# SupplementARY References

## Table 2. Non-invasive Neuromodulation Clinical Trials in Acute Migraine Treatments

### Non-invasive vagus nerve stimulation (nVNS)

Goadsby PJ, Grosberg BM, Mauskop A, Cady R, Simmons KA. Effect of noninvasive vagus nerve stimulation on acute migraine: an open-label pilot study. *Cephalalgia.* 2014;34(12):986-993.

German Clinical Trials Register. Assessment of non-invasive vagal nerve stimulation (VNS)-induced head pain-effects in refractory migraine patients: a multimodal fMRI study. Available from: http://www.drks.de/drks\_web/navigate.do?navigationId=trial.HTML&TRIAL\_ID=DRKS00009944. Identifier: DRKS00009944. Published February 8, 2016. Accessed April 3, 2018.

ClinicalTrials.gov. Non-invasive neurostimulation for the relief of migraine. Available from: https://clinicaltrials.gov/ct2/show/NCT03410628. Identifier: NCT03410628. Published January 25, 2018. Accessed April 2, 2018.

Tassorelli C, Grazzi L, de Tommaso M, et al. Noninvasive vagus nerve stimulation as acute therapy for migraine: the randomized PRESTO study. *Neurology.* 2018;91(4):e364-e373.

### External trigeminal nerve stimulation (e-TNS)

ClinicalTrials.gov. Abortive treatment of migraine with the Cefaly® abortive program device. Available from: https://clinicaltrials.gov/ct2/show/NCT03217968. Identifier: NCT03217968. Published June 7, 2018. Updated July 4, 2018. Accessed April 2, 2018.

ClinicalTrials.gov. Acute treatment of migraine using the CEFALY device. Available from: https://clinicaltrials.gov/ct2/show/NCT02411513. Identifier: NCT02411513. Published April 8, 2015. Updated December 4, 2015. Accessed April 3, 2018.

Chou DE, Shnayderman Yugrakh M, Winegarner D, Rowe V, Kuruvilla D, Schoenen J. Acute migraine therapy with external trigeminal neurostimulation (ACME): a randomized controlled trial [published online November 17, 2018]. *Cephalalgia.* doi:10.1177/0333102418811573.

### Occipital and supraorbital transcutaneous nerve stimulation (OS-TNS)

ClinicalTrials.gov. Short-term effectiveness of transcutaneous nerve stimulation in reducing migraine related pain. Available from: https://clinicaltrials.gov/ct2/show/NCT02438553. Identifier: NCT02438553. Published May 8, 2015. Updated January 7, 2016. Accessed April 2, 2018.

ClinicalTrials.gov. A randomized, double-blind clinical investigation to evaluate the use of the Relievion™ device in treating migraine. Available from: https://clinicaltrials.gov/ct2/show/NCT03185559. Identifier: NCT03185559. Published June 14, 2017. Updated March 29, 2018. Accessed April 3, 2018.

ClinicalTrials.gov. Combined occipital and supraorbital transcutaneous nerve stimulation for treatment of migraine. Available from: https://clinicaltrials.gov/ct2/show/NCT03398668. Identifier: NCT03398668. Published January 12, 2018. Updated July 6, 2018. Accessed April 3, 2018.

### Transcranial direct current stimulation (tDCS)

ClinicalTrials.gov. Transcranial direct current stimulation for migraine attack. Available from: https://clinicaltrials.gov/ct2/show/NCT01358279. Identifier: NCT01358279. Published May 23, 2011. Updated October 25, 2016. Accessed April 3, 2018.

### Transcranial alternating current stimulation

German Clinical Trials Register. Studying the efficacy of low intensity transcranial electrical stimulation in the acute treatment of migraine. Available from: http://www.drks.de/drks\_web/navigate.do?navigationId=trial.HTML&TRIAL\_ID=DRKS00011878. Identifier: DRKS00011878. Published April 21, 2017. Accessed April 3, 2018.

### Auricular transcutaneous vagus nerve stimulation

Chinese Clinical Trial Registry. Treatment of non-premonitory migraine with transcutaneous stimulation of the auricular branch of the vagal nerve (auricular t-VNS): a randomized, monocentric clinical trial on efficacy and the central mechanism of multi modality fMRI. Available from: http://www.chictr.org.cn/showproj.aspx?proj=17911. Identifier: ChiCTR-INR-17010559. Published February 7, 2017. Accessed April 3, 2018.

