**Online supplement Table 1.** Cross-sectional studies on brain morphology and outcome in schizophrenia.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author**  **(year)** | **Study design** | **Diagnostic system** | **Outcome measures** | **Definition of poor/good outcome** | **Brain areas studied** | **Covaria-**  **tes** | **MRI-procedure** | **Main findings** | **Comments** |
| Bodnar  et al. 2010 | Canada  57 FES patients,  57 healthy controls | DSM-IV (schizophrenia, schizoaffective or schizophreniform) | PANSS | Remission according to the 2005 Remission in Schizophrenia Working Group criteriaa | Amygdala, hippocampus (head, body and tail separately) | Handedness, cumulative antipsychotic  dosage | 1.5 T Siemens, slice thickness 1.0 mm | Non-remitted FES patients had smaller volume of the tail of the left hippocampus. |  |
| Brickman et al. 2004 | USA  106 schizophrenia cases, 42 normal controls | CASH (schizophrenia or schizoaffective) | PANSS | Good outcome (“non-Kraepelinian”) and poor outcome (“Kraepelinian”)b | Thalamus size | Neuroleptic treatment at  the time of scan, predominant neuroleptic for 3 years before the scan | 1.5 T GE Signa, slice thickness 1.22 mm | Poor outcome patients had smaller absolute thalami and smaller absolute and relative ventral aspects of the thalamus. | Information on neuroleptic use only for 3 years before the scan |
| Buchsbaum et al. 2003 | USA  37 schizophrenia cases, 37 healthy controls | DSM-IV  (schizophrenia or schizoaffective) | PANSS | Good outcome (“non-Kraepelinian”) and poor outcome (“Kraepelinian”)b | Caudate and putamen sizes | - | 1.5 T GE Signa, slice thickness 1.2 mm | Good outcome patients had larger relative mean putamen size but not caudate size. | Good outcome patients had larger putamen than healthy controls. Information on neuroleptic use only for 3 years before the scan |
| García-Martí  et al. 2008 | Spain  18 schizophrenia cases, 19 healthy controls | DSM-IV  (schizophrenia) | PSYRATS, BPRS, GAF | Symptom severity assessed with PSYRATS and BPRS | GM volumes | - | 1.5 T Philips Intera, slice thickness 1.25 mm | Patients with more severe symptoms had GM reductions in both left para-hippocampus and right superior temporal gyrus. | All cases had persistent auditory hallucination.  Voxel-based morphometry |
| Ha  et al. 2004 | South Korea  35 schizophrenia patients, 35 matched controls | DSM-IV  (schizophrenia paranoid type or provisional  schizophreniform disorder) | PANSS | Symptom severity assessed with PANSS | GM volumes | - | 1.5 T GE Signa, slice thickness 1.5 mm | No significant correlation was found between any regional grey matter concentrations  and PANSS symptoms or general psycho-pathology scales. | Voxel-based morphometry. Sample is  homogeneous in having positive symptoms. |
| Hulshoff Pol  et al. 2003 | The Netherlands  159  schizophrenia patients, 158 healthy controls | DSM-IV  (schizophrenia or schizophreniform disorder) | SADS-L | Illness  severity was defined by the square root of the ratio of the cumulative months of hospitalisation and the cumulative months of  illness since first symptoms | Focal WM changes in the whole brain | Age, sex and handedness | 1.5 T Philips NT, slice thickness 1.2 (T1) - 1.6 mm (T2) | Patients with more severe illness had lower density of the corpus callosum and the right anterior  commissure. | Voxel-based morphometry |
| Lui  et al. 2009 | China  68 FES patients, 68 matched healthy controls | DSM-IV  (schizophrenia) | GAF, PANSS | Severity of psychopathology assessed with GAF and PANSS | GM volume | - | 3 T GE EXCITE, slice  thickness 1.0 mm | Patients with more severe psychopatologyhad decreased GM volume in the right anterior cingulate gyrus,  right middle temporal gyrus, and right superior temporal gyrus. | Voxel-based morphometry. Antipsychotic-naive patients. |
| Mitelman  et al. 2007 | USA  104 schizophrenia, 41  healthy controls | DSM-IV (schizophrenia or schizoaffective  disorder) | PANSS, MMSE | Good outcome (“non-Kraepelinian”) and poor outcome (“Kraepelinian”)b | GM and WM morphometry across the brain | Covariates “age at the time of the scan” and “age at initiation of antipsychotic treatment” used, but results not shown. | 1.5 T GE Signa, slice thickness 1.22 mm | Poor outcome patients had lower temporal,  occipital, and to a lesser degree parietal GM volumes in both  hemispheres and lower temporal, parietal, occipital, and posterior cingulated WM volumes in the right hemisphere. | Poor outcome patients commenced neuroleptic treatment at a younger age. |
