Processing faces in Alzheimer's disease patients:
How a familiar face becomes unfamiliar

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ABSTRACT: Alzheimer's disease, a progressive neurodegenerative disorder, is the most pervasive form of dementia world-wide. Impairment in face processing is a common trait of the disorder, causing a deficit not only in the processing of emotional expressions, but also causing a deficit in face recognition. Research into the causes of impaired face recognition in Alzheimer's disease patients has found several factors at play: Abnormal temporal lobe activation in response to familiar faces, a breakdown in holistic processing of faces due to changes in frontal lobe activation, and atrophy of areas of the brain implicated in theory of mind. These neural changes are evident long prior to any alterations of behavior. Due to the progressive nature of Alzheimer's disease, patients display increasing levels of impairment in face recognition over time. At the final stages of the disorder, patients lose all ability to recognize familiar faces, and most strikingly, lose the ability to self-recognize. Further research on face recognition in Alzheimer's disease may improve our knowledge both in neurotypical face recognition, as well as aid in discovering novel ways of helping patients cope with their symptoms.

INTRODUCTION

Alzheimer's disease is the most common form of dementia, a progressive neurodegenerative disorder which affects more than 35 million people worldwide (Wong, Gilmour, and Ramage-Morin, 2016). While a major factor in Alzheimer's disease is the loss of cognitive faculties, including memory, language, and planning, a particularly difficult aspect of the disease is the burden it places on interpersonal relationships (Pant, Mukhopadhyay, and Lakshmayya, 2014). One particular aspect of impairment in interpersonal relationships is the degradation of facial processing functions. Patients with Alzheimer's disease, in contrast to other forms of dementia, exhibit impairment in processing of emotions in facial expression, which may lead to loss of appropriate behavior in social settings (Bediou et al., 2009). Further, memory impairments stemming from the disorder cause difficulties in identity recognition of both new and familiar people (Hawley and Cherry, 2004). The loss of recognition of those familiar to us is especially intriguing. In later stages of the disease, patients may even lose the ability to recognize their own face, or the face of a spouse (Kurth, Moyse, Bahri, Salmon, and Bastin, 2015). Apart from causing emotional distress both for patients and caregivers, these symptoms often lead to social withdrawal, which exacerbates psychological symptoms further (Pant et al., 2014). Recent research has explored the mechanisms of facial processing in Alzheimer's disease, both in relation to learning new faces and recognizing familiar faces.

In this article, I will examine how Alzheimer's patients process faces as compared to the neurotypical population, discuss the current hypotheses that explain what mechanisms may cause a face recognition deficit in Alzheimer's disease, as well as the neural changes that may contribute to this deficit. I will also examine how the deterioration in facial processing occurs as the disease progresses, from preclinical stage Alzheimer's disease through to late-stage Alzheimer's disease patients. The purpose of this article is to examine how Alzheimer's disease affects the processing of both new and familiar faces, with the intent of understanding face-specific deficits in Alzheimer's disease.

The progressive nature of Alzheimer's disease is such that patients will continue to cognitively deteriorate until total loss of faculties, usually occurring at about ten years after initial diagnosis. As such, psychometric scales are used to qualitatively define a patient's stage of progression in the disease. The Global Deterioration Scale (GDS) may be used to assess primary degenerative dementia at seven stages of progression, where stage one represents no cognitive decline, and stage seven represents very severe cognitive decline (Reisberg, Ferris, de Leon, and Crook, 1982). In this article, I will refer to these seven stages as a quantifier for the stage of progression associated with a certain level of face recognition impairment.

