

Evaluating the Effectiveness of Noninvasive ADHD & Autism Treatments on Response Inhibition

Nicholas Ratnesar, Peter Sells BS

Abstract

In this study, the effectiveness of new hypothesized treatment methods for ADHD and Autism including Transcranial Magnetic Stimulation, Interactive Metronome Therapy, and Primitive Reflex Therapy on response inhibition was studied based on clinical data from 14 individuals at Neurofit Connections. This clinical data included the initial and most recent response inhibition test scores. These scores evaluate the ability of patients to regulate undesired responses such as unintended motor functions and thoughts. The treatment methods used in combination were found to be effective in improving response inhibition scores in the paired groups for all admitted individuals and the ADHD only paired groups, creating a need for future, more specialized research into these developing methods and potential clinical integration of these noninvasive methods into future treatment of ADHD and Autism.

Introduction

ADHD and Autism are both prominent neurodevelopmental disorders that are becoming increasingly common in the pediatric population. The complex and multifaceted nature of both disorders has made it difficult to understand the increasing rates and develop effective treatment. For ADHD and Autism, improved awareness and screening are likely to be a key factor in rising diagnosis rates (Khadka et al., 2024). While the increasing contribution of environmental influences remains a topic of ongoing research (Yoo, 2013). The growing prevalence of ADHD and Autism has raised concerns among healthcare professionals and parents alike, necessitating further research into the methods used to treat Autism and ADHD. This study aims to investigate the effectiveness of new noninvasive treatments such as transcranial magnetic stimulation, primitive reflex therapy, and interactive metronome training, utilized by Neurofit Connections. Current research regarding transcranial magnetic stimulation and primitive reflex therapy indicates potential benefits in improving cognitive function and overall symptoms in Autism (Melillo et al., 2023), (Chen et al., 2024). A systematic review of transcranial cranial magnetic stimulation in ADHD revealed it may be effective in reducing ADHD symptoms (Chen et al., 2024). However, standardized practices for transcranial magnetic stimulation and primitive reflex therapy are not clearly defined, and current research typically evaluates executive function or general symptoms of the disorders, so while effectiveness is demonstrated, the underlying mechanisms behind these treatments are not completely understood. The evidence behind Interactive Metronome therapy was circumstantial in preliminary studies (Cospers et al., 2009), suggesting the need for more rigorous studies to evaluate its effectiveness in treating ADHD and Autism. The goal of this study is to analyze the general effectiveness of these interventions at improving a significant contributing factor to both disorders. Understanding the general effectiveness of these noninvasive therapies on response inhibition could provide valuable insights into the driving factors behind these treatments, in addition to building a foundation for future research and the development of standardized and well-researched treatment protocols.

Response inhibition became a clear target of the study as a result of the significant impairments observed in both ADHD and Autism. ADHD resulted in more frequent errors in tasks requiring inhibitory control (Lee et al., 2024), while individuals with Autism exhibited greater latency in tasks requiring inhibitory control (Johnston et al., 2011). The Pronounced errors made Creyos's double-trouble test an excellent metric for assessing response inhibition abilities for both disorders because it produces a standardized score that considers both latency and accuracy of inhibitory control (Creyos Online Cognitive Tasks, n.d.).

We compared the results of Creyos Double Trouble Assessment (CDTA) scores recorded by Neurofit Connections prior to treatment to the most recent scores of Neurofit Connections patients to explore how

the use of new noninvasive treatments utilized for both Autism and ADHD contribute to the improvement of response inhibition in affected individuals.

Individual Causes of Autism and ADHD

Autism and ADHD are complex conditions with many contributing factors. Genetic factors play a significant role in the development of both disorders. DNA abnormalities such as Nucleotide deletion and duplication in sections of DNA are known to increase the likelihood of both disorders, including specific chromosomal regions like 15q11-q13 and 16p13.11, which have been associated with both Autism and ADHD (Bădescu et al., 2016), (Shinawi et al., 2011). Neurotoxins like Lead and Mercury are environmental factors associated with both disorders (Xi & Wu, 2021). The complexity of both disorders has made it difficult to fully understand their etiology and develop treatment methods.

Impact of Autism and ADHD on Response Inhibition

Autism and ADHD are both complex conditions with many contributing factors making it difficult to fully understand their etiology and develop effective treatment methods.

