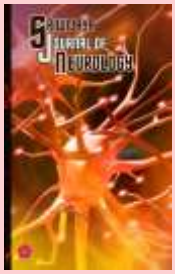

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Transcranial Magnetic Stimulation for the Treatment of Chronic Dizziness: A Randomized Controlled Trial in Bandung, Indonesia

Zahra Amir[1*], Nabila Saraswati[2], Made Swastika[2], Zainal Abidin Hasan[3], Aisyah Andina Rasyid[3], Hasrita Soleiman[2], Bernadette Wilson[4]

[1]Department of Psychiatry, CMHC Research Center, Palembang, Indonesia

[2]Department of Otorhinolaryngology, Phlox Institute, Palembang, Indonesia

[3]Department of Otorhinolaryngology, CMHC Research Center, Palembang, Indonesia

[4]Department of Otorhinolaryngology, Skopje National Hospital, Skopje, North Macedonia

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***Corresponding author:**
Zahra Amir

E-mail address:
zahra.amir@cattleyacenter.id

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A B S T R A C T

Introduction: Chronic dizziness is a debilitating condition with limited treatment options. Transcranial magnetic stimulation (TMS) has shown promise in treating various neurological conditions. This randomized controlled trial investigated the efficacy and safety of TMS in treating chronic dizziness in Bandung, Indonesia. **Methods:** Participants with chronic dizziness (≥ 3 months) were randomly assigned to receive either active TMS or sham TMS for 10 sessions over two weeks. The active TMS group received 1 Hz stimulation over the right dorsolateral prefrontal cortex (DLPFC), while the sham group received placebo stimulation. The primary outcome was the change in Dizziness Handicap Inventory (DHI) score from baseline to four weeks post-intervention. Secondary outcomes included changes in Vertigo Symptom Scale (VSS) scores, Hospital Anxiety and Depression Scale (HADS) scores, and quality of life measures. Safety was assessed through monitoring of adverse events. **Results:** A total of 60 participants completed the study (30 in each group). The active TMS group showed a significantly greater improvement in DHI scores compared to the sham group ($p < 0.001$). Significant improvements were also observed in VSS, HADS, and quality of life measures in the active TMS group. No serious adverse events were reported. **Conclusion:** This study provides evidence for the efficacy and safety of TMS in treating chronic dizziness in the Indonesian population. TMS may be a valuable therapeutic option for patients with chronic dizziness who have not responded to conventional therapies.

1. Introduction

Chronic dizziness, a common and debilitating condition characterized by persistent dizziness lasting for three months or longer, significantly impacts an individual's quality of life. The sensation of dizziness, often described as a feeling of spinning, lightheadedness, or unsteadiness, can lead to difficulties with balance, gait, and daily activities. These difficulties often result in falls, social isolation, and anxiety, further diminishing the overall well-being of affected individuals. The prevalence of chronic dizziness increases with age, affecting approximately 30% of adults over 65 years old. This age-related increase can be attributed to various factors, including the cumulative effects of age-related physiological changes, the presence of underlying medical conditions, and the use of multiple medications. The impact of chronic dizziness on the elderly population is particularly significant, as it can lead to a decline in functional independence, an increased risk of falls and

fractures, and a reduced quality of life. The underlying causes of chronic dizziness are diverse, encompassing a wide range of conditions that affect the vestibular system, the sensory system responsible for maintaining balance and spatial orientation. Peripheral vestibular disorders, such as benign paroxysmal positional vertigo (BPPV) and vestibular neuritis, involve dysfunction of the inner ear or the vestibular nerve, which transmits signals from the inner ear to the brain. Central vestibular disorders, on the other hand, involve dysfunction of the brainstem or cerebellum, the parts of the brain responsible for processing vestibular information. In addition to vestibular disorders, other conditions such as anxiety and depression can also contribute to chronic dizziness. Anxiety and depression can exacerbate dizziness symptoms through complex interactions between the vestibular system and the emotional centers in the brain. The presence of anxiety or depression can heighten a person's sensitivity to dizziness sensations, leading to increased distress and functional impairment.[1-3]