DISCUSSION

Face recognition in Alzheimer's disease

In the healthy brain, the processing of familiar faces has been examined extensively (Johnston and Edmonds, 2009). Face preferential regions, such as the fusiform face area, are important in facial processing, independent of whether the face is familiar or unfamiliar (Rossion, Schiltz, and Crommelinck, 2003). However, when processing familiar faces, there are two additional regions of the brain that are involved. Medial temporal lobe structures, including the hippocampus, amygdala, and the perirhinal cortex, along with inferior regions of the temporal cortex, respond abruptly when a person recognizes a face as familiar (Ramon, Vizioli, Liu-Shang, and Rossion, 2015). Interestingly, the medial temporal lobe is an area highly implicated in the pathology of Alzheimer's disease. Atrophy of the medial temporal lobe, in particular the hippocampus and the amygdala, has been well-documented as a biomarker for Alzheimer's disease (Visser, Verhey, Hofman, Scheltens, and Jolles, 2002). Atrophy of these regions in Alzheimer's disease patients may play a role in the breakdown of their face recognition processes as the disease progresses.

A remaining question is, what aspect of cognition are the face recognition deficits in Alzheimer's disease specifically attributed to? There has been speculation that the perceived deficit in facial recognition is actually due to a breakdown in semantic stages of recognition, as Alzheimer's patients commonly have trouble remembering names of familiar people (Werheid and Clare, 2007). Hodges, Salmon, and Butters (1993) looked at the processing of familiar faces

in Alzheimer's disorder by spontaneous and cued naming of famous faces. In a group of mildly impaired Alzheimer's patients, performance in identifying famous faces declined with increasing symptom severity. While patients were able to still spontaneously name famous people, they took longer to recognize and identify faces, and could not identify and name as many faces as the control group. Conditions of semantic cueing did not improve their naming abilities. The researchers concluded that Alzheimer's patients may have a breakdown in the pre-semantic stages of facial processing. As such, there must be a breakdown of facial processing in a stage prior to name retrieval.

An alternative hypothesis posits that Alzheimer's patients are impaired at the perceptual level of face processing, i.e., their ability to holistically process a face is impaired. Lavellée et al. (2016) investigated the processing of upright and inverted faces and cars in mildly impaired Alzheimer's patients. The inversion effect, in which it takes longer to process inverted faces versus upright faces, occurs because people normally process faces as an integrated whole, and are impaired in this ability when a face is inverted (Taubert, Apthorp, Aagten-Murphy, and Alais, 2011). Compared to controls, patients in the study showed a reduced inversion effect for faces, but not for cars. The researchers suggest that Alzheimer's disease patients are impaired in higher-level visual processing that requires holistic representation. Holistic processing of faces has been heavily implicated in the ability to recognize a face, such that the loss of holistic processing in Alzheimer's patients may be a direct link to the loss in recognition of familiar faces (Richler et al., 2011).

What then, is the neural basis for the loss of familiar face recognition? Certain prefrontal brain regions have been associated with familiarity recognition. This includes the bilateral superior frontal cortex, as well as the right middle orbital gyrus (Montaldi, Spencer, Roberts, and Mayes, 2006). Failure to activate these regions when exposed to familiar stimuli has been documented in patients with early stage Alzheimer's disease (Donix et al., 2013). There are also notable differences in cerebellar activity in patients with Alzheimer's disease, with a higher activation of the right cerebellum for unfamiliar stimuli in Alzheimer's patients as compared to controls. Alzheimer's patients have less activation in the medial frontal cortex, which has been associated with explicit access to contextual information surrounding a stimulus. In addition, Alzheimer's patients present with a reduced ability to recruit frontal brain regions during the perception of personally familiar stimuli (Li et al., 2015). Together, a reduction in access to contextual knowledge and episodes surrounding a familiar stimulus translates to reduced ability to recognize familiar stimuli in everyday life (Donix et al., 2013).

