Autonomic Dysfunction in Psychiatric Disorders

Psikiyatrik Bozukluklarda Otonom Disfonksiyon

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BSTRACT

The autonomic nervous system and its dysfunction are associated with many diseases. For a healthy individual, it is essential that the sympathetic and parasympathetic systems are balanced and functioning at a high capacity. Psychiatric disorders often exhibit disruptions in the activity of the vagus nerve, which can lead to autonomic dysfunction. People with psychiatric disorders, including panic disorder, depression, bipolar disorder, schizophrenia, post-traumatic stress disorder, anxiety disorders, and substance addiction, often show reduced heart rate variability. Heart rate variability is a reliable marker for assessing autonomic functions, and decreased heart rate variability in individuals with psychiatric disorders can lead to an increased risk of sudden cardiac death. Autonomic dysfunction is observed in psychiatric disorders, and it occurs during the course of the illness, not necessarily at its onset. Autonomic dysfunction accelerates the progression of the disease. Therefore, controlling autonomic functions is crucial. This can help reduce disease symptoms and decrease the morbidity and mortality caused by autonomic dysfunction."

Keywords: Autonomic dysfunction, heart rate variability, psychiatric disorders

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Otonom sinir sistemi ve disfonksiyonu birçok hastalıkla ilişkilidir. Sağlıklı bir birey için sempatik ve parasempatik sistemin dengede olması ve kapasitesinin yüksek olması gerekir. Psikiyatrik hastalıklarda vagus sinirinin aktivitesinde bozulmalar vardır. Bu bozulmalar otonom disfonksiyona sebep olabilir. Panik bozukluğu, depresyon, bipolar bozukluk, şizofreni, travma sonrası stres bozukluğu, anksiyete bozuklukları ve madde bağımlılığı dahil olmak üzere psikiyatrik bozuklukları olan kişilerde kalp atış hızı değişkenliğinde azalmalar görülmektedir. Kalp atış hızı değişkenliği otonom fonksiyonların belirlenmesinde güvenilir bir belirteçtir ve kalp atış hızındaki azalmalar psikiyatrik bozuklukları olan hastalarda ani kardiyak ölüm riskine neden olmaktadır. Psikiyatrik hastalıklarda otonom disfonksiyon görülmektedir. Otonom disfonksiyon hastalığın başlangıcında değil hastalık sürecinde gerçekleşmektedir. Otonom disfonksiyon hastalık progresyonunu hızlandırmaktadır. Bu yüzden otonom fonksiyonlar kontrol edilmelidir. Böylece hastalık semptomları bu sayede azalabilir ve otonom disfonksiyonun neden olduğu morbidite ve mortalite azaltılabilir.

Anahtar sözcükler: Otonom disfonksiyon, kalp hızı değişkenliği, psikiyatrik bozukluklar

Introduction

The autonomic nervous system (ANS) regulates involuntary physiological processes such as heart rate, blood pressure, sexual arousal, and digestion. It is a subcomponent of the peripheral nervous system. The autonomic nervous system includes the sympathetic, parasympathetic, and enteric nervous systems. The sympathetic nervous system (SNS) and parasympathetic nervous system (PNS) contain afferent fibers and efferent fibers that provide motor output and sensory input to the central nervous system (CNS) (Waxenbaum et al. 2023). The sympathetic and parasympathetic systems are constantly active, and their basic activity levels are defined as sympathetic and parasympathetic tonus. The former is located in the systemic arterioles, and the latter in the intestines. While parasympathetic activity (parasympathetic tone) predominates in the heart at rest, sympathetic activity increases with exertion (Guyton et al. 2003).

Psychiatric disorders might lead to an increased risk of death. Approximately 60% of this increased risk is due to cardiovascular and comorbid physical diseases (Robson and Gray 2007). Studies show that the risk of cardiovascular disease increases approximately 2-3 times in psychiatric disorders. Autonomic regulation of the heart plays an integral role in cardiovascular function (Anderson et al. 1989). If autonomic dysfunction occurs, psychiatric disorders may follow. Poor cardiac autonomic regulation has been associated with heart failure, and increased vagal input (vagal nerve stimulation) is protective against ventricular fibrillation and sudden cardiac death. Heart rate variability (HRV), the assessment of beat-to-beat variation in the heart over time, provides a reliable index of cardiac autonomic function (Alvares et al. 2016).

Healthy autonomic cardiac control is characterized by a high degree of variability in heart rate, which helps protect against myocardial infarction and other future cardiac events. In contrast, lower parasympathetic input to the sinoatrial node can cause sudden and non-sudden cardiac death (La Rovere et al. 2003). Prospective evidence has shown that reductions in HRV are associated with a greater incidence of first cardiac events and subsequent development of cardiovascular disease in patients without known cardiovascular disease. Hence, reductions in HRV have been recognized as a marker for various disease states (Alvares et al. 2016).

