**Abstract**

According to DSM criteria, autism impairs socio-emotional reciprocity (Criterion A1). The cognitive model suggests that autism impacts emotion perception due to disrupted interoception. Given the vagus nerve's important function in interoception, vagus nerve electrical stimulation may increase self and other emotion perception. Reduced restlessness and increased emotional regulation in autistic children may lead to greater behavioral therapy results. Twenty eligible autistic children and their families were recruited using convenience sampling. Ten children in the intervention group received vagus nerve electrical stimulation, while the other 10 were in the control group which received routine rehabilitation. Changes were assessed using the Sensory Profile questionnaire and facial emotion recognition photos. Statistical results showed significant differences in facial emotion recognition, emotion perception and regulation, calmness, and improved sensory state in the children. Vagus nerve stimulation decreases sympathetic activity and increases parasympathetic activity, leading to overall calmness, reduced restlessness, decreased aggression, and improved social behaviors.

**Enhancing Emotion Perception and Regulation in Children with Autism: The Impact of Vagus Nerve Electrical Stimulation**

Autism is a neurological condition that causes long-term social communication and interaction problems and repetitive and limited behavior, hobbies, and activities. Autism symptoms are usually visible by age two. If the symptoms are minor, identification may arise after two years, especially if the child has major developmental delays before 18 months. Infants with this condition exhibit distinctive characteristics from birth. By six months, they still display a lack of dependency on their mother, exhibit no response to physical contact, seldom cry but may exhibit heightened irritability, and by the age of six months, they still fail to engage with their mother, demonstrate disinterest, lack smiling, babbling, or predictable reactions, and exhibit delayed or absent interest in toys.

By six to 12 months, the infant with autism may also be disinterested in social play, shows no affection, lacks verbal and nonverbal communication, and shows hyper or hypo reactivity to stimuli. Parents are usually the first to notice their child is different compared to other children developmentally. Early on, parents may attribute their child's lack of response to their environment to deafness; but later realize their child can hear but does not react like other children their age. This is when parents consult a pediatrician or clinician experienced in childhood developmental disorders.

Speech in children with this disorder is characterized by echolalia (repeating heard words and phrases verbatim). In these children, harmful behaviors like biting, head banging, avoidance behaviors like tantrums and crying, expressing anger and irritation, and soiling clothes with feces or urine, are very common. Most of the time parents clearly notice their child's lack of interest in being held, obsessive interest in sameness and lack of change in the environment, self-stimulating behaviors (like flapping hands, rocking, spinning), self-injurious behaviors (like head banging, hitting or biting themselves), lack of eye contact with others (avoiding eye to eye looks) and preoccupation with inanimate objects.

Autism is considered a spectrum because its manifestations are highly diverse and heterogeneous. For example, some patients have very severe verbal and cognitive impairments, while others have astonishing mental abilities and talents. On one extreme of the autism spectrum, individuals have an IQ below 40, while on the other extreme, there are bright individuals with exceptionally high intelligence. Nevertheless, they all encounter difficulties in terms of social-emotional reciprocity. For example, these individuals exhibit abnormal social behaviors such as touching, licking, or shoving others, which may be intended as an attempt at interaction. They are unable to provide comfort to individuals who are distressed and exhibit inadequate or incomplete responses to eye contact, displays of affection, words of encouragement, admonishments, and indirect cues from others. These challenges may stem from defective social cognition or emotion perception.

Autism spectrum disorder occurs in all parts of the world, across all economic and social levels, and in all racial and ethnic groups. Based on existing perspectives on the etiology of this disorder, it can be said that researchers have so far been unable to accurately determine the cause of autism spectrum disorder, although they have inconsistently identified that various factors such as genetic, hereditary, air pollution, lifestyle, etc. may play a role in its occurrence. What is clear, however, is that this disorder is associated with abnormalities in the natural development of the nervous system (neural connections) in early childhood. There are no medications to treat autism spectrum disorder, and medications only reduce ancillary symptoms. In answer to the question "How should autism disorder be treated?" it can be said: Any action that leads to the patient's improvement or even prevention of worsening condition can be considered a treatment. Reducing restlessness in children with autism is likely to lead to significant progress in behavioral therapy. Moreover, augmenting emotional regulation has the potential to alleviate deficiencies in social interaction observed in individuals with autism.

**Statement of Problem**

Many studies indicate a significant increase in the prevalence of autism since 1980. The Centers for Disease Control and Prevention estimated the prevalence of autism to be 1 in 59 births in 2018. Despite extensive research, the cause of autism remains unknown. One of the methods used to understand the complexities of cognition is cognitive modeling. Based on the diagnostic criteria for autism, namely impairment in social-emotional interaction as outlined in DSM 5 criterion 1, it can be inferred that autism is characterized by difficulties in emotional functioning. The cognitive model considered in this study is autism as a disorder of interoception (inner understanding) which causes impairment in understanding emotions. When Sherrington first described interoception in 1906, his definition reflected limited knowledge of basic reflexes and visceral senses (Sherrington, 1906).

Today, interoception presents a complex phenomenon by which sensory information reaches conscious awareness such that an individual's perception of these incoming messages may influence human behavior (Cameron, 2001). The basis of the interoceptive process involves how sensory messages related to internal bodily experiences such as hunger, thirst, visceral and muscular senses, pain, body temperature, itching, touch, vasomotor activities, choking sensations come to conscious awareness (Dobbin, 2015; Craig, 2003). The anterior insula, by integrating bottom-up sensory information from the body and top-down predictive information from higher levels in frontal and sensory-motor areas, plays a key role in the interoceptive process as an integrative center for emotional and physiological perceptions (Gu et al., 2015; Calì et al., 2015).