| Mitelman  et al. 2005 | USA  37 schizophrenia patients, 37 controls | DSM-IV (schizophrenia or schizoaffective disorder) | PANSS | Good outcome (“non-Kraepelinian”) and poor outcome (“Kraepelinian”)b, severity of positive symptoms | The cingulate arch | Brain volume, age | 1.5 T GE Signa, slice thickness 1.2 mm | Poor outcome patients had bilateral GM deficits in posterior cingulate and retrosplenial cortices. |  |
| Mitelman  et al. 2003 | USA  37 schizophrenia patients, 37 controls | DSM-IV (schizophrenia or schizoaffective disorder) | PANSS | Good outcome (“non-Kraepelinian”) and poor outcome (“Kraepelinian”)b | Cortical GM, WM and  CSF volumes | In some analysis covariates age and/or brain volume were used, but mainly only unadjusted results reported. | 1.5 T GE Signa, slice thickness 1.2 mm | Patients with poor outcomes had smaller GM volumes in the temporal and occipital lobes, but no difference  between groups was found for  total frontal lobe volume. |  |
| Molina  et al. 2010 | Spain  44 schizophrenia patients, 41 healthy controls | DSM-IV  (schizophrenia) | PANSS | Good outcome (“non-Kraepelinian”) and poor outcome (“Kraepelinian”)b | GM volumes | Age and gender | 1.5 T Philips Gyroscan, slice thickness 1.1-1.5 mm | Poor outcome patients had smaller putamen and caudate nuclei. | Voxel-based morphometry |
| Paillére-Martinot  et al. 2001 | France  20 male schizophrenia patients, 20 matched healty controls | DSM-IV  (schizophrenia) | PANSS | Symptom severity assessed with PANSS | GM and WM volumes | Age | 1.5 T GE Signa, slice thickness 1.5 mm | Patients with more negative symptoms had decreased WM volumes in cingulated regions bilaterally and right internal capsule region. | Only males. Voxel-based morphometry. |
| Pressler  et al. 2005 | USA  30 male schizophrenia patients, 30 healthy male controls | DSM-III-R  (schizophrenia) | SANS, SAPS | Psychotic symptom dimension was the sum of global scores for hallucinations and delusions from the SANS/SAPS. | Insular GM volume  and cortical surface size | Total brain volume for volume measures, total cortical surface area for surface area measures | 1.5 T GE Signa, slice thickness 3.0 or 4.0 mm | Patients with more severe psychotic symptoms had greater decreases in right insular  cortex area. | No clear distinction between good and poor outcome groups |
| Rossi  et al. 2000 | Italy  56 schizophrenia patients, 32 matched healthy controls | DSM-III-R  (schizophrenia) | K-MS, SCS | Patients with a score ≤ 4 on the SCS were considered as having a poor outcome | Brain volume, lateral and 3rd ventricles, temporal lobes, caudate nucleus, putamen, amygdala, hippocampus | Age | 0.25 T  Ansaldo, slice thickness 5.0 mm | Poor outcome patients had left and right ventricular enlargement. | Controls were medical students and volunteers working in clinical and administrative areas. |
| Staal  et al. 2001 | The Netherlands  45 schizophrenia patients, 23 healthy controls | DSM-IV  (schizophrenia) | PANSS, DAS, GAS, and MMSE | Poor-outcome: hospitalised for more than 50% of their total duration of illness and continuously  hospitalised over the past 3 years. Good-outcome: hospitalised for less than 10% of their total duration of illness and not hospitalised during the past year. | ICV and volumes of the cerebrum,  GM and WM, lateral and 3rd ventricles, frontal lobes, thalamus, and cerebellum | ICV | 1.5 T Philips, slice thickness 1.6 mm | No statistically significant differences were observed between the two outcome groups. |  |
| van Haren et al. 2003 | The Netherlands  109 schizophrenia patients | DSM-IV  (schizophrenia or related psychotic disorder) | PANSS, MADRS, GSDS, CAN | Outcome measures: need for care, social functioning, symptoms, duration of hospitalisations | Cerebrum, cerebral GM and WM, lateral and 3rd ventricles, cerebellum | Age at inclusion, sex, ICV, cumulative neuroleptic medication, drug abuse, duration of untreated psychosis | 1.5 T Philips NT (Utrecht), 1.5 T Siemens Magnetom Vision, (Amsterdam and Groningen), slice thickness 1.2 mm | No significant correlations were found between the MRI and outcome measurements | Multi-center study. Two MRI scanners from different manufacturers. |
| Wilke  et al. 2001 | Germany  48 schizophrenia patients, 48 matched controls | DSM-IV  (schizophrenia) | BPRS, GAF | Illness severity measured with GAF only | GM and CSF differences | Age, sex,  and absolute individual GM/CSF-volume | 1.5 T GE Signa, slice thickness 0.9–1.4 mm | Patients with lower GAF-score had  GM reduction in the left inferior frontal gyrus and inferior parietal lobule. | Voxel-based morphometry |

