

Data supplement to Doerig et al. Amygdala response to self-critical stimuli and symptom improvement in psychotherapy for depression. *Br J Psychiatry* doi: 10.1192/bjp.bp.114.149971

## **DS1 Structural MRI data acquisition and voxel-based morphometry**

### ***Structural MRI data acquisition***

Images were acquired on a Philips Achieva 3 Tesla whole-body MRI unit equipped with an eight-channel head coil using a sensitivity encoded single shot echo-planar sequence (SENSE, acceleration factor R=2). A T1-weighted gradient echo sequence (turbo field echo) with a spatial resolution of  $0.94 \times 0.94 \times 1.00 \text{ mm}^3$  (matrix:  $240 \times 240$  pixels; 160 slices), field of view =  $240 \times 240 \text{ mm}^2$ , echo time (TE)=3.7 ms, repetition time (TR)=8.06 ms, flip angle=8° was applied.

### ***Voxel-based morphometry***

Structural images were analyzed using voxel-based morphometry (VBM 8) toolbox (<http://dbm.neuro.uni-jena.de/vbm8/>) using default parameters and employing a Diffeomorphic Anatomical Registration Through Exponentiated Lie algebra approach (DARTEL),<sup>38</sup> from the statistical parametric mapping software (SPM8; <http://www.fil.ion.ucl.ac.uk>). Images were bias-corrected, tissue classified, and normalized to MNI space using linear (12-parameter affine) and nonlinear transformations, within a unified model,<sup>39</sup> including high-dimensional DARTEL normalization. GM and WM segments were modulated only by the nonlinear components to preserve actual GM and WM values locally (modulated GM and WM volumes). Homogeneity of GM and WM images was checked using the covariance structure of each image with all other images, as implemented in the check data quality function. Based on these results, three healthy subjects were excluded from the group analysis because mean covariance for data was below 2 standard deviations. Patient and control groups did not differ in age ( $P=.54$ ), sex distribution ( $P=.10$ ), marital status ( $P=.46$ ), or highest level of education ( $P=.20$ ). The modulated GM images were smoothed with a Gaussian kernel of 8-mm full-width-at-half-maximum. The left and right amygdala masks were defined from the wfupickatlas/aal from the SPM toolbox and mean GM volumes across these masks were calculated using MarsBaR (<http://marsbar.sourceforge.net/>) from the SPM toolbox.

## **References**

38. Ashburner J. A fast diffeomorphic image registration algorithm. *Neuroimage*. 2007; **38**: 95-113.
39. Ashburner J, Friston KJ. Unified segmentation. *Neuroimage*. 2005; **26**: 839-51.

**Table DS1: Cortical brain areas with enhanced activity in MDE patients compared to control participants for the contrast self-critical>neutral**

Anatomical region	Hemisphere	Cluster size (voxel)	<i>t</i> (df 49)	<i>P</i> corrected Cluster-level	MNI coordinates x y z (mm)		
Fusiform	Right	236	4.47	0.040	40	-54	-18
	Right		4.46		40	-44	-18
	Right		3.62		30	-62	-16
Occipital inferior	Left	1632	5.98	<0.001	-28	-76	-6
Fusiform	Left		5.70		-36	-58	-16
	Left		4.72		-36	-44	-12
Precentral	Right	246	4.74	0.027	46	-6	42
	Right		3.32		42	-2	56
Cuneus	Right	412	4.29	0.004	20	-68	36
Occipital superior	Right		3.69		28	-78	20
Occipital middle	Right		3.67		32	-68	16

**Note.** Clusters significant at  $P < 0.001$  ( $\kappa > 10$ ) on whole brain level after statistical correction (FWE correction at cluster level,  $P < 0.05$ ) are reported. Multiple peaks within the same label are shown on subsequent lines. Regions are labeled according to the AAL-atlas.

**Table DS2: Details of the responder analysis including covariates**

Covariate (pre)	Anatomical region	MNI coordinates x y z (mm)	<i>t</i> (df 18)	Cluster size (voxel)
BDI-II	Right Amygdala	24, 2, -20	4.12	22
STAI trait	Right Amygdala	26, 0, -22	4.65	40
Comorbid anxiety	Right Amygdala	26, 0, -22	4.80	38

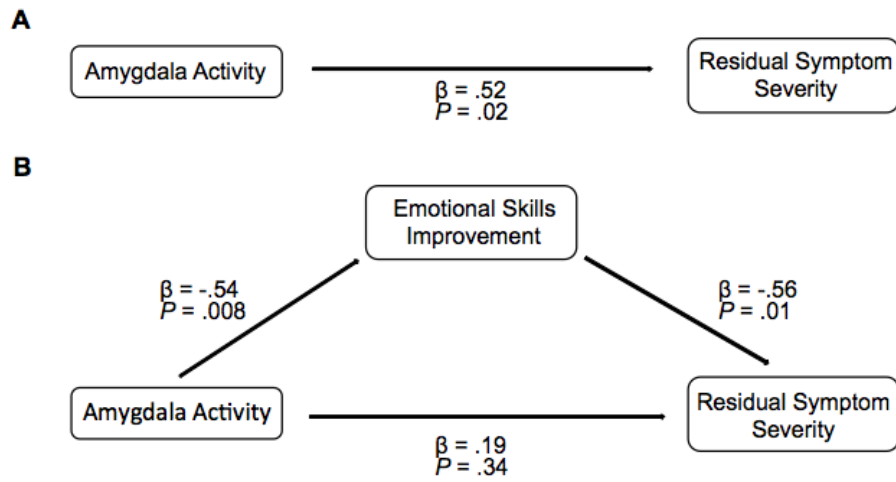
**Note.** Clusters significant at  $P < 0.001$  unc. ( $\kappa > 10$ ). Regions are labeled according to the AAL-atlas.

**Table DS3: Mediation analyses (last observation carried forward).**

Independent variable (IV)	Mediating variable (M)	Dependent variable (DV)	Effect of IV on M (a)	Effect of M on DV (b)	Direct effect (c')	Indirect effect (ab)	Total effect (c)	N
Amygdala activity	ERSQ	BDI-II follow-up	$\beta = -.54^{**}$	$\beta = -.80^{**}$	$\beta = -.05$	$\beta = .43^a$	$\beta = .53^*$	21
Amygdala activity	DAS	BDI-II follow-up	$\beta = -.01$	$\beta = .37$	$\beta = .51^*$	$\beta = -.004$	$\beta = .51^*$	20

**Note.** Amygdala activity = mean beta values of 6 mm right amygdala sphere, M and DV = residualized gain scores.  $\beta$  = standardized regression coefficients. \* $P < .05$ . \*\* $P < .01$ . <sup>a</sup>Significant point estimate ( $P < .05$ ). BDI-II data of three patients at follow-up replaced with data at post using last observation carried forward technique.

**Fig. DS1: Mediation path model.**



**Figure DS1.** Mediation path model of right amygdala activity (mean beta values), residual symptom severity post and emotional-skill acquisition. Standardized regression coefficients ( $\beta$ ) for the direct (**A**) and the indirect (**B**) paths are given. \* $P < .05$ . \*\* $P < .01$ .