**Emotion Theories**

Emotion theories emphasize the necessity of understanding bodily states for emotion recognition. To Damasio's theory, understanding bodily states and consequently emotions is necessary in all social situations including decision making. James-Lange Theory believes that the emotions that are felt are the perception of bodily changes. This indicates that what we experience as emotion is the label we apply to our responses. For example, we are afraid because we flee (James, 1884). Whereas two-factor theory of Schachter-Singer infers that emotional states are based on two factors of emotional arousal and cognitive labeling. In other words, the emotion we feel is our interpretation of states of arousal (Schachter and Singer, 1962). Richard Lazarus's appraisal theory posits that emotions arise from the assessment of information derived from both the external world and internal bodily states (Lazarus and Smith, 1988). Damasio's Somatic Marker Hypothesis proposes that emotions have a significant impact on decision making by assigning somatic markers to different possibilities, which are linked to specific emotions. Somatic markers enhance decision-making accuracy by removing unfavorable choices and minimizing intricacy. Damasio (1996) posits that decision making is a cognitive process influenced by emotions and feelings, challenging the conventional belief that emotions hinder decision making. The facial feedback theory argues that facial expressions can elicit corresponding emotional experiences internally. Tomkins proposes that facial expressions can be categorized as either positive or negative. Based on Neal and Chartrand (2011), facial expression may effectively differentiate between good and negative emotions.

Like Damasio's somatic marker hypothesis, social and personal situations are strongly linked with positive and negative emotions. Emotions arise from bodily changes caused by punishment or reward, satisfaction or pain, joy or sorrow. Emotional experiences often influence voluntary decisions. Whether these emotions are unconscious or conscious, they generate signals like "continue", "stop", and "change direction" that help make sound choices. These somatic signals or interoceptive information do not necessarily have to be consciously received. In other words, one may not be consciously aware of the process in one of these games or tasks (for example, in the Iowa gambling task, appropriate somatic emotional states are really created and sent to subcortical and cortical processing structures, especially the somatosensory and insular cortex).

In the somatic marker hypothesis, this anatomical system, known as the "body loop", can then act rapidly in neural processing, enabling the individual to engage in or avoid a specific action. After emotions have been expressed and experienced at least once, the individual will be able to construct representations of these emotional experiences in the insular/somatosensory cortex. Therefore, after an emotion is learned, one of these chains of physiological events may directly activate the somatosensory/insular cortex without passing through the body and compared to when the emotion appeared in the body, a weaker image of the bodily emotional state is recalled. This system is known as the "as if body loop". In this neural system, which enables activation of a somatic emotional state, multiple neural regions are involved including the ventromedial prefrontal cortex, primary and secondary somatosensory cortex, and insula.

Bechara and Damasio (2005) proposed the somatic marker hypothesis for patients with ventromedial prefrontal cortex (VM) lesions who despite having normal intelligence had abnormalities in their emotions, feelings, and decision making. In this theory, the neural basis for these deficits stems from impaired activity of somatic states (emotional signals) that operate covertly and overtly leading to deviations in decision making. The VM prefrontal cortex is not the only region involved.

Figure 1. Body Loop and As If Body Loop Diagram

Deficits in the “as if body loop” can lead to disregarding or forgetting rewards and punishments, and disorders manifesting as impulsivity or poor emotional control, resulting in antisocial behaviors. Understanding bodily states is equivalent to understanding the “body loop” from Damasio's somatic marker hypothesis and understanding the “as if body loop” is equivalent to understanding others' emotions (affective TOM). Understanding bodily states or the necessity to understand the “body loop” for emotion understanding is a prerequisite for understanding the “as if body loop” or understanding others' emotions.

Physiological changes in the body or understanding interoception is necessary for understanding emotional states. Impairment in sensory processing is one of the diagnostic criteria for autism, which may occur as hyposensitivity or hypersensitivity to superficial senses, deep sense, pain, temperature, etc. (American Psychiatric Association, 2013). Therefore, interoception or understanding bodily states and consequently understanding emotional states is impaired in these children, leading to a condition known as alexithymia, which in turn leads to impaired communication and social interaction, and according to DSM-5 criterion 1, autism increases.

It seems that proper emotional processing is vital for successful social behavior (Blair, 2007). The relationship between emotional regulation and prosocial decision making is supported by extensive studies (Eisenberg, 2000). It can be said that deficits in social-emotional interaction such as abnormal social behaviors, decreased common interests, emotions, and feelings, and even defects in nonverbal communication such as poor body language or deficiencies in understanding and using gestures and cues lead to behavioral adaptation problems in various social contexts and ultimately friendship problems. All these deficiencies may be rooted in understanding emotions, in other words rooted in understanding bodily states or interoception.

