## Supplementary Material

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**Supplementary Method 1: Data acquisition and magnetic resonance imaging parameters**

T1-weighted high resolution anatomical images were acquired before the first ECT session (M=11.06 days, SD=18.58 days before ECT onset) and within a few days after the last ECT session (M=3.63 days, SD=4.32 days after ECT cessation) as well as two years later (M=795 days, SD=98.42 days) employing a 3D fast gradient echo sequence ('Turbo Field Echo', TFE), TR=7.4 ms, TE=3.4 ms, FA=9°, 2 signal averages, inversion prepulse every 814.5ms, acquired over a field of view of 256(FH)x204(AP)x160(RL) mm, phase encoding in AP and RL direction, reconstructed to cubic voxels of 0.5x0.5x0.5 mm.

**Supplementary Method 2: ECT-associated changes in suicidality and delusion**

Drawing from the work by Lattuada and colleagues (Lattuada, Serretti, Cusin, Gasperini, & Smeraldi, 1999), we employed three specific items (items 2, 15 and 20) from the HDRS (Hamilton, 1960) to form a subscale for measuring delusion. Additionally, item 3 of the HDRS (Hamilton, 1960) was utilized to evaluate suicidality, following previously established practices in the literature (Kellner et al., 2005). First, paired t-tests were conducted to investigate changes in suicidality and delusion within the ECT group from t0 to t1 and from t1 to t2. Second, score changes were calculated reflecting immediate (t0 vs. t1), delayed (t0 vs. t2) and long-term (t1 vs. t2) changes in delusion and suicidality. Higher change scores were indicative of an increase in either delusion or suicidality, respectively. Spearman's correlation coefficient was used to examine associations of short-term ∆GMVpost-baseline changes with immediate or delayed changes in suicidality and delusion, and of long-term ∆GMVfollow-up-post changes with long-term changes in suicidality and delusion.

**Supplementary Result 1: 3x3 ANOVA on HDRS and BDI scores**

A significant group x time interaction on HDRS scores was found (*F*(4, 136)=16.999, *p*<.001, *ηp2*=.333) resulting from a significant decrease of HDRS scores from t0 to t1 (*MDiff-ECT*=14.118, *MDiff-TAU*=10.879; both *p*<.001) and t0 to t2 (*MDiff-ECT*=13.118, *MDiff-TAU*=12.636;both *p*<.001) in both MDD groups. No significant changes in HDRS scores from t0 to t1 (*MDiff-HC*=-.143; *p*>.99) and to t2 (*MDiff-HC* = -.476;*p=*.702) were found in the HC group. No significant differences were found between t1 and t2 in any group (all *p*≥.416). There was a significant main effect of group (*p*<.001, *ηp2*=.682) with both MDD groups showing significantly higher HDRS scores than the HC group at all time points (all *p*<.001), while the ECT and TAU group did not differ significantly from each other at all time points (all *p*≥.135).

A significant group x time interaction on BDI scores was found (*F*(4, 114)=7.174, *p*<.001, *ηp2*=.201) resulting from a significant decrease of BDI scores from t0 to t1 (*MDiff-ECT*=11.933, *MDiff-TAU*=11.630; both *p*<.001) and t0 to t2 (*MDiff-ECT*=11.267, *MDiff-TAU*=14.111;both *p*<.001) in both MDD groups. No significant changes in BDI scores from t0 to t1 (*MDiff-HC*=1.833; *p*>.99) and to t2 (*MDiff-HC* =.722;*p>*.99) were found in the HC group. No significant differences were found between t1 and t2 in any group (all *p*≥.374). There was a significant main effect of group (*p*<.001, *ηp2*=.592) with both MDD groups showing significantly higher BDI scores than the HC group at all time points (all *p*<.001), while the ECT and TAU group did not differ significantly from each other at all time points (all *p*≥.072).

**Supplementary Result 2: Associations between short-term and long-term grey matter volume change in the ECT group**

Using Spearman's correlation, GMV changes between t0 and t1 were associated with GMV changes between t1 and t2in four clusters of the significant interaction. Analyses revealed significant negative associations between short-term GMV change and long-term GMV change in the ECT group (Cluster 1: *r*=-.598, *p*=.011; Cluster 2: *r*=-.522, *p*=.031; Cluster 3: *r*=-.596, *p*=.012; Cluster 4: *r*=-.809, *p*<.001). This indicates that those with the largest GMV increase following ECT had the strongest GMV decline in the long-term.

**Supplementary Result 3: ECT-associated changes in suicidality and delusion**

Paired t-tests showed a significant decrease of suicidality (Mbaseline=1.471, SDbaseline=.875; Mpost=.529, SDpost=.717) and delusion (Mbaseline=1.020, SDbaseline=.416; Mpost=.412, SDpost=.479) within the ECT group from t0 to t1 (suicidality: *T(16)*=5.191, *p*<.001; delusion: *T(16)*=4.510, *p*<.001). There was no significant change in suicidality (Mpost=.529, SDpost=.717; Mfollow-up=.529, SDfollow-up=.800) or delusion (Mpost=.412, SDpost=.479; Mfollow-up=.392, SDfollow-up=.517) within the ECT group from t1 to t2 (suicidality: *T(16)*=.000, *p*>.999; delusion: *T(16)*=.223, *p*=.826).

There were no significant associations of short-term GMVpost-baseline change or long-term GMVfollow-up-post change with immediate (all *p*≥.080), delayed (all *p*≥.143) or long-term (all *p*≥.104) changes in suicidality and delusion (**Supplementary Table 8**).

