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Autonomic brain functioning and age-related health concerns

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ABSTRACT

The autonomic nervous system (ANS) regulates involuntary bodily functions such as blood pressure, heart rate, breathing, and digestion, in addition to controlling motivation and behavior. In older adults, the ANS is dysregulated, which changes the ability of the ANS to respond to physiological signals, regulate cardiovascular autonomic functionality, diminish gastric motility, and exacerbate sleep problems. For example, a decrease in heart rate variability, or the variation in the interval between heartbeats, is one of the most well-known alterations in the ANS associated with health issues, including cardiovascular diseases and cognitive decline. The inability to perform fundamental activities of daily living and compromising the physiological reactivity or motivational responses of older adults to moving toward or away from specific environmental stimuli are significant negative consequences of chronic and geriatric conditions that pose grave threats to autonomy, health, and well-being. The most updated research has investigated the associations between the action responsiveness of older adults and the maintenance of their physiological and physical health or the development of mental and physical health problems. Once autonomic dysfunction may significantly influence the development of different age-related diseases, including ischemic stroke, cardiovascular disease, and autoimmune diseases, this review aimed to assess the relationship between aging and autonomic functions. The review explored how motivational responses, physiological reactivity, cognitive processes, and lifelong developmental changes associated with aging impact the ANS and contribute to the emergence of health problems.

1. Introduction

The autonomic nervous system (ANS) is a subcategory of the peripheral nervous system (PNS) that coordinates involuntary physiological functions by conducting signals through autonomic neurons from the central nervous system (CNS) to glands, smooth muscles, and cardiac muscle (McCorry, 2007; Gordan et al., 2015; Waxenbaum et al., 2023). The balance, called homeostasis, of these physiological functions, such as heart rate, blood pressure, digestion, and respiration, are maintained by the two distinct branches of ANS, which are the sympathetic nervous system (SNS) and parasympathetic nervous system (PNS) (McCorry, 2007; Gordan et al., 2015; Waxenbaum et al., 2023; Weissman and Mendes, 2021) as illustrated briefly in Fig. 1.

The ANS is dynamic and continuously adapts to internal and external stimuli. It regulates physical and mental health by maintaining the balance between SNS and PNS through a complex interaction of neuronal and hormonal signals (McCorry, 2007; Weissman and Mendes, 2021; Tindle and Tadi, 2023; Green et al., 2017). For example, the "fight or flight" reaction, triggered in response to stress or danger, is frequently linked to the SNS and causes an increase in heart rate, blood pressure, and breathing rate to prepare the body for action (Weissman and Mendes, 2021). However, the PNS is frequently connected to rest and encourages processes like digestion and restoring energy (Weissman and Mendes, 2021; Tindle and Tadi, 2023). The SNS and PNS systems, along with allied systems, including the enteric, vascular, and hemodynamic systems, as shown in Fig. 2, form a complex network of interconnected and interdependent physiological processes (Stratton et al., 1987; Clinic, 2022; Sheng and Zhu, 2018; Lipsitz et al., 1993). For example, the

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sympathetic and enteric systems work together to regulate digestive functions, with the sympathetic system promoting food decomposition and the enteric system regulating food transport through the digestive tract (Lipsitz et al., 1993). In a similar manner, the sympathetic and parasympathetic systems work together to regulate cardiovascular function, with the sympathetic system increasing blood pressure and the parasympathetic system lowering blood pressure. In addition, the vascular and hemodynamic systems, which regulate blood flow and blood pressure, are also intricately connected to how the sympathetic and parasympathetic systems function (Stratton et al., 1987; Clinic, 2022; Sheng and Zhu, 2018; Lipsitz et al., 1993). Consequently, it is essential to understand that the ANS functions in a highly coordinated and interconnected manner to maintain overall physiological homeostasis, despite the fact that dividing the ANS into distinct categories can assist in comprehending the essential functions of these systems.

Autonomic imbalance has been identified as a significant factor in the etiology and clinical progression of several diseases, including mainly cardiovascular diseases (Hadaya and Ardell, 2020). For instance, long-term increases in SNS activity have been linked to hypertension (DeLalio et al., 2020), aortic and ventricular wall thickening (Borovac et al., 2020), endothelial dysfunction (Baqar et al., 2019), and renal failure (Kaur et al., 2017). The National Health and Nutrition Examination Survey and longitudinal aging studies such as the Framingham Heart Study (Burt and Harris, 1994; Mahmood et al., 2014) and the Baltimore Longitudinal Study (AlGhatrif et al., 2013) have revealed a steady increase in systolic blood pressure (systolic hypertension) and a steady decrease in diastolic blood pressure with age (Wang et al., 2023). Cardiovascular diseases are the leading cause of mortality among those aged 65 and older, and hypertension plays at least some role in this manner (Wu et al., 2015). Similarly, a decrease in PNS activity is associated with an increase in the development of arrhythmia and age-related cardiac deaths (Freeling and Li, 2015; Oveisgharan et al., 2022). The ANS is one of the body organs that is dysregulated with advancing age, and the effects of aging on the structures and functions of body organs are illustrated in Fig. 3.

