The social cognition of attachment:
Preliminary results from functional imaging of Capgras delusion

Georges Naasan,[1] Rochelle Hudson,[2] Regina Cesaro,[2] Zimbul Albo,[4] Alan Lerner,[1] Anthony Jack[3]

[1] Department of Neurology, Case Western Reserve University – Medical Center, Cleveland, OH
[2] Department of Cognitive Science, Case Western Reserve University, Cleveland, OH
[3]Director of Brain, Mind and Consciousness Lab, Department of Cognitive Science, Case Western Reserve University, Cleveland, OH
[4] Department of Neurology and Department of Neuroscience, Baylor College of Medicine, Houston, TX

CWRU
Department of Cognitive Science
Transdisciplinary approaches to the mind

Definitions and Background:

Delusions (per DSM-IV)**:** A fixed false belief based on incorrect inference about external reality that is firmly sustained despite what almost everybody else believes and despite what constitutes incontrovertible and obvious proof or evidence to the contrary. The belief is not one ordinarily accepted by other members of the person's culture or subculture.

Delusional Misidentification Syndrome (DMS): A group of delusions involving the false belief that the identity of a person, place or object has been modified. It is prevalent in 15.8% of patients with Alzheimer's disease (AD), 16.6% of patients with Lewy Body Dementia (DLB) and 8.3% of patients with Semantic Dementia (SD)[1].

Capgras Delusion: A specific DMS whereby loved ones are believed to be replaced by identical looking impostors. It was first described in 1923 by Capgras and Reboul-Lachaux. It is prevalent in 13.3% of patients with AD[1].

Capgras versus Prosopagnosia

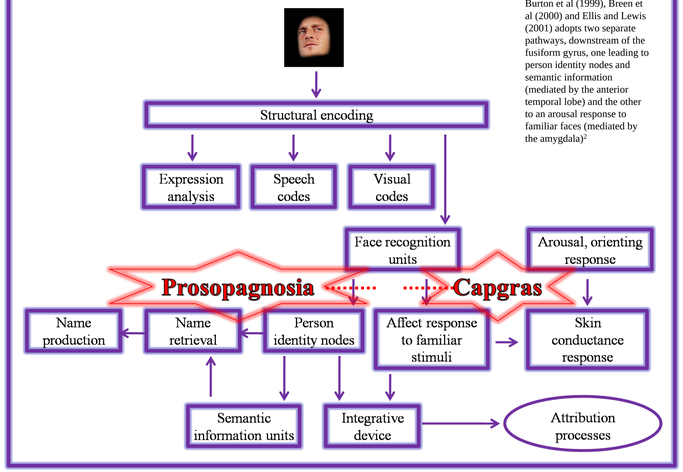

Figure 5. This model of face processing proposed by Burton et al (1999), Breen et al (2000) and Ellis and Lewis (2001) adopts two separate pathways, downstream of the fusiform gyrus, one leading to person identity nodes and semantic information (mediated by the anterior temporal lobe) and the other to an arousal response to familiar faces (mediated by the amygdala)[2]

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Results

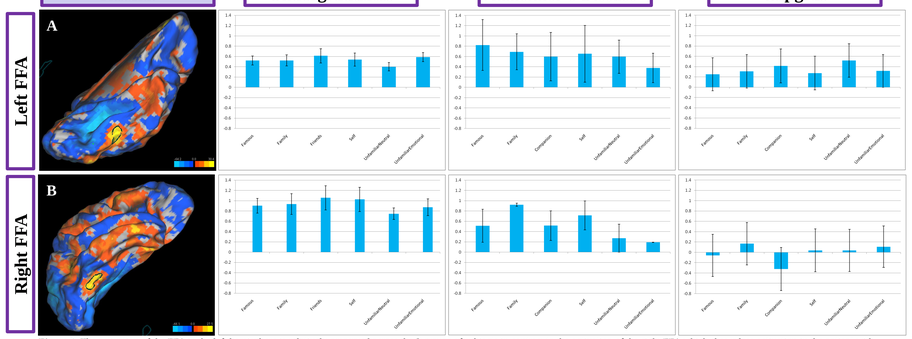

Figure 1. The activation of the FFA in the left hemisphere is relatively preserved across the 3 groups of subjects in contrast to the activation of the right FFA which shows less activation in the patient with Capgras delusion as compared to both the undergraduates and AD groups, mostly pronounced to faces of the spouse. Of note, FFA was defined through a contrast of (Adult Faces)-(Houses) from undergraduates fMRI data (Images A and B for left and right respectively).

