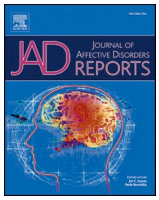
Journal of Affective Disorders Reports 10 (2022) 100407

Contents lists available at ScienceDirect

Journal of Affective Disorders Reports

journal homepage: www.sciencedirect.com/journal/journal-of-affective-disorders-reports



Brief Report

Transcranial direct current stimulation effects in late life depression: A meta-analysis of individual participant data

Rachael M. Rimmer [a], Sergi G. Costafreda [b], Julian Mutz [c], Katherine Joseph [a], Andre R. Brunoni [d], Colleen K. Loo [e], Frank Padberg [f], Ulrich Palm [f,g], Cynthia H.Y. Fu [a,h,*]

[a] School of Psychology, University of East London, London, UK
[b] Division of Psychiatry, Faculty of Brain Sciences, University College London, London, UK
[c] Social Genetic and Developmental Psychiatry Centre, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK
[d] Service of Interdisciplinary Neuromodulation, Institute of Psychiatry, Hospital das Clínicas da Faculdade de Medicina da USP, Department of Psychiatry and Department of Internal Medicina, Faculdade de Medicina da USP; University of São Paulo, São Paulo, Brazil
[e] Department of Psychiatry & Black Dog Institute, University of New South Wales, Sydney, Australia
[f] Department of Psychiatry and Psychotherapy, LMU University Hospital Munich, Germany
[g] Medical Park Chiemseeblick, Hospital for Psychosomatics, Bernau-Felden, Germany
[h] Centre for Affective Disorders, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK

ARTICLE INFO

Keywords:
Transcranial direct current stimulation
Late life depression
Geriatric depression
Major depressive disorder
Individual participant data
Meta-analysis

ABSTRACT

Background: Late life depression (LLD) refers to major depressive disorder (MDD) in adults over 65 years. LLD is associated with high morbidity and poor treatment outcomes. Transcranial direct current stimulation (tDCS) is a novel treatment for MDD. Efficacy in LLD though is unclear. Our aim was to investigate tDCS efficacy by pooling randomised controlled trials (RCT) in an individual participant data meta-analysis.
Methods: Databases were searched for sham controlled RCTs of tDCS in MDD and bipolar depression. Individual participant data (IPD) were requested. Primary outcome was change in depressive symptoms. Bayesian multilevel modelling meta-analysis was conducted with individual participants nested within studies.
Results: 6 RCTs were eligible, consisting of 43 participants (22 women), mean age 69.2 years. Active anodal tDCS over left dorsolateral prefrontal cortex (n = 19) was associated with an improvement in depressive severity, effect size 0.14 (95% credible interval [-0.44;0.15]) as compared to sham tDCS, which was not statistically significant. There was an 82% probability that tDCS treatment has a modest but non-null effect in improving depressive symptoms. Acceptability was high with no significant differences in discontinuation rates between active and sham groups.
Limitations: The total sample size was small, limiting power.
Discussion: In LLD, tDCS demonstrates a modest but non-null effect in improving depressive symptoms. Acceptability was high as measured by discontinuation rates. tDCS is a potential novel treatment option in LLD, though large scale RCTs in LLD are required to investigate this important clinical application.

1. Introduction

Late life depression (LLD) refers to major depressive disorder (MDD) in adults 65 years or older (Lebowitz et al., 1997). LLD is typically associated with comorbid neurological, medical and psychiatric disorders and shows a poorer clinical response relative to younger age groups (Tham et al., 2016). Aetiological mechanisms in LLD are multiple and complex, involving age- and disease-related processes, including immunological dysregulation, genetic liability and cerebrovascular changes (Alexopoulos, 2019). The most common treatments are antidepressant medication and psychotherapy. Psychotherapy has demonstrated efficacy in LLD with comparable effect sizes to antidepressants (Cuijpers et al., 2006; Huang et al., 2015). However, antidepressant adherence rates are low in LLD, in which 11–21% do not start treatment and 33–38% discontinue treatment early (Holvast et al., 2019). Antidepressants are also associated with increased rates of adverse effects, including anticholinergic effects, such as diarrhoea, nausea, and dizziness, and might be contraindicated with other medications taken in this

* Corresponding author at: University of East London, Arthur Edwards Building, Water Lane, London E15 4LZ, UK.
E-mail address: c.fu@uel.ac.uk (C.H.Y. Fu).

https://doi.org/10.1016/j.jadr.2022.100407
Received 12 August 2022; Accepted 16 August 2022
Available online 19 August 2022

age group (Krause et al., 2019).