**Supplementary Table 1:** Details on psychopharmacological treatment in patient groups

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Supplementary Table 1.** Details on psychopharmacological treatment in patient groups | | | | | |
|  | ECT group*n*=17 | | TAU group *n*=33 | |  |
|  | Mean (SD) | | Mean (SD) | | *p*-valuea |
| No. of patients under psychopharmacological medication at t0 (yes/no)b | 17/0 | | 32/1 | | .468 |
| No. of patients under psychopharmacological medication at t1 (yes/no)b | 16/1 | | 33/0 | | .159 |
| No. of patients under psychopharmacological medication at t2 (yes/no)b | 17/0 | | 23/10 | | .011 |
| Medication load index at t0 | 4.06 (1.78) | | 2.12 (.96) | | <.001 |
| Medication (no/yes), No. of patients at t0 | | | | | |
| Antidepressants |  | |  |  |  |
| NaSSA | 10/7 | | 29/4 | | - |
| Tricyclics | 14/3 | | 31/2 | | - |
| NDRI | 17/0 | | 33/0 | | - |
| SSRI | 16/1 | | 23/10 | | - |
| SSNRI | 6/11 | | 18/15 | | - |
| MAO-Inhibitors | 17/0 | | 33/0 | | - |
| Other | 16/1 | | 26/7 | | - |
| Antipsychotics | 6/11 | | 19/14 | | - |
| Mood stabilizer | 12/5 | | 33/0 | | - |
| Medication load index at t1 | 4.41 (2.06) | | 2.70 (1.36) | | .001 |
| Medication (no/yes), No. of patients at t1 | | | | | |
| Antidepressants |  | |  | |  |
| NaSSA | 8/9 | | 26/7 | | - |
| Tricyclics | 14/3 | | 31/2 | | - |
| NDRI | 16/1 | | 32/1 | | - |
| SSRI | 16/1 | | 26/7 | | - |
| SSNRI | 5/12 | | 14/19 | | - |
| MAO-Inhibitors | 17/0 | | 33/0 | | - |
| Other | 16/1 | | 26/7 | | - |
| Antipsychotics | 8/9 | | 19/14 | | - |
| Mood stabilizer | 13/4 | | 31/2 | | - |
| Medication load index at t2 | 4.88 (2.60) | | 1.39 (1.44) | | <.001 |
| Medication (no/yes), No. of patients at t2 | | | | | |
| Antidepressants |  |  |  |  |  |
| NaSSA | 9/8 | | 31/2 | | - |
| Tricyclics | 16/1 | | 33/0 | | - |
| NDRI | 15/2 | | 31/2 | | - |
| SSRI | 16/1 | | 28/5 | | - |
| SSNRI | 7/10 | | 18/15 | | - |
| MAO-Inhibitors | 16/1 | | 32/1 | | - |
| Other | 15/2 | | 30/3 | | - |
| Antipsychotics | 5/12 | | 28/5 | | - |
| Mood stabilizer | 9/8 | | 30/3 | | - |
| Δ Medication load index t0 – t1b | -.35 (2.18) | | -.58 (1.17) | | ECT: .514 TAU: .008 |
| Δ Medication load index t0 – t2b | -.82 (2.72) | | .73 (1.96) | | ECT: .230 TAU: .041 |
| Δ Medication load index t1 – t2b | -.47 (2.98) | | 1.30 (2.13) | | ECT: .524 TAU: .001 |
| ECT, electroconvulsive therapy; TAU, treatment as usual; NaSSA, noradrenergic and specific serotonergic antidepressant; NDRI, norepinephrine and dopamine reuptake inhibitors; SSRI, selective serotonin reuptake inhibitors; SSNRI, selective serotonin and norepinephrine uptake inhibitors; MAO-Inhibitors, monoamine oxidase inhibitors. a Comparing patients from the ECT and the TAU group by using the unpaired two-tailed *t*-test except where noted.  b *p*-values were obtained using repeated measures *t*-tests within each group. | | | | | |

**Supplementary Table 2:** Characteristics of electroconvulsive therapy

|  |  |  |
| --- | --- | --- |
| Supplementary Table 2. Characteristics of electroconvulsive therapy | | |
| Variable | Mean (SD) | Range |
| **ECT series between t0 and t1a** |  |  |
| Number of ECT sessions | 12.71 (5.86) | 5 - 30 |
| Number of days between first and last ECT session | 35.5 (18.05) | 14 - 91 |
| Stimulus intensity (%) | 47.91 (21.36) | - |
| Pulse frequency (Hz) | 37.51 (12.15) | - |
| Seizure duration EEG (sec) | 40.42 (10.81) | - |
| Seizure duration EMG (sec) | 20.47 (7.61) | - |
| Postictal suppression index (%) | 82.70 (19.26) | - |
| **ECT sessions between t1 and t2b** |  |  |
| Number of additional ECT sessions | 5.43 (3.74) | 1 - 12 |
| ECT, electroconvulsive therapy. a Information regarding characteristics of electroconvulsive therapy was missing for *n*=1 patient in the ECT group. Two patients in the ECT group had received an ECT series before study participation (2.3 and 6 years respectively). b *N*=7 patients in the ECT group underwent additional ECT sessions between t1 and t2. | | |

**Supplementary Table 3:** Extracted clusters showing significant GMV increase from t0 to t1 in the rmANOVA in the ECT group

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Supplementary Table 3.** Extracted clusters showing significant GMV increase from t0 to t1 in the rmANOVA in the ECT group. | | | | | | | | | |
| Cluster | Anatomical regions | Side | Cluster sizea | Peak voxel coordinates | | | *T*-valueb | *PFWE*-value | *ηp²* |
| x | y | z |
| Cluster 1 | Hippocampus/ parahippocampal gyrus (g.)/ amygdala/ laterale geniculate nucleus/ pars reticula/ pallidum | R | 1614 | 34 | -18 | -12 | 11.72 | <.001 | .842 |
| Cluster 2 | Insula/ rolandic operculum/ putamen/ inferior frontal g. | R | 1121 | 38 | 0 | 20 | 9.81 | <.001 | .728 |
| Cluster 3 | Middle temporal pole/ superior temporal pole/ parahippocampal g./ inferior temporal g./ posterior orbitofrontal cortex/ fusiform g. | R | 908 | 30 | 18 | -30 | 7.52 | <.001 | .771 |
| Cluster 4 | Insula/ rolandic operculum/ inferior frontal g./ putamen/ precentral g. | L | 583 | -34 | -4 | 20 | 7.92 | <.001 | .583 |
| Cluster 5 | Hippocampus/ posterior cingulate cortex/ medial pulvinar nucleus/ precuneus/ lateral pulvinar nucleus | R | 234 | 9 | -20 | 21 | 5.57 | .001 | .639 |
| Cluster 6 | Hippocampus/ laterale geniculate nucleus | L | 272 | -34 | -26 | -4 | 5.53 | .001 | .449 |
| a Only significant clusters (*pFWE*<.001) with cluster size *k*≥100 are reported. b *df*=44. | | | | | | | | |  |

