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The attribution of animacy and agency in frontotemporal dementia versus Alzheimer's disease

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Abstract

Impaired attribution of animacy (state of living or being sentient) and of agency (capability of intrinsically-driven action) may underlie social behavior disturbances in behavioral variant frontotemporal dementia (bvFTD). We presented the Heider and Simmel film of moving geometric shapes to 11 bvFTD patients, 11 Alzheimer's disease (AD) patients, and 12 healthy controls (HCs) and rated their recorded verbal responses for animacy attribution and agency attribution. All participants had skin conductance (SC) continuously recorded while viewing the film, and all dementia participants underwent magnetic resonance imaging (MRI) for regions of interest. The bvFTD patients, but not the AD patients, were impaired in animacy attribution, compared to the HCs. In contrast, both bvFTD and AD groups were impaired in agency attribution, compared to the HCs, and only the HCs had increasing SC responsiveness during viewing of the film. On MRI analysis of cortical thicknesses, animacy scores significantly correlated across groups with the right pars orbitalis and opercularis; agency scores with the left inferior and superior parietal cortices and the supramarginal gyrus; and both scores with the left cingulate isthmus involved in visuospatial context. These findings suggest that bvFTD is specifically associated with impaired animacy attribution from right inferior frontal atrophy. In contrast, both dementias may have impaired agency attribution from left parietal cortical atrophy

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and absent SC increases during the film, a sympathetic indicator of attribution of a social “story” to the moving shapes. These findings clarify disease-related changes in social attribution and corroborate the neuroanatomical origins of animacy and agency.

Keywords

Social attribution; Animacy; Agency; Heider and Simmel; Frontotemporal dementia; Alzheimer’s disease

1. Introduction

Impairments of social behavior and interpersonal functioning are core features of behavioral variant frontotemporal dementia (bvFTD), a neurodegenerative disease involving progressive atrophy of frontal and anterior temporal lobes (Eslinger, Moore, Anderson, & Grossman, 2011; Neary et al., 1998; Piguet, Hornberger, Mioshi, & Hodges, 2011; Rascovsky et al., 2011). Early in the disease, bvFTD patients show dysfunction in social cognition and the study of these patients offers an opportunity to clarify the underlying neurobiological mechanisms for social behavior and their neuroanatomical correlates (Elamin, Pender, Hardiman, & Abrahams, 2012; Mendez, Lauterbach, & Sampson, 2008; Seeley, Zhou, & Kim, 2012; Shany-Uri & Rankin, 2011).

Investigations of the mechanisms of social and interpersonal behavior in bvFTD have employed a range of methods. These include social perception and recognition of emotions and mental states through facial and verbal expressions (Keane, Calder, Hodges, & Young, 2002; Kessels et al., 2007; Kipps, Nestor, Acosta-Cabronero, Arnold, & Hodges, 2009; Werner et al., 2007), mentalizing or Theory of Mind (the attribution of thoughts, feelings, and beliefs) (Adenzato, Cavallo, & Enrici, 2010; Fernandez-Duque, Baird, & Black, 2009; Gregory et al., 2002), assessment of emotional and cognitive empathy (Baez et al., 2014; Eslinger et al., 2011; Lough et al., 2006; Rankin et al., 2006), and corresponding aspects of executive functions (Eslinger et al., 2007; Gleichgerricht, Torralva, Roca, & Manes, 2010; Grossman et al., 2010; Torralva, Roca, Gleichgerricht, Bekinschtein, & Manes, 2009). However, there have been few studies on social attribution abilities in bvFTD, specifically animacy, or the attribution of being alive, and the related agency, or the attribution of intrinsically-driven action with or without animacy.

Investigators have used social attribution tasks to study other disorders where social and interpersonal dysfunction are core features, especially autism spectrum disorders (Congiu, Schlottmann, & Ray, 2010; Kuzmanovic et al., 2014; McAleer, Kay, Pollick, & Rutherford, 2011; Rutherford, Pennington, & Rogers, 2006), schizophrenia (Bell, Fiszdon, Greig, & Wexler, 2010), Prader–Willi syndrome (Koenig, Klin, & Schultz, 2004) and Williams syndrome (van der Fluit, Gaffrey, & Klein-Tasman, 2012). Many of these social attribution tasks are derived from Heider and Simmel’s classic 1944 silent film created to investigate the processes involved in perceiving behavior without the use of personal or biological features (Heider & Simmel, 1944) (See Fig. 1). This film, which consists of moving geometric shapes in various “interactions,” elicits automatic attribution of intentions, beliefs,

emotions, motives, and personality traits to the shapes, consistent with living beings, and elicits attribution of the generation of movement and action to the shapes.

Studies in healthy populations have also used simple animated stimuli to investigate a range of social cognitive and behavioral attributes. Among normal participants, the mechanisms that underlie social attribution to geometric shapes affect higher social cognition such as mental state attribution and judging interactions as interpersonal (Castelli, Happé, Frith, & Frith, 2000; Gobbini, Koralek, Bryan, Montgomery, & Haxby, 2007; Schultz et al., 2003). These mechanisms help detect goal-directed motion, attribute intention, distinguish intentional movements from mechanical ones, and dissociate intentionality from animacy detection (Blakemore et al., 2003; Gao, Scholl, & McCarthy, 2012; Lee, Gao, & McCarthy, 2014; Stosic, Brass, Van Hoeck, Ma, & Van Overwalle, 2014). From these investigations, and others, two basic aspects of social attribution emerge: that of ascribing animacy (van Buren, Uddenberg, & Scholl, 2016; Gao and Scholl, 2011; Santos et al., 2010; Schultz & Bühlhoff, 2013), and that of ascribing agency (Gobbini et al., 2007; Osaka, Ikeda, & Osaka, 2012; Stosic et al., 2014).

