**Supplementary Online Content**

eAppendix 1. Study protocol

eAppendix 2. CBT protocol

eFigure 1. CONSORT diagram

eFigure 2: ANOVA for memory consolidation – logical memory test

eFigure 3. Mean number of responses during the Alternative Beliefs Exercise by group

eFigure 4: Mean ratings of perceived helpfulness of CBT sessions by group

eFigure 5: Mean ratings of perceived change in distress following CBT session by group

eTable 1. Demographics and clinical characteristics of participants who completed study visits through week 12 vs non-completers.

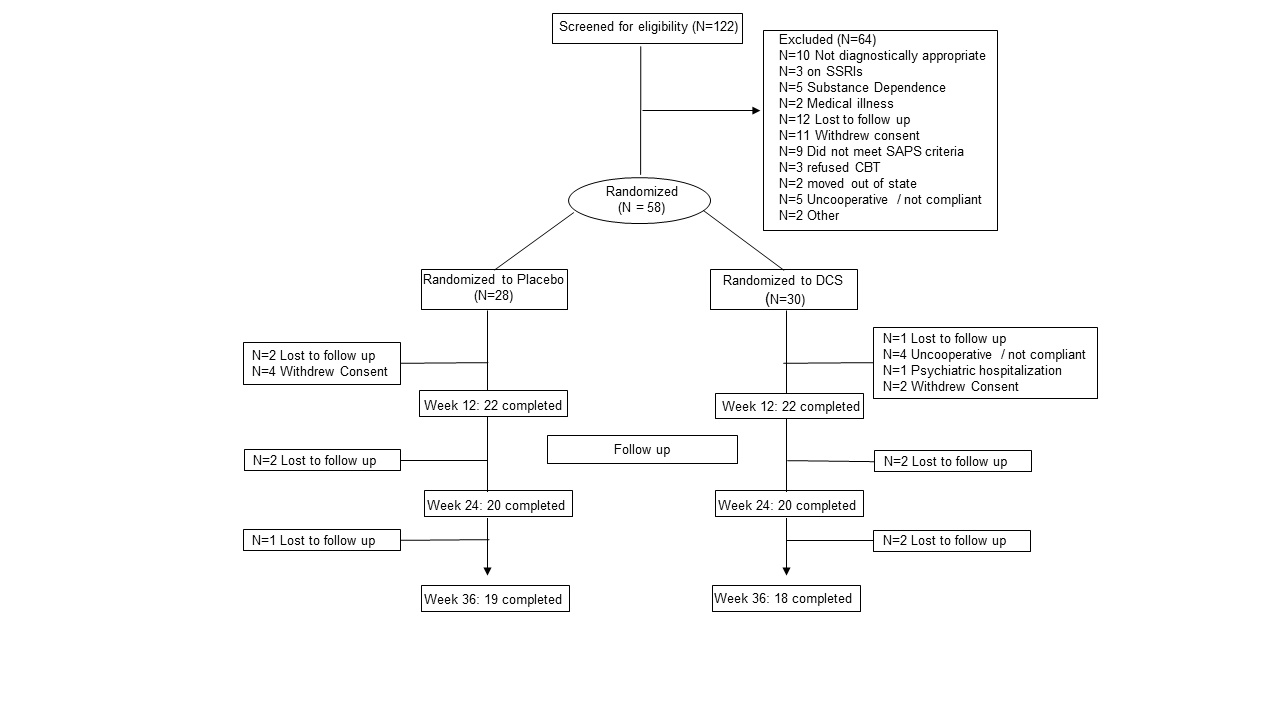
eTable 2. Medication use in randomized study sample.

eTable 3. Linear Mixed Models for repeated measures (Primary analyses)

