

Supplementary Data

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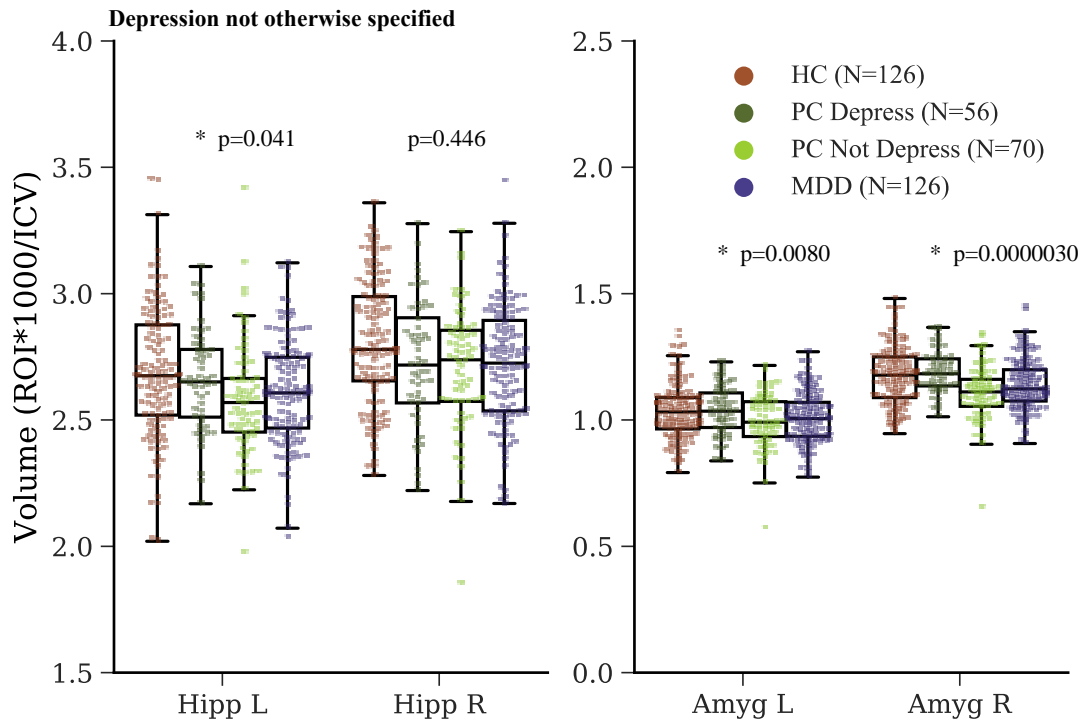
eTable 1. Group Comparisons of Hippocampal and Amygdalar Volumes

