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**Altered hippocampal function in major depression  
despite intact structure and resting perfusion**

**Supplementary Material**

**Contents**

Control condition of spatial memory task .....	2
fMRI task behavioral results .....	2
Whole-brain fMRI analysis .....	4
Hippocampal volumes and blood flow results.....	7
fMRI ROI analysis in reduced sample.....	8

## Control condition of spatial memory task

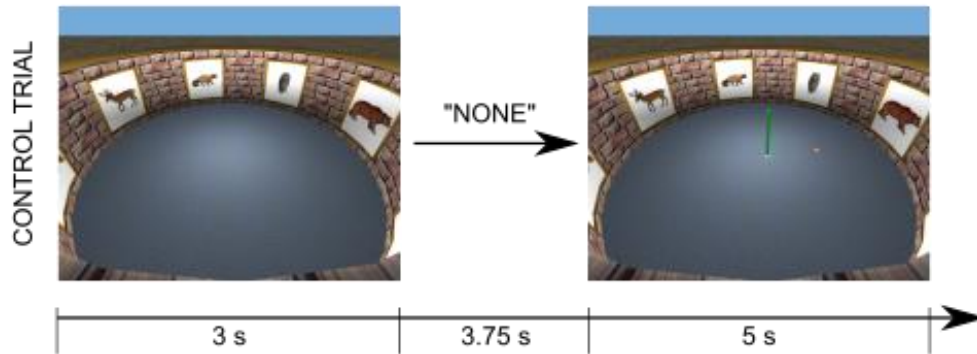


Figure S1: Trial structure of the control condition of the fMRI task. Only the empty arena with its landmarks was shown during encoding. During retrieval participants were instructed to press the button that corresponded to the disc that was indicated by the green pole marker.

## fMRI task behavioral results

Table S1: Behavioral findings of fMRI task

Source	SS	df	MS	F	p
<b>Errors</b>					
<i>Within-subject effects</i>					
Condition (egocentric, allocentric)	1.395	1	1.395	<b>97.004</b>	<b>&lt;.001</b>
Condition x group	0.027	1	0.027	1.860	.183
Error (condition)	.417	29	0.014		
Rotation angle (45, 90, 135 degrees)	0.519	2	0.259	<b>22.388</b>	<b>&lt;.001</b>
Angle x group	0.000	2	0.000	0.004	.996
Error (angle)	0.672	58	0.012		
Condition x angle	0.379	2	0.189	<b>13.296</b>	<b>&lt;.001</b>
Condition x angle x group	0.067	2	0.034	2.354	.104
Error (condition x angle)	0.826	58	0.014		
<i>Between-subject effects</i>					
Group	0.115	1	0.115	1.477	.234
Between	2.266	29	0.078		
<b>Response Time</b>					
<i>Within-subject effects</i>					
Condition (egocentric, allocentric)	34.702	1	34.702	<b>63.550</b>	<b>&lt;.001</b>
Condition x Group	0.663	1	0.663	1.212	.280
Error (condition)	15.836	29	0.546		
Rotation angle (45, 90, 135 degrees)	2.339	2	1.169	<b>16.705</b>	<b>&lt;.001</b>
Angle x group	0.211	2	0.105	1.506	.230
Error (angle)	4.060	58	0.070		
Condition x angle	0.572	2	0.286	<b>3.690</b>	<b>0.031</b>

Condition x angle x group	0.378	2	0.189	2.438	0.096
Error (condition x angle)	4.499	58	0.078		
<i>Between- subject effects</i>					
Group	0.977	1	0.977	0.779	.385
Between	36.378	29	1.254		

SS=Sum of square, df=degrees of freedom, MS=mean square; Results with p<.05 in bold.

