Fear Processing and Social Networking in the Absence of a Functional Amygdala

Benjamin Becker, Yoan Mihov, Dirk Scheele, Keith M. Kendrick, Justin S. Feinstein, Andreas Matusch, Merve Aydin, Harald Reich, Horst Urbach, Ana-Maria Oros-Peusquens, Nadim J. Shah, Wolfram S. Kunz, Thomas E. Schlaepfer, Karl Zilles, Wolfgang Maier, and René Hurlemann

Background: The human amygdala plays a crucial role in processing social signals, such as face expressions, particularly fearful ones, and facilitates responses to them in face-sensitive cortical regions. This contributes to social competence and individual amygdala size correlates with that of social networks. While rare patients with focal bilateral amygdala lesion typically show impaired recognition of fearful faces, this deficit is variable, and an intriguing possibility is that other brain regions can compensate to support fear and social signal processing.

Methods: To investigate the brain's functional compensation of selective bilateral amygdala damage, we performed a series of behavioral, psychophysiological, and functional magnetic resonance imaging experiments in two adult female monozygotic twins (patient 1 and patient 2) with equivalent, extensive bilateral amygdala pathology as a sequela of lipoid proteinosis due to Urbach-Wiethe disease.

Results: Patient 1, but not patient 2, showed preserved recognition of fearful faces, intact modulation of acoustic startle responses by fear-eliciting scenes, and a normal-sized social network. Functional magnetic resonance imaging revealed that patient 1 showed potentiated responses to fearful faces in her left premotor cortex face area and bilaterally in the inferior parietal lobule.

Conclusions: The premotor cortex face area and inferior parietal lobule are both implicated in the cortical mirror-neuron system, which mediates learning of observed actions and may thereby promote both imitation and empathy. Taken together, our findings suggest that despite the pre-eminent role of the amygdala in processing social information, the cortical mirror-neuron system may sometimes adaptively compensate for its pathology.

Key Words: Acoustic startle reflex, amygdala lesion, compensation, emotion, face, fear, fMRI, mirror-neuron system, social network

Perceiving and responding appropriately to facial expressions of emotion are critical for social cohesion, survival, and reproductive success (1) and engage a widely distributed neural network centered around the amygdala (2). The amygdala modulates cortical responses to facial expressions (3) and its size is positively correlated with that of social networks (4). A crucial question, however, is whether the social brain is dependent upon an intact amygdala. Case studies of rare patients with focal bilateral amygdala lesion show that despite their preserved ability to generate facial expressions of emotion (5), they lack any subjective experience of fear, even in the face of potent fear elicitors ([6], but see [7]) and tend to misinterpret emotional facial expressions in others, particularly fearful ones (8,9). However, there is substantial interindividual variability in this deficit (10), perhaps reflecting adaptive compensation to pathology in at least some amygdala-damaged patients. Other variables could also account for such differences between patients, including the anatomical extent of amygdala damage and genetic and environmental influences.

To investigate the brain's functional compensation for amygdala lesion, while controlling for these other variables, we performed a series of behavioral, psychophysiological, and functional magnetic resonance imaging (fMRI) experiments in two 36-year-old female monozygotic twins (patient 1 and patient 2) with selective bilateral amygdala pathology as a sequela of lipoid proteinosis due to Urbach-Wiethe disease (LP) (11–13). This rare autosomal-recessive genodermatosis is caused by mutations in the extracellular matrix protein 1 gene (*ECM1*) located on chromosome 1q21 (14,15). Interestingly, in a previous study, patient 1 displayed preserved fear recognition abilities, as opposed to patient 2, who was severely impaired (11). After genetic characterization, we first tested the twins and 15 age- and education-matched female control subjects on a behavioral facial emotion recognition task. Replicating our previous findings (11), we observed intact fear recognition in patient 1 but not in patient 2. This result may be due to her having greater sparing of amygdala tissue compared with her sister (hypothesis 1) or to functional compensation based on adaptive reorganization (hypothesis 2). The concept of lesion-induced adaptive plasticity describes the mechanisms that, following brain injury, lead to a rearrangement of cerebral organization promoting functional recovery (16). Functional recovery based on plasticity has been described for acute brain lesions such as stroke and trauma (17), as well as for slow-progressing brain lesions such as low-grade gliomas (18).