Transcranial direct current stimulation (tDCS) is a novel treatment for MDD (Woodham et al., 2021). tDCS applies a weak electrical current which modulates cortical tissue excitability, facilitating neuronal depolarization and leading to polarity-dependent neuroplasticity. The effect can extend beyond the site of stimulation to deeper brain structures, including anterior cingulate and amygdala, and is associated with changes in resting state networks (Palm et al., 2016). tDCS has demonstrated efficacy and acceptability in MDD with a course of active tDCS treatment is associated with a fourfold increased rate of clinical response (OR = 4.32, 95% CI [2.02; 9.29]) and a threefold increased rate of clinical remission (OR = 3.07, 95% CI [1.58; 5.99]) as compared to sham tDCS (Mutz et al., 2018). While age has not been found to have an impact on treatment effect (Razza et al., 2020), these meta-analyses had examined aggregate data. An individual participant data (IPD) meta-analysis synthesizes the raw individual-level data from each study, which can improve quality and reliability statistically as well as clinically, and is considered the gold standard for meta-analyses (Riley et al., 2010).

We sought to investigate efficacy and acceptability of tDCS treatment in LLD in an individual participant data meta-analysis. We examined sham-controlled RCTs of tDCS in MDD and bipolar depression and approached authors to contribute their trial data in adults aged 65 years and over.

2. Methods

2.1. Registration

The protocol was registered with PROSPERO (No: CRD42019137488) and is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (Supplementary Figure S1).

2.2. Eligibility criteria

A systematic literature search was conducted using PsycINFO (EBSCO), MEDLINE (PubMed) and PsychSource (EBSCO) databases from the first available date to 20 October 2021, key words: ((“bipolar disorder” OR “bipolar depression” OR “major depression” OR “unipolar depression” OR “unipolar disorder”) AND (“transcranial direct current stimulation” OR “tDCS”)). References of reviews and included papers were checked for additional publications.

Inclusion criteria: (i) adults aged 65 years or older; (ii) current major depressive episode with diagnosis of MDD or bipolar disorder according to DSM or ICD criteria; (iii) sham-controlled tDCS RCT; (iv) clinician-administered depressive symptom rating scale, e.g., Hamilton Depression Rating Scale (HDRS) or Montgomery-Åsberg Depression Rating Scale (MADRS); (v) being published in English. Exclusion criteria: (i) primary diagnosis other than MDD or bipolar disorder e.g., postpartum depression, psychotic depression, or secondary to a medical illness; (ii) co-initiation of any other form of treatment e.g., pharmacotherapy or cognitive control training.

2.3. Study selection and data extraction

Abstracts were independently assessed (KJ, RR), and differences were resolved by consensus with review (CF). Study level data were extracted, and authors were contacted for non-identifiable IPD and any information not available from the publication. Data consistency and completeness were checked (RR) and reviewed (CF).

2.4. Risk of bias assessment in individual studies

Methodological quality was assessed using Cochrane risk of bias tool (Higgins et al., 2021), which evaluates on basis of selection, performance, detection, attrition and reporting biases (Supplementary Figures . S2-3).

2.5. Specification of outcomes

Outcome measures were: (1) continuous measure of depressive symptoms, estimated as difference in z-scaled mood scored from baseline to study end; (2) categorical measure of clinical response, defined as a 50% or greater improvement in depressive symptoms from baseline to study end; (3) categorical measure of clinical remission, defined as MADRS $\leq$10, 17-item HDRS $\leq$7, 21-item HDRS $\leq$8, 24-item HDRS $\leq$9 at study end (Keller, 2003); (4) acceptability, defined as number of participants who did not complete either active or sham tDCS treatment arms.