**Supplementary Table 4:** Detailed information on percentages of brain areas in significant clusters from the 3x3 ANOVA

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Supplementary Table 4. Detailed information on percentages of brain areas in significant clusters from the 3x3 ANOVA | | | | |
| Peak voxel coordinates  (x/y/z) | Cluster sizea | Anatomical region | % Clusterb | % Labelc |
| **Group x time interaction effect** | | | | |
| 18/-9/-9 | 1303 | Hippocampus | 39.06 | 22.70 |
|  |  | Amygdala | 2.61 | 5.78 |
|  |  | Lateral geniculate nucleus | 1.92 | 21.97 |
|  |  | Pallidum | 1.92 | 3.77 |
|  |  | Parahippocampal gyrus | 1.30 | 0.63 |
|  |  | Pars reticula | 0.31 | 2.81 |
| 30/-2/16 | 883 | Putamen | 21.40 | 7.51 |
|  |  | Insula | 19.03 | 4.00 |
|  |  | Rolandic Operculum | 8.83 | 2.47 |
|  |  | Inferior frontal gyrus | 1.13 | 0.30 |
| -34/-8/20 | 330 | Insula | 37.58 | 2.82 |
|  |  | Putamen | 9.70 | 1.35 |
|  |  | Rolandic Operculum | 8.79 | 1.24 |
|  |  | Inferior frontal gyrus | 0.61 | 0.08 |
| -30/-22/-6 | 251 | Hippocampus | 11.55 | 1.31 |
|  |  | Lateral geniculate nucleus | 4.38 | 10.79 |
| **Post-hoc tests** | | | | |
| *ECT group: Baseline < Post* | | | | |
| 18/-9/-9 | 2066 | Hippocampus | 39.30 | 36.21 |
|  |  | Parahippocampal gyrus | 6.58 | 5.07 |
|  |  | Amygdala | 3.29 | 11.57 |
|  |  | Pallidum | 1.79 | 5.57 |
|  |  | Lateral geniculate nucleus | 1.40 | 25.49 |
|  |  | Pars reticula | 0.19 | 2.81 |
| 30/-2/16 | 1708 | Putamen | 22.48 | 15.25 |
|  |  | Insula | 19.32 | 7.87 |
|  |  | Rolandic Operculum | 15.34 | 8.30 |
|  |  | Inferior frontal gyrus | 2.87 | 1.48 |
|  |  | Supramarginal gyrus | 0.88 | 0.32 |
| -28/0/16 | 820 | Insula | 35.61 | 6.63 |
|  |  | Rolandic operculum | 21.22 | 7.43 |
|  |  | Putamen | 8.17 | 2.83 |
|  |  | Inferior frontal gyrus | 5.24 | 1.75 |
|  |  | Precentral gyrus | 0.49 | 0.05 |
| 9/-22/20 | 379 | Hippocampus | 11.61 | 1.96 |
|  |  | Medial pulvinar nucleus | 4.22 | 3.79 |
|  |  | Posterior cingulate cortex | 1.58 | 0.76 |
|  |  | Precuneus | 0.79 | 0.04 |
|  |  | Lateral pulvinar nucleus | 0.26 | 1.56 |
|  |  | Anterior pulvinar nucleus | 0.26 | 1.24 |
| -28/-20/-9 | 648 | Hippocampus | 40.90 | 12.00 |
|  |  | Lateral geniculate nucleus | 3.24 | 20.60 |
|  |  | Amygdala | 0.77 | 0.96 |
|  |  | Pallidum | 0.15 | 0.14 |
| 30/18/-30 | 864 | Superior temporal pole | 51.85 | 14.13 |
|  |  | Middle temporal pole | 34.38 | 10.56 |
|  |  | Parahippocampal gyrus | 3.24 | 1.04 |
|  |  | Orbitofrontal cortex | 1.85 | 1.20 |
| 12/0/24 | 165 | Caudate nucleus | 10.30 | 0.83 |
| *ECT group: Post > Follow-up* | | | | |
| 20/-10/-8 | 1293 | Hippocampus | 29.31 | 16.90 |
|  |  | Parahippocampal gyrus | 11.37 | 5.48 |
|  |  | Amygdala | 3.71 | 8.17 |
| **Supplementary Table 4.** Detailed information on percentages of brain areas in significant clusters from the 3x3 ANOVA | | | | |
| Peak voxel coordinates  (x/y/z) | Cluster sizea | Anatomical region | % Clusterb | % Labelc |
|  |  | Pallidum | 2.40 | 4.67 |
|  |  | Lateral geniculate nucleus | 1.24 | 14.06 |
|  |  | Superior temporal pole | 0.77 | 0.32 |
|  |  | Pars reticula | 0.31 | 2.81 |
| 30/-2/16 | 911 | Putamen | 36.33 | 13.15 |
|  |  | Insula | 15.48 | 3.36 |
|  |  | Rolandic operculum | 3.73 | 1.08 |
|  |  | Inferior frontal gyrus | 1.43 | 0.39 |
| -28/-4/16 | 1039 | Putamen | 23.58 | 10.35 |
|  |  | Insula | 12.42 | 2.93 |
|  |  | Hippocampus | 7.60 | 3.58 |
|  |  | Pallidum | 1.92 | 2.88 |
|  |  | Laterale geniculate nucleus | 1.35 | 13.74 |
|  |  | Rolandic operculum | 1.35 | 0.60 |
|  |  | Amygdala | 0.10 | 0.19 |
| 10/2/21 | 263 | Caudate nucleus | 38.02 | 4.90 |
| ECT, electroconvulsive therapy. a Only significant clusters (*pFWE*<.050) with cluster size *k*≥100 are reported.  b Percentage of the cluster occupied by the named brain area. The missing percentages are due to missing labels according to the AAL-atlas (Tzourio-Mazoyer et al., 2002).  c Percentage of the brain area lying within the cluster. | | | | |