A large body of evidence suggests that reductions in HRV are found in people with psychiatric disorders, including depression, schizophrenia, anxiety disorders, and substance abuse. Reviews have suggested that reductions in HRV provide an important mechanism contributing to the increased risk of sudden cardiac death in patients with psychiatric disorders (Licht et al. 2009, Kemp et al. 2010, Quintana et al. 2013).

Mulkey et al. (2019) argued that the central ANS is essential for maintaining cardiovascular and respiratory homeostasis in the newborn and has a critical role in supporting higher cortical functions. At birth, the central ANS matures and is vulnerable to adverse environmental and physiological influences. Critical connections are established between the ANS and the limbic system early in development to integrate psychological and body responses (Montagna and Nosarti 2016).

The Polyvagal Theory developed by Stephen Porges explained how autonomic vagal impulse modulation controls social responses and that a wide range of neuropsychiatric disorders can emerge from inadequate vagal tonus, excessive vagal reactivity, and impaired vagal balance. Under additional conditions in the fetus and neonate, such as prematurity growth restriction and environmental stress, the immature ANS can undergo "dysmature" dysmaturation. In addition to the intrauterine environment, maternal stress and health are also very important and have been shown to cause ANS changes in infants and neuropsychiatric disorders in children (Mulkey et al. 2019). The main aim of our study is to explore the functioning of the autonomic nervous system and autonomic dysfunction in psychiatric diseases and to determine the direction of variability in the autonomic system depending on these diseases. The contribution of our study to the literature is that autonomic dysfunction in psychiatric diseases has an essential role in the course of the disease, and autonomic functions should be under control in these diseases.

Polyvagal Theory and Impaired Vagal Balance

The vagus nerve (VN) is an integral autonomic nervous system component. As a mixed nerve, the VN contributes to bidirectional interactions between the brain and the gut (e.g., the brain-gut axis). The low vagal tone, assessed by heart rate variability as an indicator of sympathovagal balance, can be observed in functional gastrointestinal disorders, inflammatory bowel diseases, or various psychiatric disorders (Bonaz et al. 2016).

Polyvagal theory was first proposed by Porges in 1995. He reported that brain functions such as attention maintenance, task management, and emotional regulation are associated with cardiac vagal control based on the principles of polyvagal theory. The theory focuses on the role of two main branches of the vagal nerve. The older branch arises from the unmyelinated dorsal motor nucleus of the vagus, and the newer branch arises from the myelinated nucleus ambigus. Social responses to our environment are mediated by vagal input or vagal withdrawal through limbic system components (Porges and Furman 2011).

The polyvagal theory proposes that the parasympathetic nervous system regulates facial and head muscle movements necessary for social communication. At the age of six months and older, vagal development begins to influence social behavior and mood regulation of the behavioral state. The baby develops a 'face-heart' connection or social interaction system. This development engages muscle activity in the face/neck to communicate emotions and behavioral responses, aligning with brainstem-mediated responses in cardiovascular function. These muscles are innervated by specialized visceral efferent pathways related to the myelinated vagus, enabling the infant to display social cues and establish a parent/caregiver relationship. The gradual maturation of cerebral cortical structures and the ANS enables an individual's social participation system to develop. A wide range of neuropsychiatric disorders may be affected by inadequate vagal tonus or excessive vagal reactivity and disruption in vagal balance (Beauchaine et al. 2007, Porges and Furman 2011).

Polyvagal theory has led to the role of emotion dysregulation in psychopathology and the development of an abnormal autonomic nervous system functioning in many clinical syndromes. Polyvagal theory offers an approach to autonomic regulation as part of the mind/body connection. This approach has been studied in various contexts with proven effectiveness as a self-regulation tool that positively influences physiological and emotional outcomes in various settings. Self-regulation promotes better, clearer thinking and problem-solving

abilities, and communication as a tool to manage distress and anxiety (Bailey et al. 2020).

Autonomic imbalance, remarkably reduced parasympathetic tone, plays a role in anxiety, depression, post-traumatic stress disorder, and schizophrenia. In these conditions, sympathetic-mediated responses to stressors by the amygdala and prefrontal cortex may be inadequately compensated by the parasympathetic system (Thayer and Brosschot 2005). It disrupts the vagal balance. The immaturity of the social interaction system in preterm infants due to lower vagal activity may result in a lack of appropriate social cues to ensure normal co-regulation with parents/caregivers (Porges and Furman 2011).

In most cases, the body tries to establish homeostasis by maintaining a stable functioning. In a changing environment, the body may need to adapt to have optimal functioning, known as allostasis. Allostasis refers to the attempt to maintain optimal functioning despite different physiological and environmental demands. For example, in chronic stress situations, the body can anticipate the changing environment and enter an allostatic state where it maintains a certain level of function. There may also be an opportunity for "homeostatic" plasticity, where the nervous system retains the ability to return to the previous state when the environment returns to a more stable/normal (pre-stressor) state (Beauchaine et al. 2007).