### Single-pulse transcranial magnetic stimulation (sTMS)

Clarke BM, Upton AR, Kamath MV, Al-Harbi T, Castellanos CM. Transcranial magnetic stimulation for migraine: clinical effects. *J Headache Pain.* 2006;7(5):341-346.

Lipton RB, Dodick DW, Silberstein SD, et al. Single-pulse transcranial magnetic stimulation for acute treatment of migraine with aura: a randomised, double-blind, parallel-group, sham-controlled trial. *Lancet Neurol.* 2010;9(4):373-380.

### Repetitive transcranial magnetic stimulation (rTMS)

Almaraz AC, Dilli E, Dodick DW. The effect of prophylactic medications on TMS for migraine aura. *Headache.* 2010;50(10):1630-1633.

### Conditioned pain modulation (CPM)

ClinicalTrials.gov. Migraine treatment with Nerivio Migra neurostimulation device. Available from: https://clinicaltrials.gov/ct2/show/NCT03076515. Identifier: NCT03076515. Published March 10, 2017. Updated May 9, 2018. Accessed April 3, 2018.

ClinicalTrials.gov. Evaluation of a novel device for treatment of migraine headache. Available from: https://clinicaltrials.gov/ct2/show/NCT03361423. Identifier: NCT03361423. Published December 4, 2017. Updated July 3, 2018. Accessed April 2, 2018.

Yarnitsky D, Volokh L, Ironi A, et al. Nonpainful remote electrical stimulation alleviates episodic migraine pain. *Neurology.* 2017;88(13):1250-1255.

### Intranasal kinetic oscillation stimulation

Juto JE, Hallin RG. Kinetic oscillation stimulation as treatment of acute migraine: a randomized, controlled pilot study. *Headache.* 2015;55(1):117-127.

## Table 3. Non-invasive Neuromodulation Clinical Trials in Preventive Migraine Treatments

### Transcranial direct current stimulation (tDCS)

ClinicalTrials.gov. Effects of transcranial direct current stimulation in refractory chronic migraine and medication-overuse headache. Available from: https://clinicaltrials.gov/ct2/show/NCT01752439. Identifier: NCT01752439. Published December 19, 2012. Updated December 19, 2012. Accessed April 3, 2018.

ClinicalTrials.gov. tDCS for the treatment of migraine. Available from: https://clinicaltrials.gov/ct2/show/NCT02562196. Identifier: NCT02562196. Published September 29, 2015. Updated May 11, 2016. Accessed April 2, 2018.

ClinicalTrials.gov. Transcranial direct current simulation in chronic migraine. Available from: https://clinicaltrials.gov/ct2/show/NCT02817139. Identifier: NCT02817139. Published June 29, 2016. Accessed April 2, 2018.

ClinicalTrials.gov. Evaluation of the prophylactic efficacy of tDCS in chronic migraine (Medis). Available from: https://clinicaltrials.gov/ct2/show/NCT02120326. Identifier: NCT02120326. Published April 22, 2014. Updated May 3, 2017. Accessed April 3, 2018.

ClinicalTrials.gov. Investigation and modulation of the mu-opioid mechanisms in migraine (in vivo). Available from: https://clinicaltrials.gov/ct2/show/NCT02964741. Identifier: NCT02964741. Published November 16, 2016. Updated December 21, 2017. Accessed April 16, 2018.

ClinicalTrials.gov. Comparison between transcranial stimulation protocols with continuous current in the chronic migraine (NEUROMIG). Available from: https://clinicaltrials.gov/ct2/show/NCT03414203. Identifier: NCT03414203. Published January 29, 2018. Accessed April 2, 2018.

ClinicalTrials.gov. Neurostimulation in chronic and episodic migraine. Available from: https://clinicaltrials.gov/ct2/show/NCT03237754. Identifier: NCT03237754. Published August 3, 2017. Accessed April 2, 2018.

ClinicalTrials.gov. Anodal transcranial direct current stimulation of the visual cortex versus sham stimulation in the episodic migraine (ANODEM). Available from: https://clinicaltrials.gov/ct2/show/NCT02122757. Identifier: NCT02122757. Published April 25, 2014. Updated May 28, 2015. Accessed April 2, 2018.

