**The efficacy of non-invasive, non-convulsive electrical neuromodulation on depression, anxiety and sleep disturbance: a systematic review and meta-analysis: Supplementary Material**

**Supplementary Figure 1. Risk of bias graph**

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**Supplementary Figure 2. Risk of bias summary**

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**Supplementary Figure 3. The effects of tDCS, CES on depression and anxiety: funnel plots. (a) tDCS on depression; (b) CES on depression; (c) tDCS on anxiety. tDCS, transcranial direct current stimulation; CES, cranial electrotherapy stimulation**

**(a)**



**(b)**



**(c)**



**Supplementary Table 1. Characteristics of the included studies**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Author Year | Population | Concomitant antidepressant | Sample Size | Mean age (SD or range)  | Female (%) | Duration/Session  | Electrical device/brand | Frequency/Current | N of sessions/frequency | Electrode position | Outcome  |
| 1 Ahmadizadeh et al. 2019 | PTSD | NR | 2020 | 44.50 (2.34)43.00 (2.42) | 12 (60)14(70) | 20min | tDCS/ NeuroConn | 2 mA | 10 /once a day | Anode: F3Cathode: F4 | BDI, BAI, PCL-5, Reexperiencing, NACM |
| 2 Batista et al. 2015 | Crack-Cocaine Dependence | NR | 1917 | 30.4 (9.8)30.3 (8.4) | 0(0)0(0) | 20 min | tDCS/Striat | 2 mA | 20/ once a day | Anode: F3Cathode: F4 | HAM-D, HAMA, Craving |
| 3 Bennabi et al. 2015 | TRD  | Add on | 1212 | 60.4 (12)59.9 (15.4) | 10 (83.3)5 (45.5) | 30min | tDCS/ NeuroConn | 2 mA | 10 /twice a day | Anode: F3Cathode: FP2 | MADRS, HDRS 21, HAMA, BDI, STAI-A, MMSE |
| 4 Bianchi et al. 2017 | Postmenopausal women | Monotherapy | 1515 | 55.3 (5.6)53.8 (5.6) | 15(100)15(100) |  20min | tDCS/TCT Research Limited,CR1781195 | 2 mA | 10 /once a day | Anode:C3, C4(M1)Cathode: FP2 | HAMD, PSQI, PHQ |
| 5 Boggio et al. 2008 | MDD | Monotherapy | 21(DLPFC)9(Occipital)10 | 51.6 (7.7)46.3 (5.8)46.5 (7.1 | 7(33.3)3(33.3)3(30) | 20 min | tDCS/NR | 2 mA | 10 /once a day | tDCS**DLPFC** 🡪 Anode: F3; tDCS **Occiptal** 🡪Anode: OccipitalCathode: FP2 | HAMD, BDI |
| 6 Brunoni et al. 2013 | MDD | Monotherapy& Add on | 6349 | 41.4 (12)44.9 (13) | 42(66.7)27(55.1) | 30min | tDCS/NR | 2 mA | 10 /once a day | Anode: F3Cathode: F4 | MADRS |
| 7 Brunoni et al. 2017 | MDD | Monotherapy | 9460 | 44.6(11.8)40.9(12.9) | 64 (68)41 (68) | 30min | tDCS/Soterix  | 2 mA | 22 /15 once a day+7 sessions every week  | Anode: F3Cathode: F4 | MADRS, HAMD, BDI |
| 8 de Lima et al. 2019 | GAD | Add on | 1515 | 32(65)29 (5.05) | 10(66.7)9 (60) | 20 min | tDCS/NR | 2 mA | 5/once a day | Anode: F3Cathode: FP2 | BDI, HAMA, BAI |
| 9 Fregni et al. 2006 | FM | Add on | 11(DLPFC)11(M1)10  | 54.8 (9.3)54.2 (7.4) | 11 (100)11(100)10(100) | 20min | tDCS/NR | 2 mA | 5/once a day | tDCS DLPFC:Anode: F3tDCS M1: Anode: M1Cathode: FP2 | BDI, VAI |
| 10 Fregni et al. 2006 | MDD | Monotherapy | 99 | 47.56(10.8)45.33(9.27) | 5(55.6)6(66.7) | 20min | tDCS/NR | 1 mA | 5/once a day | Anode: F3Cathode: FP2 | HAMD-21, BDI |
| 11 Khedr et al. 2017 | FM | NR | 1818 | 31.3 (10.99)33.89(11.18) | 17(94.4)17(94.4) | 20 min | tDCS/NR | 2 mA | 5/once a day | Anode: M1Cathode: Cntralateral extra-cephalic (EC) | WPI, VAS, HAMA, HAMD |
| 12 Klauss et al. 2014 | AUD | Add on | 1617 | 44.0 (7.8) 45.5 (8.9) | 0 (0)1(5.8) | 20 min | tDCS/Striat IBRAMED | 2 mA | 5/once a day | Anode: F3Cathode: F4 | HAMD, HAMA, MMSE, OCDS |
| 13 Loo et al. 2010 | MDD | Add on | 2020 | 48.95 (10.00)45.60 (12.45) | 11(22)11(22) | 20 min | tDCS/ NeuroConn | 1 mA | 5/Once every 2 day | Anode: F3Cathode: Right orbit | HAMD, PGI, BDI, MADRS |
| 14 Loo et al. 2012 | MDD | Add on | 3129 | 47.8(12.5)48.6(12.6) | 14(45.1)14(48.2) | 30 min | tDCS/ NeuroConn | 2 mA | 15/once a day | Anode: F3Cathode: F8 | MADRS, QIDS-C, IDS |
| 15 Loo et al. 2018 | MDD | Add on | 4242 | 48.93 (12.34)46.74 (16.30) | 21(50)21(50) | 30 min | tDCS/ NeuroConn | 2.5 mA | 20/once a day | Anode: F3Cathode: F8 | MADRS |
| 16 Martin et al. 2018 | MDD | Partial use antidepressant | 5961 | 49.2 (13.6)47.3 (15.6) | 30(50.8)33(54.1) | 30 min | tDCS/NR | 2.5 mA | 20/once a day | Anode: F3Cathode: F8 | MADRS |
| 17 Martinotti et al. 2019 | SUD | NR | 1814 | 40.3 (10.1)37.6 (10.9) | 3(16.6)1(7.1) | 20 min | tDCS /E.M.S. ElectromedicalSystems, Bologna | 1.5 mA | 5/once a day | Anode: F3Cathode: F4 | Substance consumption, HAMD, HAMA, YMRS, BIS |
| 18 Nord et al. 2019 | MDD | Monotherapy | 2019 | 35.60(12.91)31.05 (8.17) | 9(45)11(57.9) | 20 min  | tDCS/ NeuroConn | 1 mA | 8/once a day  | Anode: F3Cathode: Ipsilateral deltoid | HAMD, BDI, BAI |
| 19 Pal et al. 2015 | Chronic tinnitus | NR | 2121 | 51.6(12.2)48.0(9.9) | 9(42.9)9(42.9) | 20 min | tDCS/BrainSTIM | 2 mA | 5/once a day | Anode: F3-Fz-F4 (PFC) 2 Cathodes: T3& T4 (left & right AC) | STSS Subjective Tinnitus Severity Scale, VAS, HADS, CGI |