Response inhibition can be defined as the ability to suppress responses that are inappropriate or not aligned with the current task demands, which is crucial for effective self-regulation and goal-directed behavior. ADHD results in a significant deficit in neural activity in regions associated with inhibitory control. The right inferior frontal gyrus demonstrates decreased activation, while the medial prefrontal cortex demonstrates increased activation when compared to unaffected individuals during prospective response inhibition (Bhaijiwala, 2016). The right inferior frontal gyrus (rIFG) is one of the first regions engaged in response inhibition tests involving a stop signal. It is engaged between the stop signals appearance and the reaction to the stop signal in these tests (Schaum et al., 2020), suggesting this region plays an important role in the initiation of response inhibition. A study of the medial prefrontal cortex (mPFC) in rats demonstrated that they struggled to prevent competing memories and select relevant memories, indicating the medial prefrontal cortex plays an important role in selecting previous knowledge to be utilized when deciding to inhibit a response. (Peters et al., 2013). Latency in response inhibition is associated with Autism, while research doesn't show a diminished capacity to make inhibitory decisions (Johnston et al., 2011). Deficits in response inhibition are shown to result in difficulty controlling motor responses in individuals with ADHD, which is a contributing factor to the impulsive behaviors that are a common symptom of the disorder. (Suskauer et al., 2008).

Noninvasive Treatment Methods

The Noninvasive treatment methods used by Neurofit Connections include transcranial magnetic stimulation, primitive reflex therapy, and interactive metronome training, which have shown potential in enhancing response inhibition in children with Autism and ADHD. Primitive reflex therapy aims to remove retained reflexes such as the asymmetric tonic neck reflex (ATNR) and symmetric tonic neck reflex (STNR), when these reflexes are retained for longer than intended, they can hinder the motor function of individuals with these reflexes. Systematic removal of these reflexes has been shown to improve cognitive test performance (Melillo et al., 2023). The Research surrounding primitive reflex therapy is still in its infancy, and requires further investigation to establish its efficacy in improving ADHD and Autism symptoms.

Interactive Metronome and other methods of synchronization therapy are other newly suggested methods for the treatment of Autism and ADHD. Interactive Metronome treatment involves subjects completing a physical action, such as clapping to the beat of a metronome, with a device utilized to describe the deviation of the physical action from the Metronome. The goal is to synchronize physical action with the timing of the Metronome as much as possible. (Interactive Metronome, n.d.) Interactive Metronome

training was shown to be effective in improving motor control and reaction time, but had no significant correlation with improvements in response inhibition in children affected by ADHD (Casper et al., 2009). However, A meta-analysis of Musical training studies in individuals affected with ADHD and other developmental disorders indicated that forms of musical training can help develop improved response inhibition, likely as a result of the multi-sensory demands of Musical practice, which demands the improvement of response inhibition (Jamey et al., 2023). While the effectiveness of musical training in enhancing response inhibition is prominent, Interactive Metronome's effectiveness in enhancing response inhibition requires further investigation.

Transcranial Magnetic Therapy (TMS) has been shown to stimulate brain areas by generating an electric field that can activate Neurons through the skull. It's applications are becoming increasingly prominent in research and therapy applications. However, it is difficult to accurately target specific brain regions with TMS due to anatomical differences and the lack of uniformity in electric field distribution. (Gomez-Tames et al., 2020).

Measurement of Response Inhibition

The Creyos Double Trouble Assessment (CDTA) shares many similarities with the Stroop test. In the CDTA, A subject is presented with the word red or blue, in the color red or blue, and must choose the color rather than the word itself. The Stroop test is a previously established measure of response inhibition in individuals with ADHD (Çelik et al., 2022). The Double Trouble Test uses the same principle as the Stroop test, making it well suited to measure response inhibition. It also incorporates elements that assess both latency and accuracy of response inhibition, generating a score based on both accuracy and timeliness of responses. Creating a normative score that is a factor of both inhibitory control and response times, allowing us to use it as an indicator of both autism and ADHD.

