**Supplementary Methods**

*Functional MRI image acquisition protocol*

MRI data were acquired at Copenhagen University Hospital, Righospitalet, using a 3-Tesla Siemens Prisma scanner and a 64-channel head-neck coil. We acquired two T2\*-weighted gradient echo spiral echo-planar (EPI) blood-oxygen-level-dependent (BOLD) sequences with the same parameters during performance of the spatial and verbal N-back tasks: echo time (TE) of 30 ms, repetition time (TR) of 2 s, and flip angle of 90°. The volumes consisted of 32 slices with a slice thickness of 3 mm with 25% gaps in-between and a field-of-view of 230×230 mm using a 64×64 grid. There were 300 and 230 volumes acquired for the verbal and spatial N-back tasks, respectively. The BOLD images were registered to a T1-weighted structural images acquired with a TR=1900 ms; TE=2.58 ms; flip angle=9°; distance factor=50%; field-of-view (FOV)=230×230 mm; slice thickness=0.9 mm. Further, we also acquired a standard B0 field map sequence with the same FOV and resolution as the fMRI sequence (TR=400 ms; TEs=4.92 and 7.38 ms; flip angle=60°) and used for geometric distortions correction of the BOLD images. We ensured image quality through visual inspection of each individual participant’s neuroimages. During fMRI scans, task paradigms were displayed on a screen that participants viewed through an angled mirror in the scanner.

**Supplementary Results**

*Post-hoc analysis of the effect of medication on WM-related activations*

Comparison between medicated (80%) vs. unmedicated (20%) patients revealed significantly *increased* left MFG activity during verbal N-back performance in those not receiving medication (BOLD response, M=0.47, SD=0.22) relative to those receiving medication (BOLD response, M=0.20, SD=0.25), (*t*(64)=2.36, *p*=0.021) (remaining clusters: *p*s≥0.2). Patients receiving antipsychotics (UD, n=2 (11%); BD, n=20 (43%)) displayed *increased* activity of the right MFG (dlPFC) and posterior SMG (all *p*≤0.04) during verbal N-back compared to those not receiving antipsychotics (UD, n=17 (89%); BD, n=27 (57%)) (remaining *p*s≥0.1). In contrast, patients receiving antidepressants (UD, n=11 (58%); BD, n=9 (19%)) had *lower* activity of the left SFG during visuospatial N-back (2-back>0-back), left posterior and medial SFG (dmPFC), right MFG (dlPFC), left MFG, right posterior SMG, and precuneus (all *p*≤0.02) compared to those not receiving antidepressants (UD patients, n=8 (42%); BD, n=16 (81%), remaining *p*≥0.1). There were no differences in BOLD response across the 12 clusters between patients treated vs. not treated with anticonvulsants, lithium, or other medications (all *p*≥0.2).

*Post-hoc analysis of the effect of diagnosis on WM-related activations*

Comparison between patients with unipolar (29%) vs. bipolar (71%) disorder revealed no significant differences in WM-related activations (BOLD response) across the 12 clusters:

*Visuospatial N-back task*. ROI right dlPFC (2>0) (BD: M=0.48, SD=0.37; UD: M=0.41, SD=0.29), *p*=0.5; ROI right dlPFC (2>1) (BD: M=0.19, SD=0.23; UD: M=0.11, SD=0.28), *p*=0.2; right SFG (BD: M=0.25, SD=0.26; UD: M=0.23, SD=0.27), *p*=0.8; left SFG (BD: M=0.27, SD=0.26; UD: M=0.25, SD=0.28), *p*=0.7; left OFC (BD: M= -0.38, SD=0.43; UD: M= -0.41, SD=0.47), *p*=0.8.

*Verbal N-back task*. Left dlPFC (BD: M=0.35, SD=0.29; UD: M=0.29, SD=0.27), *p*=0.4; left posterior SFG (dmPFC) (BD: M=0.32, SD=0.26; UD: M=0.25, SD=0.21), *p*=0.3; left medial SFG (BD: M=0.39, SD=0.40; UD: M=0.37, SD=0.29), *p*=0.8; right MFG (dlPFC) (BD: M=0.37, SD=0.29; UD: M=0.27, SD=0.25), *p*=0.2; left MFG (BD: M=0.24, SD=0.29; UD: M=0.22, SD=0.23), *p*=0.8; right SMG (posterior) (BD: M=0.48, SD=0.33; UD: M=0.38, SD=0.24), *p*=0.3; precuneus (BD: M=0.52, SD=0.51; UD: M=0.35, SD=0.40), *p*=0.2; left SMG (anterior) (BD: M= -0.10, SD=0.32; UD: M= -0.01, SD=0.24), *p*=0.3; left postcentral gyrus (BD: M= -0.17, SD=0.29; UD: M= -0.11, SD=0.21), *p*=0.4; left OFC (BD: M= -0.30, SD=0.43; UD: M= -0.23, SD=0.41), *p*=0.5.

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| **Supplementary Table 1.** Grouping of neurocognitive tests into cognitive domains | |
| **Cognitive domains** | **Neurocognitive test** |
| Attention and psychomotor speed | CANTAB RVP A’ |
|  | CANTAB RVP Mean Latency |
|  | RBANS Coding |
|  | RBANS Digit Span |
|  | TMT-A |
| Verbal learning and memory | RAVLT List I-V Total recall |
|  | RAVLT Immediate recall |
|  | RAVLT Delayed recall |
|  | RAVLT Recognition |
| Working memory and executive functions | CANTAB SWM Between errors |
|  | CANTAB SWM Strategy |
|  | TMT-B |
|  | Verbal Fluency (letters S+D) |
|  | WAIS-III LNS |
| Abbreviations: CANTAB=Cambridge Neuropsychological Test Automated Battery; RVP=Rapid Visual Information Processing; RBANS=Repeatable Battery for the Assessment of Neuropsychological Status; RAVLT=Rey Auditory Verbal Learning Test; TMT-A=Trail Making Test Part A; TMT-B=Trail Making Test Part B; SWM=Spatial Working Memory; WAIS-III LNS: Wechsler’s Adult Intelligence Scale 3rd edition Letter-Number-Sequencing; | |