Psychiatric disorders include panic disorder, depression, bipolar disorder, schizophrenia, post-traumatic stress disorder, sleep, attention-deficit/hyperactivity disorder, generalized anxiety disorder, substance abuse, and autism.

Panic Disorder

Panic disorder is an anxiety disorder characterized by repeated, unexpected panic attacks. Panic attacks are sudden episodes of intense fear, marked by palpitations, sweating, trembling, shortness of breath, numbness, or a feeling that something terrible will occur. The symptoms increase in intensity and reach their peak within minutes. There may be anxiety about having more episodes, resulting in avoidance of places where the episodes have occurred in the past (APA 2013).

One of methods used to assess autonomic nervous system dysfunction in the etiology of panic disorder is HRV. HRV is controlled by the sympathetic and parasympathetic (vagal) branches of the autonomic nervous system and reflects the capacity for autonomic stimulation by the parasympathetic system. A recent study evaluated HRV time domain parameters based on 24-hour Holter ECG analysis in drug-naive patients with panic disorder without any other medical or psychiatric illness. The study group consisted of 41 PD patients and 46 healthy controls. Hamilton Depression Rating Scale (HDRS), Hamilton Anxiety Rating Scale (HARS), Panic Disorder Severity Scale (PDSS), and Clinical Global Impression Scale (CGI-S) were administered to the participants. 24-hour Holter ECG results were analyzed, and time parameters were evaluated. The data obtained in the study showed a decrease in some HRV parameters reflecting parasympathetic activity in panic disorder patients (Gündüz et al. 2019).

Hong et al. (2022) examined the relationship between depression and HRV indices in patients with panic disorder. A total of 110 patients diagnosed with outpatient panic disorder participated. The medical records of panic disorder patients who applied to the outpatient clinic of Konkuk University Hospital between December 2018 and March 2020 were retrospectively analyzed. Measures used in the study included the Panic Disorder Severity Scale-Self-Report, Beck Depression Inventory (BDI-II), Insomnia Severity Index, and HRV. The results showed that HRV indices decreased in depressed patients, and the low frequency/high frequency (LF/HF) ratio decreased. HRV indices may help detect depressive symptoms in patients with panic disorder (Hong et al. 2022).

Depression

Depressive mood is depression or depression, negative expectations in the face of an event, or the delusion that expectations are going in a negative direction (Lin et al. 2011). In the presence of stress in the body or in the environment that disturbs the person, there is an increase in sympathetic nervous system activity. The sympathetic nervous system plays an active role in low depression, while the parasympathetic nervous system plays an active role in severe depression (Zwart et al. 2019).

Depression occurs in people of all ages in all regions of the world, and its global burden increased by 37.5% between 1990 and 2010. Autonomic changes are often found in altered mood states. Changes in autonomic nervous system functioning that promote vagal withdrawal are reflected in decreases in indices of HRV (HRV). Decreased HRV characterizes emotional dysregulation, reduced psychological flexibility, and defective social engagement, which are linked to prefrontal cortex hypoactivity. This evidence supports the idea that HRV may

represent a useful endophenotype for psychological/physical comorbidities (Sgoifo et al. 2015).

Thayer and Lane (2009) described a model of neurovisceral integration in the context of emotion regulation and dysregulation. According to the authors, emotional regulation is a skill with substantial health implications. HRV is a resource that can be used in situations where emotional regulation is required. The authors reported that individuals with a higher degree of baseline HRV produced context-appropriate emotional responses; further, phasic activations in HRV in response to situations requiring emotional change have facilitated effective emotional regulation.

In other words, the HRV functions as a tool that can be used to modulate emotional activation. Thus, the relationship between HRV and emotional regulation has significant implications for examining the link between physical health and specific emotional states like depression, anxiety, and anger (Thayer and Lane 2009). Other research supports the idea that HRV can be considered an index of individual capacity for psychological flexibility, self-regulation, and social engagement. Kemp et al. (2012) reported that exogenously administered oxytocin, a neuropeptide involved in human social behavior and cognition, can increase resting HRV (Sgoifo et al. 2015).

Bipolar Disorder

Bipolar disorder is a mood disorder characterized by alternating periods of depression and mania, which can range from days to weeks, during which individuals can experience a full range of emotions and return to a normal mood. The common feature of these two phases is that individuals deviate from their usual emotional state, experiencing prolonged and distinctive mood changes (Vahia 2013).

