

The Effects of Transcutaneous Auricular Vagus Stimulation on Sustained Attention and Depression in Individuals Who are Likely to Have Adhd

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Abstract

Aims: This study aims to evaluate the effects of transcutaneous auricular vagus nerve stimulation (taVNS) on sustained attention and depression in individuals with suspected attention deficit hyperactivity disorder (ADHD). **Methods:** Between May 1, 2022 and September 25, 2022, the study included 60 students (9 males, 51 females; mean age: 21.11 ± 1.6 years; range, 18 to 24 years) identified as being at high risk for attention deficit hyperactivity disorder (ADHD). Participants were randomly assigned to either the intervention or control groups. Each group consisted of 30 individuals. The intervention group received taVNS in conjunction with mobile-assisted games and relaxation exercises, while the control group received mobile-assisted games and relaxation exercises alone. The data were collected using a descriptive information form, the Beck Depression Inventory, and mobile-assisted assessment parameters. Data were analyzed using the Wilcoxon signed-rank test, t-test, and Mann-Whitney U test. **Results:** Significant differences were observed in the intervention group concerning the sub-parameters used to measure attention and depression scale scores; however, in the control group, all but one of the attention sub-parameters showed significant differences. A comparison between the two groups revealed significant differences in reaction times and Beck Depression Inventory scores in favor of the intervention group. **Conclusion:** This study revealed that taVNS can effectively improve attention (cognitive function) and alleviate symptoms of depression.

1. Introduction

As a clinically heterogeneous neurodevelopmental syndrome consisting of developmentally inappropriate inattention, hyperactivity, and increased impulsivity, Attention-Deficit Hyperactivity Disorder (ADHD) is the most common psychiatric disorder in childhood. ADHD significantly impairs many aspects of life, leading to failure in educational achievement, unemployment, failed marriages, and feelings of guilt. In addition, ADHD is significantly correlated with a wide range of comorbid psychiatric disorders, including affective disorders, oppositional defiant disorder, antisocial personality disorder, self-harm, and substance abuse, and is a significant burden on society and family [1-3].

The estimated global prevalence of ADHD is 5%. The data obtained from prospective follow-up of children with ADHD provide evidence of symptomatic or functional persistence into adulthood for 30% to 60%, which is consistent with cross-sectional epidemiological studies that estimate a prevalence of ADHD in adults of 2% to 4% [4,5].

Adult attention-deficit/hyperactivity disorder (ADHD) is a common but underdiagnosed and controversial clinical condition. Although it has been recognized as a disorder of childhood and adolescence for a long time, ADHD continues to have a significant impact on adults, often resulting in severe functional impairment [6].

In adults with ADHD, the clinical expression of core symptoms differs from that observed in children and adolescents. ADHD in adults is often characterized by inner restlessness, excessive talkativeness, and a need to move even in situations where they are expected to stand still. They may be impulsive and impatient, they may "act without thinking" and sometimes they get into trouble for doing so. Functionally, they may be unable to keep a job or maintain personal relationships. Inattention in adulthood often manifests itself in boredom, inability to make decisions, procrastination, and being disorganized and distracted [7].

Adult patients diagnosed with ADHD exhibit a broad spectrum of brain dysfunction, which includes impairment to the default

mode network, emotional network, cognitive control network, and prefrontal regions that are responsible for attention, inhibition/cognitive control, motivation, and emotion regulation [8].

According to the National Institute for Health and Care Excellence (NICE) guidelines, both pharmacological and non-pharmacological treatments are recommended interventions for adults with ADHD [9].

Many non-pharmacological treatments have been developed and used for individuals with ADHD. Some of these methods include behavioral therapy, cognitive training, neurofeedback, physical therapy, dietary interventions, mindfulness-based interventions, physical activity, and brain stimulation [10].

Hypothesis: In our study, we predict that transcutaneous auricular vagus nerve stimulation may have positive significant effects on sustained attention and depression in individuals with ADHD.