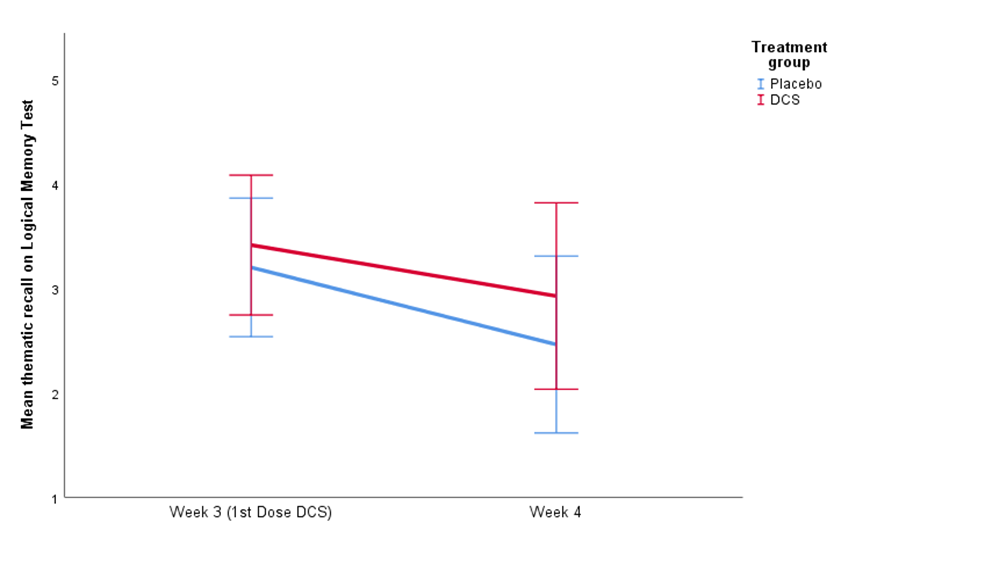
eTable 4. Linear regression analyses examining change in levels of distress and perceived benefit of CBT in predicting change in PSYRATS-D total score

eTable 5. Treatment-emergent side effects

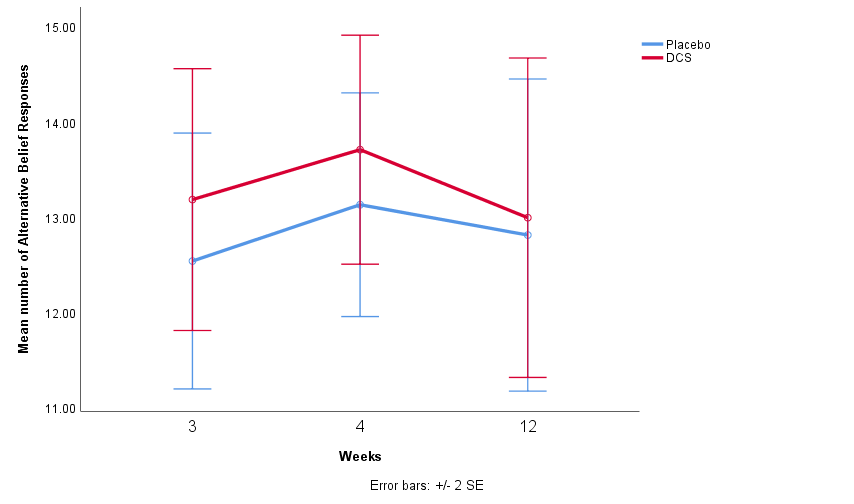
eFigure 1: CONSORT Diagram



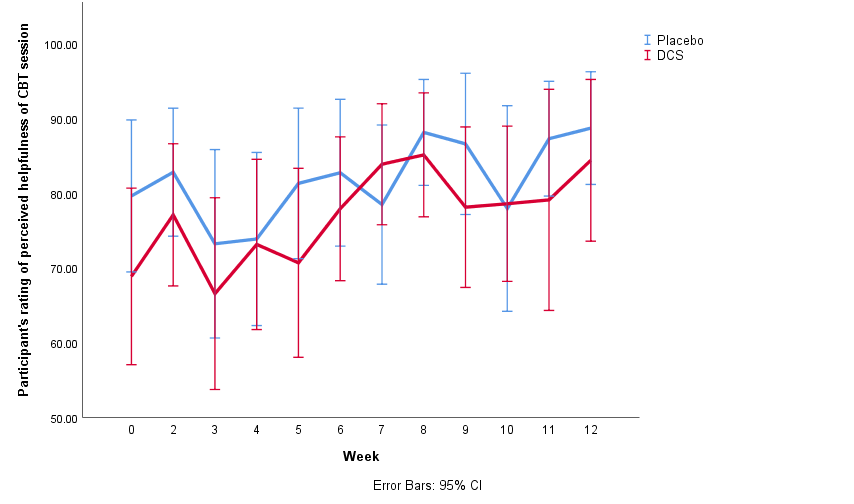
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eFigure 3. Mean number of responses during the Alternative Beliefs Exercise by group