Recent studies have focused on activating ANS through stimuli, motivation, and emotions to initiate behavior or activity (Weissman and Mendes, 2021; Kiryu et al., 2007; Cook and Artino, 2016; Chan et al., 2018a; Scheepers and Knight, 2020). The autonomic nervous activity was calculated by examining the R–R interval time series of the electrocardiogram (ECG) and sensory cues that could activate autonomic nervous activity (ANA). R–R interval is the time elapsed between two successive R waves of the QRS signal on the electrocardiogram. ECG signals were collected during cyclists' workouts for practical investigations. The subject's eye movements were also observed in connection to the image motion vectors as they watched a first-person mountain biking video to carry out virtual exercise studies. The cycling workout outcomes were classified into four unique groups using the ANA to evaluate muscular exertion. They proposed combining muscle activity and post-exercise autonomic nervous system control to evaluate weariness. An unexpected temporal pattern of trigger locations linked to ANA symptoms affected eye movement and elicited negative feelings during the virtual activity (Weissman and Mendes, 2021; Kiryu et al., 2007). Another example was shown that the ANS is the central hub for all emotions and motivated actions. The study assessed parasympathetic and sympathetic nervous system activity by measuring respiratory sinus arrhythmia (RSA), a regular change in heart rate caused by breathing, and pre-ejection period (PEP). A meta-analysis of four trials was conducted to quantify RSA and PEP at rest and during the Trier Social Stress Task, an acute stressor. There were 325 participants, 63% female and aged between 15 and 55. The association between PNS and SNS activity during tasks was measured by modeling the concurrent link between RSA and PEP responses. RSA and PEP have established a mutually beneficial partnership. Once the individual regained their calm, coactivation was observed. The level of communication between the SNS and PNS differs among individuals. There were fewer partnerships among the old females and those with a lower RSA initially, suggesting that the physiological responses of older people may be less synchronized. Individuals with a greater RSA at the beginning of the study and in a younger age bracket exhibited more vital signs of reciprocal coupling (Weissman and Mendes, 2021; Kiryu et al., 2007). Thus, intrusive stimuli activate the SNS and increase the heart rate, blood pressure, and respiration rate to prepare the body for impending threats (Weissman and Mendes, 2021; Kiryu et al., 2007). The SNS system is also activated in competitive or achievement-motivated situations, such as when an individual attempts to win a race or performs well in an interview (Weissman and Mendes, 2021). In contrast, the PNS is active during resting states and certain motivational states involving social bonding, such as seeking a friend (Weissman and Mendes, 2021; Tindle and Tadi, 2023). However, challenge states and threat situations

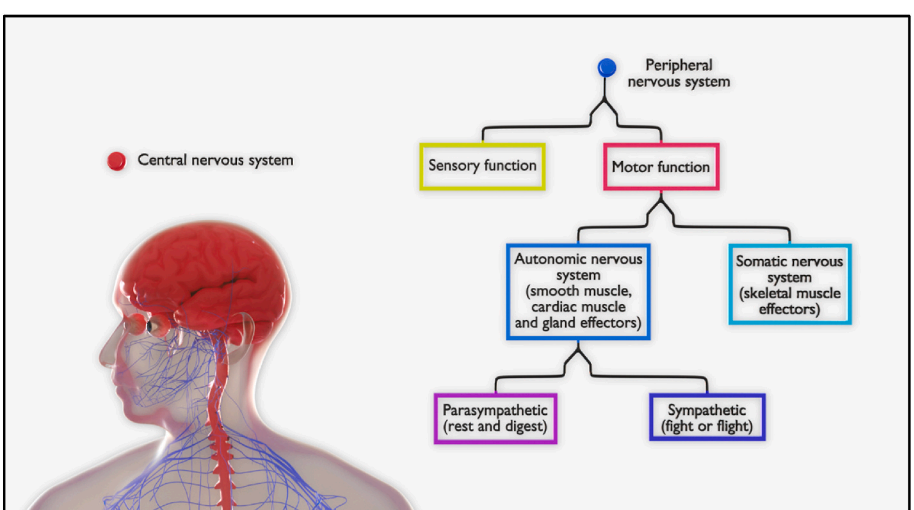

Fig. 1. Major subdivisions of the nervous system. The central nervous system (CNS) comprises of the brain and spinal cord. The brain is responsible for the processing and coordination of information, and the regulation of physiological functions and cognitive processes (McCorry, 2007; Gordan et al., 2015; Waxenbaum et al., 2023; Weissman and Mendes, 2021). The spinal cord facilitates the transmission of signals between the brain and the remainder of the body. The peripheral nervous system (PNS) comprises all nerves and ganglia outside the CNS (McCorry, 2007; Gordan et al., 2015; Waxenbaum et al., 2023; Weissman and Mendes, 2021). The PNS connects the CNS to sensory organs, muscles, and hormones throughout the body, allowing their communication and regulation.

develop psychologically when personal resources are perceived as more than situational requirements. These are accompanied by the aforementioned SNS physiological changes, which include a considerable increase in peripheral vasoconstriction and, as a result, an increase in cardiac output (Cook and Artino, 2016; Chan et al., 2018a; Scheepers and Knight, 2020; Persichini et al., 2022; Cicchetti, 2010; Charkoudian and Rabbitts, 2009). Nonetheless, personalities differ in response to unfamiliar "stressful" situations, with resilient personalities more likely to feel challenged than threatened (Karatsoreos and McEwen, 2013; Kim, 2013). Thus, ANS activity is presently used to assess effort regarding task complexity (typically measured with systolic blood pressure and, to a lesser extent, variations in heart rate) (Ernst, 2017).