Baron-Cohen's (2002) theory of mind blindness in autism supports deficits in understanding one's own and others' emotions in individuals with autism. As stated by this theory, the human cognitive model lies on a spectrum between systemizing and empathizing. Systemizers are individuals who seek rules to predict the behavior of that system. These individuals do not function well in social environments because behaviors of social systems are not even 0.1% predictable even with the best mathematical rules. Empathizers are individuals who function well in social environments, understand others' feelings, beliefs, and thoughts well, and respond appropriately to them. Males are more systematic and females are more empathic. Based on Baron-Cohen (2002), autism occurs when one's systemizing ability is very high and empathizing ability is zero. Baron-Cohen believes autism is an extremely male brain condition. Empathizing arises from recognizing others' emotions and thoughts to be able to appropriately respond to their emotions. It also causes one to predict others' behavior and be aware of others' feelings (Baron-Cohen, 2002).

Individuals with autism are described as having impaired empathy (Bird et al., 2010). Emotional dysregulation leads to maladaptive responses including irritability, poor anger control, tantrums, self-injurious behaviors, aggression, and mood disorders. Although emotional dysregulation is not considered a core symptom of autism, there is a direct relationship between the core symptoms of autism and emotional dysregulation. Repetitive and stereotyped behaviors may be a better predictor for emotional dysregulation (Samson et al., 2014). Emotional disorders are seen before other symptoms in children diagnosed with autism later (Mazefsky et al., 2012).

Interoception is mediated by the vagus nerve and hypoglossal nerves. These cranial nerves, in addition to taste, include sensory nerves that receive sensations from the viscera, lungs, aortic body, and aortic sinus (Whitehead, 2012). Given the vagus nerve's important role in interoception, it seems that vagus nerve electrical stimulation may enhance interoception and consequently improve self and other emotion understanding. Individuals who have difficulties recognizing others' emotional distress show hypoactivity in anterior insular regions (Feldman Hall et al., 2013). The anterior insula is described for temporoparietal junction tracing one's own and others' mental states (Feldman Hall et al., 2013). The temporoparietal junction is considered the site of theory of mind (Young et al., 2010).

**Vagus Nerve Stimulation**

In "The Expression of the Emotions in Man and Animals", Darwin states that emotional expression occurs through the two-way communication between the heart and brain via the pneumogastric nerve, now known as the vagus nerve (Darwin, 1872/1965). Due to limited knowledge at that time, Darwin's intuition a century later developed into Porges' polyvagal theory (2001). This theory suggests the vagus nerve is an important phylogenetic foundation that regulates emotions and social behavior. In addition, it assumes the highest level of social interaction such as facial emotion recognition is mediated by the vagus nerve (Porges, 2003).

In the context of epilepsy treatment, vagus nerve stimulation has led to improved quality of life (Morris GL 3rd et al., 1999) and improved cognition (Sackeim et al., 2001). Vagus nerve stimulation has been used as a non-pharmacological treatment for epilepsy for over 20 years (George et al., 2000; Yuan & Silberstein, 2016). The vagus nerve comprises a complex network that can regulate mood, memory, pain, and the neuroendocrine-immune axis. It is also described as a control center that integrates interoceptive information (Yuan & Silberstein, 2016).

Vagus nerve stimulation requires surgically implanting a generator in the left side of the neck which produces pulses that are embedded in the left chest. These continuously sent low frequency electrical signals to the cervical vagus nerve which transmitted to different brain regions (George et al., 2000).

INSERT FIGURE 2 HERE.

Figure 2-1: Vagus nerve stimulation implant surgery

After proving the efficacy and safety of vagus nerve stimulation, the U.S. Food and Drug Administration approved this method in 1997 for treatment of drug-resistant seizures and in 2005 for treatment-resistant depression. The most common side effects of vagus nerve stimulation using this method include surgical complaints, shortness of breath, paresthesia, headache, pain, choking sensation, sore throat, and pharyngitis (Menachem‐Ben et al., 2015). The exact mechanism of vagus nerve stimulation is still unknown. It is believed that the vagus nerve is connected to areas of the brain involved in mood regulation such as the prefrontal cortex and amygdala, which have antidepressant effects (Drevets et al., 2002).

The surgical risks and potential complications meant this method was limited to patients with major depression who failed pharmacological and electroconvulsive therapies (Daban et al., 2008). The potential therapeutic effects of the vagus nerve led to the development of non-invasive methods. In 2000, Ventureyra first introduced transcutaneous vagus nerve stimulation (tVNS) with minimal side effects such as burning and itching at the stimulation site (Ventureyra, 2000). Transcutaneous vagus nerve stimulation (tVNS) is a safe, non-invasive, and inexpensive method (Kreuzer et al., 2012). Several studies have used high intensity tVNS and observed no major side effects (Colzato et al., 2017). The rationale for tVNS through the ear is based on anatomical studies showing the ear is the only superficial location where vagus nerve afferents are distributed (Colzato et al., 2017). This stimulation activates the thick myelinated Aβ fibers of the vagus nerve auricular branch, which directly connects to the solitary tract nucleus in the brainstem (Colzato et al., 2017). The therapeutic effects appear to be based on a bottom-up neural mechanism involving propagation of electrical stimulation from the peripheral nerves to the brainstem and central structures (Shiozawa, 2014). Support for the efficacy of tVNS in treating autism spectrum disorders can be summarized in six points:

1. Improved introception, emotional understanding, and social skills

2. Regulation of the autonomic system and induction of general relaxation and reduced

restlessness

3. Modulation and increased functional brain connectivity

4. Alleviation of comorbidities such as seizures and depression

5. Improved blood-brain barrier due to reduced neuro-inflammation

6. Regulation of the immune system

INSERT FIGURE 3 HERE.