aRemission according to the 2005 Remission in Schizophrenia Working Group criteria (Andreasen NC, Carpenter Jr. WT, Kane JM, Lasser RA, Marder SR, Weinberger DR. Remission in schizophrenia: proposed criteria and rationale for consensus. Am. J. Psychiatry 2005;162: 441–449).

bKraepelinian vs. Non-Kraepelinian: Kraepelinian poor outcome patients were defined as those who met the following criteria for the previous 5 years or more: (1) continuous hospitalization, or, if living outside the hospital, complete dependence on others for food, clothing, and shelter; (2) no useful work or employment; and (3) no evidence of symptom remission (Keefe RS, Mohs RC, Losonczy MF, Davidson M, Silverman JM, Kendler KS, Horvath TB, Nora R, Davis KL. Characteristics of very poor outcome schizophrenia. Am. J. Psychiatry 1987; 144: 889–895).

Abbreviations: BPRS = Brief Psychiatric Rating Scale, CAN = Camberwell Assessment of Need, CSF = cerebrospinal fluid, DAS = Disability Assessment Schedule, FES = First episode schizophrenia, GAF = Global Assessment of Functioning, GAS = Global Assessment Scale, GM = grey matter, GSDS = Groningen Social Disabilities Schedule, ICV = inrtacranial volume, K-MS = Krawiecka-Manchester Scale, MADRS = Montgomery Åsberg Depression Rating Scale, MMSE = Mini-Mental State Examination, PANSS = Positive and Negative Syndrome Scale, SADS-L = Schedule for Affective Disorder and Schizophrenia Lifetime version, SANS = Scale for the Assessment of Negative Symptoms, SAPS = Scale for the Assessment of Positive Symptoms, SCS = Strauss-Carpenter Scale, PSYRATS = Psychotic Symptom Rating Scale, WM = white matter.