Interestingly, the SNS and PNS have been independently attributed to age-related changes in cognitive function (Knight et al., 2020). PNS has been associated with optimal cognitive aging, whereas SNS has been linked to accelerated cognitive decline (Knight et al., 2019). A measure of the SNS's activity was the heart rate variability. Comparatively, the activity of the central nervous system was assessed during two rounds of the Midlife in the United States (MIDUS) cognitive research. The data for this evaluation came from the MIDUS biomarker study, which included 764 individuals, with 56% female and the mean age being 54.1 years. Increased activity in the PNS can prevent cognitive decline in those with low SNS activity. However, this protective effect is lost when SNS activity is intense. Increased levels of the sympathetic nervous system can partially compensate for lower levels of the PNS. The most obvious manifestations of this trend were seen in people between the ages of 35 and 40 who were evaluated for their cognitive abilities for the first time. (Knight et al., 2019; Kelley and Petersen, 2007). These findings imply that, particularly in early midlife, therapies that focus on the ANS as a modifiable component in cognitive aging should take into account the impacts of both ANS branches simultaneously.

In contrast to younger adults, the consequences of failing to initiate or maintain healthy behaviors for older adults are frequently immediate and potentially lethal (Knight et al., 2019; Kelley and Petersen, 2007). Intriguingly, the research indicates that older adults are less likely to initiate behavioral changes but more likely to maintain those that do occur (Knight et al., 2019; Kelley and Petersen, 2007). Emotional distress and cognitive impairment are significant factors that undermine the efforts to make these changes (Knight et al., 2019; Kelley and Petersen, 2007). Mild cognitive impairment refers to a subtle decline in cognitive function, a normal part of aging that typically does not impair daily functioning and independence. On the other hand, dementia is diagnosed when a decline in cognitive ability impairs daily functioning and independence, but it is not considered an inevitable consequence of normal aging. Cognitive impairments types are illustrated in Fig. 4.

In this review article, we discussed how aging-related motivational responses and cognitive processes can impact the ANS and cause health problems.

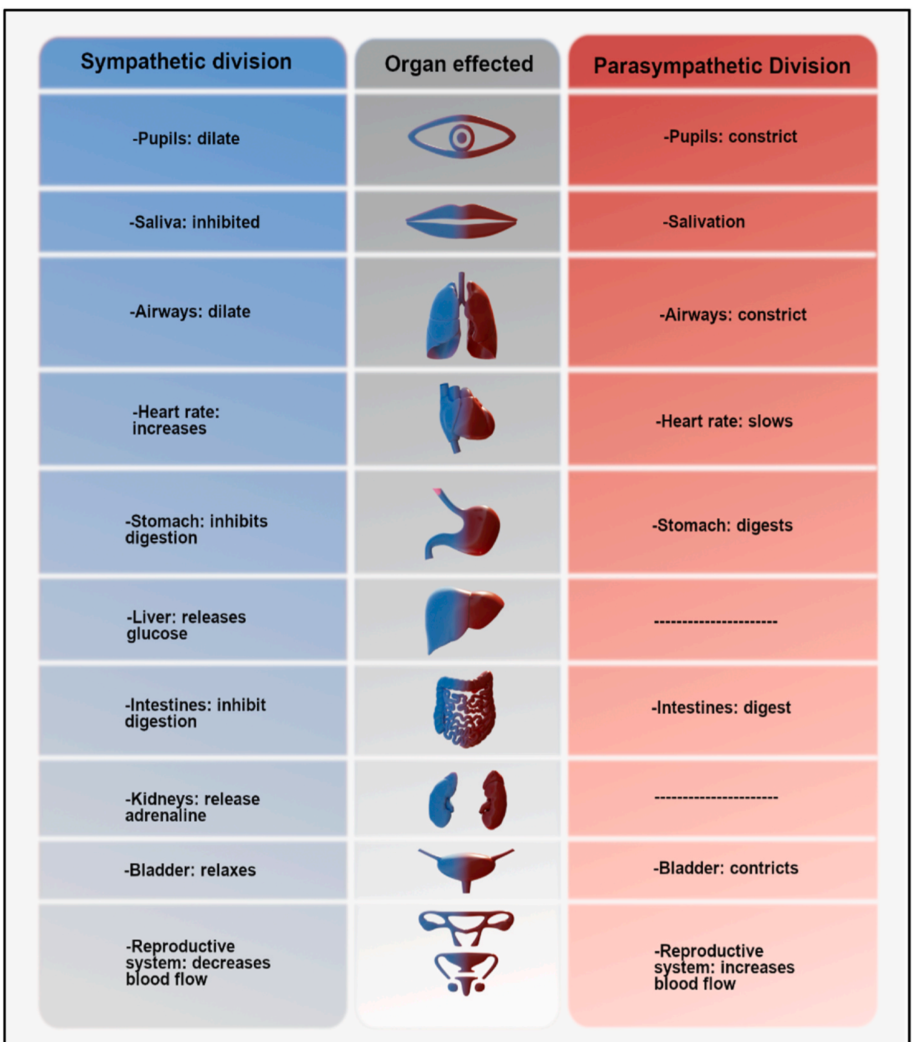

Fig. 2. The SNS and PNS systems along with the enteric, vascular, and hemodynamic systems forms a complex network of interconnected and interdependent physiological processes (Clinic, 2022).

