

Amygdala Lesion Profoundly Alters Altruistic Punishment

To the Editor:

Human decision making is not guided by rational imperatives alone but is strongly susceptible to and framed by the influence of irrational factors (1). An exquisite example is altruistic punishment, which means the human propensity to punish unfairness, even at a personal cost (2), and helps to sustain cooperation in human societies (3). Experimentally, altruistic punishment has often been operationalized using the socioeconomic ultimatum game (UG). In this task, the responder's rejections of unfair offers are thought to reflect altruistic punishment because by punishing the proposer for unfair offers, the responder also forfeits earnings (4). Rejection rates to unfair offers vary as a function of central serotonergic activity (5,6) and are biased in individuals with depressed mood ([7], but see [8]), schizophrenia ([9,10], but see [11]), and psychopathy (12). The evidence suggests that altruistic punishment is driven by negative emotions toward noncooperators (2). Consistent with this notion, single-dose administration of a benzodiazepine has been shown to decrease altruistic punishment as well as associated amygdala responses (13). Although lesion studies have often implicated the amygdala as a core generator of negative emotional arousal and emphasized its crucial role in mediating loss aversion during monetary gambles (14–16), a direct demonstration of a causal role of the amygdala in modulating altruistic punishment is still missing.

In the current study, we used the lesion method to test the hypothesis that judgments of emotional arousal and valence, as well as altruistic punishment in the UG, are causally linked to and influenced by amygdala function. Two 36-year-old female monozygotic twins with equivalent selective bilateral amygdala calcification damage following lipoid proteinosis of Urbach-Wiethe (17–19) and 12 healthy female controls (mean age \pm SD = 33.3 \pm 3.87 years) volunteered after providing written informed consent. The study was approved by the Institutional Review Board of the Medical Faculty of the University of Bonn. In previous behavioral, psychophysiological, and functional magnetic resonance imaging experiments, we have demonstrated that patient 1 but not patient 2 generated appropriate responses to fear signals, was able to form a normal-sized social network, and also exhibited normal emotional empathy for negatively valenced social stimuli, suggesting that she has developed a partial functional compensation of her amygdala damage, perhaps involving the cortical mirror-neuron system (18,19). In experimental tasks specifically addressing amygdala-hippocampal interactions during encoding of emotional episodic memories, however, both patients were severely impaired compared with controls (17,18). Thus, it would appear that patient 1's compensation for her amygdala damage does not extend to all aspects of amygdala function.

We first tested the twins against controls for their ability to judge emotional arousal and valence of 129 stimuli selected from the International Affective Picture System (IAPS) (20) (experiment 1). To visualize the quality and quantity of deviations from the mean control group ratings (Figure 1A), individual arousal and valence ratings were z-transformed and visually represented as vector maps in a two-dimensional affective space with arousal ratings along the x-axis and valence ratings along the y-axis (Figure 1, B–D). Our results revealed that both twins have lower-than-normal arousal responses to emotional IAPS stimuli (patient 1: negative, $Z = -2.02$, $p = .043$; neutral, $Z = -1.49$, $p > .05$; positive, $Z = -2.63$, $p < .01$; patient 2: negative, $Z = -5.65$, $p < .01$; neutral, $Z = -1.49$, $p > .05$;

positive, $Z = -2.12$, $p < .01$), but only patient 2 additionally displays aberrant valence judgments by rating most of the stimuli as neutral (negative, $Z = 4.59$, $p < .01$; neutral, $Z = -0.53$, $p > .05$; positive, $Z = -3.67$, $p < .01$).

Next, the twins were tested against controls on multiple iterations of the UG with varying levels of fairness (fair, unfair, and most unfair) and monetary stakes (low and high), with 10 offers randomly presented in each condition for a total of 60 trials (experiment 2). Our results revealed a behavioral pattern suggestive of overcompensation in patient 1, including excessive rejection rates for fair offers during high stakes ($Z = 3.18$, $p < .01$; Figure 1F) and significantly longer reaction times across all conditions ($Z = 2.60$, $p < .01$). In stark contrast, patient 2 displayed mostly rational behavior during the UG, i.e. a lack of altruistic punishment (Figure 1E), except during situations of extreme unfairness and high monetary stakes, in which she rejected 100% of the offers (Figure 1F). This dramatic shift to complete rejection of the most unfair offers at high stakes was significantly different from the response profile shown by controls ($Z = -4.05$, $p < .01$) and suggests that patient 2 applied a rule-based all-or-none strategy during the UG. Alternatively, it may take higher stakes and maximal unfairness to induce an arousal response, which would subsequently lead her to altruistic punishment. We note that the observed aberrations in altruistic punishment in both twins were neither due to deviant fairness attitudes (all p values $> .18$) nor to subjective differences in the perceived fairness of offers (all p values $> .11$).