**Online supplement Table 2.** Associations between volumes of grey matter, white matter, CSF and regional grey matter densities and measures of clinical outcome in schizophrenia (N=54).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Number of treatment days due to psychosis** | | **Number of treatment episodes due to psychosis** | | **Remission** | |
|  | **Beta**  **(SE)a** | **Beta**  **(SE)b** | **Beta**  **(SE)a** | **Beta**  **(SE)b** | **OR**  **(95% CI)c** | **OR**  **(95% CI)d** |
|  |  |  |  |  |  |  |
| **Whole brain** | -0.60  (3.97) | -0.46  (3.78) | -0.66  (0.02) | -0.42  (0.03) | 1.02  (0.99-1.05) | 1.02  (0.99-1.06) |
| **Total grey matter** | -0.32  (5.89) | 0.09  (5.50) | -0.53  (0.04) | -0.40  (0.04) | 0.99  (0.96-1.02) | 0.99  (0.96-1.02) |
| **Total white matter** | -0.32  (5.54) | -0.13  (4.97) | -0.17  (0.03) | -0.03  (0.03) | **1.06**  **(1.01-1.11)** | **1.07**  **(1.01-1.14)** |
| **CSF** | 0.20  (3.97) | 0.02  (3.78) | 0.23  (0.02) | 0.14  (0.03) | 0.98  (0.95-1.01) | 0.98  (0.95-1.01) |
| **Central left** | -0.17  (75.53) | -0.13  (65.49) | -0.20  (0.46) | -0.18  (0.44) | 0.88  (0.59-1.32) | 0.92  (0.59-1.45) |
| **Central right** | -0.04  (83.01) | 0.02  (72.13) | -0.03  (0.51) | 0.02  (0.49) | 0.86  (0.56-1.31) | 0.86  (0.53-1.42) |
| **Frontal left** | -0.10  (31.83) | -0.05  (27.47) | -0.23  (0.19) | -0.21  (0.18) | 1.00  (0.85-1.18) | 1.02  (0.86-1.21) |
| **Frontal right** | -0.14  (34.17) | -0.02  (30.39) | -0.17  (0.21) | -0.10  (0.21) | 0.99  (0.82-1.19) | 1.00  (0.83-1.22) |
| **Temporal left** | -0.26  (66.45) | -0.11  (62.04) | -0.14  (0.41) | -0.05  (0.42) | 0.87  (0.59-1.29) | 0.86  (0.57-1.30) |
| **Temporal right** | -0.25  (71.50) | -0.03  (67.89) | -0.27  (0.43) | -0.16  (0.46) | 0.75  (0.48-1.17) | 0.66  (0.40-1.09) |
| **Parietal left** | -0.15  (68.41) | 0.01  (61.28) | -0.21  (0.41) | -0.13  (0.42) | 0.88  (0.62-1.25) | 0.93  (0.63-1.37) |
| **Parietal right** | -0.10  (66.03) | 0.08  (59.15) | -0.12  (0.40) | -0.02  (0.40) | 0.79  (0.54-1.17) | 0.78  (0.50-1.20) |
| **Occipital left** | -0.11  (67.48) | 0.05  (60.13) | -0.08  (0.41) | 0.002  (0.41) | 0.84  (0.58-1.23) | 0.84  (0.56-1.27) |
| **Occipital right** | -0.11  (68.16) | 0.05  (61.11) | -0.22  (0.41) | -0.15  (0.41) | 0.88  (0.60-1.29) | 0.85  (0.56-1.30) |
| **Limbic left** | -0.06  (93.44) | 0.04  (81.63) | **-0.42**  **(0.52)** | **-0.40**  **(0.52)** | 1.07  (0.63-1.81) | 1.05  (0.66-1.66) |

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Limbic right** | -0.04  (87.86) | 0.13  (77.61) | -0.22  (0.52) | -0.14  (0.53) | 1.05  (0.63-1.75) | 0.90  (0.51-1.56) |
| **Insula left** | -0.09  (242.95) | 0.02  (221.48) | -0.18  (1.46) | -0.16  (1.49) | 0.62  (0.17-2.31) | 0.48  (0.11-2.06) |
| **Insula right** | -0.17  (286.32) | 0.02  (267.48) | -0.24  (1.72) | -0.16  (1.80) | 0.60  (0.13-2.84) | 0.59  (0.11-3.10) |
| **Subcortical grey nuclei left** | -0.04  (124.27) | -0.18  (112.61) | -0.13  (0.75) | -0.26  (0.75) | 0.67  (0.34-1.33) | 0.86  (0.41-1.80) |
| **Subcortical grey nuclei right** | -0.03  (127.74) | -0.06  (115.99) | 0.01  (0.78) | -0.04  (0.79) | 0.46  (0.21-1.05) | 0.56  (0.23-1.34) |
| **Cerebellum** | 0.15  (14.96) | 0.25  (14.86) | 0.08  (0.09) | 0.09  (0.10) | 0.95  (0.87-1.04) | 0.95  (0.86-1.06) |