The two core symptoms of impaired social-emotional interaction skills and restrictive, repetitive patterns of behavior and interests are seen from early childhood. Vagus nerve stimulation is a key component in regulating the nervous system, nervous system functions, and adaptive behaviors. Researchers have found vagus nerve stimulation can have positive social-emotional effects independent of seizure control (Hull et al., 2015). Studies have suggested that impaired functional connectivity within and between frontal, temporal, insular areas, and subcortical structures (such as thalamus, amygdala, hippocampus) underlies social impairment and repetitive behaviors (Cheng et al., 2015). Vagus nerve stimulation can modulate activity in cortical and subcortical regions (especially thalamus and amygdala) which may regulate disrupted brain function (Frangos et al., 2015).

Dysfunction of the immune system in autism spectrum disorder has been repeatedly reported, suggesting altered immune response in individuals with autism (Gesundheit et al., 2013). Neuroinflammation plays a role in the pathogenesis of autism. Researchers have shown several abnormalities in inflammatory and immune-inflammatory factors exist in ASD conditions. Researchers have also identified increased levels of proinflammatory cytokines and decreased levels of anti-inflammatory cytokines disrupt neurodevelopmental progression. Several inflammatory factors are increased in the brain and cerebrospinal fluid of ASD patients including TNFα, IL-1β, IL-6, IL-8, CCL8, MCP-1. Elevated plasma levels of IL-1β, IL-6, IL-8 have been correlated with maladaptive behaviors and social deficits in children with autism. Postmortem studies of brain tissue and cerebrospinal fluid from ASD individuals showed high levels of important inflammatory factors including TNFα, IL-1β, IL-6 (Mokhtari and Karimzadeh, 2017). Studies indicate reduced inflammatory cytokines due to vagus nerve stimulation (Lerman et al., 2016).

tVNS can alleviate autism co-morbidities like epilepsy (Park et al., 2003) and depression (Rong et al., 2016; Fang et al., 2016). Studies have hypothesized autism, epilepsy, and depression may overlap in origin (Rapin & Tuchman, 2002). tVNS may have a therapeutic effect on the pathway of all three disorders (Fang et al., 2016). Recently, many animal studies have not found significant differences in the anticonvulsant effect between cervical and auricular vagus nerve stimulation (Fischenich & Ellrich, 2010). New studies have shown both cervical vagus nerve stimulation and transcutaneous vagus nerve stimulation involve similar pathways in the brain (Assenza et al., 2017).

In healthy humans, cervical vagus nerve stimulation is a reliable method to modulate vagus-dependent functions such as emotion recognition, flow, or tingling (Colzato et al., 2017, 2018). It also suppresses conditioned fear (Burger et al., 2016). Vagus nerve stimulation preserves and restores the blood-brain barrier (Lopez et al., 2018; Yang et al., 2012). The neural pathway of the vagus nerve that stabilizes memory is similar to the mechanism by which emotions affect memory. Emotional arousal causes adrenaline and cortisol release from the adrenal glands. These peripheral hormones stimulate beta-adrenergic receptors which are located on vagus nerve afferents. The vagus nerve projects directly and exclusively to the solitary nucleus in the brainstem. The solitary nucleus is a relay station between peripheral adrenergic activity and the central nervous system involved in memory formation (Jacobs et al., 2015).

The solitary nucleus has extensive projections to many brainstem and forebrain areas. It has direct and indirect projections to the locus coeruleus, and several studies support the hypothesis that vagus nerve stimulation activates the locus coeruleus. Locus coeruleus neurons project to the hippocampus, the sole source of noradrenergic input to the hippocampal system. The dorsal tegmental pathway provides the majority of norepinephrine innervation to most neocortical areas in a predominantly ipsilateral fashion (Roosevelt et al., 2006).

Several known cerebellar functions that are typically bilateral and impaired in individuals with autism include sensory processing, emotional regulation, learning, attention, autonomic function, language acquisition, repetitive behaviors, sleep, inhibitory control, and differences in sensory perception due to dysfunctional locus coeruleus and norepinephrine (London, 2018). Electrical stimulation of the locus coeruleus nucleus increases neuronal responsiveness to sensory stimuli (Lecas, 2004). It has been precisely shown that vagus nerve electrical stimulation causes activation and deactivation in many brain regions with wider pulse widths causing greater activation over deactivation ratios (Mu et al., 2004).

There is extensive evidence that individuals with autism have an imbalance in their autonomic system, meaning the sympathetic system is overactive while the parasympathetic system is underactive. Heart rate variability is an index to assess autonomic balance, and studies show heart rate variability is very low in children with autism (London, 2018). Vagus nerve stimulation increases heart rate variability and decreases sympathetic outputs (Clancy et al., 2014).

Heart rate variability reflects moment-to-moment fluctuations from the interactions of body and mind and provides a meaningful assessment of sympathetic and parasympathetic balance. Heart rate variability is used to measure the balance and self-regulatory capacity of the autonomic nervous system. Autonomic nervous system function depends substantially on sympathetic and parasympathetic operations that can have additive, subtractive, or reciprocal coordinator systems. Overall, the parasympathetic is responsible for calmness and the sympathetic for arousal (Berntson et al., 2008).