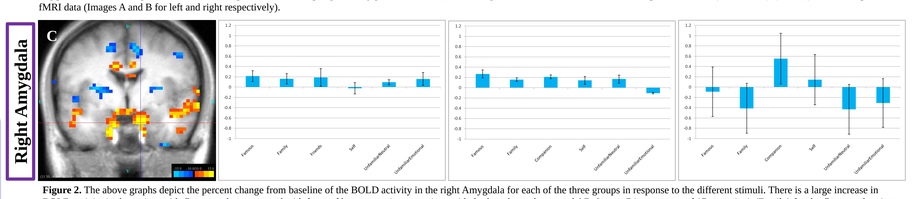

Figure 2. The above graphs depict the percent change from baseline of the BOLD activity in the right Amygdala for each of the three groups in response to the different stimuli. There is a large increase in BOLD activity in the patient with Capgras when presented with faces of her spouse, in comparison with both undergraduates and AD. Image C is a contrast of (Companion)-(Family) for the Capgras showing more activation of the Amygdala when looking at the spouse.

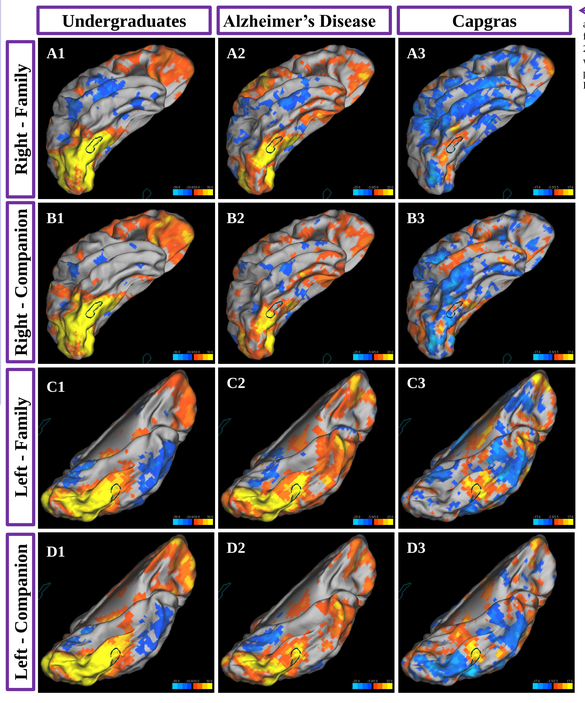

Figure 3. Activation of the right (A and B) and left (C and D) FFA when presented with faces of family members (A and C) or friends/spouse (B and D) for each of the three groups (Undergraduates, 1; AD, 2; and Capgras, 3). The decrease in activation of the Right FFA in the patient with Capgras is noticeable. There is a decrease in activation in visual processing areas on the left as well, however with relative preservation of the FFA. All the above images are contrasted with the baseline.

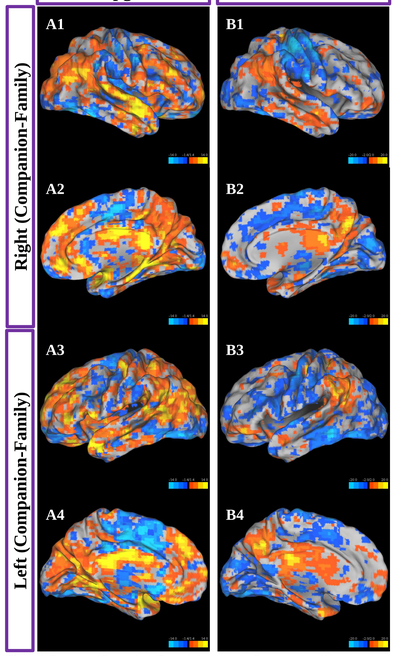

Figure 4. Contrast of (Companion)-(Family) shown for the Capgras patient (A) in comparison with both AD patients (B) in the right lateral (1), right medial (2), left lateral (3) and left medial (4) view. The patient with Capgras delusion has increased activation in frontal regions both medially and laterally which may be associated with a downstream increase in cognitive processing demand to interpret an otherwise familiar face (here, the spouse).

Materials and Methods

Participants

Our subjects included eight undergraduates, two patients with AD and one AD with a diagnosis of Capgras syndrome. Basic demographics of subjects are shown in Table 1.

	Undergraduates (n=8)	AD (n=2)	Capgras (n=1)
Age	18-24	72 and 76	76
Gender	2 males, 6 females	Both males	female
MMSE	Max score of 30 assumed	26 and 29	15 (estimated)

Table 1. Subjects' demographics

The Capgras patient was diagnosed in the clinic by her primary neurologist. She complained that her husband "is not her husband", yet he knew everything about her past and she was getting increasingly frightened of him. She still was able to identify her family members appropriately. Throughout the recruitment interview and the scanning session, she continued to behave in concordance with her delusion.