eFigure 4. Mean ratings of perceived helpfulness of CBT sessions by group



eFigure 5: Mean ratings of perceived change in distress following CBT session by group



eTable 1. Demographics and clinical characteristics of participants who completed study visits through week 12 vs non-completers

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Completers (N=44) | Non-completers (N=14) | *t*/X2 | *P* |
| Sex  Women, N (%) | 17, (38.6) | 6, (42.9) | 0.78 (1) | 0.508 |
| Race  Black  White  Hispanic  Asian  Other | 25 (56.8)  17 (38.6)  3 (6.8)  1 (2.3)  0 (0.0) | 7 (50.0)  7 (50.0)  2 (14.3)  0 (0.0)  0 (0.0) | 0.75 (1) | 0.348 |
| Age, mean (SD) | 47.60 (12.0) | 37.07 (11.0) | -2.91 | 0.005 |
| Education | 13.30 (2.7) | 12.79 (2.4) | -0.64 | 0.528 |
| Employment status  Full-time  Part-time  Unemployed | 0 (0.0)  11 (25.0)  33 (75.0) | 1 (7.1)  1 (7.1)  12 (85.7) | 4.94 (2) | 0*.*085 |
| AP treatment, mean (SD) | (N=16)  1807.06 (2233.8) | (N=4)  886.00 (639.4) | -0.80 | 0.433 |
| PSYRATS Baseline, mean (SD) | 13.68 (4.2) | 10.79 (8.3) | -1.75 | 0.086 |
| SANS Baseline, mean (SD) | 31.73 (9.5) | 31.21 (11.1) | -0.16 | 0.867 |

Note: SD=standard deviation; t=t-test statistic for continuous variables; p=p-value; X2= Chi-square test statistic categorical variables; DUP=Duration of untreated psychosis; AP = Antipsychotic treatment

eTable 2. Medication use in randomized study sample

|  |  |  |
| --- | --- | --- |
|  | D-Cycloserine (N=30) | Placebo (N=28) |
| Antipsychotic Type, N (%) |  |  |
| First Generation | 7 (23.3) | 8 (28.6) |
| Second Generation | 16 (53.3) | 15 (53.6) |
| Antipsychotic |  |  |
| Aripiprazole | 5 (16.7) | 3 (10.7) |
| Asenapine | 1 (3.3) | 0 (0.0) |
| Fluphenazine | 1 (3.3) | 4 (14.3) |
| Haloperidol | 3 (10.0) | 3 (10.7) |
| Lurasidone | 1 (3.3) | 0 (0.0) |
| Olanzapine | 4 (13.3) | 4 (14.3) |
| Paliperidone | 2 (6.7) | 0 (0.0) |
| Perphenazine | 3 (10.0) | 1 (3.6) |
| Risperidone | 0 (0.0) | 3 (10.7) |
| Quetiapine | 1 (3.3) | 3 (10.7) |
| Ziprasidone | 2 (6.7) | 2 (7.1) |
| Medication free | 9 (19.9) | 7 (25.0) |
|  |  |  |