The heterogeneity of causes underlying chronic dizziness makes diagnosis and treatment challenging. Healthcare professionals often face difficulties in pinpointing the specific cause of dizziness, as symptoms can overlap between different conditions. Moreover, the subjective nature of dizziness makes it difficult to quantify and assess the severity of the condition. Despite the availability of various therapeutic approaches, including vestibular rehabilitation, medication, and psychological interventions, a significant proportion of patients experience persistent symptoms despite treatment. Vestibular rehabilitation, a specialized form of physical therapy, aims to improve balance and reduce dizziness symptoms through exercises that promote vestibular adaptation and compensation. Medications, such as antihistamines and anticholinergics, can provide symptomatic relief by suppressing vestibular activity or reducing anxiety. Psychological interventions, such as cognitive-behavioral therapy (CBT), can help individuals manage their anxiety and improve their coping strategies for dealing with dizziness. However, the effectiveness of these conventional therapies can vary depending on the underlying cause of dizziness and individual factors. Some individuals may not respond adequately to these treatments, leaving them with persistent dizziness and its associated limitations. The search for alternative treatment options has led to the exploration of non-invasive brain stimulation techniques, such as transcranial magnetic stimulation (TMS). TMS is a non-invasive brain stimulation technique that utilizes magnetic fields to induce electrical currents in specific brain regions. It has emerged as a promising therapeutic tool for various neurological and psychiatric conditions, including depression, anxiety, and stroke rehabilitation. The application of TMS in these conditions is based on its ability to modulate cortical excitability, the responsiveness of neurons in the brain's cortex to stimulation. By delivering targeted magnetic pulses to specific brain areas, TMS can either increase or decrease cortical excitability, depending on the stimulation parameters. This modulation of cortical excitability can lead to changes in brain activity and network connectivity, potentially restoring balance and improving functional outcomes.[4-7]

Recent research suggests that TMS may also be effective in modulating vestibular pathways and alleviating symptoms of chronic dizziness. The vestibular pathways are a complex network of neural connections that transmit and process information related to balance and spatial orientation. Dysfunction within these pathways can lead to dizziness and other vestibular symptoms. The proposed mechanisms of action for TMS in chronic dizziness are multifaceted. Studies have shown that TMS can modulate cortical excitability in areas involved in vestibular processing, such as the dorsolateral prefrontal cortex (DLPFC), temporoparietal junction, and cerebellum. The DLPFC, located in the frontal lobe of the brain, plays a crucial role in cognitive control, attention, and emotional regulation, all of which can influence the perception and experience of dizziness. The temporoparietal junction, located at the intersection of the temporal and parietal lobes, is involved in integrating sensory information from different modalities, including vestibular, visual, and

somatosensory inputs. The cerebellum, located at the back of the brain, is responsible for coordinating movement and maintaining balance. By altering the activity in these brain regions, TMS may help restore the balance between excitatory and inhibitory signals within the vestibular system, thereby reducing dizziness symptoms. Additionally, TMS may exert its therapeutic effects through its impact on anxiety and depression, which often co-occur with chronic dizziness and can exacerbate its symptoms. Despite the growing body of evidence supporting the potential benefits of TMS for chronic dizziness, most studies have been conducted in Western populations.[8-10] This study aimed to evaluate the efficacy and safety of TMS in treating chronic dizziness in Bandung, Indonesia.

2. Methods

This study employed a randomized, double-blind, sham-controlled trial design, considered the gold standard for evaluating the efficacy of interventions. This design ensures the minimization of bias and the ability to draw reliable conclusions about the treatment's effectiveness. The study was conducted at the Neurology Clinic of a Private Hospital in Bandung, Indonesia, ensuring the research was carried out in a setting with appropriate medical facilities and expertise. The study protocol underwent rigorous ethical scrutiny and was approved by the CMHC's ethics committee, safeguarding the rights and well-being of the participants. All participants provided written informed consent before enrollment, ensuring their voluntary participation with full knowledge of the study's procedures and potential risks. Participants were recruited through referrals from neurologists and otorhinolaryngologists at the hospital, leveraging the expertise of specialists to identify eligible individuals. To be included in the study, participants had to meet the following criteria; Age between 18 and 70 years, ensuring the inclusion of adults within a broad age range; Diagnosis of chronic dizziness (≥ 3 months) based on clinical evaluation and diagnostic tests (e.g., audiometry, videonystagmography), ensuring participants genuinely experienced chronic dizziness; Dizziness Handicap Inventory (DHI) score ≥ 30, indicating a significant level of dizziness-related disability. Exclusion criteria were carefully defined to avoid potential confounding factors or risks associated with TMS; History of epilepsy or seizures, as TMS could potentially trigger seizures in susceptible individuals; Presence of metallic implants in the head or neck, as these could be affected by the magnetic fields generated by TMS; Pregnancy or breastfeeding, to avoid any potential risks to the fetus or infant; Current use of medications known to affect vestibular function, to prevent interactions with the effects of TMS; Severe psychiatric disorders, as these could influence the response to TMS and complicate the interpretation of results.

Eligible participants were randomly assigned to either the active TMS group or the sham TMS group using a computer-generated randomization sequence, ensuring an unbiased distribution of participants into the two groups. The allocation ratio was 1:1, meaning an equal number of participants were assigned to each group. Blinding was meticulously maintained for both participants and the treating physician, a crucial aspect of the study design. This double-blinding prevents biases that could arise if participants or the physician knew which treatment was being administered. The TMS device was programmed to deliver either active or sham stimulation with identical auditory and tactile sensations, making it indistinguishable for both the participant and the physician.