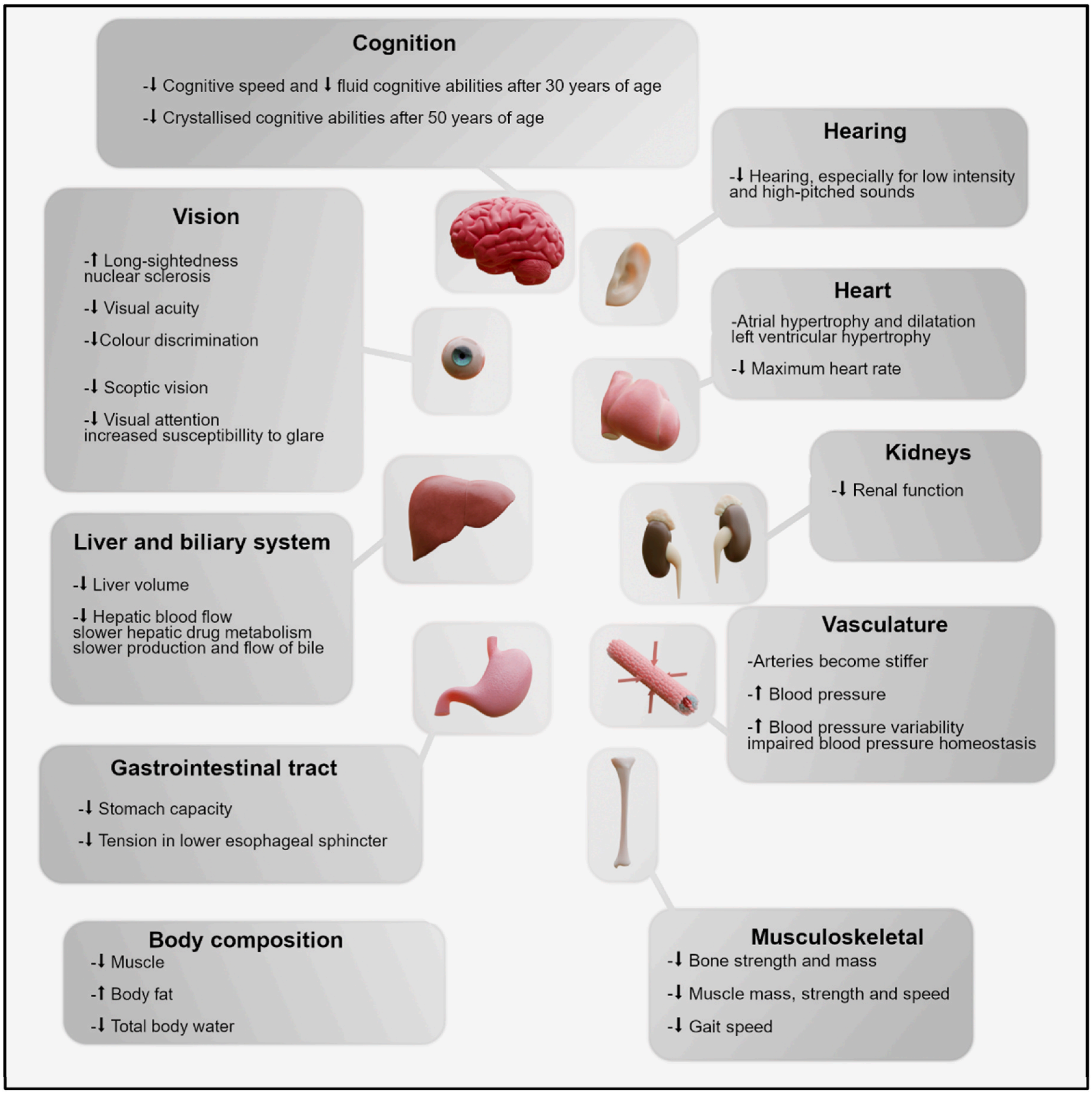

Fig. 3. The effects of normal aging on the structures and functions of body organs (Freeling and Li, 2015; Oveisgharan et al., 2022).

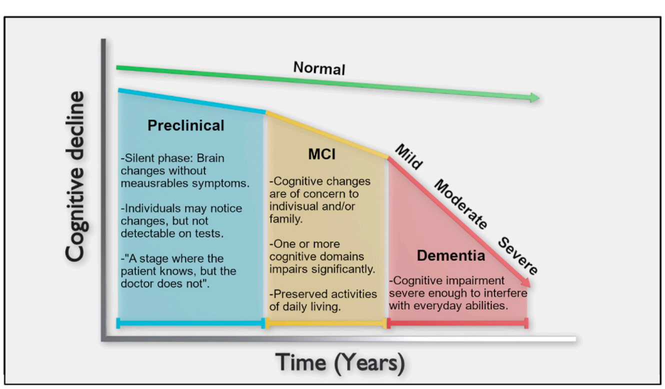

Fig. 4. Types of cognitive impairments (Knight et al., 2019; Kelley and Petersen, 2007).