| 20 Palm et al. 2012 | MDD | Add on | 1111 | 56 (12)58 (12) | 6(54.5)8(72.7) | 20 min | tDCS/ NeuroConn | 1 or 2 mA  | 10/once a day | Anode: F3Cathode: FP2 | HAMD, BDI, PANAS |
| 21 Harvey et al. 2017 | Elderly with chronic pain and insomnia  | Partial use antidepressant | 68 | 72(6)71(8) | 5(83.3)6(75) | 20min | tDCS/Soterix | 2 mA | 5/once a day | Anode：M1& Contralateral C3, C4 Cathode: FP2 | SE, ISI |
| 22 Pavlova et al. 2018 | MDD | Add on | 272120 | 36(10.8)37.0(8.8)40.1(12.2) | 17(62.9)17(80.9)15(75\_ | 30min20min | tDCS/NR | 0.5 mA | 10/once a day | Anode: F3Cathode: Contralateral orbit | HAMD |
| 23 Salehinejad et al. 2017 | MDD | Monotherapy  | 1212 | 26.8 (7.1) 25.5 (4.6) | 7(58.3)8(66.6) | 20 min | tDCS/ActivaDoseIontophoresi | 2 mA | 10/once a day | Anode: F3Cathode: F4 | CANTAB memory tests, BDI, HDRS |
| 24 Sampaio et al. 2018 | Bipolar depression | Add on | 3029 | 46.2 (11.8)45.7 (10.3 | 16 (53)24 (83) | 30min | tDCS/Soterix | 2 mA | 12/10 once a day+1 session every 2 week | Anode: F3Cathode: F4 | HAMD |
| 25 Sharafi et al. 2019 | TRD | Monotherapy | 1515 | 50.7 (10.7)43.8 (12.6) | 10 (60)6 (40) | 20min | tDCS/ENRAF | 2 mA | 10/once a day | Anode: F3Cathode: F4 | HAMD |
| 26 Taremian et al. 2019 | opium use disorder | NR | 2020 | 33. 45 (10.17)34.10 (9.31) | 00 | 20min | tDCS/NR | 2 mA | 10/once a day | Anode: F3Cathode: F4 | OCDS, BDI, BAI |
| 27 Valiengo et al. 2017 | Post stroke depression | Monotherapy | 2424 | 62.2 (12.3)61.3(10.6) | NRNR | 30 min | tDCS/ NeuroConn | 2 mA | 12/10 once a day+1 session every 2 week | Anode: F3Cathode: F4 | HAMD, MADRS, MMSE, MOCA |
| 28 Vigod et al. 2019 | Depression in pregnancy | Monotherapy | 1010 | 31.2 (4.0)33.3 (4.3) | 10(100)10(100) | 30min  | tDCS/Magstim | 2 mA | 15/once a day | Anode: F3Cathode: F4 | MADRS, EPDS, State-Trait Anxiety Inventory |
| 29 Welch et al. 2019 | MDD | Monotherapy | 95 | 49.2260.4 | 8(88.9)4(80) | 30min | tDCS/Chattanooga Ionto | 2 mA | 12/3 sessions every week | Anode: F3Cathode: F4 | HAMD-21 |
| 30 Young et al. 2020 | MS with neuropathic Pain  | Partial use antidepressant | 1515 | 51.2 (9.3)49.87 (12.9) | 11(73.3)13 (86) | 20min | tDCS/NR | 2 mA | 20/once a day | Anode: C3 or C4Cathode: Contralateral supraorbital | DASS, NPS Neuropathic Pain Scale; VAS |
| 31 Zhou et al. 2020 | MDD | Monotherapy | 4743 | 43.91 ± 1140.45 ± 8.3 | 31(65.9)29(67.4) | 30-min | tDCS | 2 mA | 20/once a day | Anode: F3Cathode: F4 | SDS, SAS, PSQI |
| 32 Blumberger et al. 2012 | TRD | Add on | 1311 | 45.3 (11.6)45.3 (11.6) | 10(76.9)10(90.9) | 20min | tDCS/CX-6650 | 2 mA | 15/once a day | Anode: F3Cathode: F4 | HRSD-17, BDI, MADRS |
| 33 Mayur et al. 2018 | MDD | Add on | 88 | 47(12.57)42.88(16.64) | 2 (25)4 (50) | 20-min | tDCS/neuroConn | 2 mA | 10/once a day | Anode: F3Cathode: F4 | MADRS, MOCA,Visual memory |
| 34 Vanderhasselt et al. 2015 | MDD | Add on | 1914 | 46.26(10.67)41(11.54) | 68%79% | 30min | tDCS /Chattanooga Ionto | 2mA | 10/once a day | Anode: F3Cathode: F4 | HAMD, BDI, PASAT, RRS |
| 35 Pohl et al. 2020 | Episodic migraine | NR | 1112 | 41(15)34 (10) | 10 (90.1)12 (100) | 20 min | tDCS/neuroConn | 1 mA | 28/once a day | Anode: OzCathode: CZ | HADS-D, HADS-A, MIDAS |
| 36 Mariano et al. 2019 | Chronic Low Back Pain | NR | 1110 | 65.7 (8.8)60.7 (11.8) | 1 (10.0)2 (18.2) | 20 min | tDCS/neuroConn | 2 mA | 10/once a day | Anode: ContralateralMastoid Cathode: FC1 | PHQ-9, GAD-7, PASS-20 |
| 37 Lisoni et al. 2020 | Borderline personality  | Add on | 1515 | 38 (10.9)42.6 (13.6) | 8(53.5)10(66.7) | 20 min | tDCS/NR | 2 mA | 15/once a day | Anode: F3Cathode: F4 | HAMD, BDI-II, BIS |
| 38 Mori et al. 2010 | MS with neuropathic Pain | NR | 109 | 44.8 (27.5)44.8 (27.5) | 5(50)6(66.7) | 20 min | tDCS/NR | 2 mA | 5/once a day | Anode:C3 or C4Cathode:Contralateral painful somatic area | BDI, VAS |
| 39 Segrave et al. 2014 | MDD | Add on | 99 | 42.6 (18.32)45.0 (10.15) | 2(22.2)4(44.4) | 20 min | tDCS/NR | 2 mA | 5/once a day | Anode: F3Cathode: F8 | MADRS, BDI |
| 40 Rose et al. 2009 | Spousal Caregivers of Alzheimer’s Disease | Monotherapy | 1919 | 71.94 (7.78)76.52 (5.60) | 14 (73.7) 11 (57.9)  | 60 mins | CES/Alpha-stim | 0.05Hz/0.1mA | 20/once a day | Ear clip electrodes | GDS, PSQI, GSDS, Sleep Onset Latency |
| 41 Bhardwaj et al. 2018 | Stroke survivors | NR | 99 | 56.06 (6.10)56.06 (6.10) | NRNR | 30 min | CES/Alpha-stim | 0.5 Hz/< 1 mA  | 20/once a day | Ear clip electrodes | DASS, PSQI |
| 42 Mischoulon et al. 2015 | TRD | Add on | 1713 | 45.5 (12.3)51.4 (11.9) | 10 (59%)7 (54%) | 20 min | CES/FW-100 Fisher Wallace Cranial Stimulator | 15, 500, 1500Hz/0.1-4 mA | 15/once a day | Scalp, over the two DLPFC | HAMD-17 |