Statistically significant results (p-value < 0.05) are marked in **bold**.

a Linear regression, adjusted with intracranial volume (ICV), sex and duration of illness

b Linear regression, adjusted with ICV, sex, duration of illness and use of antipsychotic medication

c Logistic regression, adjusted with ICV, sex and duration of illness

d Logistic regression, adjusted with ICV, sex, duration of illness and use of antipsychotic medication

**Online supplement Table 3.** Associations between volumes of grey matter, white matter, CSF and regional grey matter densities and measures of functional outcomes in schizophrenia (N=54).

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Not on disability pension** | | | | **Working at least 50% of time** | | | | **SOFAS score** | | | |
|  |  | **OR**  **(95% CI)a** | **OR**  **(95% CI)b** | **OR**  **(95% CI)c** |  | **OR**  **(95% CI)a** | **OR**  **(95% CI)b** | **OR**  **(95% CI)c** |  | **Beta**  **(SE)d** | **Beta**  **(SE)e** | **Beta**  **(SE)f** |
| **Whole brain** |  | **1.03**  **(1.00-1.05)** | 1.02  (1.00-1.04) | 1.02  (1.00-1.05) |  | 1.00  (0.98-1.02) | 1.00  (0.98-1.02) | 1.00  (0.98-1.02) |  | 0.69  (0.05) | 0.48  (0.05) | 0.64  (0.05) |
| **Total grey matter** |  | 1.02  (0.99-1.05) | 1.01  (0.99-1.04) | 1.02  (0.99-1.05) |  | 1.01  (0.98-1.04) | 1.00  (0.98-1.03) | 1.01  (0.98-1.04) |  | 0.46  (0.07) | 0.40  (0.07) | 0.51  (0.07) |
| **Total white matter** |  | 1.03  (1.00-1.06) | 1.02  (0.99-1.06) | 1.02  (0.99-1.05) |  | 1.00  (0.98-1.02) | 0.99  (0.96-1.02) | 1.00  (0.97-1.03) |  | 0.25  (0.07) | 0.08  (0.07) | 0.11  (0.08) |
| **CSF** |  | 0.98  (0.95-1.00) | 0.98  (0.96-1.00) | 0.98  (0.96-1.00) |  | 1.00  (0.98-1.02) | 1.01  (0.99-1.03) | 1.00  (0.98-1.02) |  | -0.24  (0.05) | -0.16  (0.05) | -0.23  (0.05) |
| **Central left** |  | 1.18  (0.86-1.63) | 1.22  (0.86-1.72) | 1.25  (0.88-1.77) |  | 0.98  (0.70-1.38) | 0.99  (0.70-1.39) | 0.99  (0.71-1.38) |  | 0.24  (0.89) | 0.23  (0.87) | **0.27**  **(0.83)** |
| **Central right** |  | 1.02  (0.72-1.44) | 1.04  (0.71-1.52) | 1.07  (0.74-1.56) |  | 0.78  (0.54-1.13) | 0.75  (0.50-1.11) | 0.81  (0.56-1.17) |  | -0.01  (1.02) | -0.03  (0.99) | 0.03  (0.97) |
| **Frontal left** |  | **1.17**  **(1.00-1.37)** | 1.16  (1.00-1.34) | **1.21**  **(1.02-1.43)** |  | 1.05  (0.90-1.23) | 1.04  (0.90-1.20) | 1.04  (0.89-1.22) |  | **0.31**  **(0.37)** | **0.29**  **(0.36)** | **0.30**  **(0.35)** |
| **Frontal right** |  | 1.16  (0.98-1.37) | 1.16  (0.98-1.37) | 1.20  (1.00-1.44) |  | 1.00  (0.85-1.19) | 1.00  (0.85-1.17) | 1.00  (0.85-1.19) |  | 0.21  (0.41) | 0.18  (0.41) | 0.22  (0.38) |