2. Aging-related motivational and cognitive processes affecting the ANS

Motivating rewards have a substantial impact on both value-based decision-making and cognitive control exercise. A popular science theory states that when people combine different incentives into one currency value signal, they are more likely to act responsibly and make good decisions (Karatsoreos and McEwen, 2013). However, anger eruptions may result from the potential difficulties of aging in regulating and expressing one's emotions and making decisions. There are multiple potential causes for this, including age-related changes in brain function, chronic health conditions, adverse drug reactions, and societal or environmental factors (Karatsoreos and McEwen, 2013).

2.1. Stimulus-to-motivational state cascade

When we are exposed to a stimulus, our brains interpret signals, and spontaneously determine whether to pay attention to or ignore it (Karatsoreos and McEwen, 2013). Researchers frequently attempt to comprehend the neurobiology of motivation by exposing subjects to stimuli that are predicted to elicit a specific motivational response and then interpreting the resulting physiological and neural responses as indicators of a particular motivational reflex (Kim, 2013). Multiple processes influence the stimulus-to-motivational state cascade, altering physiological responses (Kim, 2013). This cascade consists of four processes: stimulus perception, cognition, emotion, and action. The initial phase in the sequence of perceptual processes is stimulus perception (Karatsoreos and McEwen, 2013; Kim, 2013). Individuals interpret stimuli differently based on their attention and prior experiences (Karatsoreos and McEwen, 2013; Kim, 2013). A cognitive process is activated in response to stimulus perception, and emotions play a crucial role in determining the level of motivation generated in response to a stimulus (Karatsoreos and McEwen, 2013; Kim, 2013). Several neurobiological processes, including the release of neurotransmitters, the activation of specific brain regions, and the alteration of hormonal levels, are also engaged in the chain of events that leads to an action.

The stimulus persistence theory states that stimulus has a more prolonged effect on older individuals' nervous systems than younger people (Coyne et al., 1979). Researchers used the Spiral and Waterfall perceptual aftereffect displays to investigate this concept and its relationship with perceptual performance and age. Twenty-four old adults (mean age = 65.5) and twenty-four youthful adults (mean age = 24.8) were given both tasks. Based on the stimulus persistence theory, it was hypothesized that older individuals would experience prolonged aftereffects than younger individuals following each display. No evidence, however, supported this theory (Coyne et al., 1979). Also, the most significant changes in cognition associated with normal aging are declines in performance on tasks that require rapid processing or transformation of information to make decisions (Blair, 2008; Murman, 2015). These tasks include processing speed and executive cognitive function examinations (Blair, 2008; Murman, 2015). Structures and functions of the amygdala and ventromedial prefrontal cortex (vmPFC), a network of regions in the lower medial and orbital prefrontal cortices, are largely unaffected by healthy aging (Dobrushina et al., 2020; Ulus and Aisenberg-Shafran, 2022). However, when elderly individuals are exposed to unpleasant stimuli, the lateral prefrontal cortex (LPFC), which is responsible for cognitive control, decreases in size. Even though learning about rewards is less developed in elderly individuals, their responses to rewarding events do not change (Dobrushina et al., 2020; Ulus and Aisenberg-Shafran, 2022). However, age-related decline in the insular cortex's capacity to aid in interception and emotion imitation

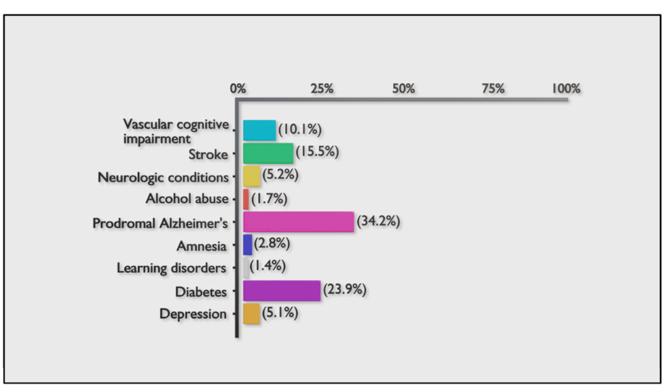

Fig. 5. Potential causes of age-related cognitive declines (Dobrushina et al., 2020; Ulus and Aisenberg-Shafran, 2022). Alzheimer's, Parkinson's and amnesia are neurodegenerative disorders that account for most cases of significant cognitive decline in the older adults. Several chronic diseases that are more prevalent in the older adults, such as diabetes, hypertension, heart disease, and renal disease, can exacerbate cognitive decline. In addition, conditions such as cerebral small vessel disease and stroke can cause decreased blood flow to the brain, impairing cognitive function. Sleep disturbances, persistent tension, and depression can also impair cognitive performance in the older adults.

requires additional research (Dobrushina et al., 2020; Ulus and Aisenberg-Shafran, 2022). The illustrative Fig. 5 highlights the various potential causes of age-related declines in cognitive function and response to any stimulus according to two studies (Dobrushina et al., 2020; Ulus and Aisenberg-Shafran, 2022).

Consequently, understanding the processes of stimulus-to-motivational cascade and the causes of age-related cognitive decline enables researchers to gain a better understanding of how motivation is generated and how it can be altered, as well as the relationships between mental states and neurobiology that change over the course of a person's lifetime.