Inclusion/Exclusion Criteria

14 Subjects were selected from Neurofit Connections that met the following criteria:

- Between the ages of 5-18
- Had taken 2 or more CDTA
- Had been treated by Neurofit Connections for at least 4 weeks
- had at least 3 weeks in between their two most recent assessments
- Lacked any characteristics inhibiting the ability of the subject to participate in the Double Trouble Assessments such as vision problems or inability to read
- Had either a formal diagnosis of Autism or ADHD, or were heavily suspected to have one or more disorders by their parents and Neurofit Connections

The admitted patients without a formal diagnosis were required to meet all but one of the following additional inclusion criteria

For Autism:

- Poor social skills
- Little to no eye contact
- Below average large scale idea recognition
- Lack of physical and emotional introspection

For ADHD

- Diminished response inhibition capabilities
- Difficulty concentrating
- Learning disability

Between the ages of 5-18, Had taken 2 or more CDTA, Had been treated by Neurofit Connections for at least 4 weeks, had at least 3 weeks in between their two most recent assessments to prevent experience from becoming a confounding factor, Lacked any characteristics inhibiting the ability of the subject to participate in the Double Trouble Assessments such as vision problems or inability to read, Had either a formal diagnosis of Autism or ADHD, or were heavily suspected to have one or more disorders by their parents and Neurofit Connections on the basis of poor social skills, little to no eye contact, lack of large scale idea comprehension, lack of physical and emotional introspection, or increased pattern recognition abilities for Autism. For individuals with ADHD, decreased response inhibition abilities, difficulty concentrating, and learning disability. Subjects still undergoing treatment were included in the data set. Subjects receiving treatment methods other than those prescribed by Neurofit Connections, such as medication, were not included in the data.

Study Design

Data regarding all previous CDTA scores were collected from each of the participants to analyze the potential impact of the noninvasive treatments on response inhibition over time. The initial CDTA scores of all admitted subjects were placed into Group 1, and the subsequent scores after treatment were placed into Group 2. This longitudinal design will allow for a comprehensive analysis of the effectiveness of noninvasive treatments on response inhibition in children diagnosed with Autism and ADHD.

Condition	Groups First Score is Included in	Groups Most Recent Score is Included in
Autism	1,2	5,6
ADHD	1,3	5,7
Both	1,4	5,8

Subjects received weekly treatment between the sampling of CDTA scores, Subjects were instructed by Neurofit Connections to perform various exercises that selectively targeted residual primitive reflexes, and utilized devices that provided transcranial magnetic stimulation, targeting different hemispheres of the frontal lobe and cerebellum at varying electrical intensities as prescribed by Neurofit Connections, along with additional techniques designed to stimulate areas of the brain that showed decreased activation compared to unaffected individuals. Individuals selected were instructed to perform these exercises for approximately 30 minutes a night and received Interactive Metronome therapy at least once a week for 10-15 minutes at Neurofit Connections.

A Shapiro-Wilk test will first be run to ensure the normality of the data with an alpha value of 0.9. A Paired T-Test will be run to compare the mean scores of response inhibition before and after treatment, comparing groups 1 to 5, 2 to 6, 3 to 7 and 4 to 8. A Paired T-Test was chosen because it allows us to

compare the scores of individuals before and after Croyos testing without differences in response inhibition abilities between trial groups becoming a confounding factor.

H0: Group 1 = Group 5, Group 3 = Group 7, Group 2 = Group 6, Group 4 = Group 8

H α : Group 1 < Group 5, Group 2 < Group 6, Group 3 < Group 7, Group 4 < Group 8,
Group will be represented by G in table

Statistical Analysis

Conditions:

Due to conducting a retrospective cohort study, the samples do not need to be randomized, selection bias is avoided due to the historical nature of the data.

There are more than 140 individuals between the ages of 5-18 who are affected by Autism or ADHD, indicating that our sample size does not interfere with the independence of samples.

For the paired groups representing all conditions, the Shapiro-Wilk test did not show a significant departure from normality, $W(14) = .97, p = .901$

For the paired groups representing Autism, the sample size is too small to perform a Shapiro-Wilk test; we will proceed with caution, and the results of this group are potentially invalid.