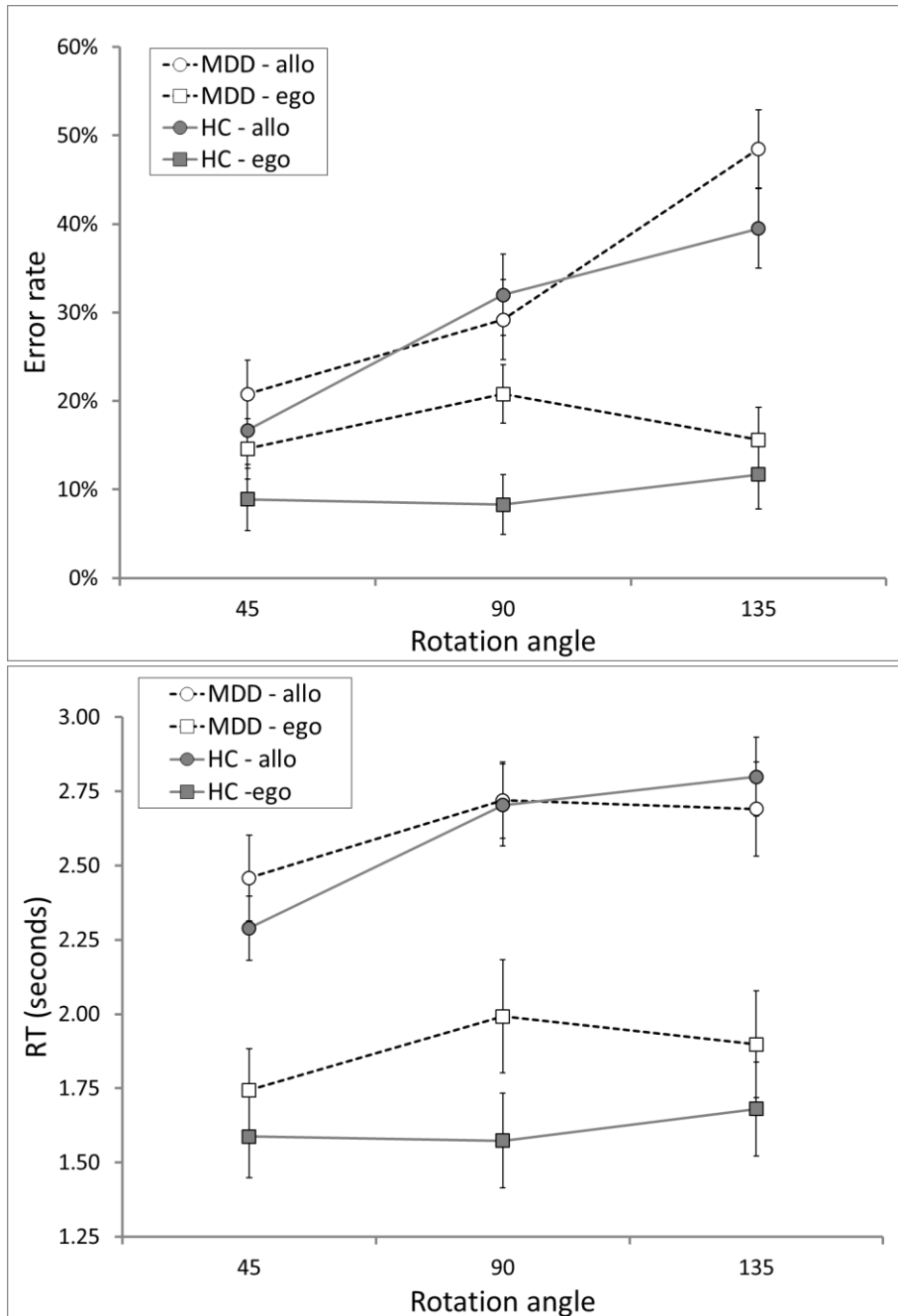


Figure S1: Behavioral findings of fMRI task (as presented in ANOVA results, table S1). Mean error rates (top) and mean reaction times (bottom). Error bars are +/- 1 standard error of mean.