| **Temporal left** |  | 1.33  (0.97-1.82) | 1.27  (0.92-1.75) | 1.34  (0.97-1.87) |  | 1.18  (0.84-1.65) | 1.14  (0.81-1.60) | 1.18  (0.84-1.66) |  | 0.16  (0.84) | 0.11  (0.86) | 0.18  (0.79) |
| **Temporal right** |  | 1.27  (0.89-1.81) | 1.29  (0.88-1.89) | 1.42  (0.97-2.09) |  | 1.15  (0.79-1.66) | 1.14  (0.77-1.70) | 1.19  (0.81-1.73) |  | 0.22  (0.88) | 0.17  (0.92) | **0.27**  **(0.82)** |
| **Parietal left** |  | 1.17  (0.87-1.58) | 1.18  (0.86-1.61) | 1.20  (0.88-1.63) |  | 0.94  (0.69-1.29) | 0.93  (0.67-1.29) | 0.96  (0.70-1.33) |  | 0.12  (0.83) | 0.09  (0.83) | 0.17  (0.77) |
| **Parietal right** |  | 0.96  (0.72-1.28) | 0.93  (0.68-1.26) | 0.98  (0.72-1.32) |  | 0.81  (0.59-1.10) | 0.73  (0.51-1.04) | 0.84  (0.61-1.15) |  | -0.05  (0.81) | -0.12  (0.80) | 0.01  (0.78) |
| **Occipital left** |  | 0.90  (0.67-1.20) | 0.85  (0.62-1.16) | 0.90  (0.67-1.22) |  | 0.96  (0.71-1.30) | 0.93  (0.68-1.29) | 0.95  (0.70-1.31) |  | -0.14  (0.81) | -0.21  (0.80) | -0.12  (0.78) |
| **Occipital right** |  | 0.92  (0.68-1.25) | 0.86  (0.62-1.19) | 0.91  (0.67-1.24) |  | 0.92  (0.67-1.27) | 0.88  (0.63-1.23) | 0.92  (0.67-1.28) |  | -0.11  (0.84) | -0.18  (0.82) | -0.10  (0.79) |
| **Limbic left** |  | 1.66  (0.98-2.80) | 1.53  (0.94-2.47) | 1.61  (0.94-2.73) |  | 1.71  (0.96-3.03) | 1.55  (0.93-2.59) | 1.69  (0.95-3.01) |  | **0.29**  **(1.08)** | **0.28**  **(1.06)** | **0.28**  **(1.01)** |
| **Limbic right** |  | 1.27  (0.85-1.91) | 1.33  (0.85-2.06) | 1.36  (0.87-2.13) |  | 0.94  (0.64-1.38) | 0.90  (0.59-1.36) | 0.94  (0.64-1.39) |  | 0.24  (1.04) | 0.21  (1.04) | 0.23  (0.98) |
| **Insula left** |  | 2.28  (0.74-7.03) | 1.95  (0.61-6.25) | 2.31  (0.69-7.75) |  | 0.99  (0.33-3.02) | 0.87  (0.25-3.01) | 0.94  (0.29-3.06) |  | 0.25  (2.94) | 0.22  (2.91) | **0.29**  **(2.73)** |
| **Insula right** |  | 3.17  (0.68-14.76) | 2.67  (0.64-11.13) | 3.49  (0.67-18.12) |  | 0.79  (0.19-3.22) | 0.76  (0.18-3.18) | 0.84  (0.19-3.63) |  | 0.27  (3.36) | 0.25  (3.49) | **0.31**  **(3.10)** |
| **Subcortical grey nuclei left** |  | 1.30  (0.75-2.24) | 1.51  (0.81-2.84) | 1.31  (0.72-2.38) |  | 1.50  (0.79-2.85) | **2.63**  **(1.07-6.47)** | 1.63  (0.81-3.31) |  | 0.21  (1.51) | **0.34**  **(1.47)** | **0.26**  **(1.40)** |
| **Subcortical grey nuclei right** |  | 0.96  (0.56-1.65) | 0.98  (0.53-1.78) | 0.95  (0.52-1.72) |  | 1.08  (0.59-1.96) | 1.38  (0.65-2.92) | 1.18  (0.60-2.35) |  | 0.03  (1.60) | 0.09  (1.59) | 0.12  (1.54) |
| **Cerebellum** |  | 0.98  (0.92-1.05) | 0.95  (0.87-1.03) | 0.95  (0.88-1.03) |  | 1.00  (0.93-1.07) | 1.00  (0.92-1.09) | 0.99  (0.91-1.08) |  | -0.09  (0.21) | -0.08  (0.21) | -0.05  (0.20) |