Major Depressive Disorder															
	Healthy Controls (N=126)		Psychiatric Controls (N=126)		Group of Interest (N=126)		Healthy Controls versus Psychiatric Controls			Healthy Controls versus Group of Interest			Psychiatric Controls versus Group of Interest		
	Mean	Std Err	Mean	Std Err	Mean	Std Err	F	p	95% CI	F	p	95% CI	F	p	95% CI
Left Hipp	2.69	2.33*10 ⁻²	2.61	1.93*10 ⁻²	2.61	1.85*10 ⁻¹	6.02	0.015	[1.47*10 ⁻² , 1.34*10 ⁻¹]	6.98	8.79*10 ⁻³	[2.00*10 ⁻² , 1.37*10 ⁻¹]	0.82	0.37	[-3.29*10 ⁻² , 8.87*10 ⁻²]
Right Hipp	2.81	2.18*10 ⁻²	2.71	2.16*10 ⁻²	2.72	2.09*10 ⁻²	10.45	1.39*10 ⁻³	[3.87*10 ⁻² , 1.59*10 ⁻¹]	8.91	3.13*10 ⁻³	[3.063*10 ⁻² , 1.50*10 ⁻¹]	0.42	0.52	[-4.62*10 ⁻² , 9.14*10 ⁻²]
Left Amyg	1.03	9.79*10 ⁻³	1.01	9.29*10 ⁻³	1.01	8.74*10 ⁻³	2.17	0.14	[-6.72*10 ⁻³ , 4.64*10 ⁻²]	3.45	0.065	[-1.49*10 ⁻³ , 5.02*10 ⁻²]	1.11	0.29	[-1.34*10 ⁻² , 4.43*10 ⁻²]
Right Amyg	1.17	9.75*10 ⁻³	1.14	9.09*10 ⁻³	1.14	8.76*10 ⁻³	4.42	0.037	[1.88*10 ⁻³ , 5.74*10 ⁻²]	6.53	0.001	[7.99*10 ⁻³ , 6.17*10 ⁻²]	4.24	0.041	[1.28*10 ⁻³ , 5.78*10 ⁻²]
Borderline Personality Disorder															
	Healthy Controls (N=114)		Psychiatric Controls (N=114)		Group of Interest (N=114)		Healthy Controls versus Psychiatric Controls			Healthy Controls versus Group of Interest			Psychiatric Controls versus Group of Interest		
	Mean	Std Err	Mean	Std Err	Mean	Std Err	F	p	95% CI	F	p	95% CI	F	p	95% CI
Left Hipp	2.69	2.38*10 ⁻²	2.61	2.00*10 ⁻²	2.63	1.93*10 ⁻²	6.78	0.010	[1.97*10 ⁻² , 1.42*10 ⁻¹]	3.68	0.056	[-1.19*10 ⁻¹ , 1.60*10 ⁻³]	0.63	0.43	[-3.27*10 ⁻² , 7.70*10 ⁻²]
Right Hipp	2.82	2.12*10 ⁻²	2.75	2.08*10 ⁻²	2.74	2.09*10 ⁻²	5.29	0.023	[9.71*10 ⁻³ , 1.27*10 ⁻¹]	7.13	8.11*10 ⁻³	[-1.38*10 ⁻¹ , -2.09*10 ⁻²]	0.15	0.703	[-6.95*10 ⁻² , 4.69*10 ⁻²]
Left Amyg	1.04	1.01*10 ⁻²	1.01	8.84*10 ⁻³	1.02	8.54*10 ⁻³	4.70	0.031	[2.65*10 ⁻³ , 5.55*10 ⁻²]	2.38	0.12	[-4.64*10 ⁻² , 5.64*10 ⁻³]	0.498	0.481	[-1.55*10 ⁻² , 3.29*10 ⁻²]
Right Amyg	1.18	9.94*10 ⁻³	1.14	8.14*10 ⁻³	1.14	8.90*10 ⁻³	9.63	2.16*10 ⁻³	[1.51*10 ⁻² , 6.77*10 ⁻²]	9.78	2.00*10 ⁻³	[-6.55*10 ⁻² , -1.49*10 ⁻²]	0.010	0.92	[-2.26*10 ⁻² , 2.50*10 ⁻²]