Lee and colleagues (2012) conducted a study to compare HRV in patients with sub-syndromal depressive phases of bipolar disorder to healthy controls and evaluate the relationship between the severity of depressive symptoms and heart rate variability. The study included 33 bipolar patients in sub-syndromal depressive phases and 59 healthy control participants. A patient was considered to be in a sub-syndromal depressive phase if their Montgomery-Åsberg Depression Rating Scale score was ≤ 10 and their Clinical Global Impression-Severity scale (CGI-S) score was ≤ 3 in the past month. After approximately 10 minutes of supine rest, all participants underwent electrocardiograms using limb electrodes for 5 minutes in a supine position. Different parameters of HRV were analyzed in both time and frequency domains. Patients with sub-syndromal depressive phases of bipolar disorder showed a decrease in HRV compared to healthy controls, and this decrease in HRV appears to be associated with the severity of symptoms in bipolar patients (Lee et al. 2012).

Schizophrenia

Schizophrenia, a term deriving from "to split," "to separate," or "to fragment," is a mental disorder characterized by changes and disruptions in an individual's behavior due to disturbances in perception and thinking. These disruptions lead to individuals distancing themselves from the external world that begins to disturb them and constructing an internal reality detached from interpersonal relationships and actuality (Goldner, 2002).

Previous studies have observed reduced vagal modulation in patients with acute schizophrenia and their first-degree relatives, implying a genetic predisposition. Heart rate and respiratory linkage were analyzed to measure central autonomic function in 19 patients, 19 relatives, and 19 matched control subjects to investigate vagal modulation. The interaction between heart rate and respiration, demonstrating asynchrony between the two-time series, was examined using the non-linear cross-ApEn parameter in all groups. Additionally, measurements of the time and frequency domains of HRV were obtained. The results suggest that autonomic dysfunction described in schizophrenia patients is also present in first-degree relatives, possibly related to alterations in brainstem activity among patients and their family members. It can be assumed that patients and family members have a shared genetic background (Berger 2010).

Research on HRV has identified reduced levels of parasympathetic activity among schizophrenia patients. HRV research indicates no abnormality in the initial sympathetic stress response in schizophrenia patients. However, evidence consistently shows that patients have a diminished capacity to recover from a stress response due to their deficiencies in parasympathetic activity. Furthermore, decreased PNS response, also known as reduced vagal tone, is associated with increased symptom severity. These findings suggest that the observed vagal tone disturbance may not solely stem from positive symptomatology but may also be present in non-psychotic relatives of schizophrenia patients. Even though the observed sympathovagal imbalance does not result from abnormally heightened sympathetic nervous system activity among patients, it leads to a general sympathetic

predominance (Montaquila et al. 2015).

Schizophrenia is a psychiatric disorder characterized by a wide range of positive, negative, and cognitive symptoms, along with an increased risk of metabolic syndrome and cardiovascular disease, which reduces life expectancy by 15-20 years. Autonomic dysfunction in the form of increased sympathetic activity and reduced parasympathetic activity is presumed to play a role in the pathophysiology and treatment of schizophrenia. This study aims to examine schizophrenia through an autonomic lens and synthesize evidence relating autonomic dysfunction to various aspects of schizophrenia pathophysiology, including symptom severity, cognitive impairment, and the development of cardiometabolic comorbidities such as metabolic syndrome and high body mass index. The review also suggests ways in which investigating autonomic dysfunction may help reduce morbidity and mortality associated with schizophrenia and its treatment. When compared to psychiatrically healthy controls, patients with schizophrenia have demonstrated reduced HRV and vagal cardiac control. Recent research has shown that HRV is decreased in schizophrenia patients compared to healthy controls and other psychiatric controls, independent of medication, age, or BMI effects. Autonomic dysfunction is a characteristic feature of other psychiatric disorders such as anxiety and mood disorders, but it is most pronounced in psychotic disorders (Stogios et al. 2021).

Post-Traumatic Stress Disorder

Post-Traumatic Stress Disorder (PTSD) is a debilitating psychiatric condition that develops in a group of individuals following a major traumatic event. The estimated global lifetime prevalence of PTSD is approximately 3.9% (Koenen et al., 2017). Diagnostic symptoms of PTSD include intrusive re-experiencing, avoidance, negative alterations in cognition and mood, and hyperarousal. Individuals with PTSD exhibit these symptoms for over a month, accompanied by severe distress and impaired functioning (Brewin 2001).

A meta-analysis has examined autonomic dysfunction indexed by HRV in PTSD. ANS function changes have been observed in various psychological disorders, including PTSD. Previous research on PTSD has found lower HRV in PTSD patients than controls, indicating altered sympathetic and parasympathetic activity, although the findings are inconsistent. This meta-analysis investigated differences in HRV indices between individuals with PTSD, both at baseline and during stress, and healthy controls. It demonstrated an association between PTSD and ANS dysfunction (Schneider and Schwerdtfeger 2020).