Statistically significant results (p-value < 0.05) are marked in **bold**.

a Logistic regression, adjusted with intracranial volume (ICV), sex and duration of illness

b Logistic regression, adjusted with ICV, sex, duration of illness and use of antipsychotic medication

c Logistic regression, adjusted with ICV, sex, duration of illness and remission

d Linear regression, adjusted with ICV, sex and duration of illness

e Linear regression, adjusted with ICV, sex, duration of illness and use of antipsychotic medication

f Linear regression, adjusted with ICV, sex, duration of illness and remission

**Online supplement Table 4**. Intercoefficient correlations (Spearman's rho) between the outcome variables.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Number of hospitalisations** | **Number of hospital treatment days** | **Remission** | **Not on disability pension** | **Working at least 50% of time** | **SOFAS** |
| **Number of hospitalisations** | - |  |  |  |  |  |
| **Number of hospital treatment days** | 0,818\*\* | - |  |  |  |  |
| **Remission** | -0,207 | -0,181 | - |  |  |  |
| **Not on disability pension** | -0,588\*\* | -0,537\*\* | 0,365\*\* | - |  |  |
| **Working at least 50% of time** | -0,421\*\* | -0,420\*\* | 0,185 | 0,581\*\* | - |  |
| **SOFAS** | -0,363\*\* | -0,353\* | 0,547\*\* | 0,555\*\* | 0,490\*\* | - |
| Remission according to the criteria by Andreasen et al. (2005); <3 score on PANSS items P1, P2, P3, N1, N4, N6, G5, and G9; yes/no), Not on disability pension = not on disability pension vs. on disability pension at the end of the year 2000, Working at least 50% of time = working at least 50% of time during the year 2000 vs. working less than 50% of time during the year 2000, SOFAS = Social and Occupational Functioning Assessment Scale.  \*\* Correlation is significant at the 0.01 level (2-tailed).  \* Correlation is significant at the 0.05 level (2-tailed). | | | | | | |

**Online supplement Table 5.** Results of principal component analysis of the outcome variables.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Course of illness** | **Cross-sectional outcome** | **Hospital treatments** | **Total** |
| Percentage of variance explained | 49.6 | 16.7 | 13.3 | 79.6 |
| Eigenvalues | 2.977 | 1.002 | 0.797 |  |
|  |  |  |  |  |
| Promax rotated solution |  |  |  | Communalities |
| Not on pension at age 34 years | 0.79 | 0.33 | 0.19 | 0.77 |
| At work at least 50% at age 34 years | 0.88 | 0.10 | 0.08 | 0.80 |
| SOFAS at age 34 years | 0.40 | 0.68 | 0.35 | 0.74 |
| Remission at age 34 years | 0.09 | 0.94 | -0.01 | 0.89 |
| Cumulative number of psychiatric treatment times | 0.58 | 0.07 | 0.57 | 0.66 |
| Cumulative number of psychiatric treatment days | 0.10 | 0.11 | 0.94 | 0.91 |

Extraction method: Principal component analysis. Rotation method: Promax with Kaiser normalization