| 43 Turner 2014 | MDE or BDII  | Partial use antidepressant | 1010 | 59.55(7.816)59.55(7.816) | 9(90)9(90) | 60min | CES/Alpha-stim | 0.5 Hz/2 mA | 21/once a day | Ear clip electrodes | BDI-II, PHQ-9 |
| 44 Rosenthal 1972 | Neurotic anxiety anddepression  | Add on | 1111 | 42.843.5 | 1010 | 30mins | CES/NR | 100Hz/0.1-0.25 mA | 5/once a day | Cathodes: OrbitsAnodes: Mastoid process | Zung self-rating depression scale |
| 45 Scallet et al. 1976 | Chronic hysteria  | NR | 55 | NRNR | NRNR | 30-40mins | CES /Neurotone 101 | 100Hz/NR | 12 session | Cathode: SupraorbitalAnode: mastoid  | Mental health self-rating symptoms scale |
| 46 BarclayBarclay 2014 | Anxiety disorder | Add on | 6055 | 42.3(14.6)42.3(14.6) | 37(47.4)41(52.6) | 60mins | CES/Alpha-Stim 100 | 0.5 Hz/0.1mA | 25/once a day | Ear clip electrodes | HAMA, HAMD |
| 47 Gong et al. 2016 | Functional Constipation | NR | 3836 | 52.45(14.38)53.17(12.11) | 25 (65.8)29 (80.6) | 30mins | CES/Alpha-Stim SCS  | 0.5 Hz/0.01-0.5mA | 15/once a day | Ear clip electrodes | SAS, SDS |
| 48 Hearst et al. 1974 | Patient with psychiatric illness | Add on | 1414 | 3740 | 1113 | 30mins | CES/Neurotone 101 | 100Hz /0.3-1.1mA | 5/once a day | Cathodes: SupraorbitalAnodes: Mastoid | SRSS |
| 49 Tillisch et al. 2020 | Veterans with anxiety& depression | Add on  | 2222 | NRNR | 00 | 60min | CES/Alpha-Stim AID | 0.5 Hz/0.1mA | 56/once a day | Ear clip electrodes | HADS, MHC-SF, PHQ, Telomere length |
| 50 LandeGragnani 2013 | Insomnia patients | Add on | 2829 | NRNR | 8(28.6)3(10.3) | 60min | CES/Alpha-Stim SCS  | 0.5 Hz//0.1mA | 5/once a day | Ear clip electrodes | Total sleep time, hours asleep |
| 51 McClure et al. 2015 | Bipolar depression | Add on  | 79 | 52.57(11.43)43.78 (18.26) | 2(28.6)6(69.7) | 20min | CES/Fisher Wallace Cranial Stimulator | 5 Hz, 500 Hz, and 15,000 Hz/2 mA | 10/once a day | Placed over the temples bilaterally | BDI, HAMD, CGI, YMRS, Q-LES-Q-SF |
| 52 Padjen et al. 1995 | AUD | NR | 2834 | 40.18(9.76)39.97(10.36) | 00 | 30 min | CES/NR | 20-200HZ/<1mA | 20/once a day | 2 Frontal2 mastoid | MAST, HAMD, HAMA, MMSE |
| 53 RohSo 2017 | Healthy postmenopausal women | NR | 2525 | 54.4 (2.8)54.8 (2.8) | 25(100)25(100) | 20mins | CES/Alpha-Stim 100 | 0.5 Hz/0.1mA | 24/3 times a week | Ear clip electrodes | K-POMS, BDNF, ACTH, Cortisol |
| 54 MellenMackey 2009 | Sheriff’s staff with depression | Add on | 1110 | NRNR | NRNR | 20min | CES/Alpha-Stim SCS | 0.5 Hz/0.1mA | 20/once a day | Ear clip electrodes | BDI, BAI, BSI |
| 55 Chen et al. 2007 | Children with mixed anxiety depressive  | Monotherapy | 3030 | 12(2.6)11(3.6) | 5(16.7)11(36.6) | 10~15min | CES/Alpha-Stim 100 | 0.5 Hz/0.01-0.5 mA | 5/once a day | Ear clip electrodes | SDS, SAS |
| 56 Wagenseil et al. 2018 | Healthy women | Monotherapy | 2515 | 26(3.07)26(3.42) | 25(100)15(100) | 60min | CES/Alpha-Stim 100 | 0.5 Hz/1 mA | 1/once a day | Ear clip electrodes | PSQI, SWS, SE, sleep onset latency |
| 57 Nikolin et al. 2020 | MDD | Add on | 3432 | 47.5 (12.0)48.8 (12.3) | 15(44.1)15(46.87) | 30 min | tRNS/NeuroConn | 0.1-640Hz/2 mA | 20/once a day | Scalp electrodes | MADRS, BDI, CGI-S |
| 58 Schecklmann et al. 2021 | MDD | Add on | 2020 | 46 (12)46 (14)  | 12 (60)8 (40) | 20-min | tRNS/NeuroConn | 100 – 650Hz/2 mA | 15/once a day | Anode: F3Cathode: F4 | HAMD, CGI |
| 59 Alexander et al. 2019 | MDD | Add on | 10 (10HZ)11(40HZ)11 | 36.3 (15.2)35.4 (11.6)38.4 (13.5) | 9 (90.0)9 (81.8)9 (81.8) | 40 min | tACS/Neuroconn | 10Hz or 40Hz/CZ: 2mAF3 F4: 1mA | 20/once a day | 2 over F3 & F43stelectrode over vertex  | MADRS, HDRS |
| 60 Wang et al. 2020 | Insomnia | Monotherapy | 3131 | 55.3(8.0)52.5(10.7) | 23(74.2)24 (77.4) | 40 min | tACS/Nexalin | 77.5 Hz/15-mA | 40/once a day | 3 over Fpz, Fp1, Fp22 over mastoid areas | TST, PSQI, SOL, SQ, SE, Daily disturbance |
| 61 Eren et al. 2018 | Persistent postural-perceptual dizziness | Add on | 109 | 38.8 (9.8)43.2 (14.1) | 6 (60)5(55.5) | 30mins | tVNS/gammaCore | NR | 20/once a day. | Positioning on the neck  | HADS, QOL  |
| 62 Hein et al. 2013 | MDD | Add on | 1819 | 45.1(12.39)46.54(12.26) | 11(61.1)11(57.89) | 15 min | tVNS/NET-1000, NET-2000, Auri-Stim | 1.5 Hz/0.6mA | 20/twice a day. | Electrodes placed in both outer ears | HAMD, BDI |
| 63 Shiozawa et al. 2015 | MDD | Add on | 2015 | 48.71(12.56)45.42(11.54) | NR(65)NR(65) | 30min | TNS/Neurodyn | 120 Hz/0-100mA | 10/once a day | Supraorbital foramen. | HAMD, BDI, MOCA |
| 64 Generoso et al. 2019 | MDD | Add on | 1212 | 39.16 (12)43.8 (11.8) | 6(50)9(75) | 30min | TNS/Neurodyn | 120hz/ 0- 100 mA. | 10/once a day | Bilateral supraorbital foramen | HAMD17, QOL, MOCA |
| 65 Lu et al. 2020 | Post stroke depression | Add on | 125133 | 65.0 (8.82)66.11 (8.37) | 55 (44)68 (51.13) | 45 min/day | PMES | 1.8Hz/10 mA | 180/once a day | Mastoid area | HAMD, MOCA, GDS |

