**Supplementary Table 1**. **Cognitive tasks classified into each domain**

| Cognitive domain | Cognitive tasks |
|---|---|
| Attention | CPT-IP(Cornblatt et al., 1988), Coding, Matching to Sample Visual Search(Robbins et al., 1994), WAIS Digits forward, WAIS Digits backward, RBANS Digit span(Rey, 1964), RBANS Coding(Rey, 1964), Rapid Visual Information Processing(Robbins et al., 1994), Stroop Color-Word Task(Golden, 1975) |
| Executive function | TMT-B(Reitan, 1958), Stroop test, BACS Tower of London(Keefe et al., 2004), NAB mazes test(Stern and White, 2003), WCST(Heaton, 1981), ID/ED(Robbins et al., 1994), Stockings of Cambridge(Robbins et al., 1994), Spatial Working Memory (strategies) (Robbins et al., 1994) Spatial span (strategies) |
| Language | RBANS picture naming(Rey, 1964) |
| Motor skills | BACS Token motor task(Keefe et al., 2004), Mcquarrie dotting(MacQuarrie, 1950), Mcquarrie tapping(MacQuarrie, 1950), Purdue Pegboard Task(Tiffin and Asher, 1948), Grooved Pegboard Test(Bohnen et al., 2007), motor task latency |
| Processing Speed | TMT-A(Reitan, 1958), Phonetic fluency, animal fluency, picture naming, RBANS Semantic fluency(Rey, 1964), Oral Fluency Test(Benton, 1968), BACS Total fluency(Keefe et al., 2004), COWAT(Benton et al., 1994), Category fluency(Spreen and Strauss, 1998), BACS Symbol coding(Keefe et al., 2004) |
| Social cognition | Facial emotion recognition task, Mayer-Salovery-Caruso emotional intelligence test(Mayer and Salovey, 2007) |
| Verbal learning/memory | BACS list learning(Keefe et al., 2004), RBANS list learning(Rey, 1964), RBANS list recall(Rey, 1964), RBANS list recognition(Rey, 1964), RBANS story memory(Rey, 1964), RBANS story recall(Rey, 1964), MAS List recall and acquisition(Williams, 1991), Hopkins Verbal learning test(Brandt and Benedict, 2001), MMA, Rey auditory verbal test(Rey, 1964) |
| Visual learning/memory | TAVEC, MAS Immediate visual recognition(Williams, 1991), RBANS Figure recall(Rey, 1964), BVMT-R(Benedict, 1997), Pattern Recognition Memory(Robbins et al., 1994), Spatial Recognition Memory(Robbins et al., 1994), Delayed Matching to Sample(Robbins et al., 1994), RBANS Figure recall(Rey, 1964) |
| Visuospatial and constructional skill | RBANS Figure copy, RBANS Line orientation |
| Working memory | WAIS(Wechsler, 1997) Digit symbol, WAIS Digits backward, arithmetic, letters and numbers, BACS Digit sequencing(Keefe et al., 2004), RBANS Digit span, WMS Spatial span (correct)(Wechsler, 1987), Letter-Number Span(Gold et al., 1997) |

BACS, Brief Assessment of Cognition; BVMT-R, Brief Visuospatial Memory Test-Revised; COWAT, controlled oral word association test; CPT-IP, Continuous Performance Test, Identical Pairs version; ID/ED, Intradimensional/Extradimensional Set-shifting; MAS, memory assessment scales; NAB, Neuropsychological Assessment Battery; RBANS, Repeatable Battery for the Assessment of Neuropsychological Status; TAVEC, Spanish version of the California Verbal Learning Test; TMT-A, Trail Making Test part A; TMT-B, Trail Making Test part B; WAIS, Wechsler adult intelligence scale; WCST, Wisconsin Card Sorting Test; WMS, Wechsler Memory Scale.