## Whole-brain fMRI analysis

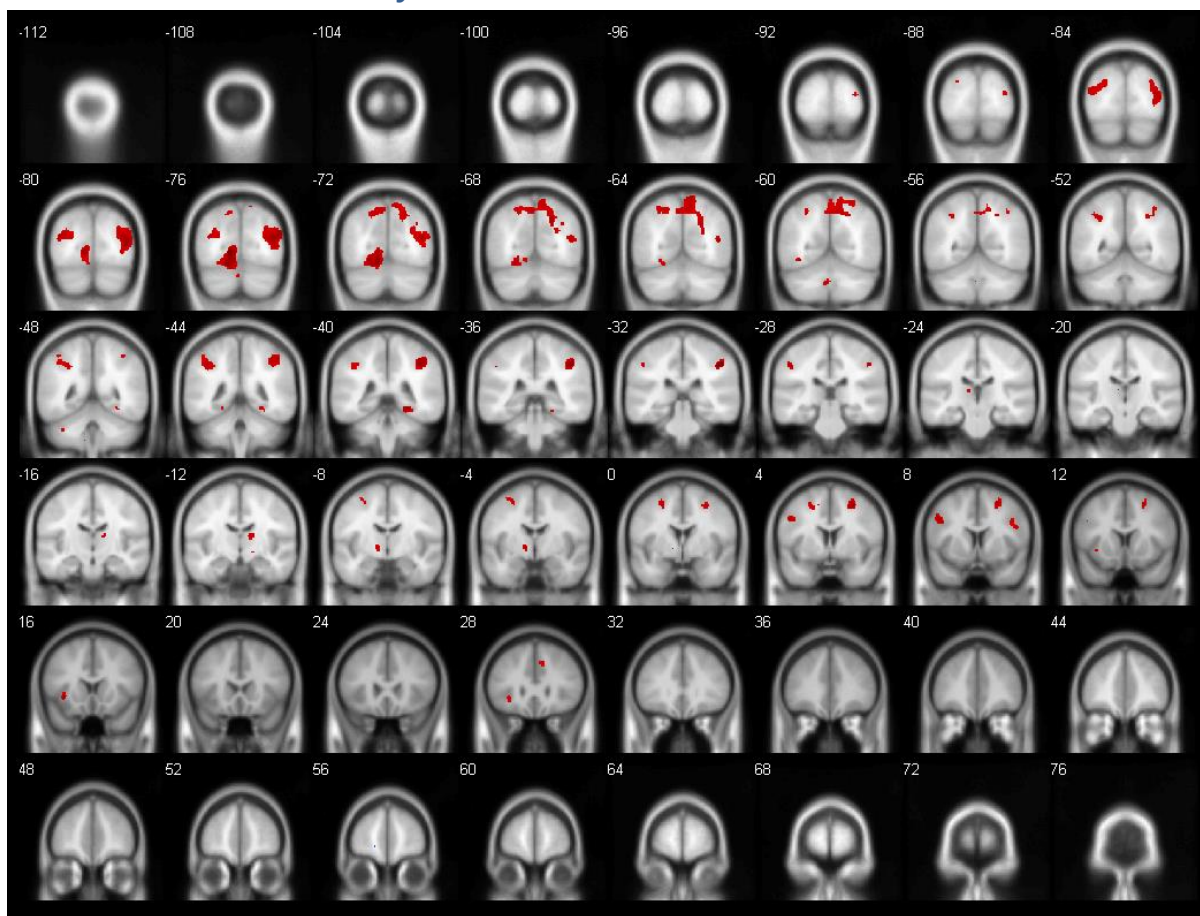


Figure S3: Results of whole-brain analysis of AvE contrast across the entire sample ( $p < .05$ , FWE-corrected). Areas in red show significant BOLD signal differences in the positive direction (i.e. allocentric condition > egocentric condition), whereas the area in blue show significant differences in the negative direction (allocentric < egocentric).