AUD, alcohol use disorder; BDI, Beck depression inventory; BIS-11, Barratt Impulsivity Scale; CES, cranial electrotherapy stimulation; CGI, Clinical global impression scale; DASS, Depression Anxiety Stress Score; HAMD, Hamilton Rating Scale for depression; HAMA, Hamilton Rating Scale for Anxiety; HADS, Hospital anxiety and depression scale; GDS, Geriatric depression scale; GSDS, General Sleep Disturbance Scale; ISI, Insomnia severe index; K-POMS, Korean version of the Proﬁle of Mood States; MADRS, Montgomery-Asberg Depression Rating Scale; MIDAS, Migraine Disability Assessment; MHC-SF, Mental Health Continuum Short Form; MOCA, Montreal Cognitive Assessment; PHQ, Patient Health Questionnaire; POMS-32, Proﬁle of Mood States; PMES, percutaneous mastoid electrical stimulator; QOL, quality of life; SDS, Zung Self-Rating Depression Scale; SAS, Zung Self-Rating Anxiety Scale; SE, sleep efficiency; SQ, sleep quality; SRSS, self-rating symptom scale; tACS, transcranial alternating current stimulation; tDCS, transcranial direct current stimulation; TNS, trigeminal nerve stimulation; tRNS, transcranial random noise stimulation; tVNS, transcutaneous electrical nerve stimulation; Q-LES-Q-SF, The Quality of Life Enjoyment and Satisfaction Questionnaire - Short Form; VAS, Visual analogue scale; WPI, Widespread pain index; YMRS, Young Mania Rating Scale