**Supplementary table 2. Quality assessment of the individual studies**

| Study | Random sequence generation | Allocation concealment | Performance bias | Detection bias | Attrition bias | Reporting bias |
|---|---|---|---|---|---|---|
| ***Aspirin*** | | | | | | |
| Laan et al., 2010 | Low | Unclear | Low | Low | Low | Low |
| Attari et al., 2017 | Low | Low | Low | Low | Low | Low |
| ***Celecoxib*** | | | | | | |
| Muller et al., 2002 | Low | Unclear | Low | Unclear | Low | Low |
| Rapaport et al., 2005 | Low | Unclear | Low | Unclear | Low | Low |
| Akhonzadeh et al., 2007 | Low | Unclear | Low | Low | Low | Low |
| Muller et al., 2010 | Low | Unclear | Low | Low | Low | Low |
| ***Omega-3 fatty acids*** | | | | | | |
| Fenton et al. 2001 | Low | Unclear | Low | Low | Low | Low |
| Peet et al., 2001 | Low | Low | Low | Low | Low | Low |
| Peet & Horrobin., 2002 | Low | Low | Low | Unclear | Low | Low |
| Emsley et al., 2002 | Low | Unclear | Low | Unclear | Low | Low |
| Emsley et al., 2006 | Low | Unclear | Low | Unclear | Low | Low |
| Wood et al., 2010 | Low | Low | Low | Low | Unclear | Low |
| Bentsen et al., 2013 | Low | Low | Low | Low | Low | High |
| Jamilian et al., 2014 | Low | Unclear | Low | Low | Low | Low |
| Boskovic et al., 2016 | Low | Unclear | Low | Low | Unclear | Low |
| Pawelczyk et al., 2016 | Low | Unclear | Low | Low | Low | Low |
| Qiao & Mei, 2017 | Low | Low | Low | Unclear | Low | Low |
| ***Estrogen*** | | | | | | |
| Kulkarni et al., 2001 | Low | Unclear | Low | Unclear | Low | Low |
| Akhonzadeh et al., 2003 | Low | Unclear | Low | Low | Low | Low |
| Kulkarni et al., 2008 | Low | Unclear | Low | Low | Low | Low |
| Kulkarni et al., 2011 | Low | Unclear | Low | Low | Low | Low |
| Ghafari et al., 2013 | Low | Unclear | Low | Unclear | Low | Low |
| Kulkarni et al., 2015 | Low | Unclear | Low | Unclear | Low | Low |
| ***SERM*** | | | | | | |
| Kulkarni et al., 2010 | Low | Unclear | Low | Low | Low | Low |

| | | | | | | |
|---|---|---|---|---|---|---|
| Usall et al., 2011 | Low | Unclear | Low | Low | Low | Low |
| Kianimehr et al., 2014 | Low | Unclear | Low | Unclear | Low | Low |
| Weickert et al., 2015 | Low | Unclear | Low | Low | Low | Low |
| Khodaie et al., 2015 | Low | Low | Low | Low | Low | Low |
| Usall et al., 2016 | Low | Low | Low | Unclear | Low | Low |
| Kulkarni et al., 2016 | Low | Low | Low | Unclear | Low | Low |
| Ji et al., 2016 | Low | Unclear | Low | Unclear | Low | Low |
| Weiser et al., 2017 | Low | Unclear | Low | Unclear | Low | Low |
| ***Minocycline*** | | | | | | |
| Levkovitz et al., 2010 | Low | Unclear | Low | Unclear | Low | Low |
| Chadhry et al, 2012 | Low | Unclear | Low | Low | High | Low |
| Ghanizadeh et al., 2014 | Low | Low | Low | Low | Low | Low |
| Khodaie-Ardakani et al., 2014 | Low | Low | Low | Low | Low | Low |
| Liu et al., 2014 | Low | Unclear | Low | Unclear | Low | Low |
| ***NAC*** | | | | | | |
| Berk et al., 2008 | Low | Low | Low | Low | Low | Low |
| Farokhina et al., 2013 | Low | Low | Low | Low | Low | Low |
| ***Pregnenolone*** | | | | | | |
| Marx et al., 2009 | Low | Unclear | Low | Unclear | Low | Low |
| Ritsner et al., 2010 | Low | Low | Low | Unclear | Low | Low |
| Marx et al., 2014 | Low | Unclear | Low | Unclear | Unclear | Low |
| Ritsner et al., 2014 | Low | Unclear | Low | Low | Low | Low |
| ***Davunetide*** | | | | | | |
| Javitt et al., 2012 | Low | Unclear | Low | Unclear | Low | Low |
| ***Erythropoietin*** | | | | | | |
| Ehrenreich et al., 2007 | Low | Low | Low | Low | Low | Low |

**Supplementary table 3. Aspirin subgroup analysis (PANSS scores).**

| PANSS domain | Variables | Trials (subjects) | ES (95% CI) | I square |
|---|---|---|---|---|
| PANSS total | baseline PANSS total < 80 | 2 (80) | 1.78 (1.29 to 2.28) | 0 |
| | baseline PANSS total > 80 | 1 (70) | .37 (-.10 to .83) | N/A |
| PANSS positive | baseline PANSS total < 80 | 2 (80) | 2.32 (1.78 to 2.87) | 73.8 |
| | baseline PANSS total > 80 | 1 (70) | .23 (-.24 to .69) | N/A |
| PANSS negative | baseline PANSS total < 80 | 2 (80) | 1.39 (.93 to 1.85) | 0 |
| | baseline PANSS total > 80 | 1 (70) | .28 (-.19 to .74) | N/A |

**Supplementary table 4. Minocycilne subgroup analysis (PANSS total score).**

| Variables | Trials (subjects) | ES (95% CI) | I square |
|---|---|---|---|
| age < 30 | 4 (144) | 0.23 (-0.60 to 1.06) | 76.4 |
| age ≥ 30 | 2 (41) | 0.81 (-0.49 to 2.12) | 87.9 |
| illness duration < 5 yr | 5 (165) | 0.37 (-0.17 to 0.90) | 77.8 |
| illness duration ≥ 5 yr | 1 (20) | 1.49 (0.80 to 2.18) | N/A |
| treatment period < 24 wk | 3 (80) | 0.42 (-0.58 to 1.43) | 87.4 |
| treatment period ≥24 wk | 3 (105) | 0.71 (0.03 to 1.39) | 76.5 |
| baseline PANSS total < 80 | 3 (56) | 1.09 (0.07 to 2.12) | 83.4 |
| baseline PANSS total > 80 | 3 (129) | 0.12 (-0.43 to 0.67) | 73.7 |