However, the loss of the ability to holistically process faces seems to be independent from the loss of processing other familiar stimuli. Another common feature in Alzheimer's patients is loss of memory for familiar locations (Pai and Jacobs, 2004). The mechanism for this ability has been found to be independent from face recognition, as impairment for scene recognition occurs earlier in the progression of the disease than does the impairment for face recognition (Cheng and Pai, 2010). Thus, there is not a generalized deficit in recognition per se, but rather separate mechanisms may be co-occurring to contribute to the loss of familiarity for different types of stimuli. Research indicates that Alzheimer's patients are better at recognizing objects such as houses than they are at recognizing faces (Kawagoe, Matsushita, Hashimoto, Ikeda, and Sekiyama, 2017). Further evidence for the specificity of facial processing impairment is indicated by deficits in emotion detection. As compared to mild cognitive impairment, patients with Alzheimer's disease are worse at detecting emotions in faces. In predementia stages of the disorder, there has been no documented impairment in emotion processing (Bediou et al., 2009). The deficit in emotional expression processing in Alzheimer's patients indicates that faces are more difficult to process in this population, and thus there is a specific deficit in holistic facial processing, rather than a general deficit in recognition of familiar stimuli.

Alzheimer's patients are not just impaired in recognizing the faces of familiar people. As the disease progresses, patients increasingly have difficulty with identifying a person, independent of face recognition processes. A final facet to explain the impairment of face recognition in Alzheimer's disease involves the ability to invoke theory of mind. Theory of mind involves the ability to understand that others have differing beliefs, and allows engagement in social and introspective behaviors (Dohnel et al., 2012). Areas of the brain implicated in theory of mind processing include prefrontal cortical areas; the medial prefrontal cortex has been implicated in conceptualizing mental states of others, while the superior frontal gyrus is implicated in self-related processes (Dohnel et al., 2012; Goldberg, Harel, and Malach, 2006). Theory of mind has been posited to be associated with face recognition processes. Impairment of this ability is well-documented in disorders such as schizophrenia and autism spectrum disorders, disorders which are also accompanied by impaired face recognition abilities (Irani et al., 2006). According to a review by Gobbini and Haxby (2007), theory of mind is necessary for familiarity recognition, as theory of mind regions of the brain are implicated in the non-visual cues of person recognition. These regions are hypothesized to act in conjunction with visual cues to invoke a mental representation of a familiar person.

In Alzheimer's disease patients, a genuine deficit in theory of mind has been documented at early stages of the disorder, and progresses as patient condition worsens (Moreau, Rausy, Viallet, and Champagne-Lavau, 2016). Furthermore, when Alzheimer's disease patients process familiar and self-face images, there is a negative correlation between connectivity in theory of mind implicated brain regions and ability to recognize faces. The current hypothesis for this phenomenon is that a decrease in the segregation of implicated neural networks leads to an increase in interference (Kurth et al., 2015). This implies that the medial prefrontal cortex and the superior frontal gyrus, regions involved in theory of mind, are implicated in the processing of familiar faces, and could explain the connection between worsened performance and unusual connectivity of these brain regions seen in Alzheimer's disease patients. This, taken with evidence from non-Alzheimer's research, implied that theory of mind plays a role in the loss of familiarity recognition in Alzheim-

er's disease. Thus, a reduced ability to invoke theory of mind in Alzheimer's patients, causing a deficit in understanding the minds of others, likely plays an indirect role in their impairment in familiar face recognition.

The time course of familiar face recognition in Alzheimer's disease

As Alzheimer's disease is neurodegenerative, it is important to examine how deficits in face recognition manifest throughout the course of the pathology. Genetic causes have been implicated in the pathology of Alzheimer's, with the discovery of autosomal-dominant Alzheimer's disease mutations. There is emerging evidence that for carriers of these mutations, dysfunction of neural circuits involved in memory occur prior to behavioral changes associated with diagnosis. In an fMRI study, carriers were shown to have abnormal activation in recognition tasks of face processing. Specifically, less activation was found in bilateral parietal regions of the brains of the subjects (Norton, Baena, Pulsifier, Lopera, and Quiroz, 2016). It is evident therefore that neural changes are taking place during the preclinical stages of the disease. In these preclinical stages, patients are still able to compensate for these neural changes and maintain normal cognitive abilities.