2.2. Respiratory sinus arrhythmia

A typical example of a stimulus-to-motivational state cascade is the SNS activity that increases the tempo and force of cardiac contractions in response to cognitive changes, emotions, or an increase in metabolic requirements, thereby reducing fluctuations in the duration of contractions (Ernst, 2017). Rapid variations in heart rate between beats are predominantly caused by PNS activity, which is predominant under conditions of rest or relaxation (Yasuma and Hayano, 2004). A RSA is a regular change in heart rate caused by breathing (Temple and Ziegler, 2011; Bush et al., 2011). During normal breathing, the heart rate increases with inhalation and decreases with exhalation, generating a periodic heart rate variability (HRV) pattern. This rhythm is caused by activating the PNS during exhalation and diminishing heart rate, while the deactivation of the PNS during inhalation increases heart rate. Thus, HRV over multiple respiratory cycles is evaluated frequently to diagnose RSA. Greater parasympathetic activity is correlated with enhanced emotional control, social skills, and physical health (Temple and Ziegler, 2011; Bush et al., 2011). In clinical research, RSA is commonly used as a non-invasive indicator of ANS function in various populations, including those with anxiety disorders, depression, autism spectrum disorders, and cardiovascular diseases. Consequently, RSA is used as a stress resilience biomarker and a predictor of medication and psychotherapy treatment response (Temple and Ziegler, 2011; Bush et al., 2011; Allen et al., 2000).

RSA frequently measures phasic vagal cardiac regulation, comprises a significant proportion of total HRV, and typically begins to decline around age 20 (Tonhajzerova et al., 2016; Suurland et al., 2018). Cardiac vagal responses are variations in heart rate that the vagus nerve, also called vagal tone, regulates and promotes during rest or relaxation (Tonhajzerova et al., 2016; Suurland et al., 2018; Porges, 2009). Recent research has linked higher vagal tone levels to enhanced cardiovascular function and emotional regulation (Tonhajzerova et al., 2016; Suurland et al., 2018; Porges, 2009). In addition, a more recent research identifies some variables, such as tension, anxiety, and physical activity, that may influence cardiac vagal responses (Suurland et al., 2018; Porges, 2009). For example, anxiety and stress can decrease vagal tone and increase heart rate. One method for measuring cardiac vagal responses is the analysis of the beat-to-beat variations in heart rate over time.

Consequently, RSA is a non-invasive method for evaluating the effectiveness of the ANS (Tonhajzerova et al., 2016; Suurland et al., 2018; Porges, 2009), and it was predicted that middle-aged individuals would have higher resting heart rates and lower resting levels of RSA than young adults (Kim, 2013; Hill et al., 2015; Christou and Seals, 1985; Mathewson et al., 2010). Moreover, it was discovered that aging is associated with a more significant task-related decline in RSA and HRV and an increase in heart rate (Christou and Seals, 1985; Mathewson et al., 2010). Individual differences in ANS reactivity are increasingly considered crucial risk factors for developing mental and physical health disorders as people age (Mathewson et al., 2010; van Beek et al., 2016).

2.3. Period of isovolumetric contraction

In cardiology, the term "period of isovolumetric contraction," or

PEP, characterizes a heart cycle phase. During the cardiac cycle, the heart undergoes a series of contractions and relaxations that permit it to circulate blood throughout the body (Temple and Ziegler, 2011; Allen et al., 2000). PEP is characterized by the contraction of the heart's ventricles when the internal pressure is insufficient for the aortic and pulmonary valves to release. It also refers to the duration between the beginning of ventricular depolarization and the beginning of left ventricular ejection (Temple and Ziegler, 2011; Allen et al., 2000). During the PEP phase, the heart attempts to generate sufficient pressure to force blood through the aortic and pulmonary valves against resistance (Temple and Ziegler, 2011; Allen et al., 2000). This stage is defined as "isovolumetric" because there is no blood ejection, and the blood volume within the ventricles remains constant (Ulus and Aisenberg-Shafran, 2022; Yasuma and Hayano, 2004). Multiple non-invasive techniques, such as echocardiography and cardiography, can determine PEP, a standard measure of cardiac function and contractility (Temple and Ziegler, 2011; Allen et al., 2000). Consequently, PEP anomalies may indicate various cardiac diseases, including myocardial ischemia, heart failure, and valve disease (Temple and Ziegler, 2011; Allen et al., 2000).

As pointed out, In the ANS, which innervates the entire body and influences virtually all physiological systems, general health, and well-being, aging is associated with structural and functional alterations (van Beek et al., 2016; Pal et al., 2014; Shimazu et al., 2005). As individuals age, their PNS activity decreases, and their SNS activity increases, which increases their risk of developing hypertension, metabolic disorders, and cognitive decline (Shimazu et al., 2005; Moodithaya and Avadhany, 2012). Numerous factors, such as increased SNS activity and PEP and decreased HRV and RSA, can negatively impact cardiovascular function as we age (van Beek et al., 2016; Pal et al., 2014; Shimazu et al., 2005; Moodithaya and Avadhany, 2012; Liu et al., 2019). Chronic medical conditions, diet, exercise, and stress may also impact cardiovascular health and alter PEP and RSA with age (Christou and Seals, 1985; Parashar et al., 2016; Visch et al., 2014; Masi et al., 2007; Barzeva et al., 2019; Sato et al., 2005; Pham et al., 2021; Okon-Singer et al., 2015; Izard, 2009; Mulkey and du Plessis, 2019). Generally speaking, more youthful individuals have a higher RSA and a lower PEP than older adults (van Beek et al., 2016; Pal et al., 2014; Shimazu et al., 2005; Moodithaya and Avadhany, 2012; Liu et al., 2019; Parashar et al., 2016; Visch et al., 2014; Masi et al., 2007; Barzeva et al., 2019; Forte et al., 2021). Therefore, middle-aged adults may be better at decision-making than older adults when confronted with high-frequency heart rate variability and enhanced autonomic responsiveness (Christou and Seals, 1985; Parashar et al., 2016; Visch et al., 2014; Masi et al., 2007; Barzeva et al., 2019; Mulkey and du Plessis, 2019; Forte et al., 2021). As opposed to baseline levels or alterations in autonomic reactivity (Mulkey and du Plessis, 2019), on-task autonomic measures typically exhibit inverse relationships. For example, more accurate performance was associated with higher pulse rates, lower levels of RSA, and lower baroreflex sensitivity, a measurement of the degree to which the baroreceptor reflex controls the heart rate (Allen et al., 2000; Sato et al., 2005). In contrast, as aging progresses, a decreased heart rate, higher levels of RSA, and greater baroreflex sensitivity were associated with more errors (Sato et al., 2005; Pham et al., 2021).