Participants in both groups received 10 sessions of TMS over two weeks (five sessions per week), ensuring a consistent and intensive treatment regimen. TMS was administered using a Magstim Rapid² stimulator (Magstim Company Limited, Whitland, UK) with a figure-of-eight coil, a widely used and well-established TMS device.

Participants in the active TMS group received 1 Hz stimulation over the right DLPFC, a brain region known to play a role in cognitive control, attention, and emotional regulation, all of which can influence the perception and experience of dizziness. The stimulation intensity was set at 110% of the resting motor threshold (RMT), a standard method for determining the appropriate stimulation intensity for each individual. RMT was determined by finding the

minimum intensity required to elicit a visible twitch in the contralateral abductor pollicis brevis muscle. Each session consisted of 10 trains of 20 pulses with an inter-train interval of 30 seconds, a protocol based on previous research and clinical experience.

Participants in the sham TMS group received placebo stimulation using a sham coil that mimicked the sound and feel of the active coil but did not deliver any magnetic stimulation. This sham stimulation serves as a control condition, allowing researchers to distinguish the genuine effects of TMS from any placebo effects.

The primary outcome measure was the change in DHI score from baseline to four weeks post-intervention, a widely used and validated measure of dizziness-related disability. The DHI is a 25-item questionnaire that assesses the impact of dizziness on daily activities, with scores ranging from 0 to 100 (higher scores indicating greater disability). Secondary outcome measures were also included to provide a more comprehensive assessment of the intervention's effects; Vertigo Symptom Scale (VSS): A 15-item scale that measures the severity of vertigo symptoms, with scores ranging from 0 to 45 (higher scores indicating greater severity); Hospital Anxiety and Depression Scale (HADS): A 14-item scale that measures anxiety and depression symptoms, with scores ranging from 0 to 21 for each subscale (higher scores indicating greater severity); Quality of Life measures: The Short Form-36 (SF-36) questionnaire, a widely used measure of health-related quality of life.

Data were analyzed using SPSS software version 26 (IBM Corp, Armonk, NY, USA), a powerful statistical software package. Descriptive statistics were used to summarize demographic and clinical characteristics, providing a clear picture of the study population. The primary outcome (change in DHI score) was analyzed using an independent samples t-test, a statistical test used to compare the means of two independent groups. Secondary outcomes were analyzed using similar methods, ensuring consistency in the statistical approach. The significance level was set at $p < 0.05$, a conventional threshold for determining statistical significance.

3. Results

Table 1 presents the demographic and clinical characteristics of the 60 participants enrolled in the study at baseline, divided into two groups: Active TMS (n=30) and Sham TMS (n=30). The table demonstrates that the two groups were largely similar in terms of their baseline characteristics. This is crucial in a randomized controlled trial as it ensures that any observed differences in outcomes can be attributed to the treatment and not pre-existing differences between the groups. The average age of participants was approximately 52 years in both groups, with a similar range (28-68 in the active TMS group and 25-70 in the sham TMS group). The proportion of females was comparable between the active TMS (63.3%) and sham TMS (66.7%) groups. Participants had experienced chronic dizziness for an average of about 12 months in both groups. Baseline DHI scores, reflecting the impact of dizziness on daily life, were similar in both groups (around 68), indicating a moderate to severe level of disability. VSS scores, measuring vertigo symptom severity, were also comparable. Both groups had similar levels of anxiety and depression symptoms as measured by the HADS. The distribution of underlying causes of dizziness (peripheral vestibular disorder, central vestibular disorder, or other/unknown) was almost identical between the two groups. The p-values provided in the table indicate that there were no statistically significant differences between the active TMS and sham TMS groups for any of the baseline characteristics. This further supports the successful randomization and comparability of the groups.

Table 2 presents the primary outcome data of the study, which is the change in Dizziness Handicap Inventory (DHI) scores from baseline to four weeks after the intervention. The DHI is a measure of dizziness-related disability, with higher scores indicating greater disability. The active TMS group showed a substantially larger mean decrease in DHI score (35.7 points) compared to the sham TMS group (8.8 points). This indicates a much greater improvement in dizziness-related disability in the active TMS group. The p-value of <0.001 indicates that the difference in DHI score changes between the two

groups is highly statistically significant. This means that the observed difference is very unlikely to be due to chance. The mean change in the active TMS group (35.7 points) is well above the threshold for clinical significance (generally 18-20 points). This suggests that the improvement experienced by participants in this group is not only statistically significant but also meaningful in terms of their daily lives and functional abilities. The 95% confidence interval for the change in DHI score in the active TMS group (30.1 to 41.3) does not include zero, further supporting the conclusion that the intervention had a real and significant effect.