It has been suggested that parasympathetic nerves mediate processes associated with social behaviors, the function of which may be an index of vagus nerve function (Stellar et al., 2015). Findings have shown vagus nerve activity correlates with empathy, compassion, and prosocial behavior to relieve others' pain (Kogan et al., 2014). Higher vagus nerve activity directly relates to better social skills, while lower vagus activity associates with better gross motor skills and cognitive processing (Roosevelt‐Doussard, 2001). Low vagus activity is accompanied by flat facial and vocal affect and lack of vocal inflection (Porges, 2001). Vagus nerve activity is indicated by respiratory sinus arrhythmia which can be considered a reflection of parasympathetic control exerted by the vagus nerve on heart rate variability (Kogan et al., 2014).

Individuals with greater vagus nerve activity have more positive emotions, social connections, emotional expression, and greater ability to regulate negative emotions in response to highly stressful factors. All these abilities are important prosocial behaviors (Wang et al., 2013; Keltner et al., 2014; Fredrickson, 2010). Vagal stimulating activities like skin-to-skin contact accelerate infant maturation and increase vagus nerve activity (Feldman and Eidelman, 2003). Vagal stimulation (like massage) increases serum levels of absorption hormones (like insulin) and gastrointestinal hormones (like gastrin) in premature infants, which in turn leads to better weight gain (Chang et al., 2003; Uvnas-Moberg, 2004). Several studies have reported massage is very beneficial for children with autism (Li et al., 2019; Silva et al., 2009).

Autism is a condition labeled as vagal hypoactivity accompanied by avoidance of eye contact and flat facial affect (Porges, 2001). Therefore, vagus nerve stimulation reduces sympathetic activity and increases parasympathetic activity, leading to general calmness, reduced restlessness, decreased aggression, and improved social behaviors. Based on the above concepts and research, this study seeks to examine whether electrical vagus nerve stimulation can improve symptoms in children with autism. The proposed framework in this study: INSERT FIGURE 4 HERE.

**Importance and Necessity of Research**

The male to female ratio for autism prevalence is 4.3:1. The number of children identified with autism has increased markedly since 1980, at least partly due to changes in diagnosis and identification of the disorder (Newschaffer et al., 2007). In 2010 in the U.S., the overall prevalence of autism was 13.4 per 1000 4-year-old children, 15.3 per 1000 in 2012, and 17 per 1000 in 2014 based on DSM-IV-TR. During each surveillance year, ASD prevalence among 4-year-old and older children for Missouri (8.5, 8.1 and 9.6 per 1000 children in 2010, 2012 and 2014, respectively) and highest in New Jersey (19.7, 22.1 and 28.4 per 1000 children, for the same years, respectively) (Christensen et al., 2018).

Few Iranian studies have addressed autism prevalence. The rate of autism among 5-year-old Iranian children was recorded at 6.26 per 10,000 for the years 2006-2008, which corresponds to a rate of 190 per 10,000 (1.9%). In 2008, the rate of 7-12-year-old pupils in Shiraz was 95.2 per 10,000. In 2015, the rate in Mahabad was 95.2 per 10,000. In 2016, the rate of 1.5-4-year-old children in Khorramabad was 1.5% (Akbarpour, 2019).

There is currently no established treatment for autism. Physicians oversee symptoms to enable patients to maintain their functionality. Available treatments enhance rehabilitation and functionality for those with autism. Individuals with persistent autism do not experience premature mortality. As a result, the expenses associated with this illness endure throughout the entirety of one's life. This imposes a significant financial burden on society, the individual, and the family. The annual cost of autism in Australia is estimated to be $5.8 billion. A study conducted in 2015 in the United States evaluated the total medical costs associated with autism, including direct, indirect, and combined charges, which amounted to $268 billion (Leigh & Du, 2015). In 2013, a different study estimated that the total cost of autism over a person's lifetime in England was £2.2 billion. The mean total expenditure per individual with autism was 223,561,841 Rials, with direct, indirect, and indirect medical expenditures accounting for 32%, 52%, and 16% respectively (Mosadeghrad et al., 2019). In light of the rising prevalence of autism, which reached a rate of one in 59 births in 2018, the researcher investigated a strategy aimed at mitigating symptoms and enhancing outcomes for patients, employing alternative therapeutic methods. Acquiring knowledge is crucial, as it can also successfully mitigate the symptoms associated with autism at a reasonable cost.

**Research and Specific Objectives**

As mentioned by previous studies, the severity of impaired functional communication is indicative of autism traits. Consequently, the objective of this study is to investigate the impact of electrical vagus nerve stimulation on children diagnosed with autism. In this study, the specific objectives are identifying the effect of electrical vagus nerve stimulation on facial emotion recognition ability, in reducing oral sensory disturbance, on fine motor skills, on attention, calmness, compliance, and ability to remain at the table in children with autism.

**Hypotheses**

This research study explored the effects of electrical vagus nerve stimulation on children with autism, focusing on reducing symptoms and enhancing important functional domains. The researchers wanted to investigate whether electrical vagus nerve stimulation not only increases accuracy of facial emotion recognition, emotional reactivity, cooperation and remaining at the table, but also reduces distractibility, sensory seeking behaviors, and sensory sensitivity in children with autism. Overall, the purpose of this study is to offer significant insights on the efficacy of electrical vagus nerve stimulation as a therapeutic intervention for autistic children. Electrical vagus nerve stimulation may have the potential to enable the creation of customized and efficient solutions for this specific demographic.