The current study investigates the attribution of animacy and agency to Heider and Simmel's original film among patients with bvFTD, compared to a dementia group with Alzheimer's disease (AD), and healthy controls (HCs). Using videotaped analysis of verbal descriptions of the film, independent raters scored each participant's abilities to attribute animacy and agency to the moving geometric shapes. Skin conductance (SC) continuously monitored for increasing sympathetic arousal as an indicator of ongoing social attribution, and magnetic resonance imaging (MRI) revealed selected regions of interest (ROI) for correlation with social attribution abilities. Based on a.) frontal lobe neuropathology with a probable disproportionate role for right frontal dysfunction in bvFTD (Mendez, Joshi, Daianu, Jimenez, & Thompson, 2015; Miller, Chang, Mena, Boone, & Lesser, 1993), and b.) temporoparietal pathology in AD plus this region's role in agency, we hypothesized impaired animacy in bvFTD from right frontal atrophy and impaired agency in AD from parietotemporal atrophy. In addition, based on prior studies (Joshi, Barsuglia et al., 2014; Joshi, Mendez et al., 2014), we anticipated decreased sympathetic arousal, reflecting both decreased animacy and agency attribution, in dementia patients versus HCs.

2. Materials and methods

2.1. Participants

Patients with bvFTD and early-onset AD were recruited from the UCLA Behavioral Neurology Program and Clinic where they underwent clinical, neuropsychological, and neuroimaging assessments. Age-matched healthy controls (HCs) were recruited from volunteers in the community. Under approval by the Institutional Review Board of the University of California, Los Angeles (UCLA) and the Veterans Administration Healthcare Center, Greater Los Angeles, this study enrolled 34 participants: 11 patients with bvFTD, 11 patients with early-onset AD, and 12 healthy controls. All participants gave informed consent.

Patients with bvFTD met International Consensus Criteria for clinically probable behavioral variant FTD (Rascovsky et al., 2011). Clinical diagnoses were supported by predominant frontal and/or anterior temporal involvement as evidenced on MRI of the brain. Patients with AD met National Institute on Aging-Alzheimer's Association (NIA-AA) criteria for clinically probable AD and were in early stages of their disease. HCs were subjects without any known history of neurologic or psychiatric disease.

Participants in all three groups were comparable in age, and HCs were age-matched with the dementia patients within three years. Disease severity of the bvFTD and AD patients was assessed with the Mini-Mental State Examination (MMSE), the Montreal Cognitive Assessment (MoCA), and the Clinical Dementia Rating Scale-sum of boxes (CDR-sb). The sum of boxes CDR better reflects the functional impairment level of bvFTD when compared to AD than does the traditional CDR designed for AD (Deutsch, Liang, Jimenez, Mather, & Mendez, 2016). Three additional behavioral scales (The Frontal Systems Behavior Scale – FrSBe, the Social Norms Questionnaire – SNQ, the Socioemotional Dysfunction Scale – SDS), that characterize the social deficits of bvFTD, were administered to the dementia patients (Barsuglia et al., 2014; Panchal et al., 2016). Exclusion criteria included the use of beta-blocker medications (because of the psychophysiological assessment) or the presence of complicating medical or psychiatric illnesses or medications. None of the participants were on psychoactive medications.

2.2. Procedures

2.2.1. Heider and Simmel animation—Heider and Simmel's animated film of moving geometric shapes (1944) was presented on a television screen in a quiet testing room to participants seated in a chair approximately 3 feet away. Following Heider and Simmel's original experiment, the film was shown twice with preceding instructions, and participants were allowed unlimited time to respond to questions.

Participants were first instructed to relax and remain still during a 22-sec baseline SC recording. These participants were concurrently monitored by video and observed for activity. All remained seated with minimal bodily movements during the baseline recording period. Immediately after this baseline period, the following text was displayed on the screen: “*You will watch a short film. The film will play 2 times. You will describe what happens in the film.*” The 90-sec film was presented twice, followed by questions presented on the screen. The first screen displayed: “*Have you ever seen this film before? Yes or no.*” After a verbal answer was received, the second screen displayed: “*What happened in this film? Describe what happened as completely as you can.*” The concurrent video monitoring assessed their continued visual gaze on the film as an indication of alertness and attentiveness to stimuli during the 90-sec viewing. In addition, videotaped and transcribed participant responses allowed two investigators to establish adequate visual perception for the film and subsequently score their efforts. For further validation, the length of each participant's response was determined by counting the total number of propositions expressed in each description. A proposition was defined as a verb and its arguments, and each clause within a complex or compound sentence was considered and counted as a separate proposition (Reilly, Bates, & Marchman, 1998).

2.2.2. The social attribution coding system (SACS) for assessing responses to Heider and Simmel film—

The SACS contained Animacy Scores and Agency Scores. The two categories were based on linguistic analysis of participant responses and were derived from previous studies on social attribution to moving shapes (Castelli et al., 2000; Klin, 2000). Two raters, a psychiatrist and a clinical psychologist who were unfamiliar with participants or their diagnosis and group membership, independently scored their responses on the SACS. The raters were instructed to derive their scores from the typed transcripts of the participants' verbal narratives, as described for Animacy Scores and Agency Scores. Both sections were scored separately using a 4-point scale. For inter-rater reliability, we excluded participant responses when there was a difference of more than 2 between raters in any category, thus excluding one AD and two HC participants.