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**Supplementary Table 2. Numbers of incorporated studies in quantitative analyses. Only items with at least 3 studies were incorporated**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Transcranial direct current stimulation, tDCS | Cranial electrotherapy stimulation, CES | Transcranial alternating current stimulation, tACS | Transcranial random noise stimulation, tRNS | Vagus nerve stimulation, VNS | Trigeminal nerve stimulation, TNS | Percutaneous mastoid electrical stimulation, PMES | Total |
| Treatment options | Current | <1mA | 2 | 8 | 0 | 0 | 1 | 0 | 0 | 11 |
| ≥1mA | 34 | 3 | 1 | 2 | 0 | 2 | 1 | 43 |
| 2mA | 28 | 2 | 1 | 2 | 0 | 0 | 0 | 33 |
| ≥2mA | 29 | 2 | 1 | 2 | 0 | 2 | 1 | 38 |
| Number of treatments | 5 | 9 | 1 | 0 | 0 | 0 | 0 | 0 | 10 |
| ≥10 | 25 | 10 | 1 | 2 | 2 | 2 | 1 | 43 |
| ≥20 | 8 | 7 | 1 | 0 | 2 | 1 | 1 | 20 |
| Targets of therapies | Depression | Targeted population | All subjects | 35 | 11 | 1 | 2 | 2 | 2 | 1 | 54 |
| Only mild depression | 9 | 2 | 0 | 0 | 1 | 0 | 0 | 12 |
| At least mild depression | 31 | 5 | 0 | 2 | 2 | 2 | 1 | 43 |
| At least moderate depression | 23 | 3 | 0 | 2 | 0 | 2 | 1 | 31 |
| Only MDD | 21 | 2 | 1 | 2 | 1 | 2 | 1 | 30 |
| Measurements | HAMD | 19 | 3 | 1 | 1 | 1 | 2 | 1 | 28 |
| BDI | 5 | 2 | 0 | 0 | 0 | 0 | 0 | 7 |
| MADRS | 7 | 0 | 0 | 1 | 0 | 0 | 0 | 8 |
| Anxiety | Targeted population | All subjects | 10 | 4 | 0 | 1 | 0 | 0 | 0 | 15 |
| Sleep disturabnce | Measurements | PSQI | 2 | 1 | 1 | 0 | 0 | 0 | 0 | 4 |
| Sleep quality | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 3 |
| Sleep efficiency | 1 | 2 | 1 | 0 | 0 | 0 | 0 | 4 |
| Sleep latency | 1 | 2 | 1 | 0 | 0 | 0 | 0 | 4 |
| Total sleep time | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 3 |
| Daily disturbance | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 3 |