**Method**

The purpose of this study is to investigate the effect of vagus nerve electrical stimulation on reducing sensory symptoms and improving emotion perception in children with autism. Considering the research objectives and hypotheses, a quasi-experimental pretest-posttest design with a control group was utilized. The sample includes all children with autism spectrum disorder in Tabriz city in 2019 who are referred to specialist psychiatrists and related treatment centers. From the above population, a sample of at least 10 people will be selected based on clinical rationale and considering inclusion and exclusion criteria. The control sample group will also be selected of at least 10 autistic children from Tabriz in 2019.

**Sample and Sampling Method**

The sample size was initially prepared as a list of 36 people who voluntarily expressed readiness. Considering the inclusion criteria, 30 people were selected, of which eight were girls and 22 were boys. Then the girls and boys were randomly assigned to two groups; the control and intervention groups, which formed this study. During data collection and obtaining consent, seven participants withdrew and two others withdrew after the pretest. To maintain group homogeneity, one girl was excluded by the researcher so that the ratio of girls to boys was equal in both groups. In this study, 20 participants, 10 per group including three girls and seven boys, were present in both groups.

A sample of 20 children with autism spectrum disorder who met the specified criteria in the DSM-5 and received a diagnosis from a specialist child and adolescent psychiatrist were selected. Ten people received only routine rehabilitation, and 10 people also received vagus nerve electrical stimulation in addition to rehabilitation.

Convenience sampling was utilized, but assignment of participants to the control and intervention groups was done at random. In experimental research, it is usually difficult to select a random sample since it requires time and obtaining informed consent from participants for ethical considerations. Therefore, the researcher must use volunteer participants. In such conditions where random sampling is not possible, replacement randomization is often used, i.e. initial sampling is done voluntarily and assignment of participants is done randomly.

**Inclusion and Exclusion Criteria**

This study included individuals without speech problems who have received a diagnosis based on DSM-5 autism diagnostic criteria by a psychiatrist. Participants should not have comorbidities such as seizures, heart problems, blindness, deafness, or other genetic abnormalities. Participants can withdraw from the study at any stage if they wish not to continue. The age range for participation is set at 9 to 14 years old to control for age. Also, equal numbers of male and female participants have been placed in the intervention and control groups to control for gender.

**Research Instruments**

*Facial Emotion Recognition Test*

The presentation of stimuli was such that the first slide was a gray page with a white +(plus sign) in the center, 2.5 degrees of vision in diameter, which was used to get the participant's attention. Simultaneously with the appearance of these gray slides, a warning sound was played to increase the participants' attention. The gray slides appeared between each trial. The display time for the next slide was set at three seconds. One emotional face from the front view was placed in the lower half of the page, and five other faces were placed side by side in the upper half of the page. All faces were without frames, and the participant had to match the emotion on the bottom of the page with one of the top images.

The images used for the recognition task were selected from the Radbound Facial Emotion Database. These images included two models, one male and one female, who were matched in potency and arousal. The implementation of the task was such that the participants were individually seated on a chair at a distance of about 30 centimeters from the display screen, and the stages of the task were simply explained to them. Before performing the main task, a practice task with 10 trials was conducted, which involved selecting the target image from among the options, to ensure that participants understood the task. The participant had to indicate the target image from among the top options by pointing. In general, they performed 36 trials, and the number of correct responses was recorded by the researcher during the experiment.

*Validity of Radbound Face Database Images*

The validity of this set has been documented by Langner et al. (2010). The images used are basic emotions, which per Baron-Cohen's view, are universal emotions. INSERT FIGURE 6 HERE.

*Sensory Profile Questionnaire*

The Sensory Profile questionnaire was developed and published by Winnie Dunn in 1999 and assesses the sensory status of children 3 to 10 years old. This questionnaire consists of 125 items. The results of the questionnaire are categorized into nine factors:

1. Factor 1 Sensory seeking: Indicates the child's sensory needs for various stimuli. According to the questionnaire scoring criteria, a child with a low score on this factor has a high need for various sensory stimuli.
2. Factor 2 Emotional reactivity: Indicates the child's reaction to emotional social issues. According to the questionnaire scoring criteria, a child with a low score on this factor exhibits a severe reaction to emotional issues such as failure, fear, and anxiety.
3. Factor 3 Low endurance/tone: Scores on this factor indicate the child's muscular endurance for various activities. According to the questionnaire scoring criteria, a child with a low score on this factor has low tolerance for daily living activities and tires quickly.
4. Factor 4 Oral sensory sensitivity: Indicates oral sensory processing in the child. According to the questionnaire scoring criteria, a child with a low score on this factor is highly sensitive to food taste, smell, and temperature.
5. Factor 5 Inattention/distractibility: Scores on this factor indicate the child's focus in daily activities. According to the questionnaire scoring criteria, a child with a low score on this factor easily loses focus due to environmental factors and is unable to continue an activity.
6. Factor 6 Poor registration: According to the questionnaire scoring criteria, a child who does not adequately perceive sensory stimuli will score low on this factor. 7
7. Factor 7 Sensory sensitivity: The child registers sensory stimuli with high intensity. According to the questionnaire scoring criteria, a child with a low score on this factor registers vestibular and proprioceptive sensory stimuli with high intensity and exhibits a severe reaction to them.
8. Factor 8 Sedentary: Indicates the child's preference in choosing the type of activity. According to the questionnaire scoring criteria, a child who scores low on this factor prefers calmer, seated activities.
9. Factor 9 Fine motor/perception: Scores on this factor indicate the child's fine motor status. According to the questionnaire scoring criteria, a child who scores low on this factor has poor eye-hand coordination.