Chinese Clinial Trial Registry. Study of migraine prevention by electrical stimulation of both mastoids behind the ears: a multicenter, randomized, double blinded controlled trial. Available from: http://www.chictr.org.cn/showprojen.aspx?proj=10807. Identifier: ChiCTR-ICR-15006273. Published April 5, 2015. Updated April 19, 2015. Accessed April 3, 2018.

Antal A, Kriener N, Lang N, Boros K, Paulus W. Cathodal transcranial direct current stimulation of the visual cortex in the prophylactic treatment of migraine. *Cephalalgia.* 2011;31(7):820-828.

Auvichayapat P, Janyacharoen T, Rotenberg A, et al. Migraine prophylaxis by anodal transcranial direct current stimulation, a randomized, placebo-controlled trial. *J Med Assoc Thai.* 2012;95(8):1003-1012.

Rocha S, Melo L, Boudoux C, Foerster Á, Araújo D, Monte-Silva K. Transcranial direct current stimulation in the prophylactic treatment of migraine based on interictal visual cortex excitability abnormalities: a pilot randomized controlled trial. *J Neurol Sci.* 2015;349(1-2):33-39.

Viganò A, D'Elia TS, Sava SL, et al. Transcranial direct current stimulation (tDCS) of the visual cortex: a proof-of-concept study based on interictal electrophysiological abnormalities in migraine. *J Headache Pain.* 2013;14:23.

ClinicalTrials.gov. Migraine--investigational treatment of migraine with noninvasive brain stimulation (tDCS-migraine). Available from: https://clinicaltrials.gov/ct2/show/NCT00521196. Identifier: NCT00521196. Published August 27, 2007. Updated March 21, 2017. Accessed April 2, 2018.

ClinicalTrials.gov. Cathodal tDCS in chronic migraine: neurophysiological study and pilot therapeutic trial (CATCHROMIG). Available from: https://clinicaltrials.gov/ct2/show/NCT02122237. Identifier: NCT02122237. Published April 24, 2014. Updated May 28, 2015. Accessed April 2, 2018.

Dasilva AF, Mendonca ME, Zaghi S, et al. tDCS-induced analgesia and electrical fields in pain-related neural networks in chronic migraine. *Headache.* 2012;52(8):1283-1295.

ClinicalTrials.gov. Occipital transcutaneous stimulation in chronic migraine (OSCRO). Available from: https://clinicaltrials.gov/ct2/show/NCT02307071. Identifier: NCT02307071. Published December 3, 2014. Updated May 28, 2015. Accessed April 2, 2018.

ClinicalTrials.gov. Optimized tDCS for the treatment of migraine. Available from: https://clinicaltrials.gov/ct2/show/NCT02562222. Identifier: NCT02562222. Published September 29, 2015. Updated May 11, 2016. Accessed April 2, 2018.

### Non-invasive vagus nerve stimulation (nVNS)

German Clinical Trials Register. Assessment of non-invasive vagal nerve stimulation (VNS)-induced head pain-effects in refractory migraine patients: a multimodal fMRI study. Available from: http://www.drks.de/drks\_web/navigate.do?navigationId=trial.HTML&TRIAL\_ID=DRKS00009944. Identifier: DRKS00009944. Published February 8, 2016. Accessed April 3, 2018.

German Clinical Trials Register. Prospective analysis and evaluation of frequency and intensity of migraine, sleeping, depression and oxytocin and CGRP-levels in patients with refractory migraine under noninvasive VNS stimulation. Available from: http://www.drks.de/drks\_web/navigate.do?navigationId=trial.HTML&TRIAL\_ID=DRKS00011089. Identifier: DRKS00011089. Published September 21, 2016. Accessed April 3, 2018.

ClinicalTrials.gov. A randomized, sham-controlled study of gammaCore® (nVNS) for prevention of episodic migraine. Available from: https://clinicaltrials.gov/ct2/show/NCT02378844. Identifier: NCT02378844. Published March 4, 2015. Updated February 19, 2018. Accessed April 2, 2018.

Silberstein SD, Calhoun AH, Lipton RB, et al. Chronic migraine headache prevention with noninvasive vagus nerve stimulation: the EVENT study. *Neurology.* 2016;87(5):529-538.