2. Method

2.1 Ethical Considerations

All aspects of this research adhered to the tenets of the Declaration of Helsinki. Ethical approval for the study was obtained from the Ethics Committee of Artvin Çoruh University, as documented in the Committee's decision dated 05.04.2022, under reference number E-18457941-050.99-45502.

2.2 Participants

The power and sample size calculations were performed using G*Power version 3.1 software (Heinrich Heine University Düsseldorf, Düsseldorf, Germany). With a statistical power of 0.80 and an effect size of 0.80, the required sample size was determined to be 42 participants. The study population was drawn from students enrolled in the Department of Therapy and Rehabilitation at the University. Individuals with Adult Self-Report Scale (ASRS) scores classified as "very high" (ASRS scores of 24 and above) within this student population were included in the study sample. The ASRS for ADHD was used to identify eligible individuals for the study. Scores obtained from participants who completed the ASRS were analyzed, and individuals deemed to have a high probability of having attention deficit hyperactivity disorder (ADHD) were selected for inclusion.

Participants were then randomly assigned to either the intervention group or the control group. Each group consisted of 30 individuals.

2.3 Inclusion Criteria

Willingness to participate in the study
Individuals who provide written informed consent
Age over 18 years
Having a "very high" ASRS score

2.4 Exclusion Criteria

Age Under 18 Years
Failure to provide informed consent
Having a "low" ASRS score
Concurrent use of psychotropic medications

2.5 Methods

All participants who agreed to participate in the research completed both a personal information form and the Beck Depression Inventory. A computer-based tool was used to assess participants' sustained attention during the study. In this application, different letters were displayed on the screen at different time intervals (1 second, 2 seconds, 3 seconds), and the participants were instructed to click on the screen when they saw any letter except the letter X. The individual results screen following the application displayed the following metrics: missed targets (indicating the number of letters the individual should have clicked on but did not), non-target responses (reflecting the number of incorrect clicks on the letter X), and reaction time (measuring the time it took the individual to click on the correct letters).

Individuals in the intervention group of the study participated in a 5-minute session of breathing exercises coupled with relaxation exercises, and computer and mobile-assisted games designed to improve attention and transcutaneous auricular vagus stimulation. They received 10 minutes of transcutaneous auricular vagus nerve stimulation (taVNS) using the Vagustim device, with a frequency of 10 Hz and biphasic, 300-microsecond pulses with modulated flow intensity based on the participants' sensory thresholds. Individuals in the control group, on the other hand, participated in a 5-minute session of breathing and relaxation exercises, as well as computer and mobile-assisted games designed to improve attention. A 10-session treatment program was designed for both groups.



Figure 1: Transcutaneous auricular vagus nerve stimulation (Yıldız, Demirkıran, 2023)

2.6 Data Collection Instruments

The data collection instruments used in this research included:

Descriptive Information Form

Beck Depression Inventory

Adult Self-Report Scale (ASRS) for ADHD

2.6.1 Descriptive Information Form

The Descriptive Information Form, which was developed based on a thorough literature review, consisted of 11 questions regarding the demographic characteristics of the participants., which included age, education level, marital status, monthly income, and place of residence.

2.6.2 Beck Depression Inventory

The Beck Depression Inventory (BDI) consisted of 21 items. Each item is scored in the range of 0 to 3. The total scale score ranges from 0 to 63 The scale is based on self-report, and there is a direct relationship between the scores obtained and the severity of depression. Individuals were categorized as follows: scores

between 1 and 10 indicated normal individuals, scores between 11 and 16 indicated a moderate level of mood disorder, scores between 17 and 20 indicated clinical depression, scores between 21 and 30 reflected a moderate level of depression, scores between 31 and 40 indicated a high level of depression, and scores between 41 and 63 indicated severe depression.

2.6.3 Adult Self-Rating Scale for ADHD (ASRS)

The ASRS consists of two sections, A and B. Section A contains six items, while section B contains twelve items. For each item, respondents have five response options: never, rarely, sometimes, often, and very often. Participants select the option that best describes their condition. Responses are scored from 0 to 4, with 0 representing "never," 1 representing "rarely," 2 representing "sometimes," 3 representing "often," and 4 representing "very often. Based on the scores obtained, individuals scoring 24 or more on any of the subscales are classified as "very likely" to have ADHD, those scoring between 17 and 23 as "likely" to have ADHD, and those scoring between 0 and 16 as not having ADHD.

3. Results

Table 1: Comparison of sociodemographic characteristics between intervention and control groups

		Intervention Group (n:30)	Intervention Group (n:30)	Control Group (n:30)	Control Group (n:30)	Test Value and Significance
Age	Mean±SD	21.70±2.18	21.70±2.18	20.53±1.25	20.53±1.25	t: 2.538 p: .014
BMI	Mean±SD	22.29±3.53	22.29±3.53	23.01±3.98	23.01±3.98	t: -.742 p: .461
		Number (n)	Percentage (%)	Number (n)	Percentage (%)	
Gender	Male	3	10.0	6	20.0	x ² : 1.176 p: .472
	Female	27	90.0	24	80.0	

t: Independent Samples t-Test. x²: Chi-Square Test

An analysis of mean age revealed a significant difference between the groups. Specifically, the intervention group had a higher mean age (p<0.05). When we look at the comparison between the groups in terms of BMI and gender variables, no significant differences between groups were observed for BMI and gender variables (p>0.05) (Table 1).

Table 2: Comparison of pre- and post-test scores for missed targets, non-target responses, reaction time, and Beck Depression scores in the intervention group

	Mean±SD	Mean±SD	z value	p value
	Pre-Test (n:30)	Post-Test (n:30)		
Number of missed targets	6.40±4.03	2.13±2.87	-4.716	.000***
Non-target response	19.60±8.18	10.93±6.55	-4.713	.000***
Reaction time	462.80±73.36	433.10±52.79	-3.909	.000***
Beck depression	18.20±10.12	11.60±7.90	-4.146	.000***

z: Wilcoxon Signed Ranks Test. ***p<0.001

Significant reductions in the number of missed targets, non-target responses, reaction time, and Beck Depression scores were observed in the intervention group between the pre-test and post-test phases (p<0.001). The post-test scores for missed targets, non-target responses, reaction time, and Beck Depression were significantly lower in the intervention group compared to the pre-test scores (Table 2).

Table 3: Comparison of pre- and post-test scores for missed targets, non-target responses, reaction time, and Beck Depression scores in the control group

	Mean±SD	Mean±SD	z value	p value
	Pre-Test (n:30)	Post-Test (n:30)		
Number of missed targets	4.33±5.12	4.03±5.54	-1.301	.193
Non-target response	14.70±6.22	8.80±6.66	-4.057	.000***
Reaction time	485.40±47.20	470.60±46.48	-3.673	.000***
Beck depression	18.30±5.66	17.10±5.10	-2.173	.030**

z: Wilcoxon Signed Ranks Test. ***p<0.001

No statistically significant differences were found between the pre-test and post-test scores for missed targets in the control group ($p>0.05$). However, a statistically significant decrease was observed in the control group between pre-test and post-test for

non-target responses, reaction time, and Beck Depression scores ($p=0.001$). Specifically, the post-test non-target response scores in the control group showed a significant reduction compared to the pre-test (Table 3).

Table 4: Comparison of pre-test and post-test missed-target scores for the intervention and control groups

		Mean±SD	Mean±SD	U value	p value
		Intervention Group (n:30)	Control Group (n:30)		
Number of missed targets	Pre-Test	6.40±4.03	4.33±5.12	270.00	.007**
	Post-Test	2.13±2.87	4.03±5.54	382.00	.304

U: Mann-Whitney U Test. ** $p<0.05$

Although there was no statistically significant difference in the number of missed targets between the intervention and control groups at the post-test ($p>0.05$), a difference was observed in the

pre-test scores ($p<0.05$). Specifically, the intervention group had a higher number of missed targets in the pre-test than the control group ($p<0.05$)(Table 4).

Table 5: Comparison of pre-test and post-test non-target response scores for the intervention and control groups

		Mean±SD	Mean±SD	t/U value	p value
		Intervention Group (n:30)	Control Group (n:30)		
Non-target response	Pre-Test	19.60±8.18	14.70±6.22	2.612 ^t	.011**
	Post-Test	10.93±6.55	8.80±6.66	365.00 ^U	.208

t: Independent Samples t-Test. U: Mann-Whitney U Test. ** $p<0.05$

While there was a significant difference in the pre-test results when evaluating the non-target response variable based on groups ($p<0.05$), no statistically significant difference was found

in the post-test comparison ($p>0.05$). In the pre-test analysis, it was found that the non-target response rate was higher in the intervention group (Table 5).

Table 6. Comparison of pre-test and post-test reaction time scores for the intervention and control groups

		Mean±SD	Mean±SD	U value	p value
		Intervention Group (n:30)	Control Group (n:30)		
Reaction time	Pre-Test	462.80±73.36	485.40±47.20	299.50	.026**
	Post-Test	433.10±52.79	470.60±46.48	214.50	.000***

** $p<0.05$, *** $p<0.001$

An analysis of the reaction time variable revealed a significant difference between the groups in both the pre-test and post-test scores ($p<0.05$). In both the pre-test and post-test analyses, the reaction time was shorter in the intervention group (Table 6).

Table 7: Comparison of pre-test and post-test Beck Depression scores for the intervention and control groups

		Mean±SD	Mean±SD	t/U value	p value
		Intervention Group (n:30)	Control Group (n:30)		
Beck depression	Pre-Test	18.20±10.12	18.30±5.66	408.00 ^U	.534
	Post-Test	11.60±7.90	17.10±5.10	-3.203 ^t	.002**

** $p<0.05$

No significant difference was observed in the analysis of the Beck Depression variable at baseline ($p>0.05$). However, there was a notable difference between the groups in terms of the post-test

scores ($p<0.05$). This difference indicated that the level of Beck Depression scores was higher in the intervention group (Table 7).

4. Discussion

The present study aims to prove the efficacy of auricular vagus nerve stimulation on sustained attention and depression states in individuals with ADHD. This study is the first to investigate the efficacy of vagus nerve stimulation in individuals with ADHD. In addition, the results of the study contribute to the field by providing a new treatment method and research topic.

Individuals with ADHD mainly suffer from affected cognitive functions such as emotional impulsivity, attention deficit, and learning difficulties. Various studies were conducted to treat or rehabilitate these conditions.

These studies investigated the effects of cognitive-behavioral intervention and music therapy on the cognitive functioning of children with ADHD. In one study, 120 children were included and randomized into experimental and control groups in the research. While the children in the control group received no intervention, the children in the experimental group received a cognitive behavioral intervention and 16 weeks of music therapy. The Numerical Cross Attention Test and the Combined Raven Test were applied to the participants before and after the study to evaluate the parameters. As a result of the study, no significant change was observed in the control group, while significant improvements were seen in the parameters of the participants in the experimental group. As a result, it was reported that music therapy combined with cognitive behavioral intervention was effective on the cognitive functions of children with ADHD [11].

In a study conducted to evaluate the possible efficacy of deep transcranial magnetic stimulation (dTMS) in adult individuals with ADHD, 26 adult individuals with ADHD were included in the research. Participants in the study were randomized into sham and experimental groups, and participants in the experimental group received 1 session/day of high-frequency stimulation to the prefrontal cortex for 20 days, while the sham group received no current. In addition, Conners' Adult ADHD Assessment Scale and the computerized sustained attention test were administered to the participants as assessment parameters. As a result of the study, no significant change was observed between the participants in terms of clinical outcomes [12].