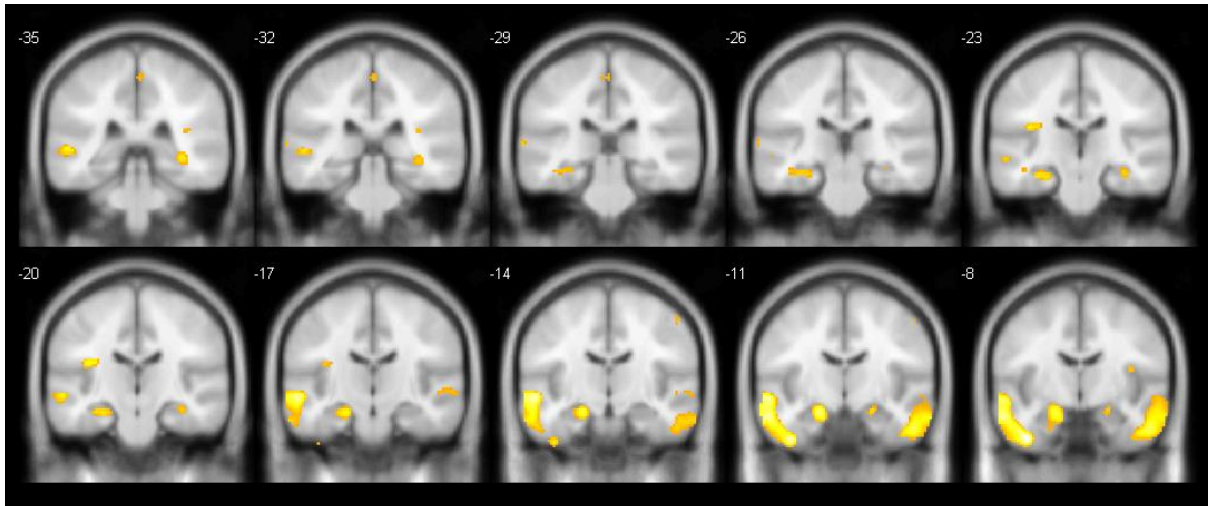


Figure S4: Pattern of findings from the whole-brain analysis of negative AvE contrast (Egocentric > Allocentric) in the healthy control group only ( $p < .005$ , uncorrected) in the hippocampal region. No hippocampal differences were seen at this level in patients.

Table S2: Whole-brain fMRI results

cluster size (voxels)	Peak location	Peak MNI coordinates (mm)	Peak T	Peak p-value (FWE)
<b>positive AvE contrast (Allocentric &gt; Egocentric)*</b>				
609	L Lingual Gyrus	-12, -76, 0	7.207	<0.001
	L Lingual Gyrus	-12, -72, -10	6.860	0.001
2611	R Supramarginal Gyrus	46, -32, 42	7.119	<0.001
	R Inferior Parietal Lobule	40, -40, 46	6.595	0.002
	R Middle Occipital Gyrus	40, -78, 16	6.513	0.003
67	R Fusiform Gyrus	24, -40, -12	6.640	0.002
143	R Superior Frontal Gyrus	26, 4, 52	6.587	0.002
312	L Middle Occipital Gyrus	-38, -80, 20	6.374	0.004
	L Middle Occipital Gyrus	-28, -76, 20	5.880	0.016
	L Superior Occipital Gyrus	-24, -86, 28	5.832	0.018
91	L Precentral Gyrus	-48, 8, 34	6.372	0.004
29	L Insula	-34, 14, -2	6.293	0.005
45	L Globus Pallidus	-12, -4, 0	6.258	0.005
40	L Inferior Parietal Lobule	-50, -28, 42	6.226	0.006
93	L Mid Frontal Gyrus	-26, 0, 54	6.052	0.010
	L Precentral Gyrus	-30, -6, 58	5.751	0.022
	L Superior Frontal Gyrus	-14, 4, 52	5.614	0.031
40	R Thalamus	14, -12, 14	6.037	0.011
27	L Cerebellum Vermis	-4, -60, -36	5.959	0.013
38	R Inferior Frontal Operculum	48, 8, 24	5.756	0.022
	R Inferior Frontal Operculum	42, 8, 32	5.601	0.033
<b>negative AvE contrast (Egocentric &gt; Allocentric)*</b> (no significant clusters)				
<b>AvE contrast, controls &gt; patients<sup>†</sup></b> (no significant clusters)				
<b>AvE contrast, patients &gt; controls<sup>†</sup></b> (no significant clusters)				

Results of whole-brain fMRI analysis \*using  $p < .05$  (FWE) at voxel level and extend-threshold of 20, <sup>†</sup> using  $p < .001$  (uncorrected) and FWE-correction at cluster level. Only the three largest local peaks of clusters are reported. L=Left, R=Right.