**Supplementary table 5. Minocycilne subgroup analysis (PANSS negative score).**

| Variables | Trials (subjects) | ES (95% CI) | I square |
|---|---|---|---|
| age < 30 | 4 (144) | 0.94 (0.27 to 1.60) | 68.4 |
| age ≥ 30 | 2 (41) | 1.02 (-0.44 to 2.48) | 89.8 |
| illness duration < 5 yr | 5 (165) | 0.77 (0.27 to 1.27) | 73.7 |
| illness duration ≥ 5 yr | 1 (20) | 1.78 (1.06 to 2.50) | N/A |
| treatment period < 24 wk | 3 (80) | 0.65 (0.13 to 1.17) | 53.6 |
| treatment period ≥24 wk | 3 (105) | 1.16 (0.30 to 2.00) | 83.8 |
| baseline PANSS total < 80 | 3 (56) | 1.14 (0.16 to 2.11) | 81.7 |
| baseline PANSS total > 80 | 3 (129) | 0.77 (0.09 to 1.44) | 81.2 |

**References**


Benedict RH. (1997) *Brief visuospatial memory test--revised: professional manual*: PAR.

Benton AL. (1968) Differential behavioral effects in frontal lobe disease. *Neuropsychologia* 6: 53-60.

Benton L, Hamsher K and Sivan A. (1994) Controlled oral word association test. *Multilingual aphasia examination* 3.

Bohnen NI, Kuwabara H, Constantine GM, et al. (2007) Grooved pegboard test as a biomarker of nigrostriatal denervation in Parkinson's disease. *Neurosci Lett* 424: 185-189.

Brandt J and Benedict RH. (2001) *Hopkins verbal learning test--revised: professional manual*: Psychological Assessment Resources.

Cornblatt BA, Risch NJ, Faris G, et al. (1988) The Continuous Performance Test, identical pairs version (CPT-IP): I. New findings about sustained attention in normal families. *Psychiatry Res* 26: 223-238.

Gold JM, Carpenter C, Randolph C, et al. (1997) Auditory working memory and Wisconsin Card Sorting Test performance in schizophrenia. *Arch Gen Psychiatry* 54: 159-165.

Golden CJ. (1975) A group version of the Stroop Color and Word Test. *Journal of personality assessment* 39: 386-388.

Heaton RK. (1981) Wisconsin card sorting test manual. *Psychological Assessment Resources*.

Keefe RS, Goldberg TE, Harvey PD, et al. (2004) The Brief Assessment of Cognition in Schizophrenia: reliability, sensitivity, and comparison with a standard neurocognitive battery. *Schizophr Res* 68: 283-297.

Lipsey MW and Wilson DB. (2001) Applied social research methods series; Vol. 49. Practical meta-analysis. Thousand Oaks, CA: Sage Publications.

MacQuarrie TW. (1950) *MacQuarrie test for mechanical ability*: California Test Bureau.

Mayer JD and Salovey P. (2007) *Mayer-Salovery-Caruso emotional intelligence test*: Multi-Health Systems Incorporated.

Reitan RM. (1958) Validity of the Trail Making Test as an indicator of organic brain damage. *Perceptual and motor skills* 8: 271-276.

Rey A. (1964) L'examen clinique en psychologie [The clinical psychological examination]. *Paris: Presses Universitaires de France*.

Robbins TW, James M, Owen AM, et al. (1994) Cambridge Neuropsychological Test Automated Battery (CANTAB): a factor analytic study of a large sample of normal elderly volunteers. *Dementia and Geriatric Cognitive Disorders* 5: 266-281.

Schulz KF, Altman DG and Moher D. (2010) CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMC Med* 8: 18.

Spreen O and Strauss E. (1998) *A compendium of neuropsychological tests: Administration, norms, and commentary*: Oxford University Press.

Stern RA and White T. (2003) *NAB, neuropsychological assessment battery: administration, scoring, and interpretation manual*: Psychological Assessment Resources.

Tiffin J and Asher EJ. (1948) The Purdue Pegboard: norms and studies of reliability and validity. *Journal of applied psychology* 32: 234.

Wechsler D. (1987) *WMS-R: Wechsler memory scale-revised*: Psychological Corporation.

Wechsler D. (1997) WAIS-III: Wechsler adult intelligence scale, administration and scoring manual. San Antonio, Texas: Psychological Corporation. *ed: Harcourt Brace*.
Williams JM. (1991) Memory assessment scales. *Odessa, FL: Psychological Assessment Resources* 199.