Functional magnetic resonance imaging (fMRI) session

All participants signed a consent form prior to scanning. A 4-Tesla Siemen-Bruker hybrid research MRI was used for the fMRI session. While in the scanner, participants were presented with 3 runs of a slide-show that randomly presents pictures from 6 different categories: faces of their own spouse (or friends for undergraduates), faces of themselves, faces of their family members, faces of famous people, and unknown faces with either a neutral or an emotional expression. Each picture was presented for 6 seconds during which the participant was asked to rate how much they liked the picture; each picture was followed by a fixation slide of either 2, 4 or 6 seconds in duration. A total of 144 pictures divided equally among categories were presented throughout the 3 runs.

To identify the fusiform face area (FFA), undergraduate subjects were shown 3 more runs of pictures from the following categories: adult faces, children's faces, mammals' faces and bodies, computers, robots and houses. The FFA was then identified by contrasting (unfamiliar and neutral) adult faces with houses, which isolated face specific activity from general visual processing demands.

Data analysis

Whole brain blood oxygenation level-dependent (BOLD) activity was analyzed through a general linear model using the Washington University, St. Louis software, fidl. Contrasts between stimuli and fixed effects regions of interest (ROIs) were created using the same software. Data from the eight undergraduates were averaged as well as data from the two AD patients. All the thresholds for the created contrasts were adjusted for the number of subjects (i.e. threshold for Capgras (n=1) was computed by dividing threshold for undergraduates (n=8) by square root of 8). Percent changes in BOLD activity was measured for each stimulus in desired ROIs.

Discussion:

The results of this first fMRI study in a patient with Capgras delusion are an initial step in understanding the neural circuitry of attachment and also those of face processing. The model of face processing proposed by Burton et al (1999), Breen et al (2000) and Ellis and Lewis (2001) is shown in figure 5[2]. The existence of two separate pathways is supported by observations that Capgras patients have decreased skin conductance response (SCR) as compared to controls when looking at familiar faces[3]. On the other hand, patients with prosopagnosia retain an intact SCR to familiar faces. The question remains: where is the affective response to familiar faces processed?

The FFA reliably activates bilaterally more for faces, as opposed to objects or places[4]. However, prior studies suggest some asymmetry of the FFA. The left FFA has been shown to be superior to the right FFA in processing facial features rather than holistic processing of faces, a property of the right FFA[5]. The left FFA has also been implicated in recognition expertise associated with stimulus classes other than faces[6]. However, many individuals show greater facial recognition accuracy for facial stimuli presented in the left visual field (which maps to the right FFA)[7]. Correspondingly the right FFA tends to activate more than the left FFA to faces[8], especially in subjects who show a more pronounced left field recognition advantage. In addition, patients with prosopagnosia who retain an intact right FFA were found to retain the recognition of emotionally charged faces as opposed to neutral faces[9]. Our study finds that the right FFA is markedly less activated in the patient with Capgras delusion, whereas the left FFA was relatively spared. The spared left FFA may drive the sense that the 'imposter' can be recognized as a 'look-alike', corresponding to spared visual expertise. The impairment in right FFA may underlie the failure to recollect the appropriate emotional memory essential to recognizing a highly attached and familiar person. Thus the two FFAs may subserve the two pathways for face processing shown in figure 5.

The decreased activation in right FFA cannot be accounted for by an overall decrease in brain activation, as might result from dementia or methodological issues. Figure 2C and Figure 4 show markedly greater brain activity in amygdala and in both social (medial) and non-social (lateral) frontal areas when the Capgras patient is shown the misidentified companion.

The amygdala is significant because patients with bilateral lesions in their amygdala rate unfamiliar faces as approachable and trustworthy, including faces rated by normal subjects as highly unapproachable and untrustworthy[10]. The increased activation of the amygdala in the Capgras patient corresponds to her finding her spouse threatening and unapproachable. The amygdala, and other social brain regions, have been implicated in the facial recognition of a mother's own child as opposed to another familiar child, underlining the importance of these regions in attachment[11].

Conclusion:

Our findings suggest that left and right FFA may mediate different forms of face identification, with left FFA being more involved in recognition of visual features, and the right FFA more being involved in emotional recognition. Frontal cognitive centers may become overactive in an attempt to reconcile the dissonant inputs of a visually familiar face that fails to evoke the corresponding emotional memory.