For studies which had used two or more depression rating scales, the scale used as the primary outcome was selected (Loo et al., 2010, Brunoni et al., 2013; Brunoni et al., 2017) (Supplementary Table S1). For studies with multiple treatment arms, only active and sham tDCS treatments arms were included. For studies with a crossover design, only the first phase parallel between-participants data were used.

2.6. Data analysis

A one-stage IPD Bayesian hierarchical model was conducted as the primary analysis. Hierarchical meta-analysis allows for modelling of individual-level covariates (age, sex, illness duration) and their potential interaction with treatment effects, while accounting for clustering of individual patients within a study (Higgins et al., 2021). One-stage Bayesian methods are recommended for meta-analysis of small trials with few participants and when heterogeneity is expected across trials, as uncertainty in estimates can be fully incorporated in the modelling (Lunn et al., 2013).

Individual study data sets were combined into a merged data set, with participants nested within studies. As studies used different rating scales (2 HDRS versions and MADRS), depressive severity scores were standardised across studies by transforming them into z-scores. For variables of interest, 4 participants had missing follow-up mood outcome, and 1 participant had missing disease duration. To maintain the intention-to-treat nature of the analysis, we assumed data were missing at random, and we imputed missing disease duration and depression scores at follow-up using a well-established multivariate imputation algorithm (van Buuren and Groothuis-Oudshoorn, 2011), resulting in multiple (n = 200) datasets with imputed missing values.

Mixed effects models with random trial-specific intercepts, treatment effects and co-variates were fitted to these data sets, with results combined into an average fitted model (Bürkner, 2017). Trial-specific treatment effects were assumed to follow a normal distribution, with the mean of this distribution representing pooled population-averaged treatment effect. We used weakly informative prior distributions so information in the dataset would be reflected in final posterior distributions. In particular, we used a weakly informative normal distribution (centred at zero and with a standard deviation of 1) as prior distribution of pooled treatment effect estimate, and similarly weakly informative half-Cauchy prior (scale parameter of 0.5) was used for between study variability. We used a Markov chain Monte Carlo algorithm to draw samples from the posterior distribution of parameters of interest (Bürkner, 2017).

Bayesian IPD meta-analysis was used to predict final depressive severity score with adjustment for baseline score, age and sex. Additional analyses explored effect of disease duration and presence of treatment-resistant depression, defined by having persistent depressive episode following at least 2 adequate treatment trials, and duration of illness. We considered fitting additional logistic regression models to predict planned categorical outcomes of treatment response and remission, however this was not possible due to the very limited number of participants with these outcomes (n = 6 clinical response; n = 3

Table 1
Clinical and demographic characteristics.

	Average	Loo (2010)	Loo (2012)	Palm (2012)	Brunoni (2013)	Brunoni (2017)	Loo (2017)
Total sample size	43 (22)	1 (0)	5 (2)	7 (5)	4 (2)	7 (3)	19 (10)
Age (yrs)	69.3 (4.22)	65.0	70.2 (5.17)	70.0 (4.83)	65.0 (0.00)	68.3 (3.45)	70.4 (4.29)
Age range	65-81	65	65-78	65-79	65	65-73	65-81
Education (yrs)	16.72 (3.57)	NR	NR	NR	NR	14.3 (3.62)	18.0 (2.89)
Unipolar depression	33	1	4	7	4	6	11
Medication (n)	15	0	1	7	0	2	5
Duration of illness (months)	145.33 (151.48)	6.00	64.00 (81.28)	219.40 (110.57)	11.00 (9.42)	87.17 (169.68)	213.89 (166.00)
Treatment resistant depression (TRD)	27	0	1	7	0	3	16

Number of participants is presented with number of female participants in parenthesis. Mean values are presented for each variable with standard deviation in parenthesis. As there was one participant from Loo et al. (2010), there is no standard deviation for age and no age range.