For the paired groups representing ADHD, The Shapiro-Wilk test did not show a significant departure from normality, $W(7) = .98, p = .995$

For the paired groups representing Both ADHD and Autism, The Shapiro-Wilk test did not show a significant departure from normality, $W(3) = .96, p = .989$

m_0 = The true mean difference between the scores before testing and the scores after testing

Initial Scores - Final Scores

Condition	H_0	H_α	n	α	\bar{x}	p	t	S_x	CI
All	$G_1 - G_5 = 0$	$G_1 - G_5 > 0$	14	0.05	-13.643	0.0000275	-5.869	8.697	(-18.629,-8.657)
Autism	$G_2 - G_6 = 0$	$G_2 - G_6 > 0$	2	0.05	-17.5	0.00272	-11.667	2.121	(-23.953,-11.046)

ADHD	$G_3 - G_7 = 0$	$G_3 - G_7 > 0$	7	0.05	-18.571	0.0003079	-6.530	7.525	(-25.297,-11.844)
Both	$G_4 - G_8 = 0$	$G_4 - G_8 > 0$	3	0.05	-8.667	0.0667	-2.457	6.110	(-19.891, 2.557)

For All Conditions, Autism and ADHD, Assume H_0 is true. Since $p < \alpha$, we reject H_0 . There is significant evidence that noninvasive treatment for individuals with Autism and ADHD works within the autism-only group, the All-conditions group, and the ADHD Group. For the following groups, our confidence interval can also be used to reject H_0 , because the interval indicates 95% confidence m_0 is between the confidence interval, and for all of the following groups 0 is not contained within the confidence interval, allowing us to reject H_0 .

For the Group with both Autism and ADHD, Assume H_0 is true. Since $p > \alpha$ we fail to reject H_0 . There is insufficient evidence to show the noninvasive treatment methods work for both ADHD and autism. This is supported by our confidence interval, the interval indicates 95% confidence ω_0 is between (-19.891, 2.557), and this interval contains our Null Hypothesis.

Confounding Factors

Due to the variety of treatment methods used by Neurofit Connections, multiple potentially confounding factors emerged during data collection. The use of different techniques to stimulate underdeveloped portions of the brain varied among individuals being treated, along with variations in how transcranial magnetic stimulation was assigned could potentially decrease the validity of the results, however, the techniques used to stimulate underdeveloped portions of the brain used alongside transcranial magnetic stimulation should have similar effects due to the same intended function if the different techniques used for stimulation were confounding. The use of all 3 treatment methods is also confounding, and being unable to block by treatment is an unfortunate consequence of conducting a retrospective cohort study. Individuals who were not formally diagnosed are also a potential confounding factor. To alleviate the consequence of this factor, individuals with uncertain diagnoses were removed from all paired groups except the paired group containing all of the conditions together. Experience/comfort with the CDTA was also another potentially confounding factor, we controlled for this by ensuring at least 3 weeks between the two most recent attempts. Lack of understanding of the test was another potentially confounding factor, we controlled for this by ensuring subjects completed the test under supervision and watched the instructional video before attempting the test for the first time, along with having practice rounds to gain comfort with the test.