## Hippocampal volumes and blood flow results

Table S3: Hippocampal Volumes

	Patients		Controls		Controls vs Patients (%TICV, df=38)
	ml	%TICV	ml	%TICV	
L anterior ROI	3.154 (0.090)	0.2230 (0.0051)	2.947 (0.082)	0.2158 (0.0051)	t=-1.001, p=.323
L posterior ROI	0.371 (0.019)	0.0263 (0.0013)	0.347 (0.024)	0.0254 (0.0018)	t=-0.399, p=.692
R anterior ROI	2.873 (0.089)	0.2034 (0.0058)	2.715 (0.084)	0.1983 (0.0043)	t=-0.695, p=.492
R posterior ROI	0.375 (0.025)	0.0265 (0.0017)	0.373 (0.026)	0.0273 (0.0019)	t=0.333, p=.741
L combined	3.525 (0.042)	0.2493 (0.0235)	3.942 (0.038)	0.2412 (0.0225)	t=-1.110, p=.274
R combined	3.247 (0.043)	0.2299 (0.0275)	3.088 (0.036)	0.2257 (0.0161)	t=-0.593, p=.557
Total	6.772 (0.082)	0.4791 (0.0490)	6.382 (0.072)	0.4669 (0.0363)	t=-0.900, p=.374

Mean (standard deviations) hippocampal volumes in ml and as percentage of total intracranial volume (TICV). R=right, L=left, ROI=region of interest

Table S4: Regional cerebral blood flow results

region	Depressed (n=20)		Control (n=20)		Significance	
	males	females	males	females	group	sex
L anterior hippocampus	34.90 (8.20)	46.46 (13.3)	40.19 (12.2)	47.95 (11.1)	F=0.81, p=.360	F=7.18, p=.011
L posterior hippocampus	44.89 (17.8)	53.15 (14.7)	44.91 (13.2)	54.08 (15.3)	F=0.01, p=.929	F=2.77, p=.105
R anterior hippocampus	34.07 (9.91)	49.49 (14.7)	41.79 (13.4)	46.17 (10.3)	F=0.21, p=.649	F=6.29, p=.017
R posterior hippocampus	35.53 (11.2)	60.20 (17.5)	47.11 (16.3)	48.42 (17.9)	F=0.01, p=.985	F=5.13, p=.030
GM	28.94 (6.83)	45.17 (9.83)	34.59 (6.92)	42.65 (9.82)	F=0.17, p=.574	F=19.04, p<.001
WM	17.96 (4.50)	26.91 (7.45)	22.46 (4.22)	26.88 (6.09)	F=1.16, p=.287	F=12.99, p=.001

Means (and standard deviation) of regional CBF in ml/100g/min of the different brain regions. The last two columns show p-values for ANOVAs with group and sex as fixed factors. L=left, R=right, GM=gray matter, WM=white matter

## fMRI ROI analysis in reduced sample

Table S5: Region-of-interest fMRI results of AvE contrast

Hippocampus ROI	Patients (n=16)	Controls (n=15)	Condition effect	Group difference
Left anterior	-0.017 (0.177)	-0.243 (0.335)	t=-2.46, <b>p=.020</b>	t=-2.316, <b>p=.031</b>
Left posterior	-0.008 (0.252)	-0.094 (0.218)	t=-1.17, p=.252	t=-1.016, p=.318
Right anterior	-0.069 (0.268)	-0.310 (0.313)	t=-3.23, <b>p=.002</b>	t=-2.291, <b>p=.030</b>
Right posterior	-0.001 (0.249)	-0.077 (0.190)	t=-0.92, p=.364	t=-0.992, p=.330

Means (and standard deviation) of the Allocentric-vs-Egocentric contrast of the retrieval phase. The condition effect column shows the result of a one-sample t-test of this contrast against 0 (across both groups). The group difference column shows the result of an independent-sample t-test for the difference between patients and healthy controls. This t-test did not assume equal variances. Bolded figures represent significant ( $p < .05$ ) results.

Table S6: Participant characteristics (reduced sample)

	Patients	Controls	group difference
Sex (f/m)	7/9	7/8	$\chi^2=0.027$ p=.870
Age (years)	44.0 (12.9)	40.8 (12.0)	t=0.713 p=.481
BDI	38.6 (11.4)	1.6 (2.6)	t=12.32 p<.001
State anxiety	47.6 (13.8)	28.6 (9.3)	t=4.449 p<.001
Trait anxiety	59.0 (12.7)	29.9 (9.2)	t=7.188 p<.001
verbal IQ	112.3 (11.9)	114.1 (5.7)	t=0.557 p=.582
HAM-D	23.3 (5.4)	0.0 (0.0)	t=16.59, p<.001