In conclusion, our study revealed impoverished emotional arousal ratings and deviant punishment behavior in both lipoid proteinosis of Urbach-Wiethe patients. Compared with patient 1, who in the past has shown relatively intact fear and emotional empathy responses as well as normal social networking abilities (18,19), the deficits observed here were more pronounced in patient 2, who exhibited aberrant arousal and valence judgments and who punished almost exclusively when emotional arousal and pecuniary interest were increased by raising the stakes in the UG. Taken together, our results provide evidence not only for the relevance of the amygdala in both emotional valence and arousal judgments but also the first causal evidence that altruistic punishment, an evolutionary important domain of socioeconomic decision making, is modulated by the amygdala. Thus, our findings corroborate the notion of altruistic punishment being an emotion-driven and impulsive act of retaliation.

Dirk Scheele^a

Yoan Mihov^a

Keith M. Kendrick^b

Justin S. Feinstein^c

Harald Reich^a

Wolfgang Maier^{a,d}

René Hurlemann^{a,*}

^aDepartment of Psychiatry, University of Bonn, Bonn, Germany; the ^bKey Laboratory for Neuroinformation, School of Life Science and Technology, University of Electronic Science and Technology of China (UESTC), Chengdu, People's Republic of China; ^cDepartment of Neurology, University of Iowa, Iowa City, Iowa; and ^dGerman Center for Neurodegenerative Diseases, Bonn, Germany.

*Corresponding author E-mail: renehurlemann@me.com.

RH is senior author. DS, YM, and KMK contributed equally to this work. RH was supported by a German Research Foundation (DFG) grant (HU1302/2-2) and by a Starting Independent Researcher Grant ('NEMO, Neuromodulation of Emotion') jointly provided by the Ministry of Innovation, Science, Research, and Technology of the German State of North Rhine-Westphalia (MIWFT) and the University of Bonn.

All authors report no biomedical financial interests or potential conflicts of interest.