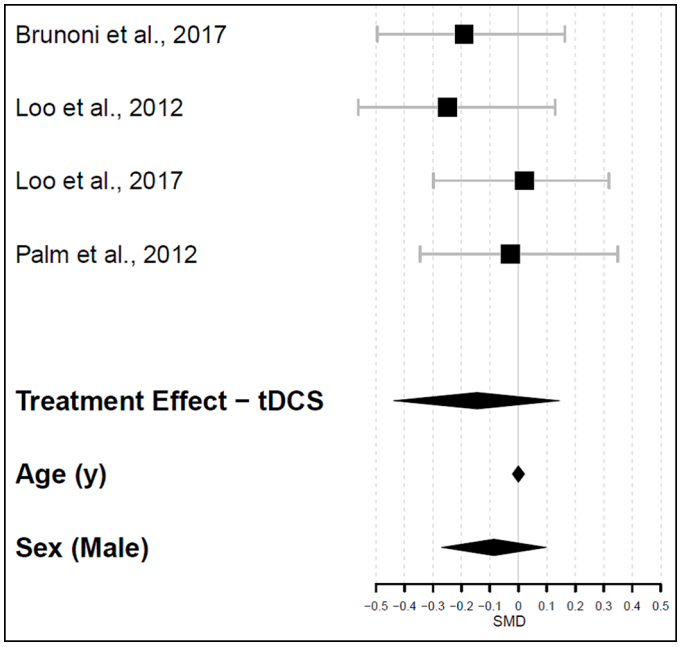


Fig. 1. Standardised mean difference of depressive scores are presented for each study, with negative scores indicating a benefit from treatment and favouring active tDCS relative to sham tDCS.

remission).

Posterior distributions obtained from Bayesian model fitting allow for direct probability statements, and we report the probability of a beneficial treatment effect of tDCS, along with point estimates and 95% credible intervals for parameters of interest. Sensitivity analysis on average pooled tDCS treatment effect, as main parameter of interest, was conducted using a two-step approach with trial-level estimates of treatment effect estimated and pooled in a second level frequentist meta-analysis, and last observation carried forward instead of imputation of missing values (Viechtbauer, 2010). All analyses were conducted using R (R Core Team, 2018).

3. Results

Total of 4336 records were assessed, and 9 studies met inclusion and exclusion criteria. Present analysis consists of 6 studies, 43 participants (22 women) (mean age 69.3 ±4.2 years, range 65-81 years), mean illness duration 145.33 ± 151.48 months, from total sample of 617 participants (Loo et al., 2010; Loo et al., 2012; Palm et al., 2012; Brunoni et al., 2013; Brunoni et al., 2017; Loo et al., 2018) (Supplementary Figure S1). Majority had unipolar depression 76.7% ($n = 33$), and 62.7% met criteria for treatment resistant depression ($n = 27$) (Table 1, Supplementary Table S1). There were no significant differences in demographics between tDCS ($n = 19$) and sham control ($n = 24$) treatment groups. There were no cases of treatment-emergent mania. Risk of bias was low for all studies (Supplementary Figures S2-S3). Authors from remaining studies had not replied to requests or were unable to share individual participant data.

Using Bayesian multilevel modelling for IPD meta-analysis, treatment with tDCS was associated with a reduction of SMD = -0.14 (95% credible interval [-0.44; 0.15]) in depression scores, relative to sham tDCS, which was not statistically significant.

Based on estimated posterior distribution of the average effect of tDCS across the studies, there is an 82% probability that tDCS treatment has at least a small effect (change in symptoms score < 0) in improving depressive symptoms in LLD. There was no evidence of significant main effects of age (change per year in SMD = 0.00 95% credible interval [-0.02;0.02]), sex (male sex SMD = -0.09 95% credible interval [-0.27;0.10]), or their interactions with treatment, though samples sizes were small. There was no evidence of significant main effect of treatment resistance or illness duration. Sensitivity analysis using a two-step IPD frequentist meta-analysis with last observation carried-forward showed similar results, with tDCS treatment associated with a reduction of -0.12 (95% confidence interval [-0.34; 0.12]) (Fig. 1).

