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Neural activities during affective processing in people with Alzheimer's disease

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Abstract

This study examined brain activities in people with Alzheimer's disease when viewing happy, sad, and fearful facial expressions of others. A functional magnetic resonance imaging and a voxel-based morphometry methodology together with a passive viewing of emotional faces paradigm were employed to compare the affective processing in 12 people with mild Alzheimer's disease and 12 matched controls. The main finding was that the clinical participants showed reduced activations in regions associated with the motor simulation system (the ventral premotor cortex) and in regions associated with emotional simulation—empathy (the anterior insula and adjacent frontal operculum). This regional decline in blood oxygen level-dependent signals appeared to be lateralized in the left hemisphere and was not related to any structural degeneration in the clinical participants. Furthermore, the regions that showed changes in neural activity differed for the 3 emotional facial expressions studied. Findings of our study indicate that neural changes in regions associated with the motor and emotional simulation systems might play an important role in the development of Alzheimer's disease.

Keywords: Alzheimer's disease; Dementia; Emotional facial expressions; Mirror neuron system

1. Introduction

Alzheimer's disease (AD) is associated with a gradual decline in brain functioning (Buckner, 2004), which eventually affects all cognitive (Bäckman et al., 2004; Buckner, 2004) and affective processing within the brain. While there have been many studies on the cognitive correlates of AD, research on affective processing in individuals with AD has been scarce. Compromised affective processing does have a very significant impact on the quality of social interactions (Phillips et al., 2010; Shimokawa et al., 2001), which then predisposes further cognitive and hence functional decline, adding to the caregiver's burden of care (Ropacki and Jeste, 2005; Scarmeas et al., 2005). Therefore, understanding the changes in affective processing in individuals with AD might be as important for the management of people with AD as the knowledge of cognitive decline that accompanies the illness.

Previous behavioral studies have provided evidence of deficits among individuals with AD in recognizing facial emotions (Guaita et al., 2009; McLellan et al., 2008), specifically in the recognition of happy, sad, and fearful expressions (Kohler et al., 2005). Impairment of facial emotion recognition cannot be explained by impairment of the recognition of faces that are affectively neutral (Hargrave et al., 2002); it appears, rather, to be associated with the

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severity of the illness (Weiss et al., 2008). The study by Wright et al. (2007) on the ability of people with AD to recognize fearful facial expressions found a significant increase in amygdala activity in individuals with AD while viewing neutral and fearful faces. Staff et al. (2011) found that AD patients with impaired emotion perception had decreased blood flow in the medial frontal lobe. Rosen et al. (2006) observed that impaired recognition of negative emotions in patients with dementia (including patients with AD, mild cognitive impairment, or frontotemporal lobar degeneration) was associated with atrophy of the right temporal gyri. Changes of brain activity during normal and pathological aging appear to be quite similar (see St. Jacques et al., 2009).

Over the past decade, a prominent finding has been the realization that observing the facial expressions of others triggers representations of the observer's own motor, somatosensory, and emotional states that are thought to allow the observer to vicariously experience what the observed individual is feeling (Atkinson and Adolphs, 2011; Gallese et al., 2004; Keysers, 2011). The realization that regions involved in motor control are important for social perception has been strongly influenced by the discovery of mirror neurons in the premotor and inferior parietal cortex of monkeys (Gallese et al., 1996; Keysers et al., 2003; Rozzi et al., 2008), which showed that primates transform the actions of others into a vicarious representation of their own corresponding actions. In the case of facial expressions, a number of studies have shown that the ventral premotor cortices (including the precentral and inferior frontal gyrus as well as the inferior frontal operculum) are activated when viewing the dynamic facial expressions of others (Budell et al., 2010; Carr et al., 2003; Grosbras and Paus, 2006; Sato et al., 2004). In light of a monkey's physiology, these results have been interpreted as indicating that the observation of other people's facial expressions triggers a motor simulation in mirror-like neurons necessary for the movement of a person's face in similar ways.

The idea that somatosensory regions are also important for recognizing facial expressions has received strong support from a lesion-mapping study by Adolphs et al. (2000), which found that lesions in the somatosensory cortex (SI) impair the recognition of facial expressions in photographs. A number of functional neuroimaging studies have provided additional evidence by showing that the observation of facial expressions triggers activity in the SI that differentiates between different facial expressions (Germine et al., 2011; Hennenlotter et al., 2005; Keightley et al., 2007; van der Gaag et al., 2007a; Winston et al., 2003). The role of the SI during the observation of facial expressions dovetails well with other mounting evidence for the role of this region in social perception more generally, including the perception of body movement, touch, and pain (Keysers et al., 2010). Together, this suggests that the brain also transforms what others do, facial expressions in particular, into a vicarious representation of what it would feel like to move one's face in that way.

Finally, there is growing evidence that the regions involved in the feeling of emotions are also vicariously recruited while viewing the feelings of emotions in others (see Bastiaansen et al., 2009 for a review). In particular, the anterior insula and the adjacent frontal operculum (jointly referred to as the insula/frontal operculum [IFO]) have been shown to be activated both when people feel an emotion (disgust or pleasure) and when they see similar emotional (disgust or pleasure) facial expressions of others (Jabbi et al., 2007; Wicker et al., 2003). A number of studies later established that a similar region is recruited when an individual experiences pain or witnesses the pain of others (Lamm et al., 2011). People who have reported to experience more empathy in everyday life have shown stronger vicarious activations in the IFO while witnessing the emotions of others (Jabbi et al., 2007; Lamm et al., 2011). The IFO is functionally connected to the ventral premotor cortex (vPMC), and the IFO seems to receive information from the region of the vPMC that is activated while viewing the facial expressions of others (Jabbi and Keysers, 2008). Therefore, it seems that motor and emotional brain regions act in unison to allow viewers to share the emotional state of others both from a motor and an affective point of view (Keysers, 2011).

From the literature reviewed above, this functional magnetic resonance imaging (fMRI) study was conducted with the aim of understanding whether seeing the emotional facial expressions of others (happiness, sadness, and fear) would trigger brain activation in the motor, somatosensory, and/or emotional simulation systems in people with AD that differed from the brain activation in control participants. Neuroimaging studies on AD-related changes in neural correlates of specific emotions have been scarce. Based on the observation of Kohler et al. (2005) that AD was associated with impaired recognition of happy, sad, fearful, and neutral expressions, in the present study, we aimed to compare patients with AD with normal controls when they were viewing happy, sad, fearful, and neutral facial expressions. We hypothesized that individuals with AD, relative to healthy controls, would show weaker blood oxygen level-dependent (BOLD) signals—when viewing all emotional facial expressions (happy, sad, or fearful faces) in neural regions involved in motor, somatosensory, or emotional simulation. Furthermore, we examined the relationship between the BOLD signals in these simulation systems when viewing emotional faces and the mental as well as the affective states of patients with AD.

2. Methods

2.1. Participants

Altogether, 24 right-handed Chinese women participated in this study approved by the Institutional Review Board of