The questionnaire scoring is based on a Likert scale (always, often, sometimes, rarely, never) and the following values were used to calculate the scores: Always = 1 point, Often = 2 points, Sometimes = 3 points, rarely = 4 points, Never = 5 points. Some studies on sensory processing based on Dunn's model have been conducted in Iran. In this regard, the study by Dehghan et al. (2015) can be mentioned, which examined the relationship between sensory processing and behavior in children with attention deficit hyperactivity disorder using the Sensory Profile questionnaire. The results indicate a significant correlation between the Sensory Profile variables and the Behavior Problems questionnaire.

The study by Jamshidian et al. (2016), on examining the effect of sensory processing on the participation of children with autism, concluded that sensory processing deficits, especially sensory sensitivity, can be an effective factor in limiting the participation of children with autism in activities. Furthermore, the results of the study by Nasaeian et al., on investigating sensory processing patterns in children with autism using the Sensory Processing Patterns questionnaire, showed that children with autism have different sensory processing patterns. These children have probable differences in low registration, sensory sensitivity and sensory seeking, and definitive differences in sensory avoidance. Asadi Gandomani et al.’s (2016) study found that the relationship between executive functions and sensory processing patterns in children with autism showed that sensory processing patterns have an inverse relationship with executive functions.

*Validity of the Sensory Profile Questionnaire*

Movallali and colleagues (2017) researched on the psychometric properties of the Sensory Profile School Form which showed that the translated Sensory Profile questionnaire has validity and reliability in Iranian children.

*Vagus Nerve Auricular Branch Electrical Stimulation Device*

This device generates a square wave with a pulse width of 300 microseconds and a frequency of 30 Hz that turns on and off every half second. The device was built by electronic engineers based on the original design and the accuracy of the current was confirmed using an oscilloscope.

**Summary of Implementation Method**

A quasi-experimental pretest-posttest design with a control group was used. First, the selected sample was randomly assigned into two experimental and control groups. The experiment was implemented such that pretest of facial emotion recognition and Sensory Profile questionnaire were administered for the experimental groups. Then, the experimental group received vagus nerve electrical stimulation in addition to routine treatments, and the control group only received sham stimulation in addition to routine treatments. Finally, posttest of facial emotion recognition and Sensory Profile were administered for both groups. Participants attended treatment sessions at the clinic. First, pretest was taken, and simultaneously with the treatment sessions, the experimental group received active stimulation and the control group received sham stimulation. Each person received 20 minutes of stimulation three sessions per week, and after 12 rehabilitation sessions, posttest was taken. Explanations about the type of study were also provided to participants after completing the test.

**Statistical Analysis of Data**

The data obtained from the experiment were analyzed using SPSS software, and pretest-posttest differences between the experimental and control groups were compared and significance of differences were determined. Due to the existence of pretest and the need to eliminate its effect, the statistical method used in this study was ANCOVA. For some factors of the Sensory Profile questionnaire that did not have normal distribution, Mann-Whitney test was used. When prerequisites of multivariate tests are not met, data transformation should be used to enable the use of intended tests (usually parametric ones).

**Findings**

The study hypothesized that electrical vagus nerve electrical stimulation can alleviate sensory problems, improves emotion perception, and overall enhance the condition of autistic children. As observed in the previous chapter, the vagus nerve auricular branch electrical stimulation variable had a significant positive effect on the overall improvement of autism symptoms in terms of enhancing facial emotion recognition and reducing sensory problems based on the Sensory Profile test. Since this is in its preliminary state in investigating the effect of vagus nerve auricular branch electrical stimulation on reducing symptoms in children with autism, unfortunately the researcher faced a scarcity of studies. The review of domestic and foreign research showed that so far, few studies have been conducted using the models of this research. The researcher had to refer to studies with related or similar topics to argue the results.

The findings regarding the facial emotion recognition hypothesis are consistent with similar results from Sellaro et al. (2018) and with results from Frindley (2018) that vagus nerve stimulation increased accuracy of facial emotion recognition, with the difference that the experimental samples were children with autism.

The findings regarding the fine motor improvement hypothesis are consistent with studies by Dousard- Roosevelt (2001). Dousard-Roosevelt found a significant correlation between high vagus nerve activity and motor skills (2001). Here, electrical vagus nerve stimulation also created a significant difference compared to the control group.

The findings regarding the emotional reactivity hypothesis are supported by extensive studies including correlation studies of high vagus nerve activity with social skills by Dousard-Roosevelt. It has also been suggested that parasympathetic nerves mediate processes associated with social behaviors, the function of which may be an index of vagus nerve function (Sellaro et al., 2018; Stellar et al., 2015). Findings have shown vagus nerve activity correlates with empathy, compassion, and the ability to recognize and express emotions, and prosocial behaviors to relieve others’ pain (Kogan et al., 2014).

Higher vagus nerve activity directly relates to better social skills, while lower vagus activity associates with better gross motor skills and cognitive processing (Roosevelt‐Doussard, 2001). Low vagus activity is accompanied by flat facial and vocal affect and lack of vocal inflection (Porges, 2001).