### External trigeminal nerve stimulation (e-TNS)

ClinicalTrials.gov. Open-trial on the prevention of chronic migraines with the CEFALY device. Available from: https://clinicaltrials.gov/ct2/show/NCT02342743. Identifier: NCT02342743. Published January 21, 2015. Updated May 1, 2017. Accessed April 2, 2018.

Schoenen J, Vandersmissen B, Jeangette S, et al. Migraine prevention with a supraorbital transcutaneous stimulator: a randomized controlled trial. *Neurology.* 2013;80(8):697-704.

Vikelis M, Dermitzakis EV, Spingos KC, Vasiliadis GG, Vlachos GS, Kararizou E. Clinical experience with transcutaneous supraorbital nerve stimulation in patients with refractory migraine or with migraine and intolerance to topiramate: a prospective exploratory clinical study. *BMC Neurol.* 2017;17(1):97.

### Transcutaneous electrical nerve stimulation

ClinicalTrials.gov. Non-pharmacological management of chronic migraine (MIGRANE). Available from: https://clinicaltrials.gov/ct2/show/NCT02953015. Identifier: NCT02953015. Published November 2, 2016. Accessed April 3, 2018.

Allais G, De Lorenzo C, Quirico PE, et al. Non-pharmacological approaches to chronic headaches: transcutaneous electrical nerve stimulation, lasertherapy and acupuncture in transformed migraine treatment. *Neurol Sci.* 2003;24(suppl 2):S138-S142.

### Transcutaneous supraorbital nerve stimulation

ClinicalTrials.gov. Migraine prevention using ActiPatch (PSWT). Available from: https://clinicaltrials.gov/ct2/show/NCT03166046. Identifier: NCT03166046. Published May 24, 2017. Updated May 16, 2018. Accessed April 2, 2018.

### Auricular transcutaneous vagus nerve stimulation

Straube A, Ellrich J, Eren O, Blum B, Ruscheweyh R. Treatment of chronic migraine with transcutaneous stimulation of the auricular branch of the vagal nerve (auricular t-VNS): a randomized, monocentric clinical trial. *J Headache Pain.* 2015;16:543.

### Cranial electrotherapy stimulation

ClinicalTrials.gov. Cranial electrotherapy stimulation in the treatment of migraine headaches. Available from: https://clinicaltrials.gov/ct2/show/NCT01265797. Identifier: NCT01265797. Published December 23, 2010. Updated February 10, 2015. Accessed April 2, 2018.

### Repetitive transcranial magnetic stimulation (rTMS)

ClinicalTrials.gov. Efficacy of rTMS in the treatment of patients with migraine. Available from: https://clinicaltrials.gov/ct2/show/NCT00316979. Identifier: NCT00316979. Published April 21, 2006. Updated June 8, 2010. Accessed April 3, 2018.

ClinicalTrials.gov. RCT versus placebo of rTMSQP over visual cortex for the prevention of chronic migraine. Available from: https://clinicaltrials.gov/ct2/show/NCT02122744. Identifier: NCT02122744. Published April 25, 2014. Updated May 28, 2015. Accessed April 3, 2018.

Clinical Trials Registry of India. Randomized placebo controlled trial evaluating role of single pulse rTMS in migraine prophylaxis. Available from: http://www.ctri.nic.in/Clinicaltrials/pmaindet2.php?trialid=5545. Identifier: CTRI/2012/2012/003165. Published March 12, 2012. Accessed April 3, 2018.

Brighina F, Palermo A, Daniele O, Aloisio A, Fierro B. High-frequency transcranial magnetic stimulation on motor cortex of patients affected by migraine with aura: a way to restore normal cortical excitability? *Cephalalgia.* 2010;30(1):46-52.

Brighina F, Piazza A, Vitello G, et al. rTMS of the prefrontal cortex in the treatment of chronic migraine: a pilot study. *J Neurol Sci.* 2004;227(1):67-71.

Conforto AB, Amaro E Jr., Goncalves AL, et al. Randomized, proof-of-principle clinical trial of active transcranial magnetic stimulation in chronic migraine. *Cephalalgia.* 2014;34(6):464-472.

Fumal A, Coppola G, Bohotin V, et al. Induction of long-lasting changes of visual cortex excitability by five daily sessions of repetitive transcranial magnetic stimulation (rTMS) in healthy volunteers and migraine patients. *Cephalalgia.* 2006;26(2):143-149.

Misra UK, Kalita J, Bhoi SK. High frequency repetitive transcranial magnetic stimulation (rTMS) is effective in migraine prophylaxis: an open labeled study. *Neurol Res.* 2012;34(6):547-551.

Teepker M, Hotzel J, Timmesfeld N, et al. Low-frequency rTMS of the vertex in the prophylactic treatment of migraine. *Cephalalgia.* 2010;30(2):137-144.

Misra UK, Kalita J, Bhoi SK. High-rate repetitive transcranial magnetic stimulation in migraine prophylaxis: a randomized, placebo-controlled study. *J Neurol.* 2013;260(11):2793-2801.

### Single-pulse transcranial magnetic stimulation

Starling AJ, Tepper SJ, Marmura MJ, et al. A multicenter, prospective, single arm, open label, observational study of sTMS for migraine prevention (ESPOUSE Study). *Cephalalgia.* 2018;38(6):1038-1048.

### Deep transcranial magnetic stimulation

Rapinesi C, Del Casale A, Scatena P, et al. Add-on deep transcranial magnetic stimulation (dTMS) for the treatment of chronic migraine: a preliminary study. *Neurosci Lett.* 2016;623:7-12.

### Caloric vestibular stimulation (CVS)

ClinicalTrials.gov. Neurostimulation device for treatment of migraine headache. Available from: https://clinicaltrials.gov/ct2/show/NCT01630044. Identifier: NCT01630044. Published June 28, 2012. Updated December 22, 2016. Accessed April 2, 2018.

ClinicalTrials.gov. A non-invasive neuromodulation device for prevention of episodic migraine headache. Available from: https://clinicaltrials.gov/ct2/show/NCT02991430. Identifier: NCT02991430. Published December 13, 2016. Updated May 17, 2018. Accessed April 2, 2018.

Wilkinson D, Ade KK, Rogers LL, et al. Preventing episodic migraine with caloric vestibular stimulation: a randomized controlled trial. *Headache.* 2017;57(7):1065-1087.

### Intranasal kinetic oscillation stimulation

ClinicalTrials.gov. Study to evaluate the efficacy of intranasal kinetic oscillation stimulation in the preventive treatment of chronic migraine. Available from: https://clinicaltrials.gov/ct2/show/NCT03400059. Identifier: NCT03400059. Published January 17, 2018. Updated July 18, 2018. Accessed April 2, 2018.

ClinicalTrials.gov. Chordate system prophylactic migraine clinical investigation. Available from: https://clinicaltrials.gov/ct2/show/NCT02243865. Identifier: NCT02243865. Published September 18, 2014. Updated December 19, 2014. Accessed April 2, 2018.

### Auditory biofeedback

Ciancarelli I, Tozzi-Ciancarelli MG, Spacca G, Di Massimo C, Carolei A. Relationship between biofeedback and oxidative stress in patients with chronic migraine. *Cephalalgia.* 2007;27(10):1136-1141.

## Table 4. Non-invasive Neuromodulation Clinical Trials in Acute and Preventive Cluster Headache Treatments

### Non-invasive vagus nerve stimulation (nVNS; acute cluster headache treatments)

Goadsby PJ, de Coo IF, Silver N, et al. Non-invasive vagus nerve stimulation for the acute treatment of episodic and chronic cluster headache: a randomized, double-blind, sham-controlled ACT2 study. *Cephalalgia.* 2018;38(5):959-969.

Silberstein SD, Mechtler LL, Kudrow DB, et al. Non-invasive vagus nerve stimulation for the acute treatment of cluster headache: findings from the randomized, double-blind, sham-controlled ACT1 study. *Headache.* 2016;56(8):1317-1332.

### Non-invasive vagus nerve stimulation (nVNS; preventive cluster headache treatment)

Gaul C, Diener HC, Silver N, et al. Non-invasive vagus nerve stimulation for PREVention and Acute treatment of chronic cluster headache (PREVA): a randomised controlled study. *Cephalalgia.* 2016;36(6):534-546.

### Transcranial direct current stimulation (tDCS; preventive cluster headache treatment)

ClinicalTrials.gov. Anodal transcranial direct stimulation (tDCS) for the treatment of chronic cluster headache (ANODECCH). Available from: https://clinicaltrials.gov/ct2/show/NCT02462395. Identifier: NCT02462395. Published June 4, 2015. Updated December 7, 2016. Accessed April 2, 2018.