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# Supplementary Materials

## **Attrition bias**

Participants who completed the follow-up study showed higher education levels and higher IQ compared to those who did not complete the study (Supplementary Table 1).

**Supplementary Table 1 Attrition Bias**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | | Completers | Non-completers | Statistics a (sig.) |
| age | Mean | 21.40 | 20.98 | -0.88 (0.382) |
| SD | 3.28 | 3.036 |
| N | 64 | 124 |
| Sex | Male (N%) | 37 (57.8%) | 85 (68.5%) | 2.14 (0.144) |
| Education (years) | Mean | 13.72 | 12.84 | **-2.64 (0.010)\*** |
| SD | 2.330 | 1.644 |
| N | 61 | 123 |
| Parental Education (years) | Mean | 14.50 | 14.38 | -0.27 (0.791) |
| SD | 2.876 | 2.792 |
| N | 64 | 124 |
| IQ | Mean | 109.92 | 104.98 | **-2.46 (0.015)\*** |
| SD | 12.146 | 13.458 |
| N | 64 | 123 |

a χ2 test was utilized for Non-parametric tests and ANOVA was applied for parametric tests.

## **Exploration of significant sex difference**

Significantly more male participants than female participants, especially in Sz (80.7%), participated in the current study. To investigate the impact of sex, we designed a two-way ANOVA model to investigate the sex by diagnostic group interaction. The ROI GM FW analysis revealed no significant sex by diagnosis interaction (F (2, 182) = 1.04, P = 0.354) or main effect of sex (F (1,182) = 3.56, p = 0.061) , while the main effect of diagnostic group remained significant (F (2,182) = 4.48, p = 0.013) (Supplementary Figure 1, panel A). The ROI WM FW analysis revealed no significant sex by diagnosis interaction (F (2, 182) = 1.21, P = 0.301), main effect of sex (F (1,182) = 0.37, p = 0.540) or main effect of diagnostic group t (F (2,182) = 1.18, p = 0.310) (Supplementary Figure 1, panel B). Therefore, we utilized ANCOVA to explore FW difference among three diagnostic groups in GM and WM respectively, while controlling sex as a covariate in the current study.



**Supplementary Figure 1: No sex by diagnostic group interactions were revealed, suggesting that the FW increase in GM in patients at baseline is independent of sex.**

## **Clinical symptoms at baseline**

Negative symptoms are significantly worse in medicated patients compared to unmedicated patients with FEPs, specifically, such significant group difference was revealed in Sz group, but not in BD group (Supplementary Table 2).

**Supplementary Table 2 Clinical symptoms at baseline**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | Schizophrenia | | | Bipolar | | | | Total | | | |
| Unmed | med | t\_test(sig.) | | Unmed | med | t\_test(sig.) | | Unmed | med | t\_test(sig.) |
| Reality | Mean | 16.17 | 15.03 | 0.74 (0.460) | | 8.45 | 8.83 | -0.20 (0.847) | | 13.68 | 13.27 | 0.30 (0.767) |
| SD | 5.929 | 6.347 | 4.967 | 5.297 | 6.659 | 6.660 |
| N | 23 | 58 | 11 | 23 | 34 | 81 |
| Disorganization | Mean | 6.39 | 6.30 | 0.12 (0.903) | | 5.64 | 5.48 | 0.16 (0.877) | | 6.15 | 6.07 | 0.12 (0.902) |
| SD | 3.677 | 2.770 | 2.767 | 2.778 | 3.386 | 2.780 |
| N | 23 | 60 | 11 | 23 | 34 | 83 |
| Poverty | Mean | 11.57 | 14.45 | **-2.20 (0.031)\*** | | 10.18 | 10.52 | -0.14 (0.813) | | 11.12 | 13.36 | **-2.13 (0.035)\*** |
| SD | 4.409 | 5.655 | 3.737 | 3.964 | 4.198 | 5.510 |
| N | 23 | 60 | 11 | 23 | 34 | 83 |

