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Hearing safety of accelerated TMS: Calculating daily noise dose of the SAINT protocol for depression

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Dear Editor,

The FDA recently approved the SAINT protocol, an accelerated transcranial magnetic stimulation (TMS) protocol, for depression. 10 intermittent theta burst (iTBS) TMS sessions are administered per day to condense the 90,000 pulse treatment into 5 days [1]. Each TMS pulse generates a loud impulse noise caused by rapid expansion of the coil.

After one 1200-pulse session of 1 Hz or 10 Hz repetitive TMS (rTMS) to the superior temporal gyrus at 100 % resting motor threshold (RMT), subjects with poor earplug fit had significant noise-induced cochlear alterations in the ear ipsilateral to the stimulus [2]. The FDA-approved rTMS treatment protocol for depression with a NeuroStar coil - 3000 daily pulses of 10 Hz rTMS to the left dorsolateral prefrontal cortex (L DLPFC) at 120 % RMT for 6 weeks, while wearing earplugs - did not significantly change subjects' auditory air conduction thresholds [3], but their subthreshold sensorineural hearing loss was not evaluated [4]. The SAINT protocol delivers 18,000 pulses daily, a 6-fold increase over previous FDA-approved TMS protocols. Though all participants in SAINT trials were required to wear hearing protection, the hearing safety of daily noise dose in accelerated TMS protocols for patients and TMS operators has not been studied.

In the SAINT protocol, the MagVenture Cool-B65 coil is used to stimulate a personalized target in the L DLPFC. Stimulation intensity, which is capped at 120 % of RMT, is depth-corrected to stimulate the target at 90 % RMT. The sound pressure level (SPL) generated by TMS decreases with distance to the coil per the inverse square law and increases linearly with the fourth power of stimulation intensity. rTMS loudness increases linearly with stimulation frequency as well. Therefore, reported sound measurements for TMS coils vary. Some exceed 80 dB(A), the American Conference of Governmental Industrial Hygienists (ACGIH) threshold for noise dosimetry, or 85 dB(A), limit A of the US Department of Defense impulse noise standard MIL-STD-1474E [5]. The National Institute for Occupational Safety and Health (NIOSH) Relative Exposure Limit defines a time-adjusted maximum daily noise dose as equivalent to 85 dB(A) for 8 hours, with a 3-dB time-intensity tradeoff for energy equivalence [6].

We calculated estimated SPL and time-adjusted noise dose of the SAINT protocol for the patient and TMS operator. We compared them to calculated noise dose of TMS protocols for which hearing safety has been assessed and standard limits for safe sound exposure. We chose SPL measurements obtained with a pressure microphone 25 cm from the coil. This avoids the confounds of measuring a node created by interference in the acoustic near-field, or using sound meters, which can average the impulse noise peak into background noise if their response time is longer than the impulse duration [7]. The measured sound pressure level 25 cm away from the MagVenture Cool-B65 operating at 20 Hz and 150 % of the average RMT was 82 dB(A) [5].

Distance from the left tragus to the L DLPFC was estimated to be 12.7 cm using mean head measurements [8] and the EEG-Locator Borckardt/Hanlon System [9]. Since RMT depends on the individual, we used 167 % and 73 % average RMT, corresponding to 120 % RMT for subjects in the top and bottom 5 percentile of RMT relative to maximum stimulator output, to represent the range [10]. iTBS delivers pulses in a pattern of 5 Hz bursts, with 3 pulses at 50 Hz per burst totaling 15 pulses/second. All sound exposure limits listed above are defined using slow-time-weighted sound meters with a 1 second time constant, making 18,000 iTBS pulses energy equivalent to 20 minutes of continuous 15 Hz noise.

The SPL at the ear of a patient with high RMT undergoing the SAINT protocol is 88.4 dB(A) for 20 minutes per day (Eq. (1)). It is 82.7 or 74.1 dB(A) for a patient with average or low RMT. The NIOSH time-adjusted threshold for 20 minutes of noise is 98.8 dB(A) (Fig. 1A). TMS noise dose from a day of SAINT treatment is energy-equivalent to 8 hours of exposure to 74.7, 69, or 60.4 dB(A) SPL with high, average, or low RMT respectively. (Eq. (2)) (Fig. 1B).

$$SPL = 82 - 6\,log_2\left(\frac{12.7cm}{25cm}\right) + 12\,log_2\left(\frac{167\%RMT}{150\%RMT}\right) + 3\,log_2\left(\frac{15\ Hz}{20\ Hz}\right) = 88.4\ dB(A) \quad \text{Eq. 1}$$