Table 1. Demographic and clinical characteristics of participants at baseline.

Characteristic	Active TMS (n=30)	Sham TMS (n=30)	p-value
Age (years)			
Mean (SD)	52.8 (11.9)	52.2 (12.7)	0.81
Range	28-68	25-70	
Gender			
Female, n (%)	19 (63.3)	20 (66.7)	0.79
Duration of dizziness (months)			
Mean (SD)	12.6 (8.4)	11.8 (7.9)	0.65
Range	3-36	3-30	
Dizziness Handicap Inventory (DHI) score			
Mean (SD)	68.2 (15.4)	67.5 (14.8)	0.85
Vertigo Symptom Scale (VSS) score			
Mean (SD)	28.5 (9.2)	27.9 (8.8)	0.72
Hospital Anxiety and Depression Scale (HADS)			
Anxiety subscale, Mean (SD)	10.3 (4.5)	9.8 (4.2)	0.61
Depression subscale, Mean (SD)	8.7 (3.9)	8.2 (3.6)	0.53
Underlying cause of dizziness			
Peripheral vestibular disorder, n (%)	15 (50.0)	16 (53.3)	0.82
Central vestibular disorder, n (%)	8 (26.7)	7 (23.3)	0.75
Other/unknown, n (%)	7 (23.3)	7 (23.3)	1.00

Table 2. Primary outcome (Change in DHI scores from baseline to four weeks post-intervention).

Group	Baseline DHI Score (Mean ± SD)	4-Week DHI Score (Mean ± SD)	Change in DHI Score (Mean ± SD)	95% CI for Change	p-value
Active TMS (n=30)	68.2 ± 15.4	32.5 ± 12.8	35.7 ± 11.2	30.1 to 41.3	< 0.001
Sham TMS (n=30)	67.5 ± 14.8	58.7 ± 13.5	8.8 ± 9.5	4.2 to 13.4	

Table 3 provides a detailed look at the secondary outcomes of the study, which further evaluate the effects of active TMS on various aspects of dizziness and quality of life; Vertigo Symptom Scale (VSS): The active TMS group showed a significantly greater reduction in vertigo symptoms compared to the sham

TMS group (p=0.002). This indicates that active TMS not only improves dizziness-related disability but also directly reduces the severity of vertigo symptoms; Hospital Anxiety and Depression Scale (HADS): The active TMS group experienced a significant decrease in anxiety symptoms compared to the sham group (p=0.015). This suggests that TMS may have a positive impact on the emotional distress associated with chronic dizziness. While there was a trend towards improvement in depression symptoms in the active TMS group, the difference was not statistically significant (p=0.028). This might indicate a less robust effect of TMS on depressive symptoms in this population; Short Form-36 (SF-36): This questionnaire assesses various domains of health-related quality of life. The active TMS group demonstrated significant improvements in several domains. Participants in the active TMS group reported a significantly greater improvement in their ability to perform physical activities (p=0.001). Active TMS led to a significant reduction in limitations in daily activities due to physical health problems (p=0.001). Participants in the active TMS group experienced a significant improvement in their ability to engage in social activities (p=0.001). Active TMS was associated with a significant improvement in mental health (p=0.005).

Table 3. Secondary outcomes.

Outcome measure	Active TMS (n=30)	Sham TMS (n=30)	p-value
Vertigo Symptom Scale (VSS)			
Baseline score (Mean ± SD)	28.5 ± 9.2	27.9 ± 8.8	0.72
4-week score (Mean ± SD)	12.8 ± 7.5	23.1 ± 8.1	
Change in score (Mean ± SD)	15.7 ± 6.8	4.8 ± 5.9	**0.002**
Hospital Anxiety and Depression Scale (HADS)			
Anxiety subscale			
Baseline score (Mean ± SD)	10.3 ± 4.5	9.8 ± 4.2	0.61
4-week score (Mean ± SD)	7.1 ± 3.8	8.9 ± 3.9	
Change in score (Mean ± SD)	3.2 ± 2.9	0.9 ± 2.5	**0.015**
Depression subscale			
Baseline score (Mean ± SD)	8.7 ± 3.9	8.2 ± 3.6	0.53
4-week score (Mean ± SD)	6.5 ± 3.1	7.5 ± 3.3	
Change in score (Mean ± SD)	2.2 ± 2.5	0.7 ± 2.1	**0.028**
Short Form-36 (SF-36) - Selected Domains			
Physical Functioning			
Baseline score (Mean ± SD)	55.3 ± 12.5	56.8 ± 11.8	0.68
4-week score (Mean ± SD)	72.1 ± 10.8	60.2 ± 11.2	
Change in score (Mean ± SD)	16.8 ± 8.9	3.4 ± 6.5	**0.001**
Role Limitations due to Physical Health			
Baseline score (Mean ± SD)	48.7 ± 15.3	49.5 ± 14.6	0.85
4-week score (Mean ± SD)	65.4 ± 13.2	53.8 ± 13.9	
Change in score (Mean ± SD)	16.7 ± 9.5	4.3 ± 7.8	**0.003**
Social Functioning			
Baseline score (Mean ± SD)	62.8 ± 10.9	61.5 ± 10.2	0.63
4-week score (Mean ± SD)	78.5 ± 8.5	66.2 ± 9.8	
Change in score (Mean ± SD)	15.7 ± 7.2	4.7 ± 6.1	**0.001**
Mental Health			
Baseline score (Mean ± SD)	68.4 ± 11.5	67.2 ± 10.8	0.69
4-week score (Mean ± SD)	81.6 ± 9.2	71.8 ± 9.9	
Change in score (Mean ± SD)	13.2 ± 6.8	4.6 ± 5.5	**0.005**