Most participants completed treatment ($n = 39$; 90.7%). Discontinuation rates were 15.8% (3/19) for active tDCS and 4.2% (1/24) for sham tDCS, which was not statistically significant (OR = 4.3, 95% CI 0.41- 45.28, $p = 0.31$).

4. Discussion

The present IPD meta-analysis demonstrates a modest but non-null effect for tDCS improving depressive symptoms in LLD. While the effect was low and did not reach statistical significance in the present IPD sample, the sample size was small, and many participants had a more treatment resistant form of depression. As tolerability and acceptability are significant limitations of current treatments in LLD, tDCS offers a potential novel treatment option. tDCS efficacy has shown an overall effect size that is low to moderate across all ages (Mutz et al., 2018; Moffa et al., 2020; Zhang et al., 2021), and full efficacy might become evident over a longer term, from 3 - 6 months (Brunoni et al., 2017). In the present analysis, outcomes were assessed immediately following the treatment period, which consisted of 5–22 sessions (Loo et al., 2010; Loo et al., 2012; Palm et al., 2012; Brunoni et al., 2013; Brunoni et al., 2017; Loo et al., 2018), and it is possible that improved outcomes might been seen with a longer follow up. Moreover, dose has been identified as a significant and independent predictor (Brunoni et al., 2016). We also considered that treatment resistant depression might contribute to efficacy, although this was underpowered in the present sample (Moffa et al., 2020).

A limitation of this meta-analysis is the small sample size, which limited power to detect an effect. IPD were collated from large RCTs of all ages, but there has not yet been a large scale RCT in LLD. There is emerging evidence for tDCS as an adjunct treatment in hard-to-treat vascular LLD and using novel montages such as high definition-tDCS in LLD (Wong et al., 2019; Zanardi et al., 2020).

In summary, the present IPD meta-analysis demonstrates that tDCS has a modest but non-null effect in improving depressive symptoms in LLD. However, the sample was small, and large-scale RCTs are required to investigate efficacy of tDCS in LLD. Acknowledging these shortcomings and the modest statistical effects, the findings provide support for further investigation into the efficacy of tDCS as a treatment for LLD and vascular depression.

Funding

This work was supported by the Rosetrees Trust [A1950] to CF. RR received funding support from UEL PhD Excellence studentship.

Declaration of Competing Interest

FP is a member of the Scientific Advisory Boards of Sooma Oy, Helsinki, Finland, and of Brainsway Inc., Jerusalem, Israel. He has received speaker's honoraria from Mag&More GmbH and the neuroCare Group. His lab has received support with equipment from neuroConn GmbH, Ilmenau, Germany, and Mag&More GmbH and Brainsway Inc. UP received speaker's honoraria from NeuroCareGroup, Munich, Germany. CF has received support with equipment from Flow Neuroscience and Neuroelectrics. All other authors declare they have no conflict of interests.

Acknowledgements

We would like to thank the participants and research team members in the clinical trials.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jadr.2022.100407.

References

Alexopoulos, G.S., 2019. Mechanisms and treatment of late-life depression. Transl. Psychiatry 9 (1), 1–16. https://doi.org/10.1038/s41398-019-0514-6.

Brunoni, A.R., Moffa, A.H., Fregni, F., Palm, U., Padberg, F., Blumberger, D.M., Loo, C.K., 2016. Transcranial direct current stimulation for acute major depressive episodes: meta-analysis of individual patient data. Br. J. Psychiatry 208 (6), 522–531. https://doi.org/10.1192/bjp.bp.115.164715.

Brunoni, A.R., Moffa, A.H., Sampaio-Junior, B., Borrione, L., Moreno, M.L., Fernandes, R. A., Benseñor, I.M., 2017. Trial of electrical direct-current therapy versus escitalopram for depression. N. Engl. J. Med. 376 (26), 2523–2533. https://doi.org/10.1056/NEJMoa1612999.

Brunoni, A.R., Valiengo, L., Baccaro, A., Zanao, T.A., de Oliveira, J.F., Goulart, A., Fregni, F., 2013. The sertraline vs electrical current therapy for treating depression clinical study: results from a factorial, randomized, controlled trial. JAMA Psychiatry 70 (4), 383–391. https://doi.org/10.1001/2013.jamapsychiatry.32.