eTable 3. Linear mixed model for repeated measures examining change in PSYRATS-D

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  |  |  | |
|  | β, (SE) | 95% CI | *P* Value | |
| **PSYRATS-D (N=53)** | **Model 1** |  | |  |
| Baseline (week 3)a | -6.20, (3.88) | -14.09, 1.70 | | 0.120 |
| Week 4 | .351, (.823) | -1.28, 1.98 | | 0.671 |
| Week 6 | .151, (.823) | -1.48, 1.78 | | 0.855 |
| Week 8 | .734, (.827) | -900, 2.37 | | 0.376 |
| Week 10 | -.007, (.835) | -1.66, 1.65 | | 0.993 |
| Week 12b | 11.49, (1.94) | 7.57, 15.42 | | 0.001 |
| Group difference at Week 12 | -.797, (1.32) | -1.82, 3.42 | | 0.547 |
| Information criteria Akaike | 1161.99 |  | |  |
| **PSYRATS-D (N=49)** | **Model 2c** |  | |  |
| Baseline (week 3)a | -6.37, (3.90) | -14.32, 1.59 | | 0.113 |
| Week 4 | 1.04, (.799) | -.540, 2.62 | | 0.195 |
| Week 6 | .996, (.799) | -.584, 2.58 | | 0.215 |
| Week 8 | 1.36, (.804) | -.225, 2.95 | | 0.092 |
| Week 10 | .624, (.831) | -1.02, 2.27 | | 0.454 |
| Week 12b | 10.93, (1.94) | 6.99, 14.87 | | 0.001 |
| Group difference at Week 12 | -.051, (1.33) | -2.70, 2.60 | | 0.969 |
| Information criteria Akaike | 1053.39 |  | |  |
| **PSYRATS-D (N=53)** | **Model 3d** |  | |  |
| SANS baseline | 6.02, (6.09) | -8.01, 20.05 | | 0.352 |
| Baseline (week 3)a | -4.01, (8.74) | -25.80, 17.78 | | 0.664 |
| Week 4 | .126, (.843) | -1.54, 1.79 | | 0.881 |
| Week 6 | -.040, (.843) | -1.71, 1.63 | | 0.962 |
| Week 8 | .544, (.847) | -1.13, 2.22 | | 0.522 |
| Week 10 | -.318, (.861) | -2.02, 1.39 | | 0.712 |
| Week 12b | 11.12, (5.45) | -1.18, 23.41 | | 0.071 |
| Group difference at Week 12 | -4.84, (2.09) | -9.69, .003 | | 0.050 |
| Information criteria Akaike | .980.145 |  | |  |
|  |  |  |  | |

**Note:** aPSYRATS total at first administration of DCS (week 3) was included as a covariate in all models; bIntercept at week 12 represents the mean PSYRATS-D total for the reference group (DCS); Treatment group (Placebo, DCS) x study visit interaction terms were included in all models. Interactions were not significant; cModel 2, participants with SAPS < 3 at baseline were excluded from the analysis; dModel 3; SANS baseline score included as a covariate; all estimates and p-values refer to fixed effects in all models.

eTable 4. Linear regression examining change in distress (models 1-3) and perceived benefit of CBT (models 4-5) in predicting change on PSYRATS-D total score

|  |  |  |  |
| --- | --- | --- | --- |
|  |  |  |  |
| **Change in level of distress following weekly CBT session** | R2 | *Β* (SE) | *p* |
| **Model 1 – Change in PSYRATS-D from week 3-12**  PSYRATS-D Week 3  Average CBT ∆ distress  ∆ Distress x Group | 0.193  0.218 | -0.468 (0.156)  -0.018 (0.058)  -0.061 (0.085) | 0.005  0.755  0.476 |
| **Model 2 – Change in PSYRATS-D from week 3-24**  PSYRATS-D Week 3  Average CBT ∆ distress  ∆ Distress x Group | 0.190  0.298 | -0.412 (0.127)  -0.034 (0.045)  0.140 (0.062) | 0.006  0.459  0.031 |
| **Model 3 – Change in PSYRATS-D from week 3-36**  PSYRATS-D Week 3  Average CBT ∆ distress  ∆ Distress x Group | 0.163  0.198 | -0.488 (0.207)  0.069 (0.066)  -0.005 (0.092) | 0.025  0.303  0.960 |
| **Perceived benefit of weekly CBT session** |  |  |  |
| **Model 4 – Change in PSYRATS-D from week 3-12**  PSYRATS-D Week 3  Average perceived benefit  Average perceived benefit x group | 0.193  0.200 | -0.451 (0.159)  0.002 (0.043)  0.008 (0.015) | 0.007  0.961  0.575 |
| **Model 5 – Change in PSYRATS-D from week 3-24**  PSYRATS-D Week 3  Average perceived benefit  Average perceived benefit x group | 0.190  0.250 | -0.410 (0.129)  -0.018 (0.036)  -0.017 (0.011) | 0.003  0.614  0.136 |
| **Model 6 – Change in PSYRATS-D from week 3-36**  PSYRATS-D Week 3  Average perceived benefit  Average perceived benefit x group | 0.163  0.194 | -0.501 (0.209)  -0.051 (0.050)  -0.005 (0.017) | 0.022  0.315  0.746 |