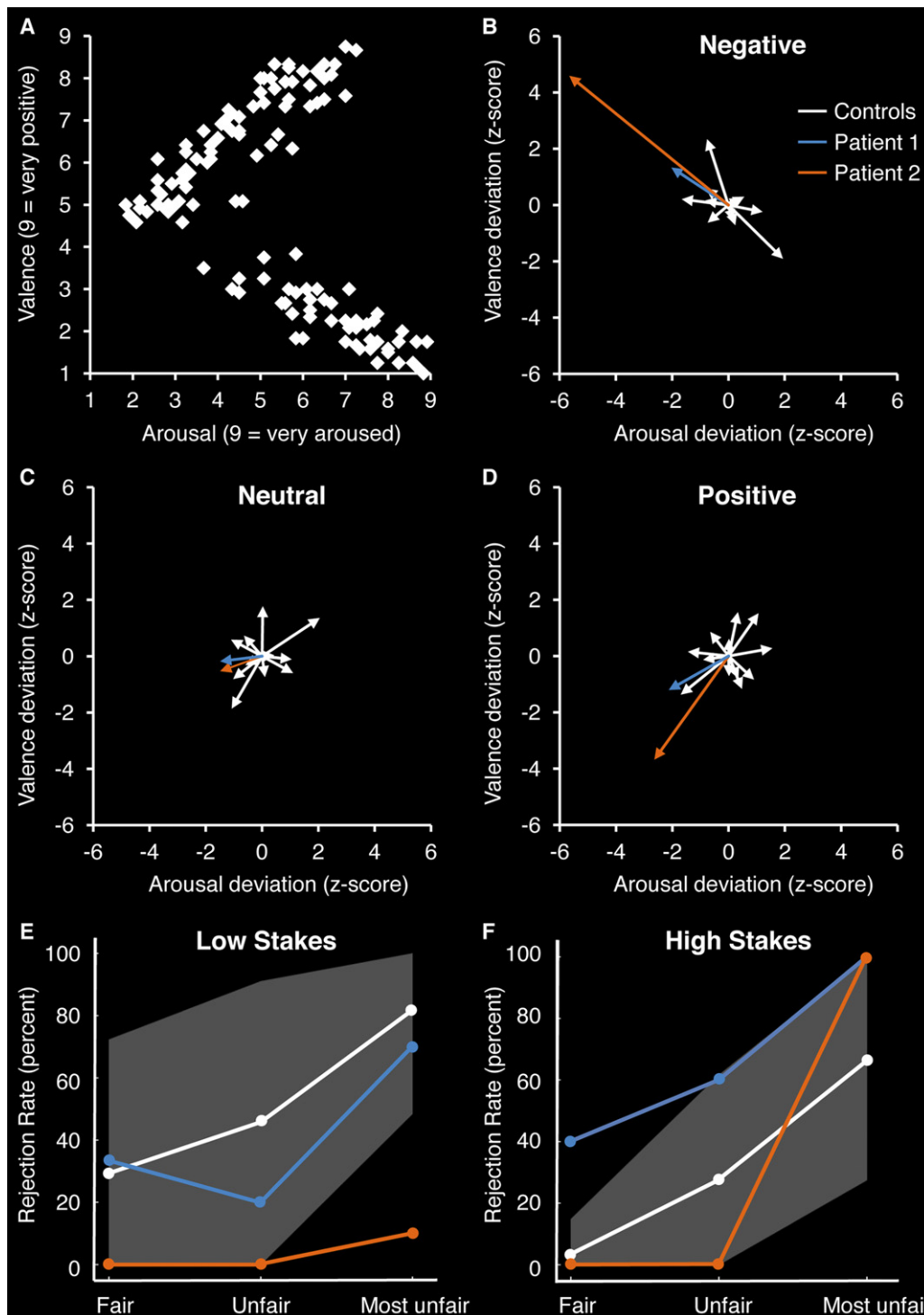


Figure 1. Emotion ratings (A–D) and ultimatum game decisions (E, F). (A) Arousal and valence ratings in the control group for 129 stimuli selected from the International Affective Picture System (IAPS), forming the characteristic “boomerang” shape of affective space (20). Vector maps for negative (B), neutral (C), and positive (D) IAPS stimuli, illustrating deviant arousal ratings in both patients and deviant valence ratings in patient 1. Rejection rates of unfair offers in the ultimatum game in percent (mean \pm 1 SD as indicated by the grey area for controls) for the low (E) and high (F) stakes conditions, demonstrating deviant altruistic punishment in both patients.

1. Camerer CF, Fehr E (2006): When does “economic man” dominates social behavior? *Science* 311:47–52.
2. Fehr E, Gächter S (2002): Altruistic punishment in humans. *Nature* 415: 137–140.
3. Henrich J, McElreath R, Barr A, Ensminger J, Barrett C, Bolyanatz A, et al. (2006): Costly punishment across human societies. *Science* 312:1767–1770.
4. Güth W, Schmittberger R, Schwartz B (1982): An experimental analysis of ultimatum bargaining. *J Econ Behav Organ* 3:367–388.

5. Crockett MJ, Clark L, Libermann MD, Robbins TW (2010): Impulsive choice and altruistic punishment are correlated and increase in tandem with serotonin depletion. *Emotion* 10:855–862.
6. Crockett MJ, Clark L, Tabibnia G, Lieberman MD, Robbins TW (2008): Serotonin modulates behavioral reactions to unfairness. *Science* 320:1739.
7. Harlé KM, Sanfey AG (2007): Incidental sadness biases social economic decisions in the Ultimatum Game. *Emotion* 7:876–881.
8. Destoop M, Schrijvers D, De Grave C, Sabbe B, De Bruijn ERA (2012): Better to give than to take? Interactive social decision-making in severe major depressive disorder [published online ahead of print January 10]. *J Affect Disorders*. doi:10.1016/j.jad.2011.12.010.
9. Czukly G, Polgár P, Tombor L, Réthelyi J, Kéri S (2011): Are patients with schizophrenia rational maximizers? Evidence from an ultimatum game study. *Psychiatry Res* 187:11–17.
10. Wischniewski J, Brüne M (2011): Moral reasoning in schizophrenia: an explorative study into economic decision making. *Cog Neuropsychiatry* 16:348–363.
11. Agay N, Kron S, Carmel Z, Mendlovic S, Levkovitz Y (2008): Ultimatum bargaining behavior of people affected by schizophrenia. *Psychiatry Res* 157:39–46.
12. Koenigs M, Kruepke M, Newman JP (2010): Economic decision-making in psychopathy: a comparison with ventromedial prefrontal lesion patients. *Neuropsychologia* 48:2198–2204.
13. Gaspic K, Mohlin E, Fransson P, Petrovic P, Johannesson M, Ingvar M (2011): Limbic justice—amygdala involvement in immediate rejections in the Ultimatum Game. *PLoS Biol* 9:e1001054.
14. Adolphs R, Russell JA, Tranel D (1999): A role for the human amygdala in recognizing emotional arousal from unpleasant stimuli. *Psychol Sci* 10: 167–171.
15. Berntson GG, Bechara A, Damasio H, Tranel D, Cacioppo JT (2007) Amygdala contribution to selective dimensions of emotion. *Soc Cogn Affect Neurosci* 2:123–129.
16. De Martino B, Camerer CF, Adolphs R (2010): Amygdala damage eliminates monetary loss aversion. *Proc Natl Acad Sci USA* 107:3788–3792.
17. Hurlmann R, Wagner M, Hawellek B, Reich H, Pieperhoff P, Amunts K, et al. (2007): Amygdala control of emotion-induced forgetting and remembering. *Neuropsychologia* 45:877–884.
18. Hurlmann R, Patin A, Onur OA, Cohen MX, Baumgartner T, Metzler S, et al. (2010): Oxytocin enhances amygdala-dependent, socially reinforced learning and emotional empathy in humans. *J Neurosci* 30: 4999–5007.
19. Becker B, Mihov Y, Scheele D, Kendrick KM, Feinstein JS, Matusch A, et al. (2012): Fear processing and social networking in the absence of a functional amygdala [published online ahead of print January 2]. *Biol Psychiatry*. doi:10.1016/j.biopsych.2011.11.024.
20. Lang PJ, Bradley M, Cuthbert B (2008): International Affective Picture System (IAPS): Affective Ratings of Pictures and Instruction Manual. Technical Report A-8. Gainesville, Florida: University of Florida.

doi:10.1016/j.biopsych.2012.01.028