**Supplementary Table 3. Sensitivity analyses for meta-analysis using leave-one-out approach**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Outcomes  | Number of studies | Effect sizes (95%CI) | Effect size p value | Heterogeneity I2 (%) |
| MADRS for all types of neuromodulationLeave one study out | 7 | 0.423 (0.012; 0.835) | 0.0439\* | 70.8% |
|  Brunoni et al. 2013 | 6 | 0.298 (-0.103; 0.698) | 0.1455 | 56.1% |
|  Loo et al. 2012 | 6 | 0.360 (-0.115; 0.835) | 0.1370 | 73.1% |
| Vigod et al. 2019 | 6 | 0.401 (-0.056; 0.858) | 0.0853 | 75.4% |
| Mayur et al. 2018  | 6 | 0.429 (-0.026; 0.883) | 0.0645 | 75.7% |
| Segrave et al. 2014 | 6 | 0.385 (-0.065; 0.834) | 0.0934 | 75.0% |
| BDI for only tDCS | 5 | 0.497 (0.099; 0.895) | 0.0144\* | 33.2% |
| Leave one study out |  |  |  |  |
|  Ahmadizadeh et al. 2019 | 4 | 0.322 (-0.045; 0.690) | 0.0855 | 0.0% |
|  de Lima et al. 2019 | 4 | 0.473 (-0.041; 0.987) | 0.0712 | 49.8% |
|  Taremian et al. 2019 | 4 | 0.495 (-0.039; 1.029) | 0.0694 | 49.7% |
| ≥ 20 sessions for only tDCS | 8 | 0.438 (0.044; 0.832) | 0.0293\* | 72.1% |
| Leave one study out |  |  |  |  |
|  Zhou et al. 2020 | 7 | 0.381 (-0.063; 0.826) | 0.0926 | 71.6% |
|  Brunoni et al. 2017 | 7 | 0.465 (-0.042; 0.973) | 0.0722 | 76.0% |
| Remission rate for only tDCS | 11 | 1.501 (0.958; 2.351) | 0.0763 | 7.1% |
| Leave one study out |  |  |  |  |
|  Brunoni et al. 2013 | 10 | 1.674 (1.075; 2.605) | 0.0225\* | 0.0% |
| Loo et al. 2018 | 10 | 1.715 (1.114; 2.639) | 0.0143\* | 0.0% |
| At least mild depression for only CES  | 5 | 0.505 (0.009; 1.001) | 0.0461\* | 65.1% |
| Leave one study out |  |  |  |  |
|  Bhardwaj et al. 2018 | 4 | 0.361 (-0.105; 0.828) | 0.1291 | 60.0% |
| Barclay 2014  | 4 | 0.578 (-0.152; 1.308) | 0.1208 | 71.4% |
|  Gong et al. 2016  | 4 | 0.385 (-0.218; 0.988) | 0.2107 | 61.7% |
| McClure et al. 2015 | 4 | 0.541 (-0.044; 1.125) | 0.0700 | 73.6% |
| Total sleep time for all types of neuromodulation | 3 | 0.474 (0.180; 0.767) | 0.0016\*\* | 0.0% |
| Leave one study out |  |  |  |  |
|  Zhou et al. 2020  | 2 | 0.454 (-0.017; 0.924) | 0.0586 | 21.3% |
| Daytime disturbance for all types of neuromodulationLeave one study out | 3 | 0.272 (-0.131; 0.675) | 0.1863 | 46.4% |
| Wang et al. 2020 | 2 | 0.482 (0.130; 0.834) | 0.0073\*\* | 0.0% |