To test hypothesis 1, both twins underwent x-ray computed tomography (CT) and high-resolution T1-weighted structural magnetic resonance imaging (MRI), enabling us to determine the anatomical extent of their amygdala damage by co-registering the two imaging modalities. Hypothesis 2 was addressed using fMRI. Specifically, we predicted that preserved fear recognition in patient 1 would be accompanied by exaggerated activity in brain regions mediating adaptive compensation.

From the Department of Psychiatry (BB, YM, DS, MA, HR, TES, WM, RH), Epileptology (WSK); Department of Radiology (HU), University of Bonn, Bonn, Germany; Key Laboratory for Neuroinformation (KMK), School of Life Science and Technology, University of Electronic Science and Technology of China, Chengdu, P.R. China; Department of Neurology (JSF), University of Iowa, Iowa City, Iowa; Institute of Neuroscience and Medicine (AM, A-MO-P, NJS, KZ), Research Center Juelich, Juelich; Department of Neurology (NJS), University of Aachen, Aachen; Division of Neurochemistry (WSK), Platform NeuroCognition, Life and Brain Center, Bonn, Germany; Department of Psychiatry and Behavioral Medicine (TES), The Johns Hopkins Hospital, Baltimore, Maryland; and German Center for Neurodegenerative Diseases (WM), Bonn, Germany.

Authors BB, YM, and DS contributed equally to this work.

Authors KMK and JSF contributed equally to this work.

0006-3223/$36.00
doi:10.1016/j.biopsych.2011.11.024

© 2012 Society of Biological Psychiatry

A related question is whether the functional compensation of patient 1 allowing accurate recognition of fearful faces extends to other amygdala-dependent domains. These include top-down interactions with brainstem structures to modulate basic reflexive (acoustic startle response [ASR]) and autonomic (skin-conductance response [SCR]) responses, as well as bottom-up interactions with cortical structures mediating mentalizing and social competence functions that can support extensive social networks (4). In two further experiments, we have tested these exciting possibilities.

Methods and Materials

Background information on Urbach-Wiethe disease and a detailed synopsis of all experimental procedures are provided in Supplement 1.

Volunteers

Two female monozygotic twins suffering from lipoid proteinosis of Urbach-Wiethe (synonyms Urbach-Wiethe disease or hyalinosis cutis et mucosae; Online Mendelian Inheritance in Man 247100) ([11–13]; see also [19–21]) and 15 age- and education-matched healthy female control subjects (Table S1 in Supplement 1) volunteered in a series of behavioral, psychophysiological, and functional MRI experiments after providing written informed consent. The study was approved by the Institutional Review Board of the Medical Faculty of the University of Bonn.

Molecular Genetics

Lipoid proteinosis of Urbach-Wiethe disease is caused by mutations in the extracellular matrix protein 1 gene (*ECM1*) located on chromosome 1q21 (Table S2 in Supplement 1) (14,15). To specify the mutation causing Urbach-Wiethe disease, *ECM1* was sequenced in both twins.

Structural Imaging

High-resolution T1-weighted structural MRI scans of both twins were acquired on a 1.5 Tesla Siemens Sonata system (Siemens, Erlangen, Germany), and magnitude images (Figures 1A[i] and 1B[i]), as well as phase images (Figures 1A[ii] and 1B[ii]) were generated (22,23). Additionally, the twins were scanned on a 16-row multidetector x-ray CT device (Brilliance 16, Philips, Best, The Netherlands), thus enabling accurate CT–MRI co-registration (PMOD 3.1, PMOD Inc., Zurich, Switzerland). To assess the lesion extent, volumes of interest were manually defined and measured in the axial, coronal, and sagittal planes. For visualization purposes, these CT-derived lesion contours were superimposed onto the MRI scans (Figures 1A[iii] and 1B[iii]).