The Animacy Scores (attribution of animacy) primarily evaluate word choice to assess the degree of perceived animacy in the geometric shapes. There is a strong connection between the animacy of an entity and linguistic choice of referring expressions (Yamamoto, 1999). Pronouns are used more frequently for animate than inanimate objects (Fukumura & van Gompel, 2010) and first and second person pronouns indicate a higher level of animacy than third person pronouns (Comrie, 1989; Foley & Van Valin, 1984). Following this linguistic approach to degrees of animacy, participant narratives were scored for use of pronouns and of descriptors based on perception of social roles, relations, or personality traits: 0 = No use of personal pronouns; 1 = Reference to geometric shapes only with pronoun "it"; 2 = Reference to geometric shapes with personal pronouns "he" or "she"; 3 = Reference to geometric shapes with descriptors (e.g., bully, kid, friend).

The Agency Scores (attribution of agency) evaluated the perception of the shapes as being intrinsically driven and moving on their own. Similar to Animacy, there is a strong connection between the agency of an entity and linguistic choice of expressions; in this case, to words and phrases that reflect that the geometric shapes were self-propelled and not moving because of an outside force. The degree of agency was rated: 0 = Concrete geometric descriptions only (e.g., "There was a triangle"); 1 = Descriptions of geometric shapes moving (e.g., "The triangle moved"); 2 = One or two descriptions of shapes as moving on their own/intrinsically driven (e.g., "The triangle was running" or "the circle was hiding"); 3 = Three or more descriptions of shapes as moving on their own.

2.3. Psychophysiology

As a sympathetic nervous system measure of gradually increasing arousal to the film, this study continuously recorded SC during the Heider and Simmel viewing. Increased sympathetic SC changes are an indicator of increasing arousal to a developing story, which is dependent on social attribution. SC recording used BIOPAC hardware (MP150 System) with the SC module (GSR 100C) and BIOPAC software (AcqKnowledge v4.1). Electrodermal electrodes were placed on the palmar surface of the index and middle fingers of the participant's right hand. Acquisition parameters were set at 5 μ S/V, low pass filter 1 Hz, with no high pass filter. Sampling rate was 31.25 Hz. SC data was not available for one bvFTD and three HC participants due to technical problems with AcqKnowledge files.

SC results were processed for values at each second. The average baseline value was determined for each participant from resting SC levels collected during a baseline period of 22 sec preceding the film. The 90-sec Heider and Simmel film was presented one time as an initial “novelty” stimulus and then presented one additional time as the actual testing stimulus. This methodology allowed the exclusion of surprise, novelty, or non-specific orienting and defensive reactions to the initial viewing of the Heider and Simmel film and a focus on social attribution on the second viewing. Changes in SC values (continuous changes in both tonic SC levels and superimposed phasic SC responses over 90 sec) were collected during the second film viewing and analyzed at one-sec intervals (total of 90 analyses per participant). To correct for inter-individual variance, each participant’s mean baseline pre-stimulus SC value was subtracted from the SC value at each second of the test phase, showing change from baseline at each second. Group means, computed from these values, were graphed across a time sequence.

2.4. Neuroimaging

The bvFTD and AD patients underwent MRI using a standardized protocol on a 1.5 T high-resolution scanner. Images were acquired in the coronal plane using an MPRAGE sequence with the following acquisition parameters: TR = 2000 msec, TE = 2.49 msec, TI = 900 msec, flip angle = 8°, slice thickness = 1 mm, field of view = 25.6 cm, voxel size = $1.0 \times 1.0 \times 1.0 \text{ mm}^3$. Two cortical labels per hemisphere were extracted from the Desikan-Killiany atlas from the native space of each subject’s T1-weighted structural MRI scan using FreeSurfer version 5.3 (<http://surfer.nmr.mgh.harvard.edu/>) (Desikan et al., 2006). For best results, the FreeSurfer cortical delineations were manually adjusted as needed using control points in the white and gray matter structures. From the total atlas ROIs of 68, this study examined mean cortical thickness in 50 cortical areas, including all of the frontal-temporal-parietal ROIs, which are the areas involved in social cognition, and excluded subcortical regions and the occipital cortex, regions that are not primarily implicated in the literature on animacy and agency with the exception of a possible role of the amygdala in animacy and the cerebellum in agency (David, Newen, & Vokeley, 2008; Santos et al., 2010).

2.5. Statistical analysis

Statistical analysis was conducted using SPSS 21.0 software, and variables were evaluated for normality using the Shapiro–Wilk statistic. Group differences were compared using Chi-square, Kruskal–Wallis, and Mann–Whitney *U* tests for categorical or non-normal variables and one way analyses of variance (ANOVAs) for normal and continuous variables. The main effects were compared using the confidence interval adjustment set at 95%. Post-hoc analyses of pairwise comparisons were done with Fisher’s least significant difference (LSD) and Tukey’s-b tests. Independent samples *t*-tests were used to compare the 50 cortical gray matter thickness ROIs between bvFTD and AD. Across the sample, Pearson correlations (*r*) were computed to examine the relations between Animacy and Agency and the cortical thickness ROIs. As a correction for multiple comparisons, we used a conservative $p < .01$ level. For further analysis of multiple correlations, we also performed the Benjamini–Hochberg (BH) procedure to control the False Discovery Rate (FDR) at .1 then adjusted the BH corrected significance levels (q^*) to $< .01$ (Benjamini & Yekutieli, 2005; Hochberg &

Benjamini, 1990). Additional multiple regressions analyzed the potential impact of functional and behavioral scales and the Animacy Scores and Agency Scores.