In a study examining gender differences in the risk of PTSD, more than 20% of over 7 million American adults and military personnel reported having PTSD, significantly associated with a heightened risk of developing cardiovascular diseases. Women have double the likelihood of developing PTSD after experiencing a traumatic event compared to men. The literature has reported increased sympathetic reactivity, decreased parasympathetic activity, higher inflammation, and autonomic dysfunction in PTSD. However, most of these findings are predominantly based on studies conducted on men. This review examines gender differences in resting and stress-related autonomic dysfunction and inflammation in PTSD. Only a limited number of studies have been conducted on women. Current data suggest an increasing trend in sympathetic nervous system output, diminished parasympathetic activity, and arterial baroreflex sensitivity in women with PTSD. There is also evidence of chronic increases in inflammation among women with PTSD. These autonomic irregularities and inflammation have also been identified in men with PTSD (Fonkoue et al. 2020).

Sleep

The autonomic nervous system plays a significant role in coordinating various physiological functions during sleep. Many untreated patients with sleep disorders will describe symptoms of autonomic dysfunction, and most patients with autonomic dysfunction have some form of sleep disorder. In a study, the current literature on autonomic disturbance in common primary sleep disorders, including obstructive sleep apnea, insomnia, restless legs syndrome, periodic limb movement disorder, narcolepsy, and rapid eye movement sleep behavior disorder, was investigated (Miglis 2016).

As individuals transition from wakefulness to sleep, parasympathetic tone increases, respiration rate slows, and respiration becomes more regular. The Botzinger complex in the lateral medulla is responsible for respiratory sinus arrhythmia. In this normal physiological phenomenon, heart rate accelerates during inspiration to accommodate increased venous return and slows during expiration. This same respiratory sinus arrhythmia is measured in the autonomic laboratory during deep breathing as HRV, an estimate of parasympathetic cardiocardiac tone. Spectral analysis of HRV in the literature typically refers to sympathetic and parasympathetic tone during sleep and is referred to as the sympathovagal balance. High-frequency RR signal (>0.15 Hz) is associated

with increased parasympathetic tone due to vagal respiratory sinus arrhythmia. In contrast, low-frequency RR signals (0.04-0.15 Hz) may be associated with increased sympathetic tone (Miglis, 2016).

Attention Deficit/Hyperactivity Disorder

Attention Deficit/Hyperactivity Disorder (ADHD) is a neurologically based mental disorder. This disorder typically manifests in childhood with symptoms such as inattention and hyperactivity, forgetfulness, impulsivity, sudden and impulsive reactions, and easy distractibility. To diagnose someone with ADHD, the symptoms should be present before age 12, persist for at least six months, and cause problems in at least two different settings (Faraone et al. 2015). Numerous studies have supported the effectiveness and tolerability of stimulants in treating ADHD. However, concerns about their cardiovascular safety have been raised in recent years. A study investigated whether time-domain analysis of HRV recorded in 24-hour electrocardiograms (ECG) could provide new insights into treatment control for ADHD. The study involved 23 children diagnosed with ADHD (19 boys and four girls), 11 of whom were given medication containing methylphenidate (MPH), while 12 children were initially examined without medication. A control group was formed with 19 children (10 boys and nine girls) without any heart or circulatory diseases. It showed significantly reduced HRV and decreased vagal tone with higher heart rates in unmedicated children with ADHD. These autonomic activation parameters improved with MPH (methylphenidate) treatment. No evidence of adverse effects of MPH on HRV was found (Buchhorn 2012).

ADHD is one of childhood's most commonly diagnosed developmental disorders, characterized by hyperactivity, impulsivity, and inattention. ADHD manifests with deficiencies in cognitive, executive, and sensorimotor functions, emotional regulation, and social adaptation in a child's development. According to current knowledge, ADHD is defined as a biological dysfunction in the central nervous system, which is associated with genetic or organic deficiencies in noradrenergic and dopaminergic neurotransmission, particularly in prefronto-striatal regions, where control of attention, arousal, and executive functions is crucial. Altered autonomic regulation is also associated with ADHD (Sekaninova 2019).

Specifically, decreased cardiac-linked parasympathetic activity associated with low HRV might represent relative sympathetic dominance in ADHD. However, the mechanisms underlying altered autonomic regulation in ADHD are not fully understood. In this context, the non-invasive assessment of central autonomic regulation using pupillometry and eye tracking can provide new insights into the neurobiological pathomechanisms underlying ADHD. Pupillary light reflex indexed by pupillometry provides crucial information about the dynamic balance between the sympathetic and parasympathetic branches of the autonomic nervous system. The balance of activity between sympathetic and parasympathetic branches depends on various factors such as genetic influences, age, accommodation status, and light conditions. After standardizing these factors, pupillary diameter measurement can identify deficits in both branches of the autonomic nervous system (Bremner 2009). Therefore, pupillary light reflex offers an optimal model for investigating central autonomic regulation/dysregulation in psychiatric disorders (Mestanikova et al. 2017).

