Elevated body weight modulates subcortical volume change and associated clinical response following electroconvulsive therapy

Opel, Nils; Narr, Katherine L.; Abbott, Christopher; Argyelan, Miklos; Espinoza, Randall; Emsell, Louise; Bouckaert, Filip; Sienaert, Pascal; Vandenbulcke, Mathieu; Nordanskog, Pia

Total number of authors: 31

Published in:
Journal of Psychiatry and Neuroscience

Link to article, DOI:
10.1503/jpn.200176

Publication date:
2021

Document Version
Publisher's PDF, also known as Version of record

Link back to DTU Orbit

Citation (APA):
Elevated body weight modulates subcortical volume change and associated clinical response following electroconvulsive therapy

Nils Opel, MD; Katherine L. Narr, PhD; Christopher Abbott, MD; Miklos Argyelan, MD; Randall Espinoza, MD, MPH; Louise Emsell, PhD; Filip Bouckaert, MD, PhD; Pascal Sienaert, MD, PhD; Mathieu Vandenbulcke, MD, PhD; Pia Nordanskog, MD, PhD; Jonathan Repple, MD; Erhan Kavakbası, MD; Martin B. Jorgensen, MD, DMSc; Olaf B. Paulson, MD, DMSc; Lars G. Hanson, PhD; Annemieke Dols, MD, PhD; Eric van Exel, MD, PhD; Mardien L. Oudega, MD, PhD; Akihiro Takamiya, MD; Taishiro Kishimoto, MD, PhD; Olga Therese Ousdal, MD, PhD; Jan Haavik, MD, PhD; Åsa Hammar, PhD; Ketil Joachim Oedegaard, MD, PhD; Ute Kessler, MD, PhD; Hauke Bartsch, PhD; Anders M. Dale, PhD; Bernhard T. Baune, MD, PhD; Udo Dannlowski, MD, PhD; Leif Oltedal, MD, PhD; Ronny Redlich, PhD

Introduction

Electroconvulsive therapy (ECT) is the most effective antidepressant option for the treatment of major depression, but the neurobiological underpinnings of treatment response to ECT remain poorly understood. Convergent evidence from neuroimaging research has pointed to an increase in grey matter volume following ECT treatment. Although most structural MRI research into ECT has focused on increases in hippocampal and amygdalar volume with ECT, several recent studies have pointed to increases in subcortical grey matter volume in other structures, including the caudate, putamen and thalamus. A recent report from the Global ECT-MRI Research Collaboration (GEMRIC) consortium suggested cortical and subcortical volume changes following ECT, with stronger...
Elevated body weight modulates subcortical volume change

Although changes in subcortical grey matter volume have been shown consistently following ECT, the relationship between change in grey matter volume and clinical response to ECT remains unclear. The extant literature on associations between neurostructural and clinical responses to ECT has revealed diverging results; some studies have reported associations between increased grey matter volume and depressive symptoms, and other studies did not find evidence for such a relationship, particularly in the hippocampus. Such disparities in terms of the presence and anatomic specificity of such relationships raise the question of whether undiscovered factors might modulate the association between ECT, change in grey matter volume and clinical response in major depression.

Emerging evidence suggests that obesity, a frequent somatic comorbidity of affective disorders, is associated with clinical and neurobiological correlates of major depression. More precisely, obesity and an elevated body mass index (BMI) have been associated with increased risk for the future development of major depression, poorer clinical response to antidepressant pharmacotherapy and a more chronic course of the disorder. Cross-sectional and longitudinal studies have consistently demonstrated that increased BMI and obesity are associated with cortical and subcortical brain structural abnormalities. Obesity has frequently been associated with reduced grey matter in similar subcortical structures for which ECT volume effects have been described, including the amygdala, hippocampus, thalamus, caudate nucleus and putamen. It has been suggested that obesity-related chronic low-grade inflammation induces neurotoxicity via kynurenine pathway activation and potentially via hypothalamic–pituitary–adrenal axis deviation, and might therefore constitute a key mechanism behind the brain structural abnormalities frequently observed in obesity.