Bürkner, P.C., 2017. brms: An R package for Bayesian multilevel models using Stan. J. Stat. Softw. 80 (1), 1–28. https://doi.org/10.18637/jss.v080.i01.

Cuijpers, P., van Straten, A., Smit, F., 2006. Psychological treatment of late-life depression: a meta-analysis of randomized controlled trials. Int. J. Geriatr. Psychiatry 21 (12), 1139–1149. https://doi.org/10.1002/gps.1620.

Higgins, J.P., Thomas, J., Chandler, J., Cumpston, M., Li, T, Page, M.J., Welch, V.A., 2021. Cochrane Handbook for Systematic Reviews of Interventions Version 6.2. The Cochrane Collaboration, pp. 33–49. Available from. www.training.cochrane.org/handbook.

Holvast, F., Oude Voshaar, R.C., Wouters, H., Hek, K., Schellevis, F., Burger, H., Verhaak, P.F., 2019. Non-adherence to antidepressants among older patients with depression: a longitudinal cohort study in primary care. Fam. Pract. 36 (1), 12–20. https://doi.org/10.1093/fampra/cmy106.

Huang, A.X., Delucchi, K., Dunn, L.B., Nelson, J.C., 2015. A systematic review and meta-analysis of psychotherapy for late-life depression. Am. J. Geriatr. Psychiatry 23 (3), 261–273. https://doi.org/10.1016/j.jagp.2014.04.003.

Keller, M.B., 2003. Past, present, and future directions for defining optimal treatment outcome in depression: remission and beyond. JAMA 289 (23), 3152–3160. https://doi.org/10.1001/jama.289.23.3152.

Krause, M., Gutsmiedl, K., Bighelli, I., Schneider-Thoma, J., Chaimani, A., Leucht, S., 2019. Efficacy and tolerability of pharmacological and non-pharmacological interventions in older patients with major depressive disorder: a systematic review, pairwise and network meta-analysis. Eur. Neuropsychopharmacol. 29 (9), 1003–1022. https://doi.org/10.1016/j.euroneuro.2019.07.130.

Lebowitz, B.D., Pearson, J.L., Schneider, L.S., Reynolds III, C.F., Alexopoulos, G.S., Bruce, M.L., Parmelee, P, 1997. Diagnosis and treatment of depression in late life: consensus statement update [Consensus Statement]. JAMA 278 (14), 1186–1190. https://doi.org/10.1001/jama.1997.03550140078045.

Loo, C.K., Alonzo, A., Martin, D., Mitchell, P.B., Galvez, V., Sachdev, P., 2012. Transcranial direct current stimulation for depression: 3-week, randomised, sham-controlled trial. Br. J. Psychiatry 200 (1), 52–59. https://doi.org/10.1192/bjp.bp.111.097634.

Loo, C.K., Sachdev, P., Martin, D., Pigot, M., Alonzo, A., Malhi, G.S., Mitchell, P., 2010. A double-blind, sham-controlled trial of transcranial direct current stimulation for the treatment of depression. Int. J. Neuropsychopharmacol. 13 (1), 61–69. https://doi.org/10.1017/S1461145709990411.

Loo, C., Husain, M., Mcdonald, W., Aaronson, S., O'Reardon, J., Alonzo, A., Lisanby, S., 2018. International randomized-controlled trial of transcranial Direct Current Stimulation in depression. Brain Stimul. 11 (1), 125–133. https://doi.org/10.1016/j.brs.2017.10.011.

Lunn, D., Barrett, J., Sweeting, M., Thompson, S., 2013. Fully Bayesian hierarchical modelling in two stages, with application to meta-analysis. J. R. Stat. Soc. Ser. C Appl. Stat. 62 (4), 551–572. https://doi.org/10.1111/rssc.12007.