In addition, a stress test revealed that middle-aged individuals had higher cardiac vagal tone than older adults, which may indicate a larger capacity to control emotional responses (Christou and Seals, 1985; Parashar et al., 2016; Visch et al., 2014; Masi et al., 2007; Barzeva et al., 2019; Mulkey and du Plessis, 2019; Forte et al., 2021). Intent, uncontrollable wrath is typically accompanied by abnormally extreme emotional and physical responses, and it can be caused by various factors, including dissatisfaction, anger, feeling threatened by loved ones, and a sense of injustice (Parashar et al., 2016; Visch et al., 2014; Mulkey and du Plessis, 2019). These factors can cause a rise in heart rate, blood pressure, and the production of stress hormones such as cortisol and adrenaline, and can be detrimental to the health and well-being of all individuals, especially older adults (Parashar et al., 2016; Visch et al., 2014; Masi et al., 2007; Mulkey and du Plessis, 2019). Aging may also impair a person's ability to regulate and express their emotions, thereby increasing the likelihood of rage. This could be caused by various factors, including aging-related changes in brain function, persistent medical conditions, adverse pharmacological effects, and social or environmental pressures (Parashar et al., 2016; Visch et al., 2014; Masi et al., 2007; Mulkey and du Plessis, 2019). Therefore, older adults should prioritize their mental and emotional health even when receiving assistance from family members and other valued ones, engaging in activities that promote relaxation and mindfulness, and developing coping strategies to manage furious or frustrated emotions.

2.4. Relations of emotions and motivation with brain neurobiology

Emotions and the neurobiology of the brain are intrinsically linked (Okon-Singer et al., 2015). The experience of emotions triggers the release of numerous neurotransmitters and hormones and the activation of specific brain regions, such as the prefrontal cortex, associated with decision-making and emotion regulation, and the amygdala, a small almond-shaped brain region, is believed responsible for processing fear and anxiety (Okon-Singer et al., 2015; Izard, 2009; Šimić et al., 2021). Dopamine, serotonin, and norepinephrine are neurotransmitters that regulate cognition and emotional responses, with low serotonin levels associated with depression and high dopamine levels associated with reward and pleasure. Moreover, tension triggers the release of hormones such as cortisol and adrenaline, which can influence the emotional state (Okon-Singer et al., 2015). These neurobiological mechanisms, in conjunction with the environment, past experiences, and cognitive processes, influence our emotional responses to various events.

The "fundamental emotions" have long been disputed by researchers (Izard, 2009). Every primary emotion, such as anger, fear, pleasure, sadness, contempt, and surprise, is associated with a unique pattern of physiological responses in the body. Generally, approach-oriented emotional states are more likely to activate SNS than emotional situations in which mobilization of energy reserves is not anticipated (Weissman and Mendes, 2021; Šimić et al., 2021). According to a study, anger is associated with producing adrenaline and other stress hormones, such as an elevated heart rate, blood pressure, and muscle tension. There is a correlation between fear and high heart rate, blood pressure, perspiration, and amygdala activity (Šimić et al., 2021). When we are joyful, endorphins, or "feel-good" chemicals, are released, and the reward and pleasure centers of the brain become more active (Šimić et al., 2021; Dfarhud et al., 2014; Paulus et al., 2013). Sadness is associated with increased activity in regions associated with processing negative emotions and decreased activity in these regions (Šimić et al., 2021; Dfarhud et al., 2014; Paulus et al., 2013). It is essential to keep in mind that there is disagreement regarding the concept of "fundamental emotions" and whether or not they have widely accepted physiological patterns. According to some experts, emotions are more nuanced and context-dependent, and there may be substantial cultural and individual differences in how people perceive and demonstrate different emotions.

The concept of active versus passive circumstances is one method for highlighting the distinctions between emotion and motivation (Dfarhud et al., 2014; Paulus et al., 2013). Frequently, emotions are regarded as passive responses to events or stimuli from the outside world or as a response to another person's suffering (i.e., observed rather than experienced) affecting the individual directly. In contrast, motivation is typically conceived of as an active process driven by internal objectives or desires, such as watching movies that elicit emotions, peering at still images of emotions, and observing the emotions of others (Dfarhud et al., 2014; Paulus et al., 2013; Jääskeläinen et al., 2022). Additionally, motivation and feelings frequently influence and influence one another, such as having a goal to work toward can generate excitement and anticipation; intense emotions such as rage can motivate someone to act to better a situation (Dfarhud et al., 2014; Paulus et al., 2013;

Jääskeläinen et al., 2022). Thus, active and passive situations can provide a valuable foundation for comprehending the complex interactions between our emotions and motivations.