Importantly, obesity-related brain structural abnormalities have been observed both in healthy people and people with depression, and these effects have also been associated with disease chronicity and previous exposure to antidepressant medication in patients with depression. Further, a recent longitudinal imaging study supported a prospective association between worse course of illness, weight gain and grey matter volume reductions in people with an affective disorder. In summary, previous research has reported associations between BMI, clinical outcomes and brain structure in people with affective disorders, and the most consistent evidence is for overlapping effects of obesity and ECT on subcortical grey matter volume. Therefore, it appeared relevant to investigate whether BMI modulates subcortical brain structural changes and clinical response following treatment with ECT. To the best of our knowledge, no study has explicitly addressed this research question to date. We aimed to investigate associations between baseline BMI, change in subcortical grey matter volume and clinical response to ECT in patients with depression. We hypothesized that increased BMI would reduce the extent of the increase in subcortical grey matter volume following ECT; be associated with poorer clinical response to ECT; and moderate the association between change in subcortical grey matter and clinical response to ECT.

Methods

Participants

The present study included data from 10 sites and 223 patients experiencing a major depressive episode (n = 200 patients with major depressive disorder; n = 23 patients with bipolar disorder; 57.8% female; mean age ± standard deviation [SD] = 52.8 ± 16.6 years; mean BMI ± SD = 25.8 ± 6.4 kg/m²) from the GEMRIC consortium for whom BMI and complete structural MRI data were available. Patients were scanned before ECT (within 1 week before the first ECT session) and after ECT completion (typically within 1 to 2 weeks after the final ECT session of the index series). Depressive symptoms were rated using the Montgomery–Åsberg Depression Rating Scale (MADRS). For sites that had used the Hamilton Depression Rating Scale, we used a validated equation to convert those scores to MADRS scores. We assessed depressive symptom change using absolute change in MADRS scores before and after ECT (ΔMADRS).

We categorized baseline body weight status using BMI (kg/m²). Patients were assigned to subgroups based on established BMI cut-offs (normal weight 18.5–25 kg/m², overweight 25–30 kg/m², obese > 30 kg/m², n = 41). Because of our focus on increased BMI in the present study, we did not include patients who were underweight (BMI < 18.5 kg/m², n = 13) in group analyses based on BMI cut-offs.

For a detailed description of ECT parameters separated by site see Oltegal and colleagues. All contributing sites received ethics approval from their local ethics committee or institutional review board. The centralized mega-analysis was approved by the Regional Ethics Committee South-East in Norway (#2018/769).

Image acquisition and postprocessing

In brief, we acquired 3-dimensional T₁-weighted structural images with a minimum resolution of 1.3 mm in any dimension at both time points using 1.5 T (1 site) or 3 T (9 sites) scanners. Image processing and analysis were performed using a pipeline optimized to increase the statistical power for detecting longitudinal cortical and subcortical anatomic change. The raw Digital Imaging and Communications in Medicine (DICOM) images and clinical/demographic information for individual patients and controls were transferred to a centralized data portal for common analyses. Images were corrected for distortions caused by scanner-specific nonlinear gradient warp, registered to a common atlas space and resampled to an isotropic 1 mm³ spatial resolution. Subcortical segmentations were performed using FreeSurfer version 5.3. Next, we used Quarc for unbiased estimates of volume change from pre- to post-treatment in all regions of interest, as previously described. Analyses of subcortical
grey matter volume for the present study included the left and right thalamus proper, the caudate, the putamen, the pallidum, the hippocampus, the amygdala and the nucleus accumbens. We ensured the quality of the segmentation by using procedures adapted from the Enhancing Neuro Imaging Genetics through Meta-Analysis (ENIGMA) consortium (http://enigma.usc.edu/). For a detailed description of MRI parameters separated by site and the GEMRIC image processing pipeline, see previous GEMRIC publications.

Statistical analyses

We performed statistical analyses in SPSS (version 25; IBM) to test the 3 formulated hypotheses by conducting 1 main analysis (1 statistical model) per hypothesis to address the following. We explored associations between baseline BMI and change in subcortical grey matter volume during ECT. Because no regionally specific hypothesis had been formulated, we applied a multivariate linear model (multivariate analysis of covariance) as the main analysis to test our hypothesis that simultaneously included grey matter volume change in all 14 subcortical regions as dependent variables. We included BMI as a predictor and age, sex, site and baseline total intracranial volume further confirmed our statistical grey matter volume that accounted for regional subcortical associations between BMI and changes in subcortical grey matter volume during ECT. (grey matter volume change, mean ± SD; left thalamus 0.0052 ± 0.0108; left putamen 0.0137 ± 0.0121). The overweight group showed grey matter volume increases that were 43.3% and 49.6%, respectively, of the increases found in the normal-weight group (grey matter volume change, mean ± SD; left thalamus 0.0068 ± 0.0106; left putamen 0.0120 ± 0.0116; Figure 2). Supplementary analyses also revealed an association between BMI and baseline subcortical grey matter volume that was driven mainly by positive associations between BMI and baseline grey matter volume in the bilateral putamen, amygdala and thalamus (Appendix 1). Additional sensitivity analyses of associations between BMI and changes in subcortical grey matter volume that accounted for regional subcortical grey matter volume at baseline further confirmed our main findings (Appendix 1).

Results

Participants

The clinical and sociodemographic characteristics of the total sample, as well as information about ECT electrode placement (right unilateral, bifrontotemporal and bitemporal) and medication, are detailed in Table 1.
Elevated body weight modulates subcortical volume change

Table 1: GEMRIC sample, clinical and sociodemographic characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value*</th>
<th>Participants†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>52.83 ± 16.30</td>
<td>223</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>25.80 ± 5.46</td>
<td>223</td>
</tr>
<tr>
<td>Montgomery–Åsberg Depression Rating Scale</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline score</td>
<td>34.54 ± 8.25</td>
<td>221</td>
</tr>
<tr>
<td>Post-treatment score</td>
<td>15.44 ± 11.55</td>
<td>219</td>
</tr>
<tr>
<td>Change in score</td>
<td>19.24 ± 12.96</td>
<td>218</td>
</tr>
<tr>
<td>% Change</td>
<td>54.50 ± 32.88</td>
<td>218</td>
</tr>
<tr>
<td>Age at first depression treatment, yr</td>
<td>36.64 ± 15.63</td>
<td>80</td>
</tr>
<tr>
<td>Time since first depression treatment, yr</td>
<td>11.09 ± 11.65</td>
<td>80</td>
</tr>
<tr>
<td>No. of depressive episodes</td>
<td>6.08 ± 11.77</td>
<td>130</td>
</tr>
<tr>
<td>Duration of current episode, wk</td>
<td>16.25 ± 24.80</td>
<td>139</td>
</tr>
<tr>
<td>No. of ECT treatments</td>
<td>11.42 ± 4.83</td>
<td>220</td>
</tr>
<tr>
<td>ECT electrode placement</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right unilateral only</td>
<td>137</td>
<td>—</td>
</tr>
<tr>
<td>Right unilateral ≥ bitemporal</td>
<td>31</td>
<td>—</td>
</tr>
<tr>
<td>Right unilateral ≥ bifrontotemporal</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>Bitemporal only</td>
<td>32</td>
<td>—</td>
</tr>
<tr>
<td>Bitemporal ≥ right unilateral</td>
<td>2</td>
<td>—</td>
</tr>
<tr>
<td>Bifrontotemporal only</td>
<td>20</td>
<td>—</td>
</tr>
<tr>
<td>Medication</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antidepressant</td>
<td>104</td>
<td>—</td>
</tr>
<tr>
<td>Selective serotonin reuptake inhibitor</td>
<td>33</td>
<td>—</td>
</tr>
<tr>
<td>Serotonin–norepinephrine reuptake inhibitor</td>
<td>52</td>
<td>—</td>
</tr>
<tr>
<td>Tricyclic antidepressant</td>
<td>22</td>
<td>—</td>
</tr>
<tr>
<td>Antipsychotic</td>
<td>87</td>
<td>—</td>
</tr>
<tr>
<td>Mood stabilizer</td>
<td>13</td>
<td>—</td>
</tr>
<tr>
<td>Lithium</td>
<td>11</td>
<td>—</td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>51</td>
<td>—</td>
</tr>
</tbody>
</table>

ECT = electroconvulsive therapy; GEMRIC = Global ECT-MRI Research Collaboration.
*Data are presented as mean ± standard deviation or n.
†The number of participants varied because data were missing for some variables.