Table 4 presents the safety and tolerability data from the study, outlining the types and frequency of adverse events experienced by participants in both the active TMS and sham TMS groups. The overall incidence of adverse events was low in both groups. 26.7% of participants in the active TMS group experienced at least one adverse event, compared to 23.3% in the sham TMS group. This difference was not statistically significant (p=0.75), suggesting that active TMS did not increase the risk of adverse events

compared to sham stimulation. The most common adverse events were mild and transient, including headache and scalp discomfort. These are commonly reported side effects of TMS and typically resolve quickly. No severe headaches or scalp discomfort were reported. A small number of participants in both groups experienced transient dizziness or tinnitus (ringing in the ears). These events were also mild and temporary. Importantly, no serious adverse events were reported in either group. This indicates that TMS, when administered according to the study protocol, is a safe intervention for individuals with chronic dizziness.

Table 4. Safety and tolerability.

Adverse event	Active TMS (n=30)	Sham TMS (n=30)	p-value
Any adverse event	8 (26.7%)	7 (23.3%)	0.75
Headache			
Mild	5 (16.7%)	4 (13.3%)	0.71
Moderate	1 (3.3%)	1 (3.3%)	1.00
Severe	0 (0%)	0 (0%)	-
Scalp discomfort			
Mild	3 (10.0%)	3 (10.0%)	1.00
Moderate	0 (0%)	0 (0%)	-
Severe	0 (0%)	0 (0%)	-
Other			
Dizziness (transient)	1 (3.3%)	1 (3.3%)	1.00
Tinnitus (transient)	1 (3.3%)	0 (0%)	0.49
Serious adverse events	0 (0%)	0 (0%)	-

4. Discussion

This randomized controlled trial (RCT) provides compelling evidence to support the growing body of literature suggesting the efficacy of transcranial magnetic stimulation (TMS) in treating chronic dizziness. The significant improvements observed in the active TMS group compared to the sham group across various outcome measures highlight the potential of this non-invasive brain stimulation technique to address a condition that often proves challenging to manage with conventional therapies. The substantial reduction in Dizziness Handicap Inventory (DHI) scores in the active TMS group underscores the potential of TMS to meaningfully improve patients' daily lives. The DHI is a well-validated, patient-reported outcome measure that captures the multi-faceted impact of dizziness on individuals' functional capacity, emotional well-being, and overall perception of handicap. A high DHI score indicates a greater degree of dizziness-related disability, reflecting the extent to which dizziness interferes with daily activities and restricts participation in social roles. In this study, the active TMS group experienced a significantly greater reduction in DHI scores compared to the sham group, suggesting that TMS can effectively alleviate the burden of dizziness and improve patients' ability to engage in everyday activities. This finding aligns with previous research demonstrating the positive impact of TMS on functional outcomes in patients with chronic dizziness. For instance, a study found that TMS applied to the right dorsolateral prefrontal cortex (DLPFC) led to significant improvements in DHI scores and balance performance in patients with persistent postural-perceptual dizziness (PPPD). Similarly, reported that TMS targeting the temporoparietal junction (TPJ) resulted in reduced DHI scores and improved gait stability in individuals with chronic subjective dizziness. The observed improvement in DHI scores in this RCT suggests that TMS may