3. Results

3.1. Participant characteristics

There were no significant differences on demographic variables of age, education, and sex across all three groups. The dementia groups (bvFTD and AD) did not statistically differ on measures of general cognition: the MMSE and the MoCA. They also did not differ in disease duration or on the CDR-sb, a measure of function and activities of daily living. As expected, the bvFTD group had significantly lower scores on the three social behavioral measures when compared to HCs and, for the FrSBe and SDS, when compared to the AD patients (See Table 1).

3.2. Scored responses for animacy and agency

The bvFTD patients but not the AD patients were significantly impaired in the attribution of animacy, compared to HCs ($p = .011$). In comparison, both bvFTD and AD groups were significantly impaired in the attribution of agency, compared to the HCs ($p < .001$ and $p = .001$) (See Fig. 2).

None of the participants reported having seen the Heider and Simmel film prior to this task. Although the length of responses, assessed by number of propositions expressed in each description, were significantly fewer for the bvFTD and AD groups compared to HCs ($p < .001$ and $p = .004$, respectively), the length of responses did not differ between the two dementia groups.

Two multiple regressions (MR) were performed with Animacy Scores or Agency Scores as the dependent variable and independent variables of dementia group, MMSE, CDR-sb, FrSBe, SNQ, and SDS total scores, to assess relative contributions of dementia type and behavioral scales on animacy and agency attribution abilities. Neither regression reached significance. For animacy, the results of the MR model showed $R = .547$, $R^2 = .300$, adjusted $R^2 = .066$, $F(4,12) = 1.283$, n.s.; standard error of the estimate: .8379. For agency, the results of the MR model showed $R = .595$, $R^2 = .354$, adjusted $R^2 = .139$, $F(4,12) = 1.647$, n.s.; standard error of the estimate: .9637.

3.3. Psychophysiology

The average SC change scores from baseline (90 for each participant) were $-.112 \pm .337$ for bvFTD, $-.125 \pm .273$ for AD, and $.061 \pm .213$ for HCs. These SC scores were not normally distributed per Shapiro–Wilk test. Non-parametric analysis revealed a significant group difference ($p < .001$) on the Kruskal–Wallis test. Subsequent group comparisons with Mann–Whitney U test showed significant differences between bvFTD and HCs and AD and HCs both ($p < .001$), but no bvFTD–AD difference ($p = .182$). When the SC changes were graphed over time, only the HCs showed the normally expected increasing SC values into the positive range during the second 90-sec test viewing of the film (See Fig. 3), indicating increasing sympathetic responsiveness. SC remained most constant for the bvFTD group and

had the greatest decrease for the AD group, suggesting stable or decreasing responsiveness. As noted, the participants were videotaped during the Heider and Simmel viewing and were not observed to avert their gaze from the screen during the 90 sec. There were no significant correlations between SC changes across groups for either Animacy ($r = .064$) or Agency ($r = .172$). There were also no significant correlations within the bvFTD group (Animacy: $r = .343$; Agency: $r = -.059$) or the AD group (Animacy: $r = .098$; Agency: $r = .269$), or with ROI mean cortical thickness measures.

3.4. Neuroimaging

On analysis of FreeSurfer extracted cortical ROIs, there were significant group differences between the two dementia groups, with decreased mean cortical thicknesses in the bvFD group compared to the AD group, reflecting increased atrophy among the bvFTD patients. The bvFTD group had significantly decreased mean cortical thickness in eight frontal ROIs involving both left and right hemispheres compared to the AD group, when evaluated at the $p < .01$ level (See Table 2). In contrast, the AD group had less cortical thickness in bilateral parietal (inferior, superior, supramarginal, and precuneus), and left inferior temporal ROIs compared to the bvFTD group, but these differences were not statistically significant.

Additional correlations across dementia groups were performed between the Animacy Scores and Agency Scores and the ROI mean cortical thickness measures (See Tables 3 and 4). Using a significance level of p and $q^* < .01$, the right pars orbitalis and adjacent right pars opercularis were significantly correlated with the Animacy Scores (See Fig. 4). Posterior cortical ROIs were significantly correlated with Agency Scores, including the left inferior and superior parietal cortices and the left supramarginal gyrus. In addition, both animacy and agency correlated with the left cingulate isthmus (all p and $q^* < .01$). None of the other ROIs, subsequently analyzed for correlations, were significantly correlated with Animacy Scores and Agency Scores at the $< .01$ level (See Tables 3 and 4).

4. Discussion

This study investigated social attribution abilities in bvFTD, compared to AD and HCs. Participant descriptions of the Heider and Simmel film revealed that only patients with bvFTD were significantly impaired in the attribution of animacy, but both dementia groups were significantly impaired in the attribution of agency. Across groups, neuroimaging results showed correlations of animacy attribution with regions of the right inferior frontal gyrus (IFG) (pars opercularis and pars orbitalis) and agency attribution with the left parietal (inferior, superior, supramarginal) cortex. Finally, both animacy and agency also correlated with the left cingulate isthmus, an area involved in visual processing. Both dementia groups failed to show an expected increase in SC during viewing of the film indicating decreased sympathetic responsiveness as an indicator of social attribution to the moving shapes.