Moffa, A.H., Martin, D., Alonzo, A., Bennabi, D., Blumberger, D.M., Benseñor, I.M., Brunoni, A.R., 2020. Efficacy and acceptability of transcranial direct current stimulation (tDCS) for major depressive disorder: an individual patient data meta-analysis. Prog. Neuropsychopharmacol. Biol. Psychiatry 99, 109836. https://doi.org/10.1016/j.pnpbp.2019.109836.

Mutz, J., Edgcumbe, D.R., Brunoni, A.R., Fu, C.H., 2018. Efficacy and acceptability of non-invasive brain stimulation for the treatment of adult unipolar and bipolar depression: a systematic review and meta-analysis of randomised sham-controlled trials. Neurosci. Biobehav. Rev. 92, 291–303. https://doi.org/10.1016/j.neubiorev.2018.05.015.

Palm, U., Hasan, A., Strube, W., Padberg, F., 2016. tDCS for the treatment of depression: a comprehensive review. Eur. Arch. Psychiatry Clin. Neurosci. 266 (8), 681–694. https://doi.org/10.1007/s00406-016-0674-9.

Palm, U., Schiller, C., Fintescu, Z., Obermeier, M., Keeser, D., Reisinger, E., Padberg, F., 2012. Transcranial direct current stimulation in treatment resistant depression: a randomized double-blind, placebo-controlled study. Brain Stimul. 5 (3), 242–251. https://doi.org/10.1016/j.brs.2011.08.005.

Razza, L.B., Palumbo, P., Moffa, A.H., Carvalho, A.F., Solmi, M., Loo, C.K., Brunoni, A.R., 2020. A systematic review and meta-analysis on the effects of transcranial direct current stimulation in depressive episodes. Depress. Anxiety 37 (7), 594–608. https://doi.org/10.1002/da.23004.

Riley, R.D., Lambert, P.C., Abo-Zaid, G., 2010. Meta-analysis of individual participant data: rationale, conduct, and reporting. BMJ (c221), 340. https://doi.org/10.1136/bmj.c221.

Tham, A., Jonsson, U., Andersson, G., Söderlund, A., Allard, P., Bertilsson, G., 2016. Efficacy and tolerability of antidepressants in people aged 65 years or older with major depressive disorder–a systematic review and a meta-analysis. J. Affect. Disord. 205, 1–12. https://doi.org/10.1016/j.jad.2016.06.013.

van Buuren, S., Groothuis-Oudshoorn, K., 2011. mice: multivariate imputation by chained equations in R. J. Stat. Softw. 45 (3), 1–67. https://doi.org/10.18637/jss.v045.i03.

Viechtbauer, W., 2010. Conducting meta-analyses in R with the metafor package. J. Stat. Softw. 36 (3), 1–48. https://doi.org/10.18637/jss.v036.i03.

Woodham, R., Rimmer, R.M., Mutz, J., Fu, C.H., 2021. Is tDCS a potential first line treatment for major depression? Int. Rev. Psychiatry 33 (3), 1–16. https://doi.org/10.1080/09540261.2021.1879030.

Wong, H.L., Chan, W.C., Wong, Y.L., Wong, S.N., Yung, H.Y., Wong, S.M.C., Cheng, P.W. C., 2019. High-definition transcranial direct current stimulation—An open-label pilot intervention in alleviating depressive symptoms and cognitive deficits in late-life depression. CNS Neurosci. Ther. 25 (11), 1244–1253. https://doi.org/10.1111/cns.13253.

Zanardi, R., Poletti, S., Prestifilippo, D., Attanasio, F., Barbini, B., Colombo, C., 2020. Transcranial direct current stimulation: a novel approach in the treatment of vascular depression. Brain Stimul. 13 (6), 1559–1565. https://doi.org/10.1016/j.brs.2020.08.013.

Zhang, R., Lam, C.L., Peng, X., Zhang, D., Zhang, C., Huang, R., Lee, T.M., 2021. Efficacy and acceptability of transcranial direct current stimulation for treating depression: A meta-analysis of randomized controlled trials. Neurosci. Biobehav. Rev. 126, 481–490. https://doi.org/10.1016/j.neubiorev.2021.03.026.