

# TMS Safety Results from Clinical Trials

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- TMS does cause physical discomfort at the stimulation site, which is tolerable and by the end of the first 1 to 2 weeks of treatment is minimal.
- Site pain, headache, and facial twitching are possible and common.
- Risk of seizures is very low (1 in 30,000 treatments).
- There is no concern regarding cognitive side effects of TMS.

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# TMS Safety: Results from Clinical Trials



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# Industry-Sponsored Randomized Trial (Neuronetics)

Most common side effect



O'Reardon, J. P., Solvason, H. B., Janicak, P. G., Simpson, S., Isenberg, K. E., Nahas, Z., ... & Damtrack, M. A. (2007). Efficacy and safety of transcranial magnetic stimulation in the acute treatment of major depression: a multisite randomized controlled trial. *Biological Psychiatry*, 62(11), 1208-1216.



Okay. So next, we'll talk about some of the side effects of TMS

So when we look at the first industry sponsored randomized trial which is the Neuronetics trial, the most common side effect was headache. And looking at the numbers, 58% of patients in the active arm had a headache. But then when you look at those who had sham treatment, 55% also had headache. So headache is very common regardless of whether you're getting active treatment or sham.

## Top 2 Adverse Effects of Active Treatment

Application site pain



Muscle twitching



✔ Magnet placement against the head

Sham in first trial: minimal physical sensation.  
After about 2 weeks, most patients tolerated it.

O'Reardon, J. P., Solvason, H. B., Janicak, P. G., Sampson, S., Isenberg, K. E., Nahas, Z., ... & Demitrack, M. A. (2007). Efficacy and safety of transcranial magnetic stimulation in the acute treatment of major depression: a multisite randomized controlled trial. *Biological psychiatry*, 62(11), 1205-1216.

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So in that study, the top two adverse effects of the active treatment was at least twice as much as sham. So definitely, application site pain was 36% versus 4% for the sham. And application site pain, what that means is where the magnet is against the head and is tapping on the head, that part hurts. So 36% of the patients said, "Wow, that does hurt" when they were getting active. And of the sham, only 4% said, "Oh, this is hurting." For muscle twitching, when the stimulation is occurring, sometimes you'll see the face muscles twitch. So in active treatment, about 21% versus 3% for sham. And remember that the sham for that first trial had minimal physical sensation. So that was not the active sham that the NIMH trial had. And in that first study, they also noted that after about two weeks, most patients really tolerated it. So they didn't report that the pain was very bothersome.

# Review of TMS: Common Side Effects

## Mechanism



Site pain

Stimulation of superficial nerves or facial muscles



Headache

Local scalp stimulation or increased cerebral blood flow



Neck pain

Person lying in a reclined position for about 40 minutes

Taylor, R., Galvez, V., & Loo, C. (2018). Transcranial magnetic stimulation (TMS) safety: a practical guide for psychiatrists. *Australasian Psychiatry*, 26(2), 189-192.



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And there's a review of TMS also that looked at the common side effects, the site pain. The thought is it's due to stimulation of superficial nerves or facial muscles. The headache was thought to be due to some of the local scalp stimulation or increased cerebral blood flow. And sometimes, there's neck pain and the thought was maybe that's because the person is lying in a reclined position, sitting there for about 40 minutes.



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It was noted that less than 2% of clinical trial patients stopped because of pain. And the usual recommendation is use over-the-counter analgesics or switch to a lower intensity stimulation if there's more pain.

# Other Side Effects

Seizures



- Theoretical risk
- In practice, very low risk
- 1 in 30,000 treatments

Early reports

- Magnet not placed in correct position
- Patient using alcohol the night before

McClintock, S. M., Reif, I. M., Carpenter, L. L., McDonald, W. M., Dubin, M., Taylor, S. F., ... & Krystal, A. D. (2018). Consensus recommendations for the clinical application of repetitive transcranial magnetic stimulation (rTMS) in the treatment of depression. *The Journal of clinical psychiatry*, 79(1).

Taylor, R., Galvez, V., & Loo, C. (2018). Transcranial magnetic stimulation (TMS) safety: a practical guide for psychiatrists. *Australian Psychiatry*, 28(2), 189-192.



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In terms of other side effects, the serious effects, there's always worry about seizures. So that's a theoretical risk. And in practice, it's very low risk, however. One in 30,000 treatments, they have noticed a seizure. And some of the early reports about seizures, sometimes they found – I think in one of the cases they found that the magnet was not placed in the correct position. And another case, the patient had been using a lot of alcohol the night before and didn't tell the doctor. So you want to be careful about those.



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# Other Side Effects



History of seizures →  TMS

- Higher frequency
- More intense protocol
- Substance use
- Adolescents



Hearing impairment  
Transient  
Earplugs used



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So there does seem to be a higher risk of seizures when the patient has a history of seizures. And so that's why we frequently will not do TMS if a patient has a history of seizures. If you use higher frequency, more intense protocol, substance use, adolescents, the worry is there might be higher risk of seizures. For hearing impairments, there have been some reports of transient hearing impairment. Earplugs are used and the thought is that those will protect the ears.



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# Cognition



TMS might help cognition.



Meta-analysis of 18 studies



No cognitive side effects of TMS

No specific enhancements on majority of cognitive tasks

Modest improvement: Trail Making Test



Interval for posttesting was not consistent.

Martin, D. M., McClintock, S. M., Forster, J. J., Lo, T. Y., & Loo, C. K. (2017). Cognitive enhancing effects of rTMS administered to the prefrontal cortex in patients with depression: A systematic review and meta-analysis of individual task effects. *Depression and anxiety, 34*(11), 1029-1039.



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In terms of cognition – so there are no cognitive side effects of TMS. Studies have looked at that and there's no concern about worsening of memory. There has been a lot of interest in whether TMS might help with cognition and I give you the reference of a meta-analysis of 18 studies for cognitive enhancements. And overall really, they didn't find any specific enhancements on the majority of cognitive tasks. There's some modest improvement for Trail Making Test performance. And some of the thoughts are: Could it be related to when people are less depressed they do better with their cognition? And one of the limitations was that the interval for the post-testing was not consistent.



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# Key Points

- TMS causes physical discomfort at the stimulation site, which is tolerable; by 1 to 2 weeks, it is minimal.
- Site pain, headache, and facial twitching are common.
- The risk of seizures is very low: 1 in 30,000 treatments.
- There are no concerns about cognitive side effects of TMS.

So the key points from this section. TMS does cause physical discomfort at the stimulation site which is tolerable. And by the end of the first one to two weeks of treatment, it's minimal. Site pain, headache and facial twitching are possible and common. The risk of seizures is very low, 1 in 30,000 treatments. And there are no concerns about cognitive side effects of TMS.