## **Antipsychotics and other Medications at the baseline scan**

Antipsychotic medications included risperidone (n=39), olanzapine (n=17), aripiprazole (n=16), ziprasidone (n=6), quetiapine (n=5), haloperidol (n=2), paliperidone (n=2), perphenazine (n=1), and iloperidone (n=1). Of the 84 patients taking antipsychotics, 66 patients (NSz = 46 and NBD = 20) were taking one medication at the time of scan; 13 patients (NSz = 11 and NBD = 2) were taking two medications; 4 patients (NSz = 2 and NBD = 2) were taking 3 medications and 1 patient with Sz was taking 5 medications. The number of medications taken was not significantly different (t (82) = 0.41; p = 0.684) between patients with Sz (Mean = 1.32, SD = 0.70) and patients with BD (Mean = 1.25; SD = 0.61) at baseline scan. Also, the number of patients with antipsychotic medication exposure versus the number of medication naïve patients did not show significant difference across two patient groups (χ² = 0.03, p = 0.853). Other medications that were taken at the time of the scan, included antidepressants (n=20), mood stabilizers (n=22), anxiolytic (n=11), and ADHD medications (n=2). Of the 34 patients not taking antipsychotics, none of them were taking other medications at the scan (Supplementary Table 3).

**Supplementary Table 3 Antipsychotics and other Medications at baseline**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Antipsychotics | N (Sz) | N (BD) | χ² (Sig.) | Other medications | N (Sz) | N (BD) | χ² (Sig.) |
| Aripiprazole | 11 | 5 | 0.03 (0.885) | Anti-depressant | 12 | 8 | 0.80 (0.371) |
| Haloperidol | 2 | 0 | mood stabilizers | 12 | 10 | 0.18 (0.670) |
| Iloperidone | 0 | 1 | Anti-anxiety | 9 | 4 | 1.92 (0.166) |
| Olanzapine | 11 | 6 | ADHD medications | 3 | 1 | 1.00 (0.317) |
| Perphenazine | 1 | 0 |  | | | |
| Paliperidone | 1 | 1 |
| Quetiapine | 3 | 2 |
| Risperidone | 31 | 8 |
| Ziprasidone | 4 | 2 |

## **Voxel-wise correlations of clinical assessments at baseline**

No significant associations were identified between psychotic symptoms and FW or between disorganization symptoms and FW in WM respectively. However, we found a positive correlation between the severity of poverty symptoms and FW in the right SLF and forceps minor (FM) (Supplementary Figure 3, red cluster). The strength of this relationship was similar between patients with Sz and BD (Fisher’s r-to-z transformation: z = 0.65, p = 0.516) (Supplementary Figure 3, scatter plot). This result indicated that FW alteration may be more sensitive to be associated with negative symptoms at the early stage of psychosis. No significant association was revealed between clinical symptoms and FA or FA-t.



Supplementary Figure 3: The severity of poverty symptoms was positively associated with FW in the right SLF and FM (red cluster), which showed the same pattern in both patients with Sz and BD (scatter plot).

## **Brain volume comparisons**

In order to demonstrate the effects of brain structure changes on diffusion measures, we calculated brain cortical GM, WM volume and intracranial volume (ICV) at baseline using SIENAX (Smith *et al.*, 2001). Gray matter ratio (GMR) and white matter ratio (WMR) were calculated by the percentage of GM/WM in ICV respectively. ANCOVA analyses with sex as a covariate showed non-significant groups difference in brain GM and WM volumes (Supplementary Table4).

**Supplementary Table 3 brain volume at baseline**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Schizophrenia | | | bipolar | | | Control | | | Stats (Sig.) |
| mean | SD | N | mean | SD | N | mean | SD | N |
| GM | 893.85 | 40.51 | 83 | 893.02 | 57.95 | 35 | 908.53 | 42.73 | 70 | 1.756 (0.176) |
| WM | 706.09 | 40.53 | 697.96 | 38.17 | 695.93 | 31.89 | 0.502 (0.606) |
| ICV | 1599.94 | 67.52 | 1590.97 | 80.39 | 1604.46 | 65.01 | 0.469 (0.627) |
| GMR | 0.559 | 0.014 | 0.561 | 0.016 | 0.556 | 0.011 | 2.978 (0.053) |
| WMR | 0.441 | 0.014 | 0.439 | 0.016 | 0.434 | 0.011 | 2.978 (0.053) |

# Supplementary References

**Smith, S. M., De Stefano, N., Jenkinson, M. & Matthews, P. M.** (2001). Normalized accurate measurement of longitudinal brain change. *J Comput Assist Tomogr* **25**, 466-75.