Table 1. Sympathetic-parasympathetic activity in psychiatric disorders		
Disorder	Sympathetic System	Parasympathetic System
Panic Disorder		Inactive
Depression (Low)	Active	
Depression(High)		Active
Bipolar Disorder	Active	
Autism	Active	
Schizophrenia	Active	Inactive
Posttraumatic Stress Disorder	Active	Inactive
Sleep	Inactive	Active
Attention Deficit/Hyperactivity Disorder	Active	Inactive/Active
Generalized Anxiety Disorder	Active	
Substance Addiction	Active	

A study on individuals with ADHD suggests that the autonomic nervous system plays a vital role in attention, self-regulation, emotional stability, and social relationships affected by ADHD. The prefrontal cortex, essential for attention, motor control, emotional regulation, and top-down autonomic control, is hypoactive in ADHD. Additionally, there is catecholaminergic dysregulation. Autonomic dysfunction has been presumed in children with ADHD. Reduced HRV and sympathetic-vagal imbalance were examined. The study included drug-free children with ADHD without any psychiatric/neurological/medical disorders and ranged from both genders

between 7 and 12 years of age. A total of 270 children with ADHD were screened, and ten participated. Short-term HRV in both the time and frequency domains was evaluated after recording the electrocardiogram after administering a behavior-shaping technique called Tell-Show-Do. Autonomic dysfunction was found in children with ADHD. A significant decrease in general HRV and sympathetic dominance was observed in children with ADHD compared to the controls (Rukmani et al. 2016).

ADHD can also be evaluated with respiratory sinus arrhythmia (RSA). RSA, a non-invasive index of parasympathetic cardiac influence, is the high-frequency rhythmic variability in heart rate during the respiratory cycle. Changes that occur in response to environmental factors are termed RSA reactivity. The suppression of RSA (RSA withdrawal) is considered an indicator of self-regulation during challenging tasks (Wang et al. 2013).

Generalized Anxiety Disorder (GAD)

Generalized Anxiety Disorder (GAD) is associated with autonomic dysfunction, notably reduced vagally mediated HRV (vmHRV), and neurostructural abnormalities (Mennin et al. 2008). Regional differences in brain morphometry are associated with vmHRV in healthy individuals. The study tested the hypothesis that focal-specific abnormalities in cortical structure in GAD may reduce vmHRV. It involved adult female patients with GAD (n = 17) and matched controls (n = 18). After characterizing symptoms and determining resting vmHRV levels derived from continuous pulse oximetry, structural magnetic resonance imaging was conducted. A preliminary analysis was conducted on only brain regions responsible for heart rate vagal control. GAD patients showed decreased resting vmHRV compared to controls. In controls, cortical thickness in the left caudal anterior cingulate cortex positively correlated with resting vmHRV. These findings expand evidence of structural abnormalities in regions involved in emotion regulation and cognition in GAD. Additionally, these results suggest that the integrity of the anterior cingulate cortex in GAD may be involved in the psychophysiological expression of GAD, and targeting this area may normalize autonomic function in GAD (Carnevali et al. 2019).

Substance Addiction

A decreased cardiovascular health status has been found in individuals suffering from alcohol addiction. Low cardiorespiratory fitness is considered an independent indicator of cardiovascular disease (Wei et al., 1999). Following ten days of acute alcohol withdrawal, physical fitness and outcomes in 22 alcohol-dependent patients were compared with matched controls. A 6-minute walk test (6 MWT) was used to analyze the relationship between autonomic dysfunction and physical fitness. Ventilation indices and gas exchanges were assessed using a portable spiroergometric system, and heart rate records were obtained. Walking distances, HRV indices, and heart rate and respiration efficiency parameters were calculated. Exhaled carbon monoxide levels were measured in all participants to account for smoking differences. Patients walked significantly shorter distances during the 6 MWT compared to healthy participants. Patients showed a significant decrease in HRV before and after the test compared to controls. However, during exercise, such a difference was not observed. Efficiency parameters showed significantly reduced efficiency in regulating physiological processes when parameters were normalized based on distance. The 6 MWT is an easily applicable tool to measure physical fitness in individuals with alcohol dependence. As seen in this study, the observed decrease in physical fitness may partly result from autonomic dysfunction, potentially leading to less efficient regulation of physiological processes during exercise (Herbsleb et al., 2013).

Autism

The autonomic nervous system regulates the functioning of the heart, bladder, and other bodily functions. When the ANS functions abnormally, individuals may experience physical symptoms such as dizziness, abnormal sweating, and digestive difficulties. Currently, it is unclear whether autistic adults experience ANS dysfunction. Therefore, the study investigated whether autistic adults report more physical symptoms related to the ANS and whether this is associated with autism, anxiety, depression, or stress. The findings suggest that ANS dysfunction observed in autism may result from co-occurring stress and anxiety. They recommended that treating stress and anxiety could effectively improve ANS-related health issues in autistic adults (Taylor et al., 2021).