eTable 1. Group Comparisons of Hippocampal and Amygdalar Volumes Continued

Alcohol Use Disorder															
	Healthy Controls (N=136)		Psychiatric Controls (N=136)		Group of Interest (N=136)		Healthy Controls versus Psychiatric Controls			Healthy Controls versus Group of Interest			Psychiatric Controls versus Group of Interest		
	Mean	Std Err	Mean	Std Err	Mean	Std Err	F	p	95% CI	F	p	95% CI	F	p	95% CI
Left Hipp	2.68	2.14*10 ⁻²	2.63	1.96*10 ⁻²	2.64	1.81*10 ⁻²	3.09	0.080	[-6.13*10 ⁻³ , 1.09*10 ⁻¹]	2.37	0.13	[-9.83*10 ⁻² , 1.21*10 ⁻²]	0.105	0.75	[-4.38*10 ⁻² , 6.11*10 ⁻²]
Right Hipp	2.8	2.02*10 ⁻²	2.74	2.13*10 ⁻²	2.74	1.89*10 ⁻²	4.54	0.034	[4.76*10 ⁻³ , 1.21*10 ⁻¹]	4.52	0.34	[-1.13*10 ⁻¹ , -4.38*10 ⁻³]	0.025	0.88	[-5.16*10 ⁻² , 6.06*10 ⁻²]
Left Amyg	1.04	9.87*10 ⁻³	1.02	8.36*10 ⁻³	1.02	8.77*10 ⁻³	1.44	0.23	[-9.80*10 ⁻³ , 4.03*10 ⁻²]	2.14	0.14	[-5.43*10 ⁻² , 6.67*10 ⁻³]	0.12	0.73	[-2.74*10 ⁻² , 1.92*10 ⁻²]
Right Amyg	1.17	9.85*10 ⁻³	1.16	8.11*10 ⁻³	1.14	8.49*10 ⁻³	1.43	0.23	[-9.90*10 ⁻³ , 4.05*10 ⁻²]	5.12	0.024	[-5.50*10 ⁻² , -3.82*10 ⁻³]	1.38	0.24	[-3.69*10 ⁻² , 9.35*10 ⁻²]
Post-Traumatic Stress Disorder															
	Healthy Controls (N=68)		Psychiatric Controls (N=68)		Group of Interest (N=68)		Healthy Controls versus Psychiatric Controls			Healthy Controls versus Group of Interest			Psychiatric Controls versus Group of Interest		
	Mean	Std Err	Mean	Std Err	Mean	Std Err	F	p	95% CI	F	p	95% CI	F	p	95% CI
Left Hipp	2.71	3.06*10 ⁻²	2.64	2.40*10 ⁻²	2.62	2.43*10 ⁻²	3.14	0.079	[1.46*10 ⁻¹ , 7.98*10 ⁻³]	5.44	0.021	[1.39*10 ⁻² , 1.68*10 ⁻¹]	0.43	0.52	[-4.52*10 ⁻² , 8.96*10 ⁻²]
Right Hipp	2.85	2.73*10 ⁻²	2.75	2.56*10 ⁻²	2.73	2.12*10 ⁻²	6.64	0.011	[-1.71*10 ⁻¹ , -2.25*10 ⁻²]	11.54	8.99*10 ⁻¹	[4.90*10 ⁻² , 1.86*10 ⁻¹]	0.39	0.53	[-4.50*10 ⁻² , 8.66*10 ⁻²]

Mean and standard error shown after divided by total intracranial volume (and multiplied by 1000 for scaling). ANCOVA results shown for major depressive disorder. Note effect of covariate (depression not otherwise specified is shown in a different figure). T-test results shown for all other disorders. Amyg: amygdala; Hipp: hippocampus; Std Err: Standard error



eFigure 1. Effect of Depression Not Otherwise Specified on Hippocampal and Amygdalar Volumes

Effect of depression not otherwise specified as a covariate in the major depression disorder versus psychiatric controls comparison. Data is divided by ICV and multiplied by 1000 for scaling. P values indicate the effect of the covariate (* $p < 0.05$). Left hippocampus: $F=4.20$; $p=0.041$; 95% CI [2.97×10^{-3} , 1.47×10^{-1}]; Depress: $2.66 \pm 2.02 \times 10^{-1}$; not Depress $2.58 \pm 2.39 \times 10^{-1}$. Right hippocampus: $F=0.582$; $p=0.446$; 95% CI [-5.01×10^{-2} , 1.13×10^{-1}]; Depress: $2.72 \pm 2.48 \times 10^{-1}$, not Depress $2.70 \pm 2.39 \times 10^{-1}$. Left amygdala: $F=7.12$; $p=8.04 \times 10^{-3}$; 95% CI [4.76×10^{-2} , 1.15×10^{-1}]; Depress: $1.04 \pm 9.37 \times 10^{-2}$, not Depress $9.94 \times 10^{-1} \pm 1.09 \times 10^{-1}$. Right amygdala: $F=22.68$; $p=3.00 \times 10^{-6}$; 95% CI [1.22×10^{-2} , 8.072×10^{-2}]; Depress: $1.19 \pm 8.24 \times 10^{-2}$, not Depress $1.11 \pm 1.09 \times 10^{-1}$. Amyg: amygdala; HC: healthy controls; Hipp: hippocampus; ICV: total intracranial volume; L: left; MDD: major depressive disorder; PC Depress: psychiatric controls with depression not otherwise specified; PC not Depress: psychiatric controls without depression not otherwise specified; R: right; ROI: region of interest.

eTable 2. Correlation Results between Psychiatric Traits and Amygdalar/Hippocampal Volumes: MDD and PC

		Trauma Score		Substance Use Score		DERS Total Score		PHQ-9		GAD-7	
		PC	MDD	PC	MDD	PC	MDD	PC	MDD	PC	MDD
Hipp L	<i>Pearson's r</i>	0.043	-0.034	-0.109	0.011	-0.022	0.074	-0.009	0.057	0.046	0.035
	<i>p value</i>	0.635	0.707	0.227	0.907	0.811	0.415	0.923	0.530	0.610	0.701
Hipp R	<i>Pearson's r</i>	0.091	0.017	-0.038	-0.080	0.005	0.091	-0.129	0.017	0.018	-0.089
	<i>p value</i>	0.316	0.854	0.673	0.378	0.952	0.314	0.152	0.849	0.844	0.324
Amyg L	<i>Pearson's r</i>	-0.105	-0.090	-0.122	-0.104	-0.039	-0.016	0.016	-0.072	-0.131	-0.088
	<i>p value</i>	0.244	0.321	0.178	0.250	0.669	0.860	0.864	0.429	0.148	0.331
Amyg R	<i>Pearson's r</i>	0.015	-0.091	-0.034	-0.105	-0.105	0.031	0.017	-0.035	-0.137	-0.058
	<i>p value</i>	0.870	0.317	0.704	0.246	0.245	0.732	0.853	0.702	0.128	0.522

Correlations for each group (PC (N=126) and MDD (N=126)) were performed between hippocampal/amygdalar volumes and psychiatric traits. Hippocampal and amygdalar volumes were divided by total intracranial volume. Trauma scores were taken from the Stressful Life Events Screening Questionnaire. Amyg: Amygdala; DERS: Difficulties in emotion regulation; GAD: Generalized anxiety disorder; Hipp: Hippocampus; L: Left; PC: Psychiatric controls; PHQ: Patient health questionnaire; MDD: Major depressive disorder; R: Right.

eTable 3. Correlation Results between Psychiatric Traits and Amygdalar/Hippocampal Volumes: BPD and PC

		Trauma Score		Substance Use Score		DERS Total Score		PHQ-9		GAD-7	
		PC	BPD	PC	BPD	PC	BPD	PC	BPD	PC	BPD
Hipp L	<i>Pearson's r</i>	0.025	-0.002	-0.033	-0.012	0.013	0.006	0.153	-0.168	0.071	-0.098
	<i>p value</i>	0.794	0.979	0.731	0.898	0.889	0.952	0.107	0.076	0.459	0.302
Hipp R	<i>Pearson's r</i>	0.035	-0.149	-0.010	-0.154	0.072	0.090	0.192	-0.114	0.120	-0.066
	<i>p value</i>	0.717	0.116	0.915	0.104	0.449	0.343	0.042*	0.232	0.208	0.488
Amyg L	<i>Pearson's r</i>	0.038	0.025	-0.136	0.024	-0.022	-0.039	0.040	-0.077	-0.042	-0.084
	<i>p value</i>	0.688	0.797	0.154	0.804	0.817	0.682	0.676	0.420	0.657	0.379
Amyg R	<i>Pearson's r</i>	0.001	0.060	-0.126	0.072	0.052	-0.041	0.166	-0.152	0.054	-0.242
	<i>p value</i>	0.993	0.532	0.186	0.450	0.589	0.668	0.081	0.110	0.572	0.010*

Correlations for each group (PC (N=114) and BPD (N=114)) were performed between hippocampal/amygdalar volumes and psychiatric traits. Hippocampal and amygdalar volumes were divided by total intracranial volume. Trauma scores were taken from the Stressful Life Events Screening Questionnaire. Amyg: Amygdala; DERS: Difficulties in emotion regulation; GAD: Generalized anxiety disorder; Hipp: Hippocampus; L: Left; PC: Psychiatric controls; PHQ: Patient health questionnaire; MDD: Major depressive disorder; R: Right. * p < 0.05.

eTable 4. Correlation Results between Psychiatric Traits and Amygdalar/Hippocampal Volumes: AUD and PC

		Trauma Score		Substance Use Score		DERS Total Score		PHQ-9		GAD-7	
		PC	AUD	PC	AUD	PC	AUD	PC	AUD	PC	AUD
Hipp L	<i>Pearson's r</i>	-0.064	-0.002	0.036	-0.141	-0.088	-0.081	-0.093	-0.132	-0.117	-0.116
	<i>p value</i>	0.463	0.982	0.683	0.104	0.315	0.355	0.286	0.127	0.178	0.181
Hipp R	<i>Pearson's r</i>	0.011	0.065	-0.019	-0.074	-0.054	0.015	-0.132	-0.067	-0.158	-0.035
	<i>p value</i>	0.899	0.456	0.830	0.393	0.534	0.865	0.129	0.439	0.069	0.688
Amyg L	<i>Pearson's r</i>	-0.025	-0.003	0.043	-0.088	-0.061	0.048	-0.131	-0.073	-0.145	-0.092
	<i>p value</i>	0.776	0.968	0.618	0.315	0.486	0.584	0.132	0.403	0.094	0.289
Amyg R	<i>Pearson's r</i>	-0.003	0.077	0.001	-0.024	-0.051	-0.038	-0.063	-0.074	-0.100	-0.166
	<i>p value</i>	0.969	0.379	0.992	0.780	0.557	0.664	0.467	0.396	0.251	0.055

Correlations for each group (PC (N=136) and AUD (N=136)) were performed between hippocampal/amygdalar volumes and psychiatric traits. Hippocampal and amygdalar volumes were divided by total intracranial volume. Trauma scores were taken from the Stressful Life Events Screening Questionnaire. Amyg: Amygdala; DERS: Difficulties in emotion regulation; GAD: Generalized anxiety disorder; Hipp: Hippocampus; L: Left; PC: Psychiatric controls; PHQ: Patient health questionnaire; MDD: Major depressive disorder; R: Right.

eTable 5. Correlation Results between Psychiatric Traits and Amygdalar/Hippocampal Volumes: PTSD and PC

		Trauma Score		Substance Use Score		DERS Total Score		PHQ-9		GAD-7	
		PC	PTSD	PC	PTSD	PC	PTSD	PC	PTSD	PC	PTSD
Hipp L	<i>Pearson's r</i>	0.183	-0.230	-0.221	0.051	0.008	0.151	-0.027	-0.094	-0.055	0.046
	<i>p value</i>	0.140	0.063	0.074	0.683	0.947	0.227	0.830	0.454	0.662	0.712
Hipp R	<i>Pearson's r</i>	0.190	-0.143	-0.153	-0.013	0.031	0.088	0.035	-0.269	0.011	-0.074
	<i>p value</i>	0.127	0.252	0.219	0.919	0.806	0.484	0.779	0.029*	0.929	0.557

Correlations for each group (PC (N=68) and PTSD (N=68)) were performed between hippocampal/amygdalar volumes and psychiatric traits. Hippocampal and amygdalar volumes were divided by total intracranial volume. Trauma scores were taken from the Stressful Life Events Screening Questionnaire. Amyg: Amygdala; DERS: Difficulties in emotion regulation; GAD: Generalized anxiety disorder; Hipp: Hippocampus; L: Left; PC: Psychiatric controls; PHQ: Patient health questionnaire; MDD: Major depressive disorder; R: Right.
* p <0.05.

eTable 6. Correlation Results between Psychiatric Traits and Amygdalar/Hippocampal Volumes: Psychiatric Patients

		Trauma Score	Substance Use Score	DERS Total Score	PHQ-9	GAD-7
Hipp L	<i>Pearson's r</i>	-0.038	-0.040	-0.026	-0.083	-0.050
	<i>p value</i>	0.382	0.364	0.548	0.059	0.256
Hipp R	<i>Pearson's r</i>	-0.019	-0.057	-0.002	-0.072	-0.055
	<i>p value</i>	0.673	0.192	0.967	0.100	0.209
Amyg L	<i>Pearson's r</i>	-0.032	-0.065	-0.050	-0.097	-0.102
	<i>p value</i>	0.463	0.138	0.259	0.027*	0.020*
Amyg R	<i>Pearson's r</i>	-0.017	-0.074	-0.063	-0.070	-0.099
	<i>p value</i>	0.707	0.092	0.149	0.112	0.025*

Correlations for each all psychiatric patients (N=522) were performed between hippocampal/amygdalar volumes and psychiatric traits. Hippocampal and amygdalar volumes were divided by total intracranial volume. Trauma scores were taken from the Stressful Life Events Screening Questionnaire. Amyg: Amygdala; DERS: Difficulties in emotion regulation; GAD: Generalized anxiety disorder; Hipp: Hippocampus; L: Left; PC: Psychiatric controls; PHQ: Patient health questionnaire; MDD: Major depressive disorder; R: Right.
* p <0.05.