**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

<table>
<thead>
<tr>
<th>Region</th>
<th>No lifetime MDD (n=448)</th>
<th>Lifetime MDD (n=162)</th>
<th>p†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean*</td>
<td>SD</td>
<td>Mean*</td>
</tr>
<tr>
<td>Rostral anterior cingulate</td>
<td>3364.37</td>
<td>72.64</td>
<td>3471.48</td>
</tr>
<tr>
<td>Insula</td>
<td>12053.26</td>
<td>125.78</td>
<td>11813.70</td>
</tr>
<tr>
<td>Thalamus</td>
<td>11597.33</td>
<td>111.61</td>
<td>11381.19</td>
</tr>
<tr>
<td>Ventral diencephalon</td>
<td>6704.75</td>
<td>73.67</td>
<td>6540.86</td>
</tr>
<tr>
<td>Putamen</td>
<td>9409.72</td>
<td>135.46</td>
<td>9173.56</td>
</tr>
<tr>
<td>Nucleus accumbens</td>
<td>970.78</td>
<td>18.34</td>
<td>935.73</td>
</tr>
<tr>
<td>Pallidum</td>
<td>3003.19</td>
<td>41.68</td>
<td>2911.07</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th></th>
<th>Pericalcarine</th>
<th>Lingual</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3462.15</td>
<td>3601.43</td>
</tr>
<tr>
<td></td>
<td>73.24</td>
<td>79.09</td>
</tr>
<tr>
<td></td>
<td>0.015</td>
<td>0.044</td>
</tr>
</tbody>
</table>

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**

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Low education level (≤ 5 years)</th>
<th>Antidepressant use</th>
<th>Head injury</th>
<th>Cardiovascular ischemic pathologies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β</td>
<td>SE</td>
<td>STβ</td>
<td>Pr &gt;</td>
</tr>
<tr>
<td>Medial orbitofrontal</td>
<td>19.73</td>
<td>85.13</td>
<td>0.017</td>
<td>0.817</td>
</tr>
<tr>
<td>Lateral orbitofrontal</td>
<td>-39.07</td>
<td>91.39</td>
<td>-0.029</td>
<td>0.669</td>
</tr>
<tr>
<td>Rostral anterior cingulate</td>
<td>-132.64</td>
<td>55.82</td>
<td>-0.183</td>
<td>0.018</td>
</tr>
<tr>
<td>Caudal anterior cingulate</td>
<td>-29.68</td>
<td>50.64</td>
<td>-0.051</td>
<td>0.558</td>
</tr>
<tr>
<td>Hippocampus</td>
<td>-1.58</td>
<td>66.77</td>
<td>-0.002</td>
<td>0.981</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Covariate</th>
<th>Low education level (≤ 5 years)</th>
<th>Antidepressant use</th>
<th>Head injury</th>
<th>Cardiovascular ischemic pathologies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β</td>
<td>SE</td>
<td>STβ</td>
<td>Pr &gt;</td>
</tr>
<tr>
<td>Amygdala</td>
<td>-2.66</td>
<td>29.39</td>
<td>-0.007</td>
<td>0.928</td>
</tr>
<tr>
<td>Insula</td>
<td>-47.49</td>
<td>96.58</td>
<td>-0.032</td>
<td>0.623</td>
</tr>
<tr>
<td>Thalamus</td>
<td>-27.14</td>
<td>86.09</td>
<td>-0.022</td>
<td>0.753</td>
</tr>
<tr>
<td>Ventral diencephalon</td>
<td>-14.26</td>
<td>56.81</td>
<td>-0.016</td>
<td>0.802</td>
</tr>
<tr>
<td>Caudate nucleus</td>
<td>-174.43</td>
<td>103.62</td>
<td>-0.149</td>
<td>0.093</td>
</tr>
<tr>
<td>Putamen</td>
<td>-208.49</td>
<td>104.03</td>
<td>-0.167</td>
<td>0.045</td>
</tr>
<tr>
<td>Nucleus accumbens</td>
<td>1.12</td>
<td>14.15</td>
<td>0.006</td>
<td>0.937</td>
</tr>
<tr>
<td>Pallidum</td>
<td>-12.08</td>
<td>32.07</td>
<td>-0.029</td>
<td>0.706</td>
</tr>
<tr>
<td>Cuneus</td>
<td>-111.61</td>
<td>59.55</td>
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<td>0.061</td>
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<td>56.33</td>
<td>-0.064</td>
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<tr>
<td>Lingual</td>
<td>-203.10</td>
<td>133.20</td>
<td>-0.116</td>
<td>0.128</td>
</tr>
</tbody>
</table>

β = regression coefficient estimated by multivariate linear regression; SE = standard error; STβ = 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*

<table>
<thead>
<tr>
<th>Brain Region</th>
<th>No lifetime MDD (n=431)</th>
<th>Lifetime MDD (n=138)</th>
<th>p‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean†</td>
<td>SD</td>
<td>Mean†</td>
</tr>
<tr>
<td>Rostral anterior cingulate</td>
<td>3350.62</td>
<td>29.35</td>
<td>3431.81</td>
</tr>
<tr>
<td>Insula</td>
<td>11968.72</td>
<td>50.46</td>
<td>11738.44</td>
</tr>
<tr>
<td>Thalamus</td>
<td>11831.79</td>
<td>44.75</td>
<td>11600.21</td>
</tr>
<tr>
<td>Ventral diencephalon</td>
<td>6808.89</td>
<td>29.58</td>
<td>6639.74</td>
</tr>
<tr>
<td>Putamen</td>
<td>9470.14</td>
<td>54.52</td>
<td>9250.33</td>
</tr>
<tr>
<td>Nucleus accumbens</td>
<td>999.18</td>
<td>7.35</td>
<td>970.77</td>
</tr>
<tr>
<td>Pallidum</td>
<td>2985.99</td>
<td>16.54</td>
<td>2885.81</td>
</tr>
<tr>
<td>Pericalcarine</td>
<td>3416.70</td>
<td>29.39</td>
<td>3555.78</td>
</tr>
</tbody>
</table>

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Lingual 10731.67 69.51 11098.32 124.93 0.011

MDD = major depressive disorder; SD = standard deviation.

*Excluding 41 participants with current MDD or taking antidepressants.

†Mean (SD) values expressed as mm$^3$ 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

<table>
<thead>
<tr>
<th></th>
<th>No Lifetime MDE (n=448)</th>
<th>First MDE &lt; 50 yrs (n=91)</th>
<th>First MDE ≥ 50 yrs (n=70)</th>
<th>p‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean†</td>
<td>SD</td>
<td>Mean†</td>
<td>SD</td>
</tr>
<tr>
<td>Rostral anterior cingulate</td>
<td>3349.00</td>
<td>28.35</td>
<td>3401.15</td>
<td>64.07</td>
</tr>
<tr>
<td>Insula</td>
<td>11957.35</td>
<td>48.83</td>
<td>11772.02</td>
<td>110.38</td>
</tr>
<tr>
<td>Thalamus</td>
<td>11808.36</td>
<td>43.51</td>
<td>11564.14</td>
<td>98.34</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Brain Structure</th>
<th>MDE</th>
<th>SD</th>
<th>Late MDE</th>
<th>SD</th>
<th>No MDE</th>
<th>SD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventral diencephalon</td>
<td>6796.51</td>
<td>28.66</td>
<td>6608.33</td>
<td>64.79</td>
<td>6649.31</td>
<td>72.81</td>
<td>0.011**</td>
</tr>
<tr>
<td>Putamen</td>
<td>9455.09</td>
<td>52.81</td>
<td>9200.91</td>
<td>119.37</td>
<td>9226.88</td>
<td>134.15</td>
<td>0.071</td>
</tr>
<tr>
<td>Nucleus accumbens</td>
<td>997.67</td>
<td>7.15</td>
<td>954.48</td>
<td>16.16</td>
<td>968.25</td>
<td>18.16</td>
<td>0.030**</td>
</tr>
<tr>
<td>Pallidum</td>
<td>2984.24</td>
<td>16.20</td>
<td>2900.17</td>
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<td>2886.44</td>
<td>41.14</td>
<td>0.020</td>
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<tr>
<td>Pericalcarine</td>
<td>3405.81</td>
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<td>3598.43</td>
<td>72.20</td>
<td>0.024*</td>
</tr>
<tr>
<td>Lingual</td>
<td>10717.52</td>
<td>67.45</td>
<td>10864.28</td>
<td>152.47</td>
<td>11162.62</td>
<td>171.35</td>
<td>0.050*</td>
</tr>
</tbody>
</table>

MDE = major depressive episode; SD = standard deviation.

‡Mean (SD) values expressed as mm$^3$ 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.