Conclusion

Autonomic dysfunction is commonly observed in psychiatric disorders. Studies conducted up to the present have raised the question of whether autonomic dysfunction is a cause of psychiatric disorders or if it develops due to these disorders. Autonomic dysfunction occurs not at the onset of psychiatric disporders but during their course.

The progression of autonomic dysfunction can accelerate and exacerbate symptoms. Therefore, autonomic functions should be monitored, potentially leading to a reduction in disease symptoms. Addressing autonomic dysfunction can also help reduce associated morbidity and mortality. Few methods are available in the literature for assessing autonomic dysfunction in psychiatric disorders, indicating a need for further research. More accurate evidence can be obtained with the development of more assessment methods. HRV should be monitored in psychiatric patients. Since decreased HRV characterizes emotional dysregulation, reduced psychological flexibility, and impaired social engagement in psychiatric illnesses, controlling HRV is essential to minimize these conditions. Situations that could potentially be caused by autonomic dysfunction in individuals with psychiatric disorders should not be overlooked.

References

Alvares GA, Quintana DS, Hickie IB, Guastella AJ (2016) Autonomic nervous system dysfunction in psychiatric disorders and the impact of psychotropic medications: a systematic review and meta-analysis. J Psychiatry Neurosci, 41:89–104.

Anderson EA, Sinkey C, Lawton W (1989) Elevated sympathetic nerve activity in borderline hypertensive humans. Evidence from direct intraneural recordings. Hypertension, 14:177-260.

APA (2013) Diagnostic and Statistical Manual of Mental Disorders, 5th ed (DSM-5). Washington DC, American Psychiatric Assocition

Bailey R, Dana D, Bailey E, Davis F (2020) The application of tahe polyvagal theory to high conflict co-parenting cases. Fam Court Rev, 58:525-543.

Beauchaine TP, Gatzke-Kopp L, Mead HK (2007) Polyvagal theory and developmental psychopathology: emotion dysregulation and conduct problems from preschool to adolescence. Biol Psychol, 74:174–258.

Berger S, Boettger MK, Tancer M, Guinjoan SM, Yeragani VK, Bär KJ (2010) Reduced cardiorespiratory coupling indicates suppression of vagal activity in healthy relatives of patients with schizophrenia. Prog Neuropsychopharmacol Biol Psychiatry, 34:406–411.

Bonaz B, Sinniger V, Pellissier S (2016) Vagal tone: effects on sensitivity, motility, and inflammation. Neurogastroenterol Motil, 28:455–462.

Brewin CR (2001) A cognitive neuroscience account of posttraumatic stress disorder and its treatment. Behav Res Ther, 39:373-393.

Buchhorn R, Conzelmann A, Willaschek C, Störk D, Taurines R, Renner TJ (2012) Heart rate variability and methylphenidate in children with ADHD. Atten Defic Hyperact Disord, 4:85–91.

Carnevali L, Mancini M, Koenig J, Makovac E, Watson DR., Meeten F et al. (2019) Cortical morphometric predictors of autonomic dysfunction in generalized anxiety disorder. Auton Neurosci, 217:41–48.

De Zwart, PL, Jeronimus BF, de Jonge P (2019) Empirical evidence for definitions of episode, remission, recovery, relapse and recurrence in depression: a systematic review. Epidemiol Psychiatr Sci, 28:544–562.

Faraone SV, Asherson P, Banaschewski T, Biederman J, Buitelaar JK, Ramos-Quiroga JA et al. (2015) Attention-deficit/hyperactivity disorder. Nat Rev Dis Primers, 1:15020.

Fonkoue IT, Michopoulos V, Park J (2020) Sex differences in post-traumatic stress disorder risk: autonomic control and inflammation. Clin Auton Res, 30:409-421.

Goldner EM, Hsu L, Waraich P, Somers JM (2002) Prevalence and incidence studies of schizophrenic disorders: a systematic review of the literature. Can J Psychiatry, 47:833–876.

Guyton AC, Hall JE, Tuan DXA, Coquery S (2003) Précis de Physiologie Médicale. Paris, Piccin.

Gündüz N, Akpınar Aslan E, Eren F, Sodan Turan H, Öztürk M, Tural Ü (2019) Analysis of 24-hour heart rate variability among panic disorder patients without previous drug treatment and comorbid disorders. Turk Psikiyatri Derg, 30:236–244.

Herbsleb M, Schulz S, Ostermann S, Donath L, Eisenträger D, Puta CW et al. (2013) The relation of autonomic function to physical fitness in patients suffering from alcohol dependence. Drug Alcohol Depend, 132:505–512.

Hong S, Park DH, Ryu SH, Ha JH, Jeon, HJ (2022) Association between heart rate variability indices and depressed mood in patients with panic disorder. Clin Psychopharmacol Neurosci, 20:737–746.