Psychophysiological theory studies the relationship between psychological processes and bodily physiological responses (Wu et al., 2020; Goldfine and Schiff, 2011; Hoffmann et al., 2018). It asserts that emotions, thoughts, and other mental states cause physical changes in the body, which affect our perception of the world. For example, when we experience a strong emotion, such as fear, our brain transmits messages to the ANS, which triggers physiological responses such as an increased heart rate, perspiration, and tense muscles. Therefore, our affective experience may be enhanced by the brain's ability to receive feedback from these physiological changes. This generalization, however, does not specify which physiological system or systems are involved, the direction of the change, the duration of the change, or whether the mental state must be conscious or can exist below conscious awareness (Wu et al., 2020; Goldfine and Schiff, 2011). Psychology, neuroscience, and medicine are a few disciplines that have utilized psychophysiological theory (Hoffmann et al., 2018). Activation of the hypothalamic-pituitary-adrenal axis (HPA) can occur, for example, during prolonged mental endeavors and extreme events (Herman et al., 2016). HPA controls various physiological functions, including metabolism, immunological responses, and the ANS. In response to particular negative feedback loops, the hypothalamus, anterior pituitary gland, and adrenal gland form the HPA axis, a network of endocrine pathways (Herman et al., 2016). The hippocampus and pituitary glands control the release of glucocorticoids (GC). GCs help maintain internal balance and assist the body in recovering from mental and physical stress. Cortisol production mainly occurs in the adrenal cortex, serving as the main glucocorticoid in humans. It is released into the bloodstream periodically and rhythmically (Herman et al., 2016). Similarly, SNS activation can occur in states of approach-oriented motivation, such as anxiety and avoidance (Salamone et al., 2015).

Even though psychophysiological theory asserts that psychological processes can cause physiological reactions in the body (Hoffmann et al., 2018; Simpson and Balsam, 2016), the mere occurrence of physiological changes does not necessarily indicate a motivational state. For example, an elevated heart rate and profuse sweating may show anxiety when confronted with a dangerous animal. The exact physiological alterations can also result from physical activity or heat exposure (McCorry, 2007; Braver et al., 2014). Moreover, psychological processes may occur without a discernible physical response (Braver et al., 2014). For example, a person may feel guilty or ashamed without noticing a change in their pulse rate or blood pressure, and gastrointestinal contractions may decrease when exposed to stressful conditions (Braver et al., 2014). Using psychophysiological measures, the relationship between psychological processes and physiological reactions can be studied (Hoffmann et al., 2018; Braver et al., 2014). Nonetheless, it is essential to interpret these measurements in the context of the individual and the specific situation. Therefore, it is essential to consider the environment and other psychological elements when evaluating physiological responses.

Several psychophysiological perspectives on aging assert that age-related alterations in the physical body may impact psychological functioning (Hoffmann et al., 2018; Dziechciaż and Filip, 2014). The socioemotional selectivity theory, one of the most well-known theories, asserts that as individuals age, they become less interested in acquiring new knowledge or experiences and more focused on emotionally gratifying relationships and experiences (Hoffmann et al., 2018; Dziechciaż and Filip, 2014). According to this hypothesis, brain and body changes associated with aging may increase our sensitivity to emotional events and interpersonal relationships (Hoffmann et al., 2018; Dziechciaż and Filip, 2014). The biopsychosocial model, which proposes that biological, psychological, and social factors interact intricately to cause aging (Hoffmann et al., 2018; Dziechciaż and Filip, 2014), is another theory used to explain aging. According to this hypothesis, changes in the immune system or hormone levels can affect the brain and social interactions. Last but not least, the neurocognitive aging theory posits that declines in cognitive function, such as memory, attention, and reasoning speed, can result from aging-related changes in the brain (Hoffmann et al., 2018; Dziechciaż and Filip, 2014). According to this hypothesis, changes in the brain associated with aging can influence how psychological processes function and individuals interact (Hoffmann et al., 2018; Dziechciaż and Filip, 2014).

Psychophysiological theory can, in general, explain how aging-related physical changes may influence psychological performance and interpersonal relationships. These concepts will aid researchers in comprehending the complex relationships between the mind and body as we age.

2.5. Relations of stress with brain neurobiology

The major causes of stress that people encounter daily are often referred to as "principal stress systems" in the context of human physiology. Many theories use these biological systems as the starting point of stress experiences and interpretation, and stress research likewise uses biological reactions as a critical source of assessment (Barzeva et al., 2019). For instance, the two biological systems referred to as the principal stress systems are the hypothalamic-pituitary-gonadal axis (HPG) and the HPA (Shirtcliff et al., 2015; Tarter et al., 2013). The HPG axis primarily regulates reproduction and hormone secretion in the ovaries in humans and other animals. This axis functions under elevated stress, leading to a reduced amplitude of the gonadotropin-releasing hormone (GnRH) pulse. Cortisol decreases the intensity of the Luteinizing Hormone (LH) pulse by affecting how the pituitary gