

Table S1: Association of subsegmental brain region volumes with lifetime major depressive disorder among 610 participants in multivariable model adjusted for age, sex, total brain volume, education level, head injury, cardiovascular ischemic pathologies, and antidepressant use

	No lifetime MDD (n=448)		Lifetime MDD (n=162)		<i>p</i> †
	Mean*	SD	Mean*	SD	
Rostral anterior cingulate	3364.37	72.64	3471.48	78.44	0.059
Insula	12053.26	125.78	11813.70	135.83	0.015
Thalamus	11597.33	111.61	11381.19	120.52	0.013
Ventral diencephalon	6704.75	73.67	6540.86	79.55	0.004
Putamen	9409.72	135.46	9173.56	146.28	0.025
Nucleus accumbens	970.78	18.34	935.73	19.80	0.014
Pallidum	3003.19	41.68	2911.07	45.01	0.005

Pericalcarine	3462.15	73.24	3601.43	79.09	0.015
Lingual	10628.71	173.68	10901.94	187.55	0.044

MDD = major depressive disorder; SD = standard deviation.

*Mean (SD) values expressed as mm³.

†Raw p-values.

Table S2: Strength of the associations with covariates evaluated using standardized regression coefficient

Covariate	Low education level (≤ 5 years)				Antidepressant use				Head injury				Cardiovascular ischemic pathologies			
	β	SE	ST β	Pr > t *	β	SE	ST β	Pr > t *	β	SE	ST β	Pr > t *	β	SE	ST β	Pr > t *
Medial orbitofrontal	19.73	85.13	0.017	0.817	305.26	168.87	0.257	0.071	204.26	122.46	0.172	0.096	22.73	112.31	0.019	0.834
Lateral orbitofrontal	-39.07	91.39	-0.029	0.669	40.36	181.80	0.030	0.824	156.89	131.63	0.116	0.234	152.22	120.44	0.112	0.207
Rostral anterior cingulate	-132.64	55.82	-0.183	0.018	164.69	111.34	0.227	0.140	69.20	80.80	0.095	0.392	-94.05	73.89	-0.129	0.203
Caudal anterior cingulate	-29.68	50.64	-0.051	0.558	31.88	100.74	0.054	0.752	68.74	72.98	0.117	0.347	-87.00	66.74	-0.148	0.193
Hippocampus	-1.58	66.77	-0.002	0.981	-302.22	132.23	-0.338	0.023	-65.49	96.23	-0.073	0.496	-207.66	87.68	-0.232	0.018

Covariate	Low education level (≤ 5 years)				Antidepressant use				Head injury				Cardiovascular ischemic pathologies			
	β	SE	ST β	Pr > t *	β	SE	ST β	Pr > t *	β	SE	ST β	Pr > t *	β	SE	ST β	Pr > t *
Amygdala	-2.66	29.39	-0.007	0.928	-15.22	58.45	-0.037	0.795	-6.87	42.37	-0.017	0.871	8.13	38.77	0.020	0.834
Insula	-47.49	96.58	-0.032	0.623	145.11	192.04	0.099	0.450	-8.18	139.27	-0.006	0.953	55.59	127.42	0.038	0.663
Thalamus	-27.14	86.09	-0.022	0.753	-190.57	171.06	-0.151	0.266	-198.76	123.86	-0.158	0.109	-178.21	113.35	-0.142	0.116
Ventral diencephalon	-14.26	56.81	-0.016	0.802	-61.05	112.96	-0.068	0.589	-126.73	81.74	-0.142	0.122	-82.67	74.87	-0.093	0.270
Caudate nucleus	-174.43	103.62	-0.149	0.093	112.70	206.53	0.096	0.585	90.99	149.70	0.078	0.543	480.79	135.62	0.410	0.0004
Putamen	-208.49	104.03	-0.167	0.045	-161.68	207.49	-0.129	0.436	116.48	150.40	0.093	0.439	45.04	137.68	0.036	0.744
Nucleus accumbens	1.12	14.15	0.006	0.937	-18.85	28.13	-0.105	0.503	-13.67	20.39	-0.076	0.503	-43.86	18.58	-0.245	0.019
Pallidum	-12.08	32.07	-0.029	0.706	50.09	63.75	0.121	0.432	2.95	46.24	0.007	0.949	-27.76	42.29	-0.067	0.512
Cuneus	-111.61	59.55	-0.142	0.061	81.48	118.74	0.103	0.493	-16.40	86.11	-0.021	0.849	79.74	78.73	0.101	0.311
Pericalcarine	-43.89	56.33	-0.064	0.436	50.10	112.08	0.074	0.655	47.00	81.23	0.069	0.563	112.09	74.21	0.165	0.131
Lingual	-203.10	133.20	-0.116	0.128	13.63	265.44	0.008	0.959	127.75	192.34	0.073	0.507	-140.00	175.97	-0.080	0.427