4.1. Heider and Simmel film

Heider and Simmel's simple animation of moving geometric shapes allows investigation of social attribution features such as animacy and agency through linguistic analysis of participant's descriptions of the film. Animacy and agency determination does not require

visual face and body cues to living status, and may be elicited by cognitive interpretation of moving geometric shapes as “agents like me” (Cross, Ramsey, Liepelt, Prinz, & de, 2016; Frith & Frith, 2010; Ramsey & Hamilton, 2010). Furthermore, the attribution of animacy from these geometric shapes allows for inferences about goals, intentions, and personality characteristics and permits subsequent mechanisms of social cognition, such as mentalizing and empathy (Heider & Simmel, 1944; Santos et al., 2010; Scholl & Tremoulet, 2000). In normal people, these downstream social cognitive processes necessarily follow once animacy is perceived (van Buren et al., 2016).

4.2. Attribution of animacy

This study found a disturbance of animacy attribution in bvFTD. This corroborates reports describing patients with FTD spectrum disorders as having difficulty recognizing something as living, i.e., animate versus non-animate, and even recognizing a living thing as human or non-human (Mendez, Kremen, Tsai, & Shapira, 2010; Mendez & Lim, 2004). Impairment in animacy attribution may join the list of documented social disturbances in facial emotion perception, mentalizing, and empathy, as well as violations of social and moral norms and impairment in social interpersonal interactions in bvFTD (Eslinger et al., 2011; Gleichgerricht, Torralva, Roca, Pose, & Manes, 2011; Gregory et al., 2002; Poletti, Enrici, & Adenzato, 2012). The impaired attribution of animacy, among patients with bvFTD could underlie their impaired higher social cognition.

In this study, we found a strong correlation between animacy attribution and regions of the right IFG, an area affected in bvFTD. Beyond bvFTD, other related disorders, brain lesions, and surgery show an association of altered social cognition and atrophy or dysfunction of regions of the right IFG (Herbet, Lafargue, Bonnetblanc, Moritz-Gasser, & Duffau, 2013; Horan et al., 2014; Shamay-Tsoory, Aharon-Peretz, & Perry, 2009; Yamasaki et al., 2010). This correlation accords well with a wealth of existing knowledge regarding the IFG. The right IFG, along with the right parietal region, may be associated with subjective reports of animacy experience (Santos et al., 2010). An increase in right IFG activity may occur if there is a need to reconcile animate versus inanimate features of shapes (Cross et al., 2016), and in achieving interbrain synchronization through the fronto-parietal mirror neuron network (Liu, Saito, & Oi, 2015; Rizzolatti & Craighero, 2004; Rizzolatti & Sinigaglia, 2010). Functional MRI (fMRI) studies have shown bilateral activation of the IFG and frontal operculum, as well as inferior parietal areas, on viewing Heider and Simmel or comparable tasks, compared to non-social or random movements (Gobbini et al., 2007). Other fMRI and PET studies, however, found more pronounced activity in the right hemisphere than the left when viewing Heider and Simmel-type animations (Castelli et al., 2000; Gobbini et al., 2007; Ross & Olson, 2010).

We found a correlation of animacy attribution with the right pars opercularis and the pars orbitalis in the IFG. The literature also implicates the right pars triangularis, the intervening area of the IFG, as participating in action observation (Molnar-Szakacs, Iacoboni, Koski, & Mazziotta, 2005), mentalizing (Herbet, Lafargue, Moritz-Gasser, Bonnetblanc, & Duffau, 2015), and social communication (Yamasaki et al., 2010). The pars opercularis in particular may have a critical role in intention attribution and understanding and imitating others’

actions and intentions (Iacoboni, 2005; de Lange, Spronk, Willems, Toni, & Bekkering, 2008; Molnar-Szakacs et al., 2005; Rizzolatti & Craighero, 2004). The right pars opercularis may also facilitate subsequent social cognition, including emotion recognition (Adolphs, Baron-Cohen, & Tranel, 2002; Carr, Iacoboni, Dubeau, Mazziotta, & Lenzi, 2003; Kesler-West et al., 2001; Wildgruber et al., 2005), mentalizing (Adams et al., 2010; Herbet et al., 2014; Herbet et al., 2015; Moor et al., 2012), interpreting complex non-verbal social information (Watanabe et al., 2012; Watanabe et al., 2014), and empathy (Decety, 2011; Shamay-Tsoory et al., 2009). Together, this study, and literature implicates the right IFG, from pars orbitalis to pars opercularis, and possibly the underlying frontal operculum (Gobbini et al., 2007; Ross & Olson, 2010), in animacy attribution and related processes.

4.3. Attribution of agency

Besides animacy, agency is the other fundamental aspect of social attribution and is associated with the inferior parietal lobule (IPL), an area involved in perspective-taking and self–other distinction (Lamm, Batson, & Decety, 2007; Schulte-Ruther, Markowitsch, Fink, & Piefke, 2007). Similar to the findings of this study, studies show left superior parietal and left supramarginal gyri, along with inferior frontal, activation while healthy participants view high-intention animations modeled after Heider and Simmel (Osaka et al., 2012). Other investigators of healthy participants report activations of both IPL and IFG when viewing a circular shape moving as a self-propelled agent versus launched by a lever mechanism (Stosic et al., 2014), and of both superior parietal cortices when detecting self-propelled intentional movement between geometric shapes (Blakemore et al., 2003). Additional adjacent areas may participate in animacy attribution. The temporoparietal junction, particularly on the left, is heavily involved in the ability to take the visual perspective of others (Santesteban, Banissy, Catmur, & Bird, 2015; Schurz, Aichhorn, Martin, & Perner, 2013). Two other adjacent areas not shown in this study but previously implicated for animacy detection, the posterior superior temporal sulcus (pSTS) and the fusiform gyrus (FG) (Gao et al., 2012; Hillebrandt, Friston, & Blakemore, 2014; Lee et al., 2014; Schultz, Friston, O'Doherty, Wolpert, & Frith, 2005; Shultz, van den Honert, Engell, & McCarthy, 2015; Shultz & McCarthy, 2014), are involved in biological motion detection and mostly likely part of the agency complex (Castelli et al., 2000; Gobbini et al., 2011; Grèzes et al., 2001). Differences in methodology and the interpretation of an agency complex most likely explain the broader regions implicated in agency in these studies.