Figure 1: Scatter plots depict the association between body mass index and change in subcortical grey matter volume (%) following treatment with electroconvulsive therapy. (A) Left thalamus ($r = -0.283, p < 0.001$). (B) Left putamen ($r = -0.281, p < 0.001$).
although the slopes indicated less absolute change in MADRS scores before and after ECT with higher BMI ($\beta = -0.094$, $p = 0.17$, $n = 218$). We found no significant association between BMI and absolute change in MADRS score in regression analyses controlling for baseline MADRS score ($\beta = -0.028$, $p = 0.64$, $n = 218$).

Clinical response was defined as symptom reduction of 50% or greater according to the MADRS. Mean BMI was greater in nonresponders ($n = 72$; BMI [mean ± SD] = 26.25 ± 6.17 kg/m²) than in responders ($n = 134$; BMI = 25.72 ± 5.25 kg/m²), but these differences were also not significant ($t_{1,204} = 0.646$, $p = 0.52$). At near-threshold significance, higher BMI was reflective of lower baseline depressive symptoms before ECT according to MADRS sum score ($\beta = -0.130$, $p = 0.054$, $n = 221$) and with a higher number of lifetime depressive episodes ($\beta = 0.170$, $p = 0.053$, $n = 130$).

Similarly, we observed no significant associations between BMI and change in the MADRS score ($F_{1,217} = 1.531$, $p = 0.22$) or clinical response ($F_{1,215} = 0.425$, $p = 0.52$) in linear models that also controlled for the presence and type of antidepressant medications.

We observed no significant association between BMI and total number of ECT sessions; slopes suggested fewer ECT sessions in patients with a higher BMI ($\beta = -0.091$, $p = 0.18$, $n = 223$).

Role of body weight in the association between grey matter volume change and depressive symptoms

The multivariate model yielded a significant BMI × ΔMADRS interaction effect on change in subcortical grey matter volume (Wilks $\lambda = 0.859$, $F_{14,167} = 1.964$, $p = 0.023$, $\eta^2 = 0.141$), but no significant main effect of BMI on change in subcortical grey matter volume (Wilks $\lambda = 0.946$, $F_{14,167} = 0.687$, $p = 0.79$, $\eta^2 = 0.054$).

Again, we observed the same pattern of results in additional sensitivity analyses controlling for the total number of ECT sessions, baseline MADRS score, antidepressant medication use and ECT electrode placement (Appendix 1).

Univariate follow-up analyses indicated that the interaction was driven primarily by BMI × ΔMADRS effects in the left and right thalamus (left: $F_{1,180} = 6.736$, $p = 0.010$, $\eta^2 = 0.036$; right: $F_{1,180} = 6.682$, $p = 0.011$, $\eta^2 = 0.036$; Appendix 1, Table S3). To further delineate the differential association between change in subcortical grey matter volume and clinical response, we conducted correlational analyses in subgroups stratified by body weight. Our findings suggested that the observed interaction was driven by positive associations between change in subcortical grey matter volume and clinical response in the normal-weight group (left thalamus: $r = 0.255$, $p = 0.017$; right thalamus: $r = 0.207$, $p = 0.055$), and negative associations between change in grey matter volume and ΔMADRS emerged in both the overweight group (left thalamus: $r = -0.153$, $p = 0.23$; right thalamus: $r = -0.153$, $p = 0.22$) and the obese group (left thalamus: $r = -0.300$, $p = 0.08$; right thalamus: $r = -0.362$, $p = 0.033$; Figure 3).

Discussion

The present study provides the first evidence for the relevance of BMI as a moderating factor of brain structural changes following ECT and their association with treatment outcome in patients with depression. We demonstrate that increased body weight modulates increases in subcortical grey volume change and depressive symptoms.
Elevated body weight modulates subcortical volume change

J Psychiatry Neurosci 2021;46(4)

Figure 3: Interaction effect of change in depressive symptoms (assessed by change in MADRS sum score) and body weight on change in subcortical grey matter volume in the left thalamus (%). Subgroups were stratified by body mass index (normal weight 18.5–25 kg/m²; overweight 25–30 kg/m²; obese > 30 kg/m²). MADRS = Montgomery–Åsberg Depression Rating Scale.
ECT research — was not significantly associated with BMI in our regional analyses, and thus appears to be unaffected by body weight status before ECT.

Because higher BMI was associated at a trend level with fewer baseline depressive symptoms, it appears relevant to consider that differences in depressive symptom profiles between patients might have contributed to the present findings, although sensitivity analyses controlling for overall baseline symptom load confirmed our findings.

Our second main finding was that body weight significantly moderated the association between change in subcortical grey matter volume and clinical symptom improvement. In the present study, we found a positive association between change in grey matter volume in the thalamus and clinical response in patients with normal weight, and an inverse association in patients who were overweight and obese. This finding adds to the notion that body weight critically interferes with brain structural changes during ECT and suggests a link between body weight, brain structural changes and clinical outcomes following ECT. As outlined in the introduction, the published literature on the associations between change in grey matter volume and clinical response to ECT is inconsistent. Our findings might help to explain this inconsistency. Because none of the previous imaging ECT studies accounted for BMI, previous reports on associations between change in grey matter volume and clinical response to ECT may have been biased by the differential distribution of BMI across study samples. Future ECT studies should account for and explicitly test body-weight-related associations with clinical and neurobiological changes following ECT.

Considering the complex etiological background of obesity involving multiple interrelated genetic and environmental factors, our finding of a body-weight-dependent relationship between increases in subcortical grey matter volume and clinical response to ECT points to the importance of considering environmental and genetic factors that could modify both neural and clinical response to ECT to expand our understanding of the neurobiological mechanisms of ECT. Furthermore, the present study raises important questions about the potential mechanisms underlying the association between BMI, brain structural changes and clinical response during ECT. It has frequently been suggested that low-grade inflammation, hypothalamic–pituitary–adrenal axis deviation and impaired neuroendocrine–crine regulation represent shared biological mechanisms of obesity and major depression.

More precisely, evidence from previous research suggests that BMI-related immunometabolic deviation such as a shift in circulating inflammatory cytokines, fatty acids and immune cells could induce central inflammation, leading to synaptic remodelling and neurodegenerative processes that could represent one explanation for our finding of a lower BMI-related increase in subcortical grey matter volume following ECT. Furthermore, the relevance of imbalances in the kynurenine pathway, leading to neurotoxic effects, is well established in both obesity and depression, and represents another promising candidate mechanism behind the mutual associations between body weight, depressive phenotype and brain structure. The latter notion is further supported by reports demonstrating associations between inflammation, kynurenine pathway metabolites and brain structural volume decline in patients with depression and schizophrenia. Furthermore, preliminary evidence suggests that ECT might interfere with serum concentrations of kynurenine pathway metabolites. Future ECT research should explore whether these mechanisms might explain the pattern of results observed in the present work.

We did not observe a significant association between increased BMI and overall poorer clinical response following ECT in patients with depression. Future research on ECT should explore the potential predictive relevance of body weight in patients with depression in other study samples before firm conclusions can be drawn.

**Limitations**

The present study had strengths and limitations. Strengths included the relatively large sample size compared with previous ECT studies. Limitations included the lack of information about weight change following ECT. All of our results were based on baseline BMI values, so we were unable to study changes in body weight during ECT and their potential associations with clinical outcomes and change in grey matter volume following ECT. Furthermore, the present data set did not allow us to differentiate between depression subtypes that might be relevant in studying BMI-related neurobiological alterations. Because recent studies have suggested that the presence and extent of obesity-related biometabolic alterations in depression might depend on the presence of atypical depressive symptoms, future studies should aim to clarify the potential associations between distinct depressive subtypes and change in grey matter volume, as well as response to ECT.

Moreover, the absence of further metabolic or anthropometric measures such as waist-to-hip ratio, body fat and metabolic and inflammatory serum markers at baseline and follow-up should be acknowledged. Cardiovascular factors closely related to increased BMI—such as insulin resistance, elevated HbA1c, physical endurance and cardiopulmonary fitness—have been associated with brain structural abnormalities and might have contributed to the findings of the present study. Because of our design, causality could not be inferred, and it is important to consider that further undiscovered factors might have contributed to the changes we observed in subcortical grey matter volume. Future studies should consider including such data to further delineate the mechanisms underlying the associations we have reported. Future research might also investigate whether altered electric field properties in obese patients could contribute to the reported changes in grey matter volume following ECT. Finally, future work should consider analyzing imaging measures that were beyond the scope of the present study, such as subcortical shape, cortical thickness, surface or gyrification change following ECT in relation to BMI.

Because subgroup analyses excluding patients who were underweight confirmed our main findings, we assume that our
Elevated body weight modulates subcortical volume change

Conclusion

The present study sheds light on the relevance of body weight as a relevant factor that modulates brain structural changes during ECT and their association with treatment outcome. Future research on ECT should account for body weight and aim to further unravel the neurobiological mechanisms and clinical implications of this finding.

Affiliations: From the Institute for Translational Psychiatry, University of Münster, Münster, Germany (Opel, Repple, Dannlowski, Redlich); Department of Psychiatry and Psychotherapy, University of Münster, Münster, Germany (Kavakbasi, Baune); the Departments of Neurology, Psychiatry, and Biobehavioral Sciences, University of California, Los Angeles, CA (Narr); the Department of Psychiatry, University of New Mexico School of Medicine, Albuquerque, NM (Abbott); the Institute of Behavioral Science, Feinstein Institutes for Medical Research, Manhasset, NY (Argyelan); the Department of Psychiatry, The Zucker Hillside Hospital, Glen Oaks, NY (Argyelan); the Department of Psychiatry, University of California, Los Angeles (Espinoza); the Department of Geriatric Psychiatry, University Psychiatric Center KU Leuven, KU Leuven, Leuven, Belgium (Emsell, Vandenbulcke); the KU Leuven, Leuven Brain Institute, Department of Neurosciences, Neuropsychiatry & Geriatric Psychiatry, University Psychiatric Center KU Leuven, Belgium (Bouckaert); the Academic Center for ECT and Neurostimulation (AcCENT), University Psychiatric Center (UPC)–KU Leuven, Kontenberg, Belgium (Sienaert); the Center for Social and Affective Neuroscience, Department of Clinical and Experimental Medicine, Linköping University, Linköping, Sweden (Nordanskg); the Psychiatric Center Copenhagen (Rigshospitalet), Mental Health Services of the Capital Region of Denmark, Copenhagen, Denmark (Jørgensen); the Neurobiology Research Unit, Rigshospitalet and University of Copenhagen, Denmark (Paulson); the Danish Research Centre for Magnetic Resonance, Centre for Functional and Diagnostic Imaging and Research, Copenhagen University Hospital Hvidovre, Denmark (Hanson); the Center for Magnetic Resonance, Department of Health Technology, Technical University of Denmark, Kgs. Lyngby, Denmark (Hanson); the GGZ in Geest Specialized Mental Health Care, Amsterdam, the Netherlands (Dols, Van Exel, Oudega); the Amsterdam UMC, Vrije Universiteit Amsterdam, Psychiatry, Amsterdam Neuroscience, Amsterdam, the Netherlands (Dols, van Exel, Oudega); the Department of Neuropsychiatry, Keio University School of Medicine, Tokyo, Japan (Takamiya, Kishimoto); the Department of Radiology, Haukeland University Hospital, Bergen, Norway (Ousdal); the Department of Biomedicine, University of Bergen, Bergen, Norway (Haavik); the Division of Psychiatry, Haukeland University Hospital, Bergen, Norway (Haavik, Hammar); the Department of Biological and Medical Psychology, University of Bergen, Bergen, Norway (Hammar); the NORMENT, Department of Psychiatry, Haukeland University Hospital, Bergen, Norway (Oedegaard, Kessler, Olgaard); the Department of Radiology, University of California, San Diego, La Jolla, California (Bartsch); the Mohn Medical Imaging and Visualization Centre, Department of Radiology, Haukeland University Hospital, Bergen, Norway (Bartsch, Olgaard); the Department of Radiology, Neurosciences, and Psychiatry, University of California, San Diego (Dale); the Center for Multimodal Imaging and Genetics, University of California, San Diego, La Jolla, California (Dale); the Department of Psychiatry, University of Melbourne, Melbourne, Australia (Baune); the The Florey Institute of Neuroscience and Mental Health, The University of Melbourne, Parkville, VIC, Australia (Baune); and the Department of Psychology, University of Halle, Halle, Germany (Redlich).

Funding: The Münster cohort was funded by the German Research Foundation (DFG, grant FOR2107 DA1151-5/1 and DA1151-5/2 to UD; SFB-TRR58, Projects C09 and Z10 to UD) and the Interdisciplinary Center for Clinical Research (IZKF) of the medical faculty of Münster (grant Dan3/012/17 to UD and SEED 11/19 to NO). For the UCLA site, work was supported by NIH/NIMH grants U01 MH110008, and R01 MH092301. For the UNM site, work was supported by NIH/NIMH Grants U01 MH111826 MJ, OP and LH (Copenhagen) report funding from the Lundbeck Foundation.

Competing interests: A. Dale reports that he was a founder of and holds equity in CorTechs Labs, Inc., and serves on its scientific advisory board; he is a member of the scientific advisory boards of Human Longevity, Inc., the Mohn Medical Imaging and Visualization Centre; he receives funding through research grants from GE Healthcare to UCSF. The terms of these arrangements have been reviewed by and approved by the University of California, San Diego in accordance with its conflict of interest policies. No other competing interests declared.


Content licence: This is an Open Access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY-NC-ND 4.0) licence, which permits use, distribution and reproduction in any medium, provided that the original publication is properly cited, the use is noncommercial (i.e., research or educational use), and no modifications or adaptations are made. See: https://creativecommons.org/licenses/by-nc-nd/4.0/

References

7. Wade BSC, Joshi SH, Njau S, et al. Effect of electroconvulsive ther-
  apy on striat al morphometry in major depressive disorder. Neuro-
  psychopharmacology 2016;41:2481-91.
8. Ousdal OT, Argylen M, Narr KL, et al. Brain changes induced by 
  electroconvulsive therapy are broadly distributed. Biol Psychiatry 
  2020;87:451-61.
  right unilateral versus bitemporal electroconvulsive therapy for 
  treatment-resistant depression. J Neuropsychiatry Clin Neurosci 
  2019;31:152-8.
 changes in amygdala nuclei, hippocampal subfields and cortical 
 thickness following electroconvulsive therapy in treatment-resistant 
11. Ghy G, Videbech P. Electroconvulsive therapy increases brain vol-
  ume in major depression: a systematic review and meta-analysis. 
12. Jorgensen A, Magnusson P, Hanson LG, et al. Regional brain vol-
  umes, diffusivity, and metabolite changes after electroconvulsive 
13. Opel N, Redlich R, Grotegerd D, et al. Obesity and major depres-
  sion: body-mass index (BMI) is associated with a severe course of 
  disease and specific neurostructural alterations. Psychoneuroen-
14. Luppino FS, de Wit LM, Bouvy PF, et al. Overweight, obesity, and 
  and obesity: evidence of shared biological mechanisms. Mol Psy 
  chiatr 2019;24:18-33.
  malities in obesity: relation to age, genetic risk, and common psy-
  chiatric disorders. Mol Psychiatry 2020 May 28 [Epub ahead of 
17. Kloiber S, Ising M, Reppermund S, et al. Midlife weight and obes-
  ity affect treatment response in major depression. Biol Psychiatry 
18. Driscoll I, Beydoun MA, An Y, et al. Midlife obesity and trajecto-
  ries of brain volume changes in older adults. Hum Brain Mapp 
  2016;38:3023-36.
  gitudinal association of body mass index and brain volume. Hum 
  Brain Mapp 2014;35:75-88.
  matter, body mass index, and waist circumference in healthy 
21. Hamer M, Batty GD. Association of body mass index and waist-to-
  circumference and gray matter volume in 2344 individuals from 
  body mass index in the Framingham heart study reveal distinct 
  is activated in human obesity and shifted toward kynurenine 
  monooxygenase activation. Obesity (Silver Spring) 2015;23:2066-74.
  mammalian brain: when physiology meets pathology. Nat Rev 
  FTO genotype or major depressive disorder, influences brain 
27. Bond DJ, Su W, Honer WG, et al. Weight gain as a predictor of 
  frontal and temporal lobe volume loss in bipolar disorder: a pro-
  Research Collaboration (GEMRIC): establishing a multi-site investi-
  gation of the neural mechanisms underlying response to electro-