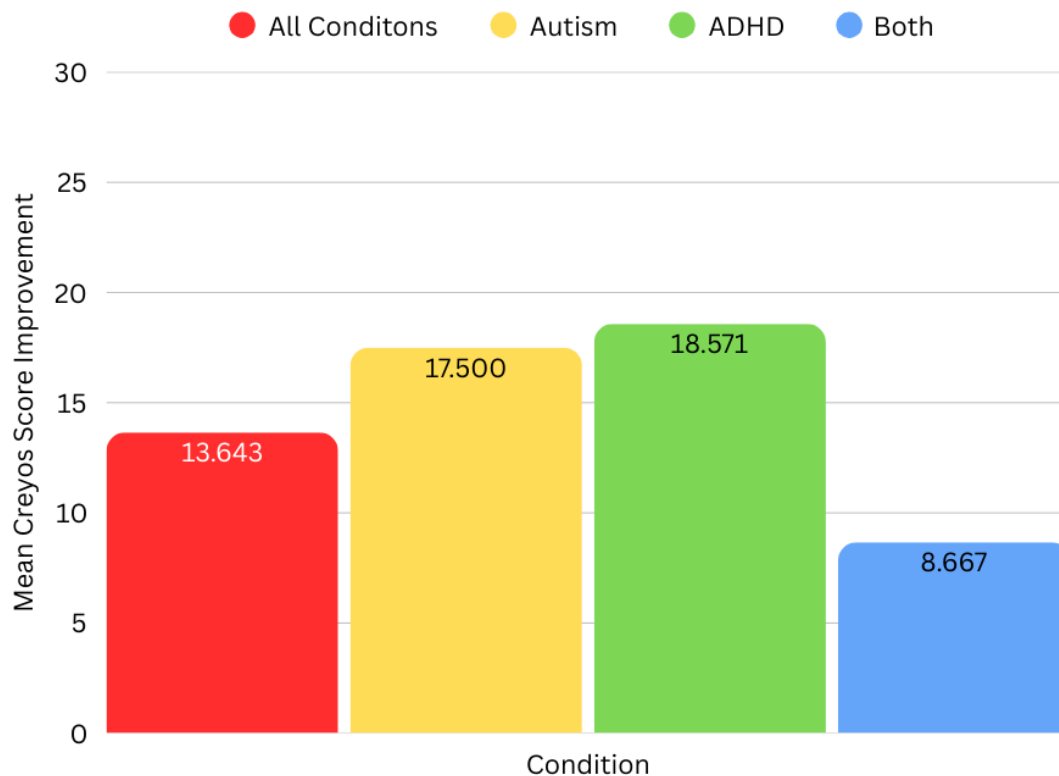
Discussion

The P-values for the paired T-Tests indicated significant improvements in response inhibition across all groups, with p-values consistently below 0.05, demonstrating the effectiveness of the noninvasive treatments administered, except for the group including scores for both ADHD and Autism. The small sample sizes of the Autism only paired groups and the both conditions paired groups likely make the results for these specific groups less reliable, but the findings from the ADHD only groups and the groups containing all disorders were significantly below our critical value, Suggesting that some combination of Interactive Metronome Therapy, Transcranial magnetic stimulation, and Primitive Reflex Therapy may effectively enhance response inhibition in children diagnosed with both ADHD and Autism. The effectiveness of these treatments highlights the potential clinical future of noninvasive treatment for autism, as individual methods and clinical supporting data become more refined.

This Graph represents the initial and final CDTA Scores of All of the individuals included in the study. Creyos score are normally distributed with an average score of 100 and a standard deviation of 15. A score of 87 or lower is considered below average, or in the bottom 20% of test scores while a score of 113 or higher is considered above average or in the top 80% of test scores.

NOTE: Will not be included in final study, here because my class requires it as part of the grade

Mean Creyos Score Improvement By Conditon



This Graph represents the mean improvement from initial score to final score for all individuals included in the study. Creyos score are normally distributed with an average score of 100 and a standard deviation of 15. A score of 87 or lower is considered below average, or in the bottom 20% of test scores while a score of 113 or higher is considered above average or in the top 80% of test scores.

References

Khadka, N., Peltier, M., Fassett, M. J., Mensah, N. A., Yeh, M., Chiu, V. Y., Oyelese, Y., & Getahun, D. (2024). Rising Trends of Childhood Attention-Deficit/Hyperactivity Disorder in a Large Integrated Healthcare Delivery System in Southern California, 2010-2021. *Jornal De Pediatria*. <https://doi.org/10.1016/j.jpeds.2024.113997>

Yoo, H. J. (2013). Recent increase in autism and ADHD: true or inflated? *Journal of Korean Medical Science*. <https://doi.org/10.3346/JKMS.2013.28.7.974>

Melillo, R., Leisman, G., Machado, C., & Carmeli, E. (2023). Identification and reduction of retained primitive reflexes by sensory stimulation in autism spectrum disorder: effects on qEEG networks and cognitive functions. *Case Reports*. <https://doi.org/10.1136/bcr-2023-255285>

Chen, Y. B., Lin, H., Wang, L., Hung, K., Brunoni, A. R., Chou, P., Tseng, P., Liang, C., Tu, Y., Lin, P.-Y., Carvalho, A. F., Hsu, C., & Ni, H. (2024). A network meta-analysis of non-invasive brain stimulation interventions for autism spectrum disorder: evidence from randomized controlled trials. *Neuroscience & Biobehavioral Reviews*. <https://doi.org/10.1016/j.neubiorev.2024.105807>

Cosper, S. M., Lee, G. P., Peters, S. B., & Bishop, E. (2009). Interactive Metronome training in children with attention deficit and developmental coordination disorders. *International Journal of Rehabilitation Research*. <https://doi.org/10.1097/MRR.0B013E328325A8CF>