**Supplementary Table 5**: Group differences in grey matter volume (*punc*<.001)

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Supplementary Table 5.** Group differences in grey matter volume (*punc*<.001) | | | | | | | | |  |
| Anatomical region | | Side | Cluster sizea | Peak voxel coordinates | | | Test statistics | | |
| x | y | z |
| **Main effect of groupb** | |  |  |  |  |  | *F*-value | *Punc*- value | *ηp²* |
| Postcentral gyrus/ supramarginal gyrus/ precentral gyrus | | R | 345 | 48 | -18 | 33 | 18.37 | <.001 | .227 |
| Inferior parietal gyrus/ supramarginal gyrus/ postcentral gyrus/ superior parietal gyrus | | R | 399 | 32 | -39 | 45 | 18.11 | <.001 | .215 |
| Inferior parietal gyrus/ postcentral gyrus/ supramarginal gyrus | | L | 539 | -51 | -30 | 36 | 12.61 | <.001 | .140 |
| **Post-hoc tests at baselinec** | |  |  |  |  |  | *T-*value | *Punc*- value | *ηp²* |
| *ECT group > HC group* | | - | - | - | - | - | - | n.s. | - |
| *ECT group < HC group* | |  |  |  |  |  |  |  |  |
| Inferior parietal gyrus/ postcentral gyrus/ supramarginal gyrus/ superior parietal gyrus | R | 575 | 32 | -39 | 45 | 5.35 | <.001 | .089 |
| Superior frontal gyrus/ anterior cingulate cortex/ middle cingulate cortex | L/R | 678 | 10 | 51 | 18 | 4.98 | <.001 | .096 |
| Fusiform gyrus/ inferior temporal gyrus/ cerebellum | L | 679 | -38 | -36 | -21 | 4.61 | <.001 | .020 |
| Inferior parietal gyrus/ postcentral gyrus/ supramarginal gyrus | L | 519 | -52 | -28 | 34 | 3.99 | <.001 | .055 |
| *ECT group > TAU group* | | - | - | - | - | - | - | n.s. | - |
| *ECT group < TAU group* | |  |  |  |  |  |  |  |  |
| Calcarine gyrus/ cuneus/ lingual gyrus | L/R | 634 | -2 | -80 | 20 | 4.18 | <.001 | .011 |
| *TAU group > HC group* | | - | - | - | - | - | - | n.s. | - |
| *TAU group < HC group* | |  |  |  |  |  |  |  |  |
| Postcentral gyrus/ supramarginal gyrus/ precentral gyrus | R | 866 | 48 | -16 | 33 | 5.84 | <.001 | .128 |
| Inferior parietal gyrus/ postcentral gyrus/ supramarginal gyrus | L | 1204 | -33 | -39 | 46 | 5.55 | <.001 | .094 |
| Postcentral gyrus/ supramarginal gyrus/ inferior parietal gyrus/ superior parietal gyrus | R | 357 | 32 | -39 | 44 | 5.10 | <.001 | .088 |
| Middle frontal gyrus/ inferior frontal gyrus/ superior frontal gyrus | R | 372 | 36 | 39 | 8 | 4.29 | <.001 | .055 |
| Superior frontal gyrus/ supplementary motor area | L | 410 | -15 | 18 | 60 | 4.27 | <.001 | .065 |
| Lingual gyrus/ cerebellum/ fusiform gyrus | R | 338 | 15 | -52 | -8 | 4.05 | <.001 | .090 |
| Gyrus rectus/ orbitofrontal cortex/ orbitofrontal gyrus/ olfactory sulcus/ ventral striatum/ middle frontal gyrus | L/R | 594 | -10 | 15 | -15 | 3.94 | <.001 | .064 |
| **Post-hoc tests at postc** | |  |  |  |  |  | *T-*value | *Punc*- value | *ηp²* |
| *ECT group > HC group* | |  |  |  |  |  |  |  |  |
| Hippocampus | R | 322 | 34 | -24 | -6 | 4.16 | <.001 | .642 |
| *ECT group < HC group* | |  |  |  |  |  |  |  |  |
| Supplementary motor area/ superior frontal gyrus | L | 380 | -10 | 12 | 62 | 5.28 | <.001 | .117 |
| Inferior parietal gyrus/ supramarginal gyrus/ postcentral gyrus/ superior parietal gyrus/ | R | 605 | 32 | -39 | 45 | 5.17 | <.001 | .136 |
| Superior frontal gyrus/ anterior cingulate cortex/ middle cingulate cortex | R | 476 | 9 | 51 | 18 | 4.40 | <.001 | .039 |
| *ECT group > TAU group* | | - | - | - | - | - | - | n.s. | - |
| *ECT group < TAU group* | |  |  |  |  |  |  |  |  |
| Calcarine gyrus/ lingual gyrus/ cuneus | L/R | 1163 | 0 | -84 | 3 | 4.22 | <.001 | .131 |
| *TAU group > HC group* | |  |  |  |  |  |  |  |  |
| Calcarine gyrus/ precuneus/ lingual gyrus | L | 367 | -22 | -54 | 8 | 4.46 | <.001 | .136 |
| *TAU group < HC group* | |  |  |  |  |  |  |  |  |
| Postcentral gyrus/ supramarginal gyrus/ precentral gyrus | R | 662 | 48 | -18 | 33 | 5.56 | <.001 | .057 |
| Inferior parietal gyrus/ postcentral gyrus/ supramarginal gyrus | L | 1064 | -33 | -39 | 46 | 5.19 | <.001 | .054 |
| Postcentral gyrus/ supramarginal gyrus/ inferior parietal gyrus/ superior parietal gyrus | R | 344 | 32 | -39 | 44 | 5.08 | <.001 | .067 |
| **Supplementary Table 5.** Whole-brain cross-sectional differences in grey matter volume (*punc*<.001) *(continued)* | | | | | | | | | |
| Anatomical region | | Side | Cluster Sizea | Peak voxel coordinates | | | Test statistics | | |
| x | y | z |
| Superior frontal gyrus/ supplementary motor area | L | 407 | -14 | 18 | 60 | 4.57 | <.001 | .079 |
| Middle frontal gyrus/ inferior frontal gyrus/ superior frontal gyrus | R | 408 | 38 | 39 | 8 | 4.53 | <.001 | .058 |
| **Post-hoc tests at follow-upc** | |  |  |  |  |  | *T-*value | *Punc*- value | *ηp²* |
| *ECT group > HC group* | | - | - | - | - | - | - | n.s. | - |
| *ECT group < HC group* | |  |  |  |  |  |  |  |  |
| Inferior parietal gyrus/ supramarginal gyrus/ postcentral gyrus/ superior parietal gyrus | R | 458 | 32 | -39 | 45 | 5.00 | <.001 | .531 |
| Anterior cingulate cortex/ superior frontal gyrus/ middle cingulate cortex | L/R | 566 | 8 | 50 | 15 | 4.65 | <.001 | .481 |
| *ECT group > TAU group* | | - | - | - | - | - | - | n.s. | - |
| *ECT group < TAU group* | | - | - | - | - | - | - | n.s. | - |
| *TAU group > HC group* | |  |  |  |  |  |  |  |  |
| Calcarine gyrus/ precuneus/ lingual gyrus | L | 356 | -22 | -54 | 9 | 4.35 | <.001 | .160 |
| *TAU group < HC group* | |  |  |  |  |  |  |  |  |
| Postcentral gyrus/ supramarginal gyrus/ inferior parietal gyrus/ precentral gyrus/ superior parietal gyrus | R | 1218 | 48 | -16 | 33 | 6.16 | <.001 | .070 |
| Inferior parietal gyrus/ postcentral gyrus/ supramarginal gyrus | L | 1246 | -32 | -39 | 45 | 5.37 | <.001 | .076 |
| Superior frontal gyrus/ supplementary motor area | L | 770 | -14 | 18 | 60 | 4.84 | <.001 | .073 |
| Middle frontal gyrus/ inferior frontal gyrus/ superior frontal gyrus | R | 387 | 33 | 42 | 9 | 4.38 | <.001 | .039 |
| Anterior cingulate cortex/ superior frontal gyrus | L | 307 | -6 | 42 | 8 | 3.96 | <.001 | .071 |
| Gyrus rectus/ orbitofrontal gyrus/ olfactory gyrus/ orbitofrontal cortex/ anterior cingulate cortex | L/R | 596 | 4 | 36 | -14 | 3.66 | <.001 | .051 |
| ECT, electroconvulsive therapy; TAU, treatment as usual; HC, healthy controls.  a Only significant clusters (*punc*<.001) with cluster size *k*≥300 are reported. b *df1*=2; *df2=*200. c *df*=200. | | | | | | | | | |