facilitate a recalibration of neural activity within brain regions involved in vestibular processing, leading to a reduction in dizziness-related symptoms and an enhanced ability to maintain balance and postural control. By modulating cortical excitability and promoting neuroplasticity, TMS may help restore the functional integrity of the vestibular system and improve the brain's ability to process and interpret sensory information related to movement and spatial orientation. The significant reduction in Vertigo Symptom Scale (VSS) scores in the active TMS group further strengthens the evidence for the therapeutic benefits of TMS in chronic dizziness. The VSS is a specific measure of vertigo symptoms, assessing the frequency, intensity, and duration of subjective experiences of spinning, tilting, or swaying. Vertigo is a particularly distressing symptom of dizziness, often accompanied by nausea, vomiting, and a sense of imbalance, which can significantly impair daily functioning and quality of life. By effectively reducing VSS scores, TMS demonstrates its potential to alleviate the core symptoms of vertigo, providing much-needed relief for patients who often struggle with the debilitating effects of this condition. The mechanism by which TMS reduces vertigo symptoms may involve its ability to modulate neural activity in key brain areas associated with vestibular processing, such as the DLPFC, TPJ, and cerebellum. These regions play a critical role in integrating sensory information from the vestibular system, visual system, and proprioceptive system to maintain balance and spatial orientation. In addition to improving vertigo symptoms, this study also found a significant reduction in anxiety levels in the active TMS group, as measured by the Hospital Anxiety and Depression Scale (HADS). Chronic dizziness is often associated with heightened anxiety, as individuals may experience fear and apprehension about experiencing dizziness in public or engaging in activities that trigger their symptoms. This anxiety can create a vicious cycle, exacerbating dizziness symptoms and further limiting daily activities. The observed improvement in anxiety levels in the active TMS group suggests that TMS may have a broader impact on emotional regulation and well-being in patients with chronic dizziness. TMS has been shown to be effective in treating anxiety disorders, including generalized anxiety disorder and panic disorder. The anxiolytic effects of TMS may be attributed to its ability to modulate activity in brain regions involved in fear and anxiety processing, such as the amygdala and prefrontal cortex. The significant improvements observed in Short Form-36 (SF-36) scores in the active TMS group provide further evidence for the positive impact of TMS on overall health-related quality of life. The SF-36 is a widely used generic health status measure that assesses eight dimensions of health, including physical functioning, role limitations due to physical health problems, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems, and mental health. In this study, participants in the active TMS group reported significant improvements in several domains of the SF-36, including physical functioning, role limitations due to physical health problems, and social functioning. These findings suggest that TMS not only alleviates dizziness symptoms but also enhances patients' overall well-being and ability to participate in social and recreational activities. The improvement in physical functioning may be directly related to the reduction in dizziness symptoms and improved balance control, allowing patients to engage in physical activities with greater ease and confidence. The reduction in role limitations due to physical health problems reflects the decreased impact of dizziness on daily activities and work productivity. Furthermore, the improvement in social functioning highlights the potential of TMS to reduce the social isolation and withdrawal that often accompany chronic dizziness. The findings of this RCT have important implications for clinical practice, suggesting that TMS may be a valuable addition to the treatment armamentarium for chronic dizziness. Chronic dizziness is a prevalent and debilitating condition that can significantly impact patients' quality of life, leading to functional limitations, emotional distress, and reduced social participation. Despite the availability of various therapeutic approaches, including vestibular rehabilitation, medication, and psychological interventions, a significant proportion of patients

experience persistent symptoms and disability. TMS offers a non-invasive, relatively safe, and well-tolerated treatment option that may be particularly beneficial for patients who have not responded adequately to conventional therapies. By modulating neural activity in key brain regions involved in vestibular processing and emotional regulation, TMS may help break the vicious cycle of dizziness, anxiety, and functional impairment, leading to improved symptom control and enhanced quality of life.[11-13]