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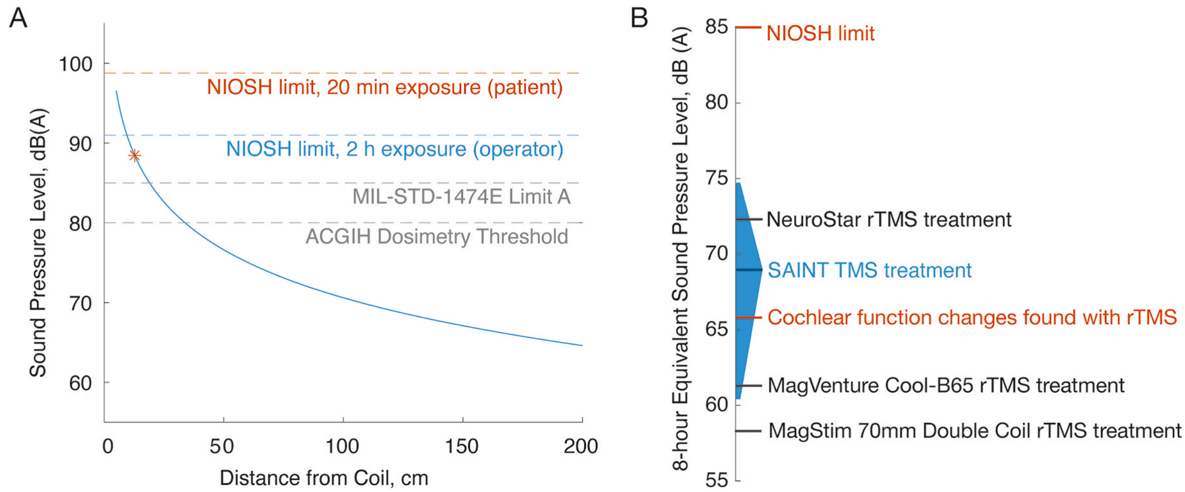

Fig. 1. Sound Pressure Level during SAINT protocol. A) Maximum SPL. Blue line represents TMS operator exposure. Distance from patient's tragus to L DLPFC marked with orange asterisk. Dotted lines show upper limits of noise exposure standards. B) 8-h SPL equivalent to daily noise dose for several TMS protocols. Range across RMT distribution for SAINT TMS shown in blue, with line marking equivalent SPL for patient with average RMT. Traditional 10Hz rTMS protocols with different coils marked in black. NIOSH limit and TMS protocol that induced significant cochlear alterations in subjects with poor earplug fit marked in orange. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

$$SPL_{eq,8h} = 82 \ - 6\ log_2\left(\frac{12.7cm}{25cm}\right) + 12\ log_2\left(\frac{167\%RMT}{150\%RMT}\right) + 3\ log_2 \left(\frac{18000\ pulses}{20\ Hz\ *\ 8\ *\ 60\ *\ 60\ s}\right) = 74.7\ dB(A) \qquad \text{Eq. 2}$$

SPL for the TMS operator decreases with their distance from the coil. It falls below 85 dB(A) at 19 cm distance from a patient with high RMT and below 80 dB(A) at 34 cm. In the SAINT protocol, each patient receives treatment for 10 minutes/hour for 10 hours [1]. An operator treating the maximum possible 6 patients per day is effectively exposed to 2 h of 15 Hz TMS noise daily, increasing their 8 h equivalent daily noise from TMS by 7.8 dB over treatment of one patient. Exceeding the NIOSH time-adjusted threshold for 2 h of noise, 91 dB(A), would require the operator's ear to remain 9.5 cm from the coil through a full day treating six patients with high RMT (Fig. 1A).

For comparison, using the same estimation method, noise from the FDA-approved 10Hz rTMS treatment protocol with the same coil is equivalent to 8 hours of 61.3 dB(A) SPL for the average patient. The 8-h equivalent SPL is 58.3 dB(A) with the Magstim 70mm Double Coil or 72.3 dB(A) with the NeuroStar coil [5]. In the rTMS protocols observed to cause noise-induced cochlear alterations in subjects with poor earplug fit [2], the 8-h equivalent SPL was 65.8 dB(A) noise at the subject's ear (Fig. 1B).