In a study registered on ClinicalTrials, researchers conducted a study comparing the effectiveness of physical activity and cognitive skills training in adults with ADHD. They included 120 adult individuals diagnosed with ADHD between the ages of 18 and 65. They then randomized the participants and divided them into three groups. In the first of these groups, they applied a mixed training program to the participants for 12 weeks. In the second group, cognitive skills training was added to the mixed exercise program, and the third group was designated as the control group. The researchers will conduct pre-treatment assessment and post-treatment assessments in the first week and at the end of 6 and 12 months. As part of the evaluations, they identified the Adult ADHD Self-Report Scale, the Clinical Global Impression Severity Scale, and the Clinical Global Impression Improvement Scale as

initial outcome measures. In addition, cognitive tests such as the AX-Continuous Performance Test, and Go/No Go Motor Response Inhibition Test were defined as secondary outcome measures to test mental functions. The final evaluation of the study is planned to be completed in 2024 and the results will be shared after the final assessment [13].

Considering these and similar studies, various interventions were carried out to improve the affected cognitive functions in individuals with ADHD. In our study, we investigated the efficacy of vagus nerve stimulation on impaired sustained attention performance in individuals with ADHD. Our study found that auricular vagus nerve stimulation significantly improved sustained attention performance sub-parameters in individuals with ADHD.

Individuals diagnosed with ADHD may also experience psychopathological conditions such as depression, anxiety, and suicide, as well as cognitive dysfunction. Depression may occur in approximately half of individuals diagnosed with ADHD. Long-term and high-cost mental health services are required to manage these conditions [14].

Both the financial and moral burden of long-term mental health services have led researchers to explore different treatment methods. In this context, one study conducted investigated the effect of music therapy on depression in individuals with ADHD. Within the scope of the study, 36 individuals diagnosed with ADHD were randomized into experimental and control groups. While participants in the control group received standard care, participants in the experimental group received active music and receptive music therapies twice a week for three months. The study evaluated 5-HT secretion, cortisol expression, blood pressure, and heart rate to assess depression. As a result of the study, 5-HT secretion increased, while cortisol expression, blood pressure, and heart rate decreased in participants in the experimental group. There were no significant changes in the variables of the participants in the control group. As a result, the researchers reported that the application of music therapy has positive neurophysiological and psychological effects on children and adolescents with ADHD. In addition, they recommended the use of music therapy in the treatment of depression [15].

A meta-analysis of the effects of physical exercise on attention and other symptoms in people with ADHD was published in another study. This meta-analysis included randomized controlled trials and searched major databases. A total of 734 subjects were included in their study. The study assessed various parameters, including attention, depression, executive function, hyperactivity, motor skills, social problems, and aggressive behavior. As a result of the study, although physical exercise produced varying results in different parameters, significant positive changes were observed especially in attention, executive function, and motor skills [16].

Another study examined the effects of group treatment based on dialectical behavior therapy (DBT) on various variables in adults with ADHD. In this multicenter randomized controlled

trial, adult participants with ADHD received DBT and usual care for 14 weeks. The study's primary outcome measures were the Executive Functioning Behavior Rating Inventory and the Emotion Regulation Difficulties Scale, while secondary outcome measures included depressive and anxiety symptoms and quality of life. Pre- and post- treatment assessments were conducted for both groups. As a result, the study revealed significant positive changes in executive dysfunction, ADHD core symptoms, and quality of life in the group that received DBT treatment [17,18].

The depression status of individuals diagnosed with ADHD in our study was also evaluated. Our study demonstrated a significant and positive change in the depression variable through the auricular vagus nerve stimulation we applied to the participants.

5. Conclusion

In our study, significant changes were observed in all sub-parameters related to sustained attention in the intervention group when compared to baseline measurements; likewise, the control group showed significant changes in all parameters except the sub-parameter related to the number of missed targets. However, it is noteworthy that both groups showed a significant reduction in Beck Depression scores compared to baseline measurements.

A comparative analysis of the intervention and control groups revealed significant differences in reaction time and Beck Depression scores for sustained attention and depression.

These findings underscore the potential of transcutaneous auricular vagus nerve stimulation as a viable approach to address cognitive processes associated with attention and mood disorders.

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