**Online supplement Table 6.** Associations between volumes of grey matter, white matter, CSF and regional grey matter densities and three outcome factors (N=54).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Course of illness** | | **Cross-sectional outcome** | | **Hospital treatments** | |
|  | **Beta**  **(SE)a** | **Beta**  **(SE)b** | **Beta**  **(SE)a** | **Beta**  **(SE)b** | **Beta**  **(SE)a** | **Beta**  **(SE)b** |
|  |  |  |  |  |  |  |
| **Whole brain** | 0.54  (<0.01) | 0.47  (<0.01) | 0.69  (<0.01) | 0.60  (<0.01) | 0.66  (<0.01) | 0.05  (<0.01) |
| **Total grey matter** | 0.32  (0.01) | 0.36  (0.01) | -0.03  (<0.01) | -0.05  (0.01) | 0.39  (0.01) | -0.03  (0.01) |
| **Total white matter** | 0.23  (0.01) | 0.09  (0.01) | 0.81  (<0.01) | 0.68  (<0.01) | 0.28  (0.01) | 0.09  (0.01) |
| **CSF** | -0.20  (<0.01) | -0.16  (<0.01) | -0.25  (<0.01) | -0.21  (<0.01) | -0.24  (<0.01) | -0.02  (<0.01) |
| **Central left** | 0.11  (0.06) | 0.12  (0.06) | <-0.01  (0.06) | <0.01  (0.06) | 0.19  (0.07) | 0.15  (0.06) |
| **Central right** | -0.07  (0.07) | -0.07  (0.07) | -0.05  (0.06) | -0.06  (0.06) | 0.06  (0.07) | -0.01  (0.06) |
| **Frontal left** | 0.27  (0.03) | 0.26  (0.03) | 0.08  (0.02) | 0.06  (0.02) | 0.10  (0.03) | 0.04  (0.02) |
| **Frontal right** | 0.17  (0.03) | 0.17  (0.03) | 0.04  (0.03) | 0.03  (0.03) | 0.14  (0.03) | <0.01  (0.03) |
| **Temporal left** | 0.22  (0.06) | 0.22  (0.06) | -0.04  (0.05) | -0.07  (0.05) | 0.28  (0.06) | 0.11  (0.05) |
| **Temporal right** | 0.23  (0.06) | 0.24  (0.06) | -0.09  (0.06) | -0.12  (0.06) | 0.27  (0.06) | 0.06  (0.06) |
| **Parietal left** | 0.09  (0.06) | 0.11  (0.06) | -0.05  (0.05) | -0.05  (0.05) | 0.18  (0.06) | 0.01  (0.05) |
| **Parietal right** | -0.09  (0.06) | -0.12  (0.06) | -0.10  (0.05) | -0.14  (0.05) | 0.14  (0.06) | -0.03  (0.05) |
| **Occipital left** | -0.12  (0.06) | -0.14  (0.06) | -0.16  (0.05) | -0.19  (0.05) | 0.15  (0.06) | -0.02  (0.05) |
| **Occipital right** | -0.08  (0.06) | -0.10  (0.06) | -0.09  (0.05) | -0.12  (0.05) | 0.16  (0.06) | 0.01  (0.05) |
| **Limbic left** | **0.36**  **(0.07)** | **0.38**  **(0.07)** | 0.08  (0.07) | 0.09  (0.07) | 0.08  (0.08) | -0.04  (0.07) |
| **Limbic right** | 0.13  (0.07) | 0.12  (0.08) | 0.11  (0.07) | 0.10  (0.07) | 0.04  (0.08) | -0.13  (0.07) |
| **Insula left** | 0.15  (0.21) | 0.15  (0.21) | -0.02  (0.19) | -0.02  (0.19) | 0.13  (0.22) | 0.01  (0.19) |
| **Insula right** | 0.13  (0.24) | 0.16  (0.25) | 0.01  (0.22) | 0.03  (0.23) | 0.21  (0.25) | <0.01  (0.23) |
| **Subcortical grey nuclei left** | 0.18  (0.11) | **0.30**  **(0.11)** | -0.07  (0.10) | 0.03  (0.10) | 0.07  (0.11) | 0.17  (0.10) |
| **Subcortical grey nuclei right** | <-0.01  (0.11) | 0.07  (0.11) | -0.17  (0.10) | -0.10  (0.10) | 0.06  (0.12) | 0.07  (0.10) |
| **Cerebellum** | -0.09  (0.02) | -0.06  (0.02) | -0.13  (0.01) | -0.10  (0.01) | -0.13  (0.02) | -0.24  (0.01) |

P-values ≤ 0.05 are marked in **bold**.

a Linear regression, adjusted with ICV, sex and duration of illness

b Linear regression, adjusted with ICV, sex, duration of illness and use of antipsychotic medication