The safety profile observed in this randomized controlled trial (RCT) further strengthens the existing body of evidence supporting the safety and tolerability of TMS as a therapeutic intervention. The absence of serious adverse events and the low incidence of mild, transient side effects are consistent with findings from numerous studies across various neurological and psychiatric conditions. This reassuring safety profile, coupled with the demonstrated efficacy of TMS in treating chronic dizziness, positions it as a promising treatment option, particularly for patients who may not tolerate or have not responded to conventional therapies. The most commonly reported adverse events in this study, namely headache and scalp discomfort, are typically mild and transient, resolving spontaneously without requiring intervention. These side effects are often attributed to the stimulation of scalp muscles and nerves by the magnetic pulses delivered during TMS. The fact that these side effects were reported with similar frequency in both the active and sham TMS groups suggests that they may not be directly related to the magnetic stimulation itself but rather to the overall procedure or the placebo effect. The mild nature of these side effects is further underscored by the fact that none of the participants in either group discontinued treatment due to adverse events. This high tolerability is crucial for ensuring patient adherence to the TMS treatment protocol, which typically involves multiple sessions over several weeks. The absence of serious adverse events in this study is particularly noteworthy and aligns with the broader safety profile of TMS established through extensive research. TMS has been investigated in a wide range of neurological and psychiatric disorders, including depression, anxiety, stroke, Parkinson's disease, and chronic pain, with a consistently low incidence of serious adverse events. The safety of TMS is attributed to its non-invasive nature. Unlike surgical interventions or deep brain stimulation, TMS does not involve any incisions or implantation of electrodes, thereby minimizing the risk of infection, bleeding, or other complications. Furthermore, the magnetic fields used in TMS are relatively weak and focused, limiting their effects to the targeted brain regions and minimizing the potential for unintended effects on other organs or tissues. The safety and tolerability of TMS compare favorably to other treatment modalities commonly used for chronic dizziness, such as medication and vestibular rehabilitation. Medications, including antihistamines, benzodiazepines, and antiemetics, are often prescribed to manage dizziness symptoms but can be associated with a range of side effects, such as drowsiness, sedation, cognitive impairment, dry mouth, and constipation. These side effects can significantly impact patients' quality of life and may limit their ability to drive, operate machinery, or perform daily activities. Vestibular rehabilitation therapy (VRT), a form of physical therapy designed to improve balance and reduce dizziness symptoms, is another commonly used treatment for chronic dizziness. While generally safe and effective, VRT can sometimes exacerbate dizziness symptoms in the short term, particularly during the initial stages of therapy. This can be discouraging for patients and may lead to treatment discontinuation. In contrast to medication and VRT, TMS does not appear to cause any significant cognitive or functional impairment. This makes it a particularly attractive treatment option for patients who cannot tolerate the side effects of medication or who have experienced an exacerbation of symptoms with VRT. Furthermore, TMS may be suitable for patients who have not responded adequately to medication or VRT, offering a potential alternative or adjunctive treatment strategy. The safety of TMS has been demonstrated in various populations, including older adults and individuals with medical comorbidities. This is particularly relevant in the context of chronic dizziness, as the condition is more prevalent in older adults and often

co-occurs with other medical conditions, such as cardiovascular disease, diabetes, and anxiety disorders. Studies have shown that TMS is well-tolerated in older adults, with no increased risk of adverse events compared to younger individuals. Similarly, TMS has been safely used in patients with various medical comorbidities, including hypertension, diabetes, and heart disease. These findings support the use of TMS in a broad range of patients with chronic dizziness, regardless of age or medical history. While TMS has a favorable safety profile, certain contraindications and safety considerations should be taken into account to ensure patient safety and minimize the risk of adverse events. TMS should not be used in individuals with metallic implants in the head or neck, such as pacemakers, aneurysm clips, or cochlear implants, as the magnetic fields generated by TMS can potentially cause these implants to heat up, malfunction, or become dislodged. TMS should also be used with caution in individuals with a history of seizures, as it may lower the seizure threshold and increase the risk of seizure induction. However, the risk of seizure induction with TMS is generally low, particularly when appropriate safety guidelines are followed, such as careful screening of patients, appropriate stimulation parameters, and close monitoring during treatment sessions. Other safety considerations include the potential for hearing loss, particularly when TMS is applied to the temporoparietal region. To mitigate this risk, it is essential to use appropriate hearing protection during TMS sessions and to monitor patients for any changes in hearing.[14-16]

While the exact mechanisms underlying the therapeutic effects of TMS in chronic dizziness are not fully understood, several hypotheses have been proposed. One prominent theory is that TMS modulates cortical excitability in brain regions involved in vestibular processing. Cortical excitability refers to the responsiveness of neurons in the brain's cortex to stimulation. By altering cortical excitability, TMS can influence the activity and communication patterns of neurons within specific brain regions and networks. The DLPFC, located in the frontal lobe of the brain, plays a crucial role in cognitive control, attention, and emotional regulation, all of which can influence the perception and experience of dizziness. Studies have shown that TMS can modulate cortical excitability in the DLPFC, leading to changes in brain activity and network connectivity. These changes may help restore the balance between excitatory and inhibitory signals within the vestibular system, thereby reducing dizziness symptoms. In addition to the DLPFC, other brain regions involved in vestibular processing, such as the temporoparietal junction (TPJ) and cerebellum, may also be modulated by TMS. The TPJ, located at the intersection of the temporal and parietal lobes, is involved in integrating sensory information from different modalities, including vestibular, visual, and somatosensory inputs. The cerebellum, located at the back of the brain, is responsible for coordinating movement and maintaining balance. By altering the activity in these brain regions, TMS may help improve the brain's ability to process and interpret sensory information related to movement and spatial orientation, leading to a reduction in dizziness symptoms. Another potential mechanism is the impact of TMS on anxiety and depression. Chronic dizziness is often associated with heightened levels of anxiety and depression, which can create a vicious cycle of symptom exacerbation. Anxiety and depression can heighten a person's sensitivity to dizziness sensations, leading to increased distress and functional impairment. TMS has been shown to be effective in treating both anxiety and depression. The antidepressant and anxiolytic effects of TMS may be attributed to its ability to modulate activity in brain regions involved in mood regulation and emotional processing, such as the prefrontal cortex, amygdala, and hippocampus. By reducing anxiety and depression symptoms, TMS may help break the vicious cycle of symptom exacerbation and improve overall well-being in patients with chronic dizziness. In addition to the mechanisms described above, other potential mechanisms of action of TMS in chronic dizziness have been proposed. TMS may promote neuroplasticity, the brain's ability to reorganize and adapt, by inducing changes in synaptic strength and connectivity. This may help the brain compensate for vestibular dysfunction and improve