Lee, K., Cho, I. H., Park, J., Choi, H., & Cheon, K.-A. (2024). Response inhibition as a critical executive function in differentiating attention-deficit/hyperactivity disorder from autism spectrum disorder: a comprehensive attention test study. *Frontiers in Psychiatry*. <https://doi.org/10.3389/fpsy.2024.1426376>

Johnston, K., Johnston, K., Madden, A. K., Bramham, J., & Russell, A. (2011). Response Inhibition in Adults with Autism Spectrum Disorder Compared to Attention Deficit/Hyperactivity Disorder. *Journal of Autism and Developmental Disorders*. <https://doi.org/10.1007/S10803-010-1113-9>

Creyos Online Cognitive Tasks. (n.d.). Creyos Online Cognitive Tasks. <https://creyos.com/online-cognitive-tasks>

Bădescu, G. M., Filfan, M., Sandu, R. E., Surugiu, R., Ciobanu, O., & Popa-Wagner, A. (2016). Molecular mechanisms underlying neurodevelopmental disorders, ADHD and autism. *Romanian Journal of Morphology and Embryology*.

Shinawi, M., Sahoo, T., Maranda, B., Skinner, S. A., Skinner, C., Chinault, C., Zascavage, R. R., Peters, S. U., Patel, A., Stevenson, R. E., & Beaudet, A. L. (2011). 11p14.1 microdeletions associated with ADHD, autism, developmental delay, and obesity. *American Journal of Medical Genetics Part A*. <https://doi.org/10.1002/AJMG.A.33878>

Xi, T., & Wu, J. (2021). A Review on the Mechanism Between Different Factors and the Occurrence of Autism and ADHD. *Psychology Research and Behavior Management*. <https://doi.org/10.2147/PRBM.S304450>

Bhaijiwala, M. (2016). *The Neural Substrates of Response Inhibition in Attention Deficit Hyperactive Disorder (ADHD)*.

Schaum, M., Pinzuti, E., Sebastian, A., Lieb, K., Fries, P., Mobascher, A., Jung, P., Wibrall, M., & Tuescher, O. (2020). Cortical network mechanisms of response inhibition.*bioRxiv*.
<https://doi.org/10.1101/2020.02.09.940841>

Peters, G. J., David, C. N., Marcus, M. D., & Smith, D. M. (2013). The medial prefrontal cortex is critical for memory retrieval and resolving interference.*Learning & Memory*.
<https://doi.org/10.1101/LM.029249.112>

Suskauer, S. J., Simmonds, D. J., Fotedar, S., Blankner, J. G., Pekar, J. J., Denckla, M. B., & Mostofsky, S. H. (2008). Functional magnetic resonance imaging evidence for abnormalities in response selection in attention deficit hyperactivity disorder: Differences in activation associated with response inhibition but not habitual motor response.*Journal of Cognitive Neuroscience*.
<https://doi.org/10.1162/JOCN.2008.20032>

Interactive Metronome. (n.d.).

https://www.interactivemetronome.com/?utm_source=google&utm_medium=paid&utm_campaign=branding&utm_source=google&utm_medium=ppc&utm_campaign=multiview_google&gad_source=1&gad_campaignid=22232434729&gbraid=0AAAAA-2XBBNFEW55s0k-11rSDNvow6LUz&gclid=CjwKCAjw_pDBBhBMEiwAmY02NuSyC68tXLW2N4kwOVe23ixurwPe_YmryVIOMaRf3GTH2HSCuiejOhoC_p4QAvD_BwE&gclsrc=aw.ds

Jamey, K., Foster, N. E. V., Hyde, K. L., & Bella, S. D. (2023). Does Music Training Improve Inhibition Control in Children? A Systematic Review and Meta-Analysis.*bioRxiv*.
<https://doi.org/10.1101/2023.02.08.527718>

Gomez-Tames, J., Laakso, I., & Hirata, A. (2020). Review on Biophysical Modelling and Simulation Studies for Transcranial Magnetic Stimulation.*arXiv: Neurons and Cognition*.
<https://doi.org/10.1088/1361-6560/ABA40D>

Çelik, H. E. A., Küçükgöncü, S., Erdogan, A. A., & Özerdem, A. (2022). Response Inhibition and Interference Control in Adult Attention Deficit Hyperactivity Disorder.*Nöropsikiyatri Arşivi*.
<https://doi.org/10.29399/npa.28192>