**Supplementary Table 6:** Results of the group x time interaction (controlling for depression severity)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Table 2. Results of the group x time interaction (controlling for depression severity) | | | | | | | |
| Anatomical region | Side | Cluster sizea | Peak voxel coordinates | | | Test statistics | |
| x | y | z |
| **Group x time interaction effectb** |  | | | | | *F-*value | *pFWE*- value |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Hippocampus/ lateral geniculate nucleus/ amygdala/ pallidum/ parahippocampal gyrus/ pars reticula | R | 1201 | 20 | -10 | -8 | 36.53 | <.001 |
| Putamen/ insula/ rolandic operculum/ inferior frontal gyrus | R | 812 | 30 | -2 | 16 | 33.35 | <.001 |
| Insula/ putamen/ rolandic operculum/ inferior frontal gyrus/ precentral gyrus | L | 390 | -28 | 0 | 16 | 19.08 | <.001 |
| Hippocampus/ lateral geniculate nucleus | L | 279 | -30 | -22 | -6 | 14.23 | <.001 |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Post-hoc testsc from baseline to post** |  |  |  |  |  | *T-*value | *pFWE*- value |
| *ECT group: Baseline < Post* |  |  |  |  |  |  |  |
| Hippocampus/ lateral geniculate nucleus/ amygdala/ pallidum/ parahippocampal gyrus/ pars reticula | R | 1279 | 28 | -20 | -8 | 10.33 | <.001 |
| Putamen/ Insula/ rolandic operculum/ inferior frontal gyrus/ supramarginal gyrus | R | 1075 | 30 | -2 | 16 | 10.16 | <.001 |
| Insula/ rolandic operculum/ putamen/ inferior frontal gyrus/ precentral gyrus | L | 676 | -28 | 0 | 16 | 8.56 | <.001 |
| Hippocampus/ medial pulvinar nucleus/ lateral pulvinar nucleus/ precuneus/ posterior cingulate cortex/ anterior pulvinar nucleus | R | 338 | 10 | -21 | 21 | 7.30 | <.001 |
| Hippocampus/ lateral geniculate nucleus/ amygdala | L | 458 | -28 | -20 | -9 | 6.35 | <.001 |
| *TAU group: Baseline < Post* | - | - | - | - | - | - | n.s. |
| *HC group: Baseline > Post* | - | - | - | - | - | - | n.s. |
| **Post-hoc testsc from post to follow-up** |  |  |  |  |  | *T-*value | *pFWE*- value |
| *ECT group: Post > Follow-up* |  |  |  |  |  |  |  |
| Hippocampus/ parahippocampal gyrus/ amygdala/ pallidum/ lateral geniculate nucleus/ superior temporal pole/ pars reticula | R | 907 | 30 | -2 | 16 | 9.84 | <.001 |
| Putamen/ insula/ rolandic operculum/ inferior frontal gyrus | R | 1287 | 20 | -10 | -8 | 9.84 | <.001 |
| Putamen/ insula/ hippocampus/ pallidum/ laterale geniculate nucleus/ rolandic operculum/ amygdala | L | 1063 | -28 | -4 | 16 | 7.93 | <.001 |
| Caudate nucleus | R | 259 | 10 | 2 | 21 | 6.46 | <.001 |
| *TAU group: Post > Follow-up* | - | - | - | - | - | - | n.s. |
| *HC group: Post > Follow-up* | - | - | - | - | - | - | n.s. |
| **Post-hoc testsc from baseline to follow-up** |  |  |  |  |  | *T-*value | *pFWE*- value |
| *ECT group: Baseline < Follow-up* | - | - | - | - | - | - | n.s. |
| *TAU group: Baseline > Follow-up* | - | - | - | - | - | - | n.s. |
| *HC group: Baseline > Follow-up* | - | - | - | - | - | - | n.s. |
| ECT, electroconvulsive therapy; TAU, treatment as usual; HC, healthy controls.  a Only significant clusters (*pFWE*<.050) with cluster size *k*≥100 are reported.  b *df1*= 4; *df2*=199.  c *df*=199. | | | | | | | | |