La Rovere MT, Pinna GD, Maestri R (2003) Short-term heart rate variability strongly predicts sudden cardiac death in chronic heart failure patients. Circulation, 107:565-635

Lee JS, Kim B, Hong Y, Joo YH (2012) Heart rate variability in the subsyndromal depressive phase of bipolar disorder. Psychiatry Clin Neurosci, 66:361–366.

Licht CMM, de Geus EJC, van Dyck R, Penninx BW. (2009) Association between anxiety disorders and heart rate variability in The Netherlands Study of Depression and Anxiety (NESDA). Psychosom Med, 71:508-518.

Lin HP, Lin HY, Lin WL, Huang AC (2011) Effects of stress, depression, and their interaction on heart rate, skin conductance, finger temperature, and respiratory rate: sympathetic-parasympathetic hypothesis of stress and depression. J Clin Psychol, 67:1080–1091.

Kemp AH, Quintana DS, Gray MA (2010) Impact of depression and antidepressant treatment on heart rate variability: a review and meta-analysis. Biol Psychiatry, 67:1067-1141.

Koenen KC, Ratanatharathorn A, Ng L (2017) Posttraumatic stress disorder in the world mental health surveys. Psychol Med, 47:2260-2274.

Quintana DS, McGregor IS, Guastella AJ (2013) A meta-analysis on the impact of alcohol dependence on short-term restingstate heart rate variability: implications for cardiovascular risk. Alcohol Clin Exp Res, 37:23-32.

Mennin DS, Heimberg RG, Fresco DM, Ritter MR (2008) Is generalized anxiety disorder an anxiety or mood disorder? Considering multiple factors as we ponder the fate of GAD. Depress Anxiety, 25:289–299.

Miglis MG (2016) Autonomic dysfunction in primary sleep disorders. Sleep Med, 19:40-49.

Mulkey SB, du Plessis AJ (2019) Autonomic nervous system development and its impact on neuropsychiatric outcome. Pediatr Res, 85:120–126.

Montagna A, Nosarti C. (2016) Socio-emotional development following very preterm birth: pathways to psychopathology. Front Psychol, 7:80.

Montaquila JM, Trachik BJ, Bedwell JS (2015) Heart rate variability and vagal tone in schizophrenia: A review. J Psychiatr Res, 69:57–66.

Porges SW, Furman SA. (2011) The early development of the autonomic nervous system provides a neural platform for social behavior: A polyvagal perspective. Infant Child Dev, 20:106–124

Rukmani MR, Seshadri SP, Thennarasu K, Raju TR, Sathyaprabha TN (2016) Heart rate variability in children with attention-deficit/hyperactivity disorder: A pilot study. Ann Neurosci, 23:81–88.

Robson D, Gray R (2007) Serious mental illness and physical health problems: a discussion paper. Int J Nurs Stud, 44:457–466

Schneider M, Schwerdtfeger A (2020) Autonomic dysfunction in posttraumatic stress disorder indexed by heart rate variability: a meta-analysis. Psychol Med, 50:1937–1948.

Sekaninova N, Mestanik M, Mestanikova A, Hamrakova A, Tonhajzerova I. (2019). Novel approach to evaluate central autonomic regulation in attention deficit/hyperactivity disorder (ADHD). Physiol Res, 68:531–545.

Sgoifo A, Carnevali L, Alfonso M deL, Amore M (2015) Autonomic dysfunction and heart rate variability in depression. Stress, 18:343–352.

Stogios N, Gdanski A, Gerretsen P, Chintoh AF, Graff-Guerrero A, Rajji TK et al. (2021) Autonomic nervous system dysfunction in schizophrenia: impact on cognitive and met abolic health. NPJ Schizophr, 7:22.

Taylor EC, Livingston LA, Callan MJ, Ashwin C, Shah P (2021) Autonomic dysfunction in autism: The roles of anxiety, depression, and stress. Autism, 25:744–752.

Thayer JF, Brosschot JF (2005) Psychosomatics and psychopathology: looking up and down from the brain. Psychoneuroendocrinology, 30:1050–1058

Vahia VN (2013) Diagnostic and Statistical Manual Of Mental Disorders 5: A quick glance. Indian J Psychiatry, 55:220–223.

Wang T-S, Huang W-L, Kuo TB, Lee G-S, Yang CC (2013) Inattentive and hyperactive preschool-age boys have lower sympathetic and higher parasympathetic activity. J Physiol Sci, 63:87-94.

Waxenbaum JA, Reddy V, Varacallo M (2023) Anatomy, Autonomic Nervous System. In: StatPearls. Treasure Island (FL), StatPearls Publishing.

Wei M, Kampert JB, Barlow CE, Nichaman MZ, Gibbons LW, Paffenbarger RS et al. (1999) Relationship between low cardiorespiratory fitness and mortality in normal-weight, overweight, and obese men. JAMA, 282:1547–1553.

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