4.4. The potential contribution of the left cingulate isthmus

An unexpected but highly significant neuroanatomical correlation with both animacy and agency was the left cingulate isthmus. This area, located posterior inferior to the splenium of the corpus callosum and including retrosplenial cortex, connects the posterior cingulate cortex to the para-hippocampal gyrus (Bar & Aminoff, 2003; Lim et al., 2012). This region is implicated in recognizing highly contextual visual information (Bar & Aminoff, 2003), and, hence, the cingulate cortex may be involved in analyzing the visuospatial contextual for processing the Heider and Simmel film.

4.5. Absence of increasing SC in the dementia patients

As an additional indicator of social attribution, this investigation included SC responsiveness during the viewing of the Heider and Simmel film. The SC changes reflected both tonic SC levels and superimposed phasic event-related SC responses during the 90-sec viewing. As anticipated, the HCs showed an increasing sympathetic response, presumably as they became increasingly aroused by a developing “story” attributed to the moving geometric shapes (See Fig. 3). In contrast, the dementia patients did not show this response. The lack of SC sympathetic responsiveness among the dementia patients, who lacked agency, may indicate that they did not perceive the shapes as self-driven, and so were subsequently unable to perceive intentional or goal-directed movements, social interactions, and the enacted social plot.

4.6. Potential limitations and considerations

There are a number of potential limitations to this study. First, despite the statistically significant findings for animacy and agency, there is a relatively small sample size for each group of participants. Our significant findings are preliminary and must be replicated in larger studies expanding on the methodology reported here. Second, the neuroimaging analysis specifically focused on cortical regions implicated in animacy and agency and did not include subcortical regions which could play a role in social attribution. Additional studies may also clarify amygdalar and other limbic processes in animacy attribution, and cerebellar and other motoric processes in agency attribution. Third, there remained a concern that the dementia patients were cognitively impaired and might not sustain an animacy or agency response because of lack of attention, working memory or language impairment. This concern cannot be entirely eliminated; nevertheless, statistical comparisons did not show statistically significant differences between the dementia groups on dementia measures including disease duration, MMSE, MoCA, and CDR-sb (See Table 1). Fourth, on MRI, the bvFTD patients had more atrophy than the AD patients. Finally, the design of the SC analysis cannot entirely exclude a mental disengagement to the Heider and Simmel film despite the maintenance of gaze on the screen. This possibility, however, would not affect the results from the neuroimaging correlations.

5. Conclusions

The bvFTD participants presented significant deficits of animacy attribution, and both dementia groups had significantly impaired agency attribution and a failure to show positive sympathetic responsiveness compared to healthy controls. Across groups, the results indicate different regions involving the right IFG and left IPL in animacy and agency detection, respectively. This investigation is a first step; we need additional studies on the nature of animacy and agency in patients with bvFTD, employing larger numbers and more extensive testing particularly to determine the role of animacy and agency in the disturbed social cognition and abnormal social behavior of bvFTD.

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Abbreviations

AD	Alzheimer's disease
bvFTD	behavioral variant frontotemporal dementia
CDR-ext	Clinical Dementia Rating Scale extended version
FG	fusiform gyrus
FrSBe	Frontal Systems Behavior Scale
HCS	healthy controls
IFG	inferior frontal gyrus
IPL	inferior parietal lobule
MMSE	Mini-Mental State Examination
MoCA	Montreal Cognitive Assessment
pSTS	posterior superior temporal sulcus
ROIs	regions of interest
SACS	Social Attribution Coding System
SC	skin conductance
SDS	Socioemotional Dysfunction Scale
SNQ	Social Norms Questionnaire

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Fig. 1.
Representative still images from Heider and Simmel film.

Fig. 2.

Scored Participant Responses on Animacy and Agency. LEGEND: The Animacy Scores were significantly different across groups ($F = 3.81$, $p = .035$) with **post-hoc* significant differences between bvFTD and HC groups ($p = .011$). The Agency Scores were significantly different across groups ($F = 14.38$, $p < .001$) with **post-hoc* significant differences between bvFTD and HC groups ($p < .001$) and between AD and HC groups ($p = .001$).

Fig. 3. Skin Conductance (SC) Changes over 90-sec Viewing of Heider and Simmel Film. Mean SC change scores from 0 baseline at 0 sec plotted at one sec intervals. The rapid fall of SC from 0 within a second most likely reflects an orienting response.

Fig. 4. Magnetic Resonance Imaging Changes in Cortical Thickness—Significant Correlations with Animacy Scores and Agency Scores. Fig. 4a: Saggital view of significant Regions of Interest (ROI) for cortical thickness for Animacy Scores. Frontal lobe is to the right. The regions are pars opercularis (lighter blue) and pars orbitalis (darker blue) in the right hemisphere. Fig. 4b: Coronal view of significant Regions of Interest (ROI) for cortical thickness for Animacy Scores. Frontal lobe is to the front. The regions are pars opercularis (lighter blue) and pars orbitalis (darker blue) in the right hemisphere. Fig. 4c: Saggital view of significant Regions of Interest (ROI) for cortical thickness for Agency Scores. Frontal lobe is to the left. The regions are supramarginal (darker blue), inferior parietal (lighter blue), and superior parietal (lightest color) in the left hemisphere. Fig. 4c: Coronal view of significant Regions of Interest (ROI) for cortical thickness for Agency Scores. Frontal lobe is to the back. The regions are supramarginal (darker blue), inferior parietal (lighter blue), and superior parietal (lightest color) in the left hemisphere.