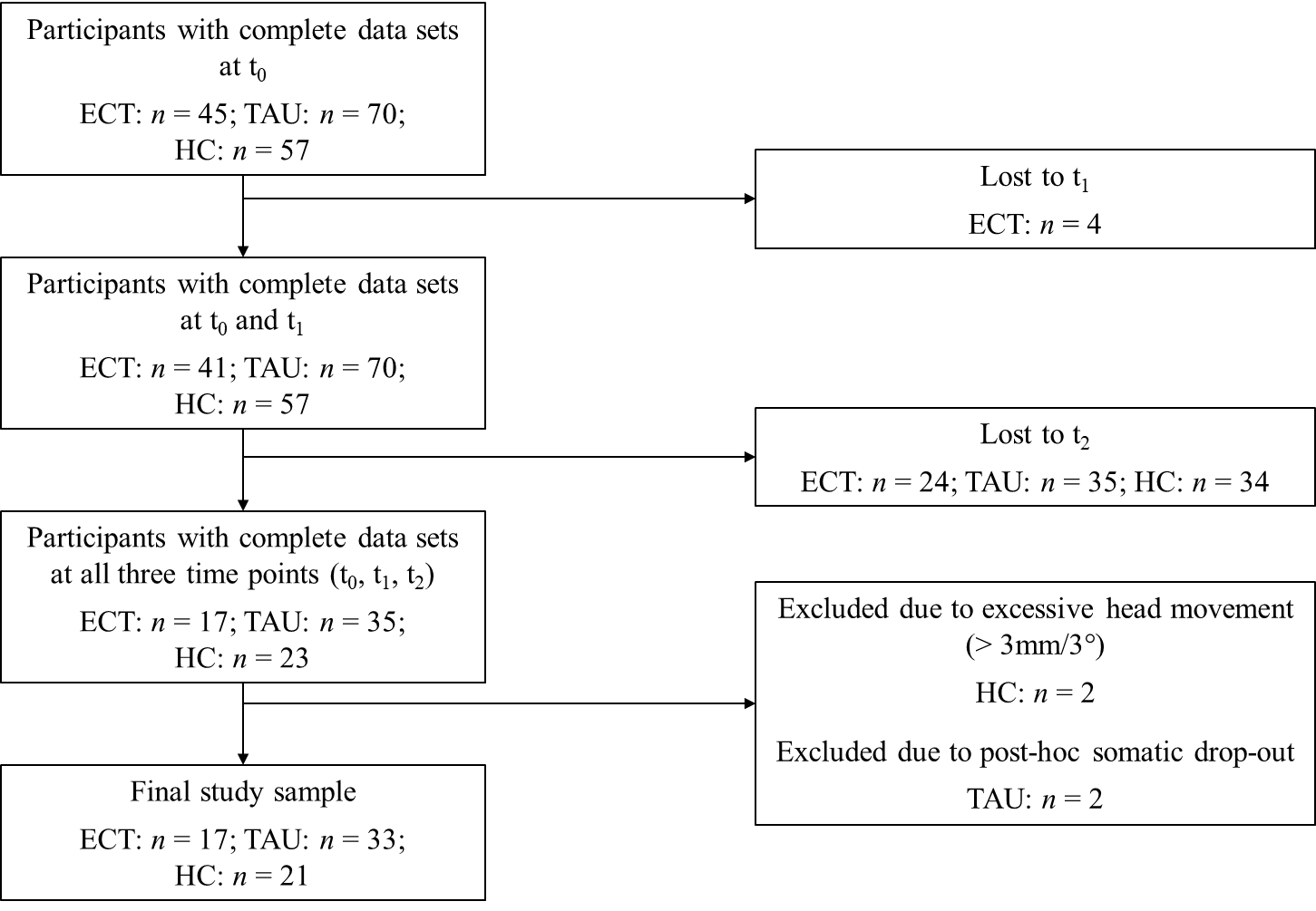
**Supplementary Table 7**: Associations of grey matter volume changes with clinical outcome measures (controlling for covariates)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Supplementary Table 7.** Associationsa of grey matter volume changes with clinical outcome measures (controlling for covariates) | | | | | | | |
| ∆ GMV changes | | ∆ HDRS score change | | ∆ BDI score changeb | | Number of depressive episodes | |
|  | | *r* | *p* | *r* | *p* | *r* | *p* |
| **Short-term grey matter volume change and immediate clinical outcome variablesc** | | | | | | | |
| *t0 vs t1* | | *t0 vs t1* | | *t0 vs t1* | | - | |
| Cluster 1 | | .486 | .056 | .433 | .466 | **-** | **-** |
| Cluster 2 | | **.593** | **.015**e | .057 | .841 | **-** | **-** |
| Cluster 3 | | .156 | .564 | -.106 | .708 | **-** | **-** |
| Cluster 4 | | **.564** | **.023** | .296 | .283 | **-** | **-** |
| Cluster 5 | | .105 | .698 | -.300 | .278 | **-** | **-** |
| Cluster 6 | | .287 | .281 | .492 | .062 | **-** | **-** |
| **Short-term grey matter volume change and delayed clinical outcome variablesc** | | | | | | | |
| *t0 vs t1* | *t0 vs t2* | | | *t0 vs t2* | | *t0 vs t2* | |
| Cluster 1 | | .406 | .118 | .175 | .532 | .423 | .102 |
| Cluster 2 | | **.638** | **.008**e | .330 | .229 | .476 | .063 |
| Cluster 3 | | .019 | .944 | .108 | .701 | -.249 | .353 |
| Cluster 4 | | **.512** | **.043** | **.530** | **.042** | **.500** | **.048** |
| Cluster 5 | | .172 | .523 | -.060 | .832 | .254 | .342 |
| Cluster 6 | | .258 | .336 | **.611** | **.016** | .474 | .420 |
| **Long-term grey matter volume change and long-term clinical outcome variablesd** | | | | | | | |
| *t1 vs t2* | | *t1 vs t2* | | *t1 vs t2* | | *t1 vs t2* | |
| Cluster 1 | | -.114 | .673 | **-.721** | **.004**e | -.275 | .302 |
| Cluster 2 | | -.228 | .396 | **-.752** | **.002**e | -.383 | .143 |
| Cluster 3 | | -.243 | .363 | -.530 | .051 | .008 | .976 |
| Cluster 4 | | -.165 | .542 | -.476 | .085 | -.194 | .472 |
| Cluster 5 | | .019 | .945 | **-.546** | **.043** | -.371 | .157 |
| Cluster 6 | | -.328 | .215 | -.304 | .290 | -.368 | .160 |
| GMV, grey matter volume; HDRS, Hamilton depression rating scale; BDI, Beck depression inventory. a Correlation analyses using Spearman’s correlation coefficient.  b Information regarding BDI score changewas missing for *n*=1 patient in the ECT group.  c Correlation analyses were controlled for the number of ECT sessions.  d Correlation analyses were controlled for the GMV change between baseline and post.  e No correction for multiple comparisons was made. With a Bonferroni-adjusted *p*-value of .016, only these correlation results remain significant. | | | | | | | |