balance control. TMS may reduce neuroinflammation, which has been implicated in the pathophysiology of chronic dizziness. TMS may facilitate vestibular habituation, the process of reducing the response to a repeated vestibular stimulus. This may help patients with chronic dizziness become less sensitive to movements or situations that trigger their symptoms.[17,18]

The findings of this study have important implications for clinical practice. Chronic dizziness is a common and debilitating condition that can significantly impact patients' quality of life. Despite the availability of various therapeutic approaches, including vestibular rehabilitation, medication, and psychological interventions, a significant proportion of patients experience persistent symptoms despite treatment. TMS may offer a new treatment option for these patients who have not responded to conventional therapies. Current treatments for chronic dizziness have several limitations. Vestibular rehabilitation, while effective for some patients, requires active participation and adherence to a structured exercise program. Medication can provide symptomatic relief but may be associated with side effects such as drowsiness and cognitive impairment. Psychological interventions, such as cognitive-behavioral therapy (CBT), can be helpful for managing anxiety and depression associated with dizziness but may not directly address the underlying vestibular dysfunction. TMS offers a non-invasive, well-tolerated treatment option that may be particularly beneficial for patients who have not responded to or cannot tolerate conventional therapies. The findings of this study suggest that TMS can significantly reduce dizziness-related disability, vertigo symptoms, and anxiety levels, leading to improvements in overall quality of life. The integration of TMS into clinical practice for chronic dizziness requires careful consideration of patient selection, treatment protocols, and clinical expertise. TMS may be most appropriate for patients with chronic dizziness who have not responded to conventional therapies or who have contraindications to medication or vestibular rehabilitation. Factors such as age, duration of dizziness, underlying medical conditions, and psychological comorbidities should be considered when selecting patients for TMS treatment. The optimal TMS protocol for chronic dizziness is still under investigation. Factors such as stimulation frequency, intensity, duration, and location may influence treatment efficacy. Clinicians should stay informed about the latest research and clinical guidelines to ensure the use of evidence-based TMS protocols. The administration of TMS requires specialized training and expertise. Clinicians should be knowledgeable about TMS safety protocols, potential side effects, and patient monitoring procedures. Collaboration with neurologists, otolaryngologists, and other healthcare professionals may be necessary to ensure comprehensive patient care. TMS may be particularly beneficial for certain subtypes of chronic dizziness, such as persistent postural-perceptual dizziness (PPPD) and vestibular migraine. PPPD is a chronic dizziness disorder characterized by persistent non-vertiginous dizziness, unsteadiness, and hypersensitivity to motion stimuli. Vestibular migraine is a type of migraine associated with vertigo or dizziness. Studies have shown that TMS can significantly reduce dizziness symptoms and improve postural control in patients with PPPD. TMS has also been found to be effective in reducing migraine frequency and severity, which may indirectly improve dizziness symptoms in patients with vestibular migraine.[19,20]

5. Conclusion

This randomized controlled trial provides compelling evidence for the efficacy and safety of TMS in treating chronic dizziness in the Indonesian population. TMS significantly improved Dizziness Handicap Inventory scores, Vertigo Symptom Scale scores, Hospital Anxiety and Depression Scale scores, and quality of life measures compared to sham stimulation. No serious adverse events were reported. Our findings suggest that TMS may be a valuable therapeutic option for patients with chronic dizziness who have not responded to conventional therapies. Further research is needed to determine the optimal TMS protocols and to evaluate the long-term effects of TMS in this population. This study has several

strengths, including its randomized controlled design, the use of a sham TMS control group, and the comprehensive assessment of outcome measures. However, it also has some limitations. The study was conducted at a single center in Indonesia, so the findings may not be generalizable to other populations. The sample size was relatively small, and the follow-up period was limited to four weeks. Further research is needed to confirm our findings and to evaluate the long-term effects of TMS in larger and more diverse populations. Despite these limitations, our study provides important evidence for the efficacy and safety of TMS in treating chronic dizziness. TMS may be a promising new treatment option for this debilitating condition.

6. References

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