\*p<0.05, \*\*p<0.01

**Supplementary Table 4. Publication bias of electrical neuromodulation on depression, anxiety and sleep disturbance. (a) only tDCS; (b) only CES; (c) all types of neuromodulation**

1. **Only tDCS**

|  |  |
| --- | --- |
|  | Egger’s linear regression test |
| Number of studies | t value | p value | Publication bias |
| Depression: targeted population |  |  |  |  |
|  All subjects | 35 | 1.370 | 0.1799 | Not significant |
| At least mild depression | 31 | 1.067 | 0.2947 | Not significant |
| At least moderate depression | 23 | 1.017 | 0.3208 | Not significant |
| Only MDD patients | 21 | 1.411 | 0.1746 | Not significant |
| Depression: measurements |  |  |  |  |
|  HAMD | 19 | 1.387 | 0.1834 | Not significant |
| BDI | 5 | -# | -# | -# |
| MADRS | 6 | -# | -# | -# |
| Anxiety: targeted population |  |  |  |  |
| All subjects | 11 | 0.895 | 0.3969 | Not significant |
| Treatment options: current |  |  |  |  |
| ≥ 1mA | 34 | 1.432 | 0.1618 | Not significant |
| 2mA | 28 | -0.382 | 0.7056 | Not significant |
| ≥ 2mA | 29 | 0.080 | 0.9368 | Not significant |
| Treatment options: number of treatments |  |  |  |  |
| 5 sessions | 9 | -# | -# | -# |
| ≥ 10 sessions | 25 | 1.068 | 0.2966 | Not significant |
| ≥ 20 sessions | 8 | -# | -# | -# |
| Binary outcomes |  |  |  |  |
| Response rate | 11 | 0.164 | 0.8736 | Not significant |
| Remission rate | 11 | -0.272 | 0.7921 | Not significant |

1. **Only CES**

|  |  |
| --- | --- |
|  | Egger’s linear regression test |
| Number of studies | t value | p value | Publication bias |
| Depression: targeted population |  |  |  |  |
|  All subjects | 11 | 0.411 | 0.6910 | Not significant |
| At least mild depression | 5 | -# | -# | -# |
| At least moderate depression | 3 | -# | -# | -# |
| Depression: measurements |  |  |  |  |
| HAMD | 3 | -# | -# | -# |
| Anxiety: targeted population |  |  |  |  |
|  All subjects | 4 | -# | -# | -# |
| Treatment options: current |  |  |  |  |
| < 1mA | 8 | -# | -# | -# |
| ≥ 2mA | 3 | -# | -# | -# |
| Treatment options: number of treatments |  |  |  |  |
| ≥ 10 sessions | 10 | 0.444 | 0.6687 | Not significant |
| ≥ 20 sessions |  7 | -# | -# | -# |

1. **All types of neuromodulation**

|  |  |
| --- | --- |
|  | Egger’s linear regression test |
| Number of studies | t value | p value | Publication bias |
| Depression: targeted population |  |  |  |  |
| All subjects | 54 | 1.819 | 0.0746 | Not significant |
| Only mild depression  | 12 | -0.165 | 0.8727 | Not significant |
| At least mild depression  | 43 | 1.499 | 0.1415 | Not significant |
| At least moderate depression | 31 | 1.451 | 0.1574 | Not significant |
|  Only MDD patients | 30 | 1.335 | 0.1927 | Not significant |
| Depression: measurements |  |  |  |  |
|  HAMD | 28 | 1.257 | 0.2198 | Not significant |
|  BDI  | 7 | -# | -# | -# |
| MADRS | 7 | -# | -# | -# |
| Anxiety: targeted population |  |  |  |  |
| All subjects | 15 | 0.031 | 0.9761 | Not significant |
| Sleep disturbance: measurements |  |  |  |  |
| PSQI | 4 | -# | -# | -# |
| Sleep quality  | 3 | -# | -# | -# |
| Sleep efficiency | 4 | -# | -# | -# |
| Sleep latency  | 4 | -# | -# | -# |
| Total sleep time | 3 | -# | -# | -# |
| Daily disturbances | 3 | -# | -# | -# |
| Treatment options: current |  |  |  |  |
| <1mA | 11 | 1.580 | 0.1485 | Not significant |
| 1mA | 5 | -# | -# | -# |
| ≥ 1mA | 43 | 1.601 | 0.1170 | Not significant |
| 2mA | 33 | 0.101 | 0.9200 | Not significant |
| ≥ 2mA | 38 | 0.704 | 0.4861 | Not significant |
| Treatment options: number of treatments |  |  |  |  |
| 5 sessions | 10 | 0.953 | 0.3684 | Not significant |
| ≥ 10 sessions | 43 | 1.676 | 0.1013 | Not significant |
| ≥ 20 sessions | 20 | 1.124 | 0.2758 | Not significant |