Eventually, neural changes overtake the brain's ability to compensate, and cognitive decline begins. Once behavioral changes are evident in the progression of Alzheimer's disease, face recognition will deteriorate in a more or less linear manner. In the mild cognitive impairment stage of Alzheimer's disease, there is evidence that patients are still able to identify familiar faces at the same rate as healthy individuals (Hodges et al., 1993). The major difference is length of time for recognition to occur; patients need more time to recognize a familiar face, and have more trouble identifying familiar faces by name (Hodges et al., 1993). So, while at the earlier stages of Alzheimer's disease patients will still be able to recognize familiar people, it is more difficult and time-consuming.

Patients with mild cognitive impairment (GDS stages 2 and 3) due to Alzheimer's disease will also not have difficulty recognizing recent photographs of themselves, which is a deficit that appears as the disease progresses. With moderate cognitive impairment (GDS stages 4 and 5), patients become better at recognizing more dated photographs of both themselves and their spouses in comparison to more recent images. Moderately impaired patients will also perform worse both on time taken to recognize familiar faces and on rate of recognition (Kurth et al., 2015). This indicates that with disease progression, patients are worse at recognizing familiar faces in general, and their mental representations of themselves and familiar people are likely to be temporally inaccurate.

Despite a decline in the ability to recognize familiar faces, there is evidence that Alzheimer's patients are still able to acquire representations of faces in the earlier to intermediate stages of the disorder. In a study by Hawley and Cherry (2004), patients with moderate Alzheimer's (GDS stage 4 and 5) were able to learn face-name recognition. Patients were trained to learn faces and names based on pictures, and were subsequently tested both in picture conditions and on live person transfer abilities, i.e., recognizing the people from the images in real life. Improvements were displayed over a two-week period, and maintenance of learned information was displayed. Thus, the ability to acquire familiarity of a face is still preserved at some level at these stages, and is displayed at a functional, real-world level. However, it is unclear from this study at what stage the ability to learn or recognize faces is lost, and whether it is consistent across Alzheimer's patients.

In the final and most severe stages of Alzheimer's disease (GDS Stage 6 and 7), patients have often lost all ability to recognize familiar faces and, most notably, can no longer recognize their own faces. Biringer and Anderson (1992) tested self-recognition in Alzheimer's patients in stages 5, 6, and 7 on the GDS scale, by presenting the patients with a mirror after marking their foreheads with paint. At stages 6 and 7, there was no response to the mark on the forehead, while the ability to self-recognize was still intact in GDS stage 5 patients. This provides evidence that patients at the final stages of the disease have lost all concept of the self and theory of mind. Without a concept of the self, the ability to recognize one's own face is lost, as well as the recognition of loved ones.

CONCLUSION

In conclusion, there are several neural processes implicated in the graded impairment of face recognition throughout the progression of Alzheimer's disease. The breakdown in face recognition is pre-semantic, meaning patients are not just impaired in ability to name familiar people, but are truly losing the ability to recognize the faces themselves. There is a loss of the ability to holistically process faces, and is a specific deficit for faces rather than a generalized deficit in the ability to recognize. Theory of mind brain regions are implicated in familiarity recognition, and deficits in theory of mind in Alzheimer's patients further impairs face recognition. Although there is no clear, unified answer for the deficit in face recognition exhibited by Alzheimer's patients, it may be due to a combination of the deterioration of theory of mind and holistic face processing abilities. Finally, the neurodegenerative nature of the disease is such that as the disease progresses, patients become increasingly impaired in their ability to recognize faces. Changes are evident in the connectivity of face recognition neural networks in Alzheimer autosomal dominant mutation carriers long prior to any observable behavioral effects of face recognition loss. The disease eventually progresses to the point that patients often have no recognition of their own face at the final stages in the pathology.

Understanding the deficits in face recognition in Alzheimer's disease patients both on a behavioral and neural basis may allow us to further our understanding of how familiar faces are processed in healthy patients. Furthermore, as research progresses, this may lead to a more complete understanding of the mechanisms behind the pathology and, consequently, novel ways to alleviate the social burdens placed on Alzheimer's patients and their caregivers due to the loss of face recognition.

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