β = regression coefficient estimated by multivariate linear regression; SE = standard error; ST β = standardized regression coefficient (computed by dividing the original estimates by the sample standard deviation of the ROI volume).

*Adjusted for age, sex, and total brain volume.

Table S3: Association of subsegmental brain region volumes with past major depressive disorder among 569 participants*

	No lifetime MDD (n=431)		Lifetime MDD (n=138)		<i>p</i> ‡
	Mean†	SD	Mean†	SD	
Rostral anterior cingulate	3350.62	29.35	3431.81	52.75	0.184
Insula	11968.72	50.46	11738.44	90.70	0.028
Thalamus	11831.79	44.75	11600.21	80.44	0.013
Ventral diencephalon	6808.89	29.58	6639.74	53.16	0.006
Putamen	9470.14	54.52	9250.33	97.99	0.053
Nucleus accumbens	999.18	7.35	970.77	13.21	0.063
Pallidum	2985.99	16.54	2885.81	29.74	0.004
Pericalcarine	3416.70	29.39	3555.78	52.82	0.023

Lingual	10731.67	69.51	11098.32	124.93	0.011
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MDD = major depressive disorder; SD = standard deviation.

*Excluding 41 participants with current MDD or taking antidepressants.

†Mean (SD) values expressed as mm³ adjusted for age, sex, and total brain volume.

‡Raw p-values.

Table S4: Association between ROIs and lifetime major depressive episode as a function of age at first episode

	No Lifetime MDE (n=448)		First MDE < 50 yrs (n=91)		First MDE ≥ 50 yrs (n=70)		<i>p</i> ‡
	Mean†	SD	Mean†	SD	Mean†	SD	
Rostral anterior cingulate	3349.00	28.35	3401.15	64.07	3541.18	72.00	0.045*
Insula	11957.35	48.83	11772.02	110.38	11657.00	124.05	0.042
Thalamus	11808.36	43.51	11564.14	98.34	11597.12	110.51	0.030

Appendix 1 to Ancelin ML, Carriere L, Artero S, et al. Lifetime major depression and grey matter volume. J Psychiatry Neurosci 2018.

DOI: 10.1503/jpn.180026

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Ventral diencephalon	6796.51	28.66	6608.33	64.79	6649.31	72.81	0.011**
Putamen	9455.09	52.81	9200.91	119.37	9226.88	134.15	0.071
Nucleus accumbens	997.67	7.15	954.48	16.16	968.25	18.16	0.030**
Pallidum	2984.24	16.20	2900.17	36.61	2886.44	41.14	0.020
Pericalcarine	3405.81	28.42	3517.80	64.24	3598.43	72.20	0.024*
Lingual	10717.52	67.45	10864.28	152.47	11162.62	171.35	0.050*

MDE = major depressive episode; SD = standard deviation.

†Mean (SD) values expressed as mm³ and adjusted for age, sex, and total brain volume.

‡Global raw p-values when comparing early (1), late (2) onset and no lifetime MDE (0); significant 2 by 2 comparisons (Bonferroni-adjusted p-value, <0.05): *2 vs. 0, **1 vs. 0.