A study found that vagus nerve stimulation improves social-emotional well-being without seizure control (Hull et al., 2015). Reduced sensory disturbances may improve emotional reactivity. As mentioned before of Dehghan et al.’s (2015) use of the Sensory Profile questionnaire, their study examined the relationship between sensory processing and behavior in children with ADHD. The results showed a significant correlation between Sensory Profile variables and behavioral problem questionnaire scores.

Jamshidian et al. (2016) examined how sensory processing affects autism participation. They found that sensory processing deficits, especially sensory sensitivity, can limit autism children's activity participation. Thus, reduced sensory issues likely improved autism symptoms. This study's increased attention and reduced distractibility contradict previous findings. Routine exercises to improve attention may have not made a difference compared to the control group.

Studies on the sensory seeking and sensory sensitivity hypotheses were hard to find to compare. In their studies, Lecas (2004) and London (2018) linked sensory processing deficits to dysfunctional locus coeruleus and norepinephrine. Electrical stimulation of the locus coeruleus nucleus increases sensory neuronal responsiveness (Lecas, 2004). Several studies suggest vagus nerve stimulation activates locus coeruleus (Roosevelt et al., 2006).

The positive effect of vagus nerve stimulation treatment has shown to decrease sympathetic activity and enhance parasympathetic activity which increased sitting at the table in children with autism. This results in a state of increased tranquility, reduced restlessness, decreased aggression, and enhanced social behaviors in children with autism. Because of an imbalance in autistic individual’s autonomic system, evidence indicated that this exhibition of imbalance is characterized by heightened activity in the sympathetic system and reduced activity in the parasympathetic system. So, a heart rate variability may be utilized since it serves as a metric for evaluating autonomic equilibrium. Research indicates that children with autism exhibit significantly reduced heart rate variability (London, 2018). Vagus nerve stimulation enhances heart rate variability and reduces sympathetic outputs (Clancy et al., 2014).

Based on the current studies, there appears to be a notable correlation between electrical vagus nerve stimulation and the improvement of autism symptoms in individuals. This electrical stimulation activates the widespread brain network, reduces restlessness, and stress by targeting the parasympathetic nature of the vagus nerve. Additionally, it increases activity in the insular cortex, which is responsible for understanding one's own emotional states. Furthermore, with greater certainty, electrical vagus nerve stimulation has a discernible impact in mitigating symptoms in children diagnosed with autism spectrum disorders. Moreover, it can be employed in conjunction with other customary treatments.

Repeating this experiment and similar experiments using other tools on larger samples and different age ranges, the results of this research can be extensively utilized, because reducing restlessness and understanding emotions relates to all aspects of life and directly and indirectly affects social interaction and quality of life of children with autism and the autistic individual's family. Considering rehabilitation principles, this method can be used alongside other routine treatments. Based on the principles of cognitive rehabilitation, if a specific section of the nervous system is stimulated and repaired, and the neural connections in that area are enhanced, the rehabilitation impact can be long-lasting, especially when there is sufficient sleep between sessions and exercises. Hence, this approach can be employed to enhance the manifestations of autism.

**Limitations**

Because of the experimental nature and many stages of the experiment and intervention, finding a random sample was difficult. Thus, convenience sampling was used for this study. From an ethical standpoint, no group exclusively got active stimulation. The two groups receiving routine rehabilitation therapies of occupational therapy and speech therapy were given active stimulation for the intervention group and sham stimulation for the control group. As a result of the experimental nature of the study and the need to conduct follow-ups per rehabilitation principles, necessary follow-ups were not performed. By the cause of the sanctions on Iran, constructing the electrical vagus nerve stimulation device faced many problems. Due to the aversive nature of electrical stimulation and restlessness in children with autism, electrical stimulation was applied in half-second bursts. The sample size was small considering the coincidence of the research being conducted with the coronavirus pandemic. As a result, generalizing the findings to the whole population should be done cautiously.

**Suggestions for Future Research**

Based on the discoveries made in this work, several recommendations for further research in this field emerged. Due to the relatively weaker nature of the auricular branch of the tenth cranial nerve, it is recommended to explore the potential benefits of repeating electrical stimulation on other branches to optimize the therapeutic effect. Furthermore, the design and implementation of a specialized device for improved regulation of current flow, acting as a current limiter, may enhance the precision and safety of electrical stimulation procedures.

To improve the applicability of the findings, it is advisable for future research to duplicate the intervention using bigger and more varied populations. Hence in future studies, incorporating a variety of instruments may enhance the overall applicability of the results. Since this research is a preliminary study, it is essential to continue to explore this investigation by assessing the long-term efficacy of the intervention through follow-up phases. Moreover, broadening the range by doing analogous research on diverse age cohorts would provide a full comprehension of the intervention's suitability.

Given the favorable outcomes shown in terms of improved focus and compliance in children with autism, it is advisable to replicate such studies in the context of children with ADHD as well. Investigating the suitability of this intervention in conditions linked to autonomic dysfunction and evaluating heart rate variability (HRV) as a measure of autonomic well-being could provide significant knowledge. Regarding facial emotion identification, it may be beneficial to evaluate each emotion separately to have a more detailed knowledge. Additionally, expanding this research to include the recognition of body language could provide a holistic view of socio-emotional functioning. The purpose of these guidelines is to promote the overall comprehension and utilization of electrical vagus nerve stimulation in different clinical and research areas.

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