Experiment 1

The twins and 15 matched control subjects were tested on a behavioral facial emotion recognition task. Specifically, subjects were exposed, in a computer-based paradigm, to photographs depicting angry, disgusted, fearful, happy, neutral, and sad facial expressions of 12 different individuals selected from the validated

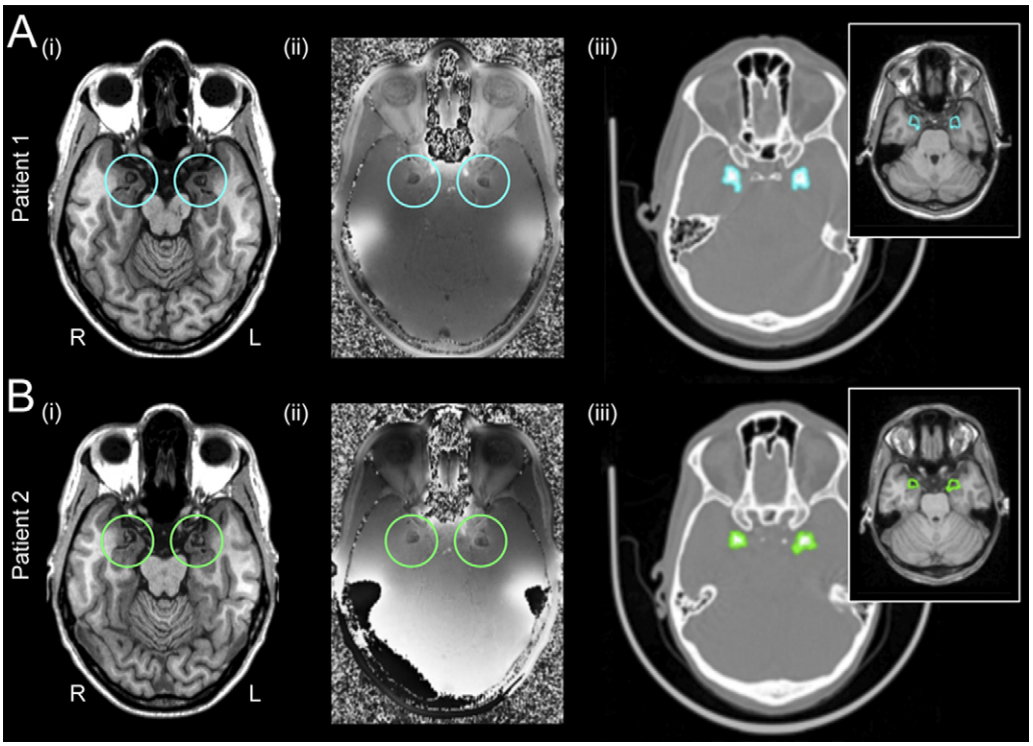

Figure 1. Lesion imaging. Lipoid proteinosis of Urbach-Wiethe led to selective bilateral calcification lesions of the amygdala in patient 1 **(A)** and patient 2 **(B)**, however, without significant volumetric differences between them. (i) Displayed are high-resolution axial (horizontal) T1-weighted magnetic resonance imaging sections of the anterior medial temporal lobes with circles indexing the focal bilateral amygdala calcification damage. Magnetic resonance images are derived from reconstructed five-average data sets acquired with .8 mm isotropic resolution. In the conventional magnitude images, the lesion signal is reduced compared with intact tissue due to the combined effect of enhanced intravoxel dephasing (susceptibility inhomogeneities) and calcification (reduced water content). (ii) Due to differential susceptibility between calcified regions and intact tissue, the amygdala lesions can be delineated more accurately in the phase images. (iii) Projection of the individual calcifications as measured by x-ray computed tomography onto high-resolution magnetic resonance imaging, documenting equivalent, extensive amygdala damage in both twins. L, left; R, right.

Download English Version:

https://daneshyari.com/en/article/4178161

Download Persian Version:

https://daneshyari.com/article/4178161

Daneshyari.com