eTable 5. Treatment emergent side effects

|  |  |  |
| --- | --- | --- |
| **Symptom** | **Placebo** | **DCS** |
| Trouble sleeping | 10 | 5 |
| Nightmares or sleep disturbances | 8 | 6 |
| Drowsy or sleepy | 7 | 3 |
| Nervous or hyper | 2 | 5 |
| Weakness or fatigue | 11 | 4 |
| Irritable | 7 | 5 |
| Poor memory | 6 | 6 |
| Trouble concentrating | 7 | 5 |
| Feeling strange or unreal | 2 | 3 |
| Hearing or seeing things | 2 | 0 |
| Abnormal sensations | 2 | 3 |
| Numbness or tingling | 3 | 3 |
| Dizziness or faintness | 5 | 1 |
| Headache | 3 | 6 |
| Blurred vision | 5 | 2 |
| Ringing in ears or trouble hearing | 2 | 1 |
| Stuffy nose | 4 | 5 |
| Dry mouth | 4 | 2 |
| Drooling or increased salivation | 0 | 4 |
| Muscle cramps or stiffness | 12 | 4 |
| Muscle twitching or movements | 3 | 2 |
| Trouble sitting still | 0 | 2 |
| Tremor or shakiness | 2 | 1 |
| Poor coordination or unsteadiness | 2 | 1 |
| Slurred speech | 0 | 0 |
| Heartbeat rapid or pounding | 0 | 2 |
| Trouble catching breath or hyperventilating | 1 | 2 |
| Chest pain | 3 | 4 |
| Nausea or vomiting | 4 | 2 |
| Stomach or abdominal cramps | 3 | 5 |
| Constipation | 2 | 1 |
| Diarrhea | 2 | 4 |
| Difficulty starting urination | 2 | 3 |
| Frequent need to urinate | 5 | 5 |
| Menstrual irregularities | 0 | 0 |
| Loss of sexual interest | 3 | 4 |
| Problems with sexual arousal | 4 | 2 |
| Delayed or absent orgasm | 5 | 2 |
| Sweating excessively | 0 | 2 |
| Fluid retention or swelling | 1 | 0 |
| Appetite decreased | 1 | 0 |
| Appetite increased | 5 | 6 |
| Weight gain | 4 | 4 |
| Weight loss | 1 | 1 |
| Skin rash or allergy | 2 | 2 |
| Diminished mental acuity or sharpness | 8 | 5 |
| Difficulty finding words | 3 | 1 |
| Apathy emotional difference | 2 | 2 |
| Dizziness upon standing | 2 | 0 |
| Bruising | 0 | 1 |
| Hair thinning loss | 0 | 0 |
| Hot flashes | 2 | 2 |
| Clenching teeth at night | 1 | 2 |
| Straight taste in mouth | 1 | 0 |
| Unable to sit still | 0 | 2 |

**Note**: Side effects were assessed using the Systematic Assessment for Treatment Emergent Events (SAFTEE). Participant responses at each visit were compared to symptom responses at Week 2 (one week before baseline and the week prior to the start of medication administration). A side effect was defined as an increase of 2 points on an item on the SAFTEE. Individuals who reported a side effect in multiple weeks (i.e. at week 4 and 5) were only counted one time. Table reports the total number of participants reporting an increase in a side effect by 2 or more points on the SAFTEE at least one time during the study.