**Supplementary Table 8:** Associations of grey matter volume changes with suicidality and delusion

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Supplementary Table 8.** Associationsa of grey matter volume changes with suicidality and delusion | | | | | |
| ∆ GMV changes | | ∆ change in suicidalityb | | ∆ change in delusionb | |
|  | | *r* | *p* | *r* | *p* |
| *t0 vs t1* | | *t0 vs t1* | | *t0 vs t1* | |
| Cluster 1 | | .140 | .592 | .220 | .395 |
| Cluster 2 | | .219 | .398 | .436 | .080 |
| Cluster 3 | | .358 | .158 | .417 | .096 |
| Cluster 4 | | .383 | .129 | .411 | .101 |
| Cluster 5 | | .203 | .433 | .279 | .279 |
| Cluster 6 | | .166 | .523 | -.082 | .754 |
| *t0 vs t1* | *t0 vs t2* | | | *t0 vs t2* | |
| Cluster 1 | | .014 | .956 | .074 | .778 |
| Cluster 2 | | .279 | .278 | .164 | .529 |
| Cluster 3 | | .370 | .143 | .371 | .143 |
| Cluster 4 | | .227 | .381 | .338 | .185 |
| Cluster 5 | | .214 | .410 | .119 | .649 |
| Cluster 6 | | -.130 | .618 | -.001 | .996 |
| *t1 vs t2* | | *t1 vs t2* | | *t1 vs t2* | |
| Cluster 1 | | -.149 | .569 | .212 | .413 |
| Cluster 2 | | -.173 | .506 | .408 | .104 |
| Cluster 3 | | -.248 | .338 | -.082 | .755 |
| Cluster 4 | | -.124 | .636 | .146 | .577 |
| Cluster 5 | | -.149 | .569 | .321 | .209 |
| Cluster 6 | | -.173 | .506 | -.045 | .865 |
| GMV, grey matter volume; HDRS, Hamilton depression rating scale; BDI, Beck depression inventory. a Correlation analyses using Spearman’s correlation coefficient.  b Changes in suicidality and delusion were assessed via specific items from the HDRS (Hamilton, 1960). | | | | | |

