult to elicit and measure objectively in the clinic. Second, our results may also provide insight into potential intervention strategies to improve social behaviour of patients. Specifically, based on the current findings, it is unsurprising that bvFTD patients have difficulty in understanding complex social situations such as sarcasm, where external contexts are in direct competition with opposing, and often subtle facial expression cues. Psychoeducation for carers of the importance of providing external and consistent emotional cues when interacting with patients may thus improve the patients’ ability to understand interactions. Here, we focused on body language as the contextual information of interest; however, evidence suggests that other types of external contextual cues exert similar effects. Thus, information from environmental scenes (e.g. being at a wedding versus a funeral), vocal prosody (i.e. emotional tone of voice) and other faces, are all influential when recognizing emotions from faces (for reviews see Barrett *et al.*, 2011; Hassin *et al.*, 2013). While future studies will be necessary to confirm this, our results indicate that provision of congruent contextual information irrespective of modality, may improve emotion perception in both bvFTD and semantic dementia patients.

In summary, this study has demonstrated the importance of including context when assessing social cognition in clinical syndromes, something that is currently lacking in existing clinical tests [with some notable exceptions, e.g. The Awareness of Social Inference Test (TASIT) (McDonald *et al.*, 2003; Honan *et al.*, 2016; Kumfor *et al.*, 2017), the Social cognition and Emotional Assessment (SEA) (Bertoux *et al.*, 2012)]. From a theoretical perspective, our results suggest that the parahippocampal gyrus, amygdala, fusiform and precentral gyrus are key structures in forming context-target associations and using information from facial expressions and body language to perceive

emotions in others. While examination of context is only a recent advance in social neuroscience, a move towards understanding how we interpret emotions in more realistic situations will be helpful to both improve theories of emotion and increase our knowledge of clinical syndromes, which are characterized by a profound breakdown in the ability to participate in complex human social interactions.

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Supplementary material

Supplementary material is available at *Brain* online.

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