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| #1 |  (((((((("non invasive brain stimulation"[All Fields]) OR ("electrical neuromodulation"[All Fields])) OR ("transcranial direct current stimulation"[All Fields])) OR ("cranial electrotherapy stimulation"[All Fields])) OR ("transcutaneous vagus nerve stimulation"[All Fields])) ) OR ("transcranial random noise stimulation"[All Fields])) OR ("transcranial alternating current stimulation"[All Fields])) OR ("trigeminal nerve stimulation"[All Fields]) | 7402 |

**Pubmed**

**Medline, PsycInfo, PsycArticles, CINAHL**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| # | Query | Limiters/Expanders | Last Run Via | Results |
| S4 |  | Expanders - Apply equivalent subjectsNarrow by Methodology: - clinical trialSearch modes - Find all my search terms | Interface - EBSCOhost Research DatabasesSearch Screen - Advanced SearchDatabase - MEDLINE;APA PsycInfo;APA PsycArticles;CINAHL | 600 |
| S3 | ( S1 AND S2 ) AND randomized controlled trials | Expanders - Apply equivalent subjectsSearch modes - Find all my search terms | Interface - EBSCOhost Research DatabasesSearch Screen - Advanced SearchDatabase - MEDLINE;APA PsycInfo;APA PsycArticles;CINAHL | 4,820 |
| S2 | depression OR anxiety OR ( insomnia or sleep disorders or sleep disturbance )   | Expanders - Apply equivalent subjectsSearch modes - Find all my search terms | Interface - EBSCOhost Research DatabasesSearch Screen - Advanced SearchDatabase - MEDLINE;APA PsycInfo;APA PsycArticles;CINAHL | 1,500,173 |
| S1 | cranial electrotherapy stimulation OR transcranial direct current stimulation OR ( non invasive brain stimulation or nibs ) OR vagus nerve stimulation OR transcranial alternating current stimulation | Expanders - Apply equivalent subjectsSearch modes - Find all my search terms | Interface - EBSCOhost Research DatabasesSearch Screen - Advanced SearchDatabase - MEDLINE;APA PsycInfo;APA PsycArticles;CINAHL | 1,500,173 |
|  | ( non invasive brain stimulation or nibs ) OR ( transcranial direct current stimulation or tdcs ) OR cranial electrotherapy stimulation OR transcutaneous vagus nerve stimulation OR ( vagus nerve stimulation or nvns ) OR ( transcutaneous electrical nerve stimulation or tens )  | Expanders - Apply equivalent subjectsSearch modes - Find all my search terms | Interface - EBSCOhost Research DatabasesSearch Screen - Advanced SearchDatabase - MEDLINE;APA PsycInfo;APA PsycArticles;CINAHL | 1,001,637 |

**Embase**

|  |  |  |
| --- | --- | --- |
| No. | Query | Results |
| #4 | #1AND #2 AND #3 | 773 |
| #3 | 'depression'/exp OR depression OR 'anxiety'/exp OR anxiety OR 'insomnia'/exp OR insomnia OR 'sleep disorder'/exp OR 'sleep disorder' | 878,958 |
| #2 | 'depression'/exp OR depression OR 'anxiety'/exp OR anxiety OR 'insomnia'/exp OR insomnia OR 'sleep disorder'/exp OR 'sleep disorder' |  1,189,297 |
| #1 | 'transcutaneous electrical nerve stimulation'/exp OR 'transcutaneous electrical nerve stimulation' OR 'transcranial direct current stimulation'/exp OR 'transcranial direct current stimulation' OR 'cranial electrotherapy stimulator'/exp OR 'cranial electrotherapy stimulator' OR 'transcranial alternating current stimulation'/exp OR 'transcranial alternating current stimulation' OR 'trigeminal nerve stimulation'/exp OR 'trigeminal nerve stimulation' OR 'transcutaneous vagus nerve stimulator'/exp OR 'transcutaneous vagus nerve stimulator' OR 'transcranial random noise stimulation'/exp OR 'transcranial random noise stimulation' | 18,884 |