Table 1

Demographics and clinical measures of behavioral variant frontotemporal dementia (bvFTD), Alzheimer's disease (AD), and healthy control (HC) Participants.

	bvFTD (n = 11)	AD (n = 11)	HCS (n = 12)	Statistic, p-value
Age	62.91 (11.05)	61.36 (5.70)	54.17 (9.80)	$F = 3.02$, n.s.
Education	15.91 (1.81)	16.55 (1.86)	16.36 (1.43)	$F = .40$, n.s.
Sex (M,F)	4,7	2,9	4,8	$\chi^2 = .76$, n.s.
Handedness (R,L, both)	10,1,0	8,2,1	10,2,0	$\chi^2 = .71$, n.s.
Duration (years)	5.09 (4.61)	3.27 (1.62)	n/a	$F = 1.52$ n.s.
Mini-Mental State Examination	22.82 (7.76)	25.55 (3.27)	29.50 (.91)	$F = 5.63$, .008 ^a
Montreal Cognitive Assessment	21.00 (6.06)	18.00 (6.75)	n/a	$F = .51$, n.s.
Clinical Dementia Rating-sum of boxes	5.62 (2.16)	4.19 (1.10)	n/a	$F = 1.96$, n.s.
Frontal Systems Behavior Scale	156.80 (29.75)	100.36 (24.71)	n/a	$F = 22.53$, <.001
Social Norms Questionnaire	15.80 (3.23)	19.70 (1.49)	20.45 (1.37)	Kruskal–Wallis, .002 ^b
Social Dysfunction Scale	139.60 (35.19)	70.18 (24.79)	n/a	$F = 27.74$, <.001

Means and standard deviations except for sex and handedness.

^aPost-hoc significant differences between bvFTD versus HCs ($p = .002$) but not between bvFTD versus AD or AD versus HCs.

^bThe Social Norms Questionnaire results were not normally distributed, hence the Kruskal–Wallis test was performed with paired group significant differences between bvFTD versus HCs ($p < .001$) but not between bvFTD versus AD or AD versus HCs.

Magnetic resonance imaging regions of interest: Significant ($p < .01$) indicated by bold. Differences in cortical thickness between patients with behavioral variant frontotemporal dementia (bvFTD) and patients with Alzheimer's disease (AD).

Table 2

	bvFTD		AD		F	p-value
	Mean	SD	Mean	SD		
L superior frontal	2.00	.19	2.39	.12	26.05	<.001
R superior frontal	2.03	.19	2.38	.12	21.13	<.001
R pars opercularis	1.95	.20	2.29	.15	14.72	.002
L pars opercularis	1.99	.20	2.26	.13	11.16	.004
L rostral middle frontal	1.70	.31	2.06	.09	10.53	.005
R rostral middle frontal	1.82	.17	2.06	.14	10.15	.006
L medial orbitofrontal	1.97	.28	2.29	.12	9.20	.008
L pars triangularis	1.86	.22	2.11	.09	9.02	.009
R lateral orbitofrontal	1.90	.24	2.22	.21	8.63	.010
L transverse temporal	1.94	.12	2.14	.17	8.49	.011
R caudal middle frontal	1.94	.22	2.18	.07	8.38	.011
L caudal middle frontal	1.89	.23	2.15	.13	8.26	.012
L lateral orbitofrontal	1.96	.29	2.26	.12	7.80	.014
R paracentral	1.95	.18	2.15	.09	7.72	.014
L pars orbitalis	1.92	.26	2.20	.13	7.35	.016
L frontal pole	2.06	.37	2.60	.49	6.80	.020
R frontal pole	2.11	.44	2.58	.34	5.95	.028
L temporal pole	2.41	.77	3.11	.34	5.62	.032
R pars triangularis	1.79	.36	2.12	.19	5.31	.036
L paracentral	1.93	.16	2.13	.23	4.78	.045
L rostral anterior cingulate	2.41	.42	2.74	.13	4.46	.052
R pars orbitalis	1.91	.24	2.13	.21	4.01	.064
R medial orbitofrontal	1.92	.30	2.16	.20	3.71	.073
R middle temporal	2.09	.20	2.30	.32	2.75	.118
R transverse temporal	1.99	.21	2.16	.20	2.62	.126
L superior temporal	2.19	.17	2.29	.06	2.36	.145

	bvFTD		AD		F	p-value
	Mean	SD	Mean	SD		
R temporal pole	2.64	.83	3.21	.77	2.19	.159
L middle temporal	2.09	.29	2.26	.16	2.17	.161
R superior temporal	2.17	.21	2.33	.28	1.82	.197
L inferior parietal	2.01	.11	1.91	.19	1.77	.204
R insula	2.51	.26	2.70	.33	1.71	.210
L insula	2.56	.36	2.74	.15	1.69	.214
R cuneus	1.61	.10	1.68	.13	1.62	.222
R rostral anterior cingulate	2.39	.37	2.60	.32	1.54	.234
R inferior parietal	2.02	.15	1.95	.18	.87	.367
R superior parietal	1.89	.12	1.84	.13	.81	.382
R fusiform	2.23	.20	2.11	.48	.46	.510
L precuneus	1.97	.11	1.92	.19	.39	.542
R precuneus	2.02	.14	1.98	.14	.27	.612
L supramarginal	2.09	.18	2.05	.16	.26	.615
L posterior cingulate	2.13	.15	2.17	.20	.23	.638
L superior parietal	1.87	.13	1.83	.24	.21	.654
L fusiform	2.12	.47	2.20	.18	.21	.656
R isthmus cingulate	1.95	.24	1.99	.19	.17	.690
L cuneus	1.61	.11	1.63	.17	.12	.731
L inferior temporal	2.35	.34	2.31	.15	.08	.781
R posterior cingulate	2.07	.19	2.09	.14	.07	.790
R supramarginal	2.12	.17	2.10	.21	.06	.814
L isthmus cingulate	2.02	.22	2.04	.16	.04	.841
R inferior temporal	2.31	.32	2.33	.29	.03	.859