**Supplementary Figure 1:** Flow diagram visualizing the participant dropout process

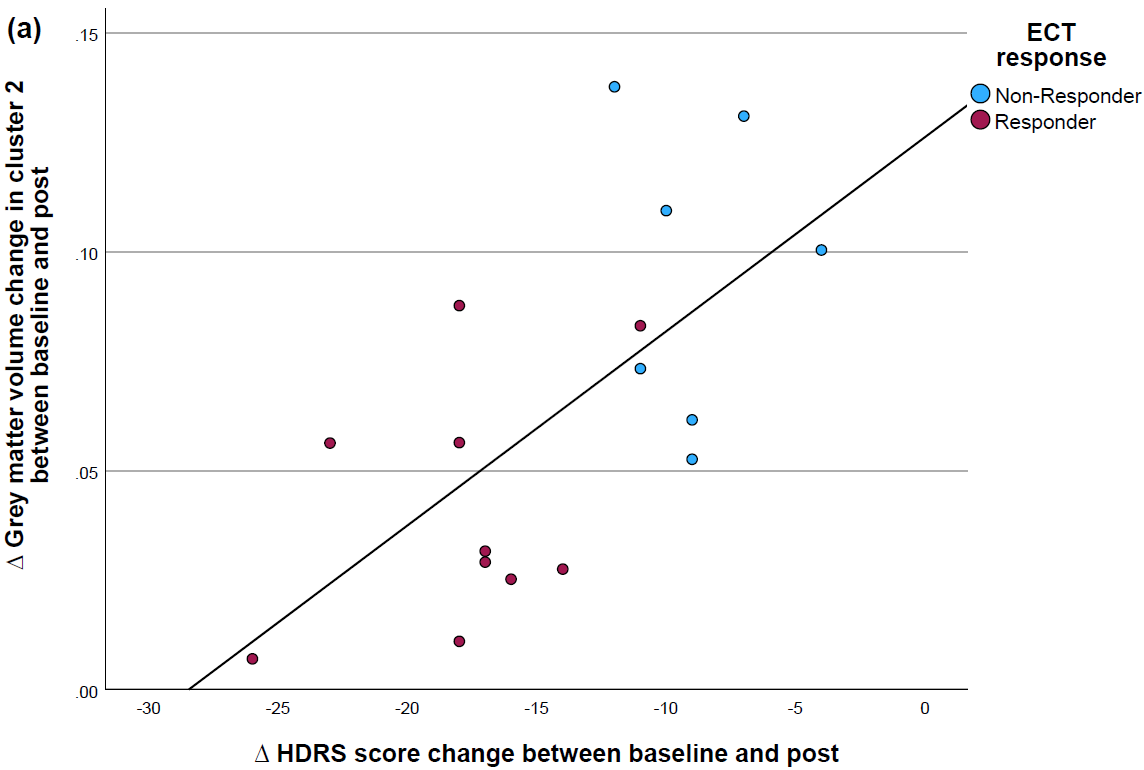
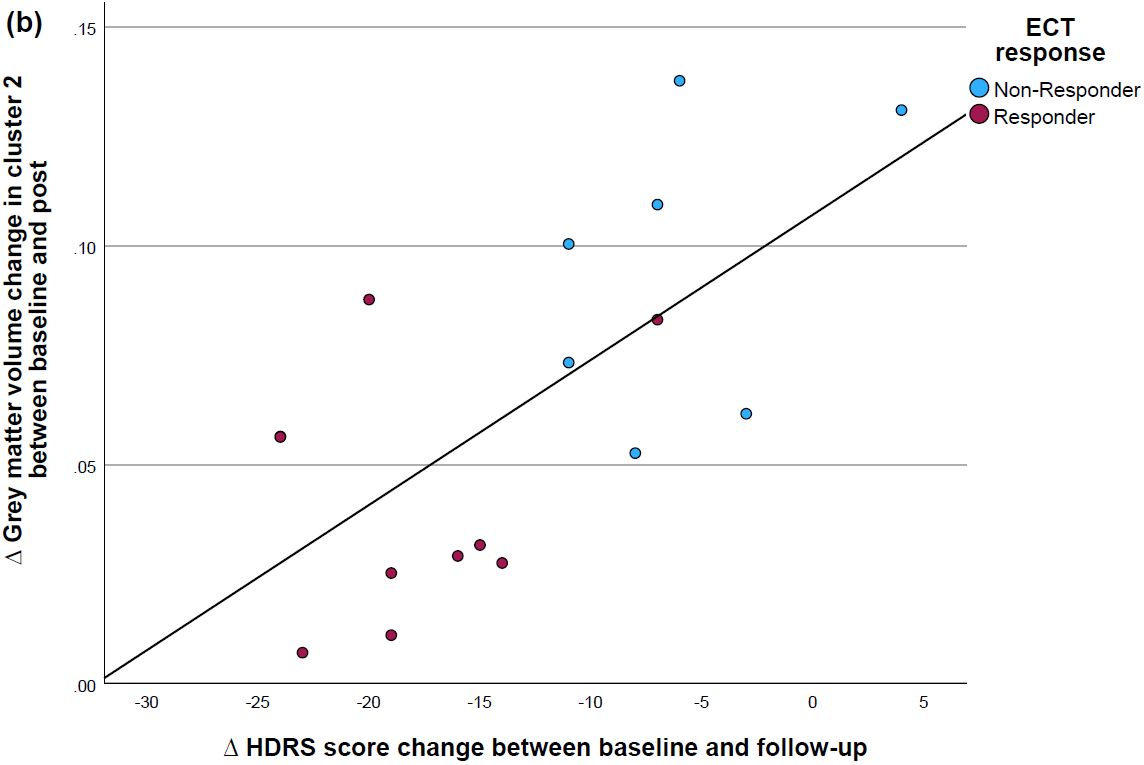
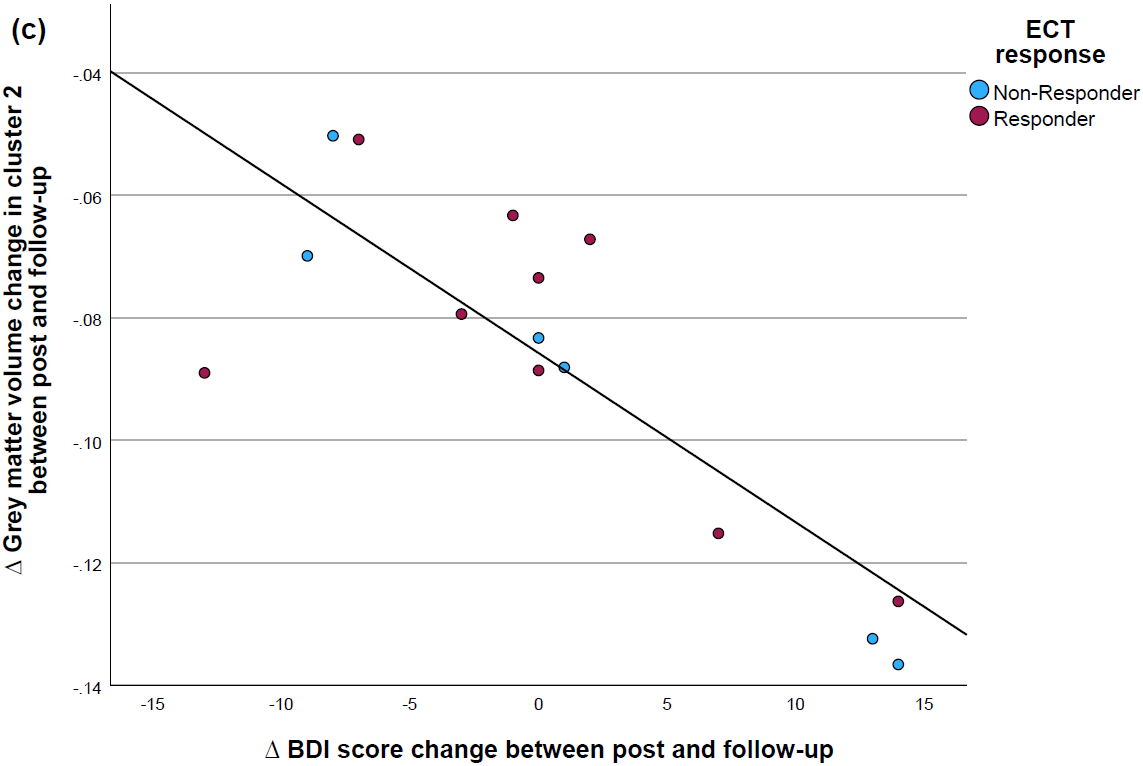


Supplementary Figure 1. Flow diagram visualizing the participant dropout process. ECT = Electroconvulsive therapy, TAU = Treatment as usual, HC = Healthy controls, t0 = Baseline assessment, t1 = Post assessment, t2 = Follow-up assessment.

**Supplementary Figure 2:** Distribution of additional ECT treatments in the ECT group

**Supplementary Figure 2. Distribution of additional ECT treatments in the ECT group.** The distribution of additional ECT treatments between t1 and t2 in responder and non-responder and the varying disease progression between t1 and t2 in the respective groups. There was no significant difference in rates of additional ECT treatment between response groups (χ²(1)=2.837, *p*=.092). a Information on additional ECT treatment between t1 and t2 was missing for *n*=1 patient in the ECT group. b according to DSM-IV (Wittchen, Wunderlich, Gruschwitz, & Zaudig, 1997). ECT = Electroconvulsive therapy, t0 = Baseline assessment, t1 = Post assessment, t2 = Follow-up assessment.

**Supplementary Figure 3:** Grey matter volume changes associated with clinical outcome

**Supplementary Figure 3. Grey matter volume changes associated with clinical outcome.** Scatterplots of the association between **(a)** short-term ∆ GMV change (computed as GMV post – GMV baseline) and immediate HDRS score change (computed as post – HDRS baseline), (b) short-term ∆ GMV change (computed as GMV post – GMV baseline) and delayed HDRS score change (computed as HDRS follow-up – HDRS baseline) and (c) long-term ∆ GMV change (computed as GMV follow-up – GMV post) and long-term HDRS score change (computed as BDI follow-up – BDI post) in cluster 2 (see **Table 3**). Colours indicate ECT response group. Continuous line: regression line.

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