All calculated daily noise doses are under the duration-adjusted NIOSH relative exposure limits. SPL at the patient's ear can exceed MIL-STD-1474E limit A for impulse noise, the strictest threshold, and require noise dosimetry per the ACGIH threshold. In line with prior recommendations that TMS patients wear hearing protection, properly inserted standard earplugs (rated at 35 dB noise reduction with good fit) bring the patient's exposure below all identified noise limits. A SAINT protocol operator's noise exposure meets all identified standards with no noise dosimetry required if their ear remains >34 cm from the coil.

Occupational sound exposure limits are thresholds based on noise levels that cause permanent threshold shifts in audiometry studies. However, noise-induced cochlear synaptopathy without significant threshold shift is a growing concern in audiology [4]. Symptoms, including tinnitus and difficulty understanding conversations, impact quality of life, a particular concern for patients with depression. Cochlear function changes have been observed with experimental rTMS protocols that are within noise exposure limits [2], so these limits do not capture all relevant mechanisms. We demonstrate that the daily noise exposure from the SAINT protocol and from traditional rTMS protocols can exceed the daily TMS noise exposure that induced significant cochlear alterations in subjects with poor earplug fit. Cochlear changes may occur with quieter protocols as well. Therefore, ensuring proper fit of hearing protection is important for risk management in TMS patients and operators. Additionally, earplug fit varies in practice, and our findings do not account for varying head geometry, bone conduction, noise from other components of the TMS system, or time-varying sound damping that may influence true noise level delivered to the ear during TMS. Therefore, thorough audiometric testing is needed to understand the effect of TMS on hearing.

CRediT authorship contribution statement

Bianca N. De: Conceptualization, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Brent R. Carr:** Conceptualization, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Cole EJ, Stimpson KH, Bentzley BS, Gulser M, Cherian K, Tischler C, et al. Stanford accelerated intelligent neuromodulation therapy for treatment-resistant depression. Am J Psychiatr 2020;177:716–26. https://doi.org/10.1176/appi.ajp.2019.19070720.

[2] Tringali S, Perrot X, Collet L, Moulin A. Repetitive transcranial magnetic stimulation: hearing safety considerations. Brain Stimul 2012;5:354–63. https://doi.org/10.1016/j.brs.2011.06.005.

[3] O'Reardon JP, Solvason HB, Janicak PG, Sampson S, Isenberg KE, Nahas Z, et al. Efficacy and safety of transcranial magnetic stimulation in the acute treatment of major depression: a multisite randomized controlled trial. Biol Psychiatr 2007;62:1208–16. https://doi.org/10.1016/j.biopsych.2007.01.018.

[4] Chen F, Zhao F, Mahafza N, Lu W. Detecting noise-induced cochlear synaptopathy by auditory brainstem response in tinnitus patients with normal hearing thresholds: a meta-analysis. Front Neurosci 2021;15:778197. https://doi.org/10.3389/fnins.2021.778197.

[5] Koponen LM, Goetz SM, Tucci DL, Peterchev AV. Sound comparison of seven TMS coils at matched stimulation strength. Brain Stimul 2020;13:873–80. https://doi.org/10.1016/j.brs.2020.03.004.

[6] Understanding noise exposure limits: occupational vs. General Environmental Noise | Blogs | CDC n.d. https://blogs.cdc.gov/niosh-science-blog/2016/02/08/noise/. [Accessed 22 September 2023].

[7] Goetz SM, Lisanby SH, Murphy DLK, Price RJ, O'Grady G, Peterchev AV. Impulse noise of transcranial magnetic stimulation: measurement, safety, and auditory neuromodulation. Brain Stimul 2015;8:161–3. https://doi.org/10.1016/j.brs.2014.10.010.
[8] Mir-Moghtadaei A, Caballero R, Fried P, Fox MD, Lee K, Giacobbe P, et al. Concordance between BeamF3 and MRI-neuronavigated target sites for repetitive transcranial magnetic stimulation of the left dorsolateral prefrontal cortex. Brain Stimul 2015;8:965–73. https://doi.org/10.1016/j.brs.2015.05.008.
[9] Borckardt J, Hanlon C. EEG-Locator Borckardt/Hanlon System, http://clinicalresearcher.org/eeg/index.php/. [Accessed 22 September 2023].
[10] Desbeaumes Jodoin V, Miron J-P, Lespérance P. Safety and efficacy of accelerated repetitive transcranial magnetic stimulation protocol in elderly depressed unipolar and bipolar patients. Am J Geriatr Psychiatr 2019;27:548–58. https://doi.org/10.1016/j.jagp.2018.10.019.

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