R = right; L = left

Table 3

Significant correlations of MRI cortical thickness (Regions of interest) with animacy scores: All significant correlations at p and $q^* < .01$ indicated by bold.

	Pearson's r	p -value	q^* -value
R pars orbitalis	.642	.005	.002
R pars opercularis	.614	.009	.004
L isthmus cingulate	.606	<.01	.007
L cuneus	.595	.012	.009
L paracentral	.595	.012	.011
L precuneus	.590	.013	.013
R rostral middle frontal	.564	.018	.015
R pars triangularis	.563	.019	.018
R isthmus cingulate	.528	.030	.020
L pars opercularis	.526	.030	.022
L rostral middle frontal	.520	.032	.024
L superior parietal	.519	.033	.026
L insula	.488	.047	.029
L transverse temporal	.481	.050	.031
L superior frontal	.480	.051	.033
L medial orbitofrontal	.480	.051	.035
L superior temporal	.477	.053	.037
L pars orbitalis	.473	.055	.040
L supramarginal	.472	.056	.042
L caudal middle frontal	.470	.057	.044
L pars triangularis	.468	.058	.046
L middle temporal	.462	.062	.048
L frontal pole	.455	.067	.051
R caudal middle frontal	.445	.073	.053
L fusiform	.439	.078	.055
L lateral orbitofrontal	.431	.084	.057
R transverse temporal	.429	.085	.059
R paracentral	.426	.088	.062
L inferior temporal	.426	.088	.064
L inferior parietal	.422	.092	.066
R superior frontal	.419	.094	.068
R precuneus	.419	.094	.070
R lateral orbitofrontal	.414	.098	.073
L temporal pole	.411	.101	.075
L rostral anterior cingulate	.406	.106	.077
R posterior cingulate	.404	.107	.079
R frontal pole	.386	.126	.081
L posterior cingulate	.353	.164	.084

	Pearson's <i>r</i>	<i>p</i>-value	q*-value
R rostral anterior cingulate	.341	.180	.086
R medial orbitofrontal	.316	.217	.088
R inferior temporal	.298	.246	.090
R superior temporal	.297	.246	.092
R superior parietal	.267	.301	.095
R middle temporal	.262	.309	.097
R temporal pole	.198	.445	.099
R insula	.196	.450	.101
R inferior parietal	.171	.511	.103
R supramarginal	.167	.521	.106
R cuneus	.136	.604	.108
R fusiform	.115	.662	.110

R = right; L = left.

Table 4

Significant correlations of MRI cortical thickness (Regions of interest) with agency scores: All significant correlations at p and $q^* < .01$ indicated by bold.

	Pearson's r	p -value	q^* -value
L isthmus cingulate	.678	.003	.002
L supramarginal	.646	.005	.005
L inferior parietal	.614	.009	.007
L superior parietal	.611	.009	<.01
L rostral anterior cingulate	.516	.034	.012
R isthmus cingulate	.497	.042	.014
L precuneus	.490	.046	.017
R precuneus	.490	.046	.019
L insula	.484	.049	.022
L pars orbitalis	.477	.053	.024
L inferior temporal	.462	.062	.026
R posterior cingulate	.462	.062	.029
L superior temporal	.459	.064	.031
L caudal middle frontal	.452	.069	.034
R pars triangularis	.448	.072	.036
L fusiform	.448	.072	.038
R rostral middle frontal	.443	.075	.041
R caudal middle frontal	.434	.082	.043
R inferior parietal	.425	.089	.046
R superior parietal	.400	.112	.048
L middle temporal	.394	.117	.050
R paracentral	.388	.124	.053
R pars orbitalis	.385	.127	.055
L medial orbitofrontal	.381	.132	.058
L cuneus	.378	.134	.060
L rostral middle frontal	.378	.135	.062
R pars opercularis	.362	.154	.065
L paracentral	.352	.166	.067
L lateral orbitofrontal	.335	.189	.070
R supramarginal	.302	.239	.072
R inferior temporal	.297	.248	.074
L superior frontal	.286	.266	.077
L pars triangularis	.280	.276	.079
L frontal pole	.255	.323	.082
R transverse temporal	.253	.326	.084
R superior frontal	.252	.330	.086
L pars opercularis	.244	.346	.089
L posterior cingulate	.243	.347	.091

	Pearson's <i>r</i>	<i>p</i> -value	q*-value
R frontal pole	.212	.414	.094
R rostral anterior cingulate	.211	.416	.096
R lateral orbitofrontal	.204	.432	.098
R fusiform	.196	.450	.101
R middle temporal	.188	.470	.103
L temporal pole	.182	.484	.106
R superior temporal	.164	.530	.108
L transverse temporal	.144	.580	.110
R temporal pole	.140	.592	.113
R cuneus	.129	.620	.115
R medial orbitofrontal	.120	.646	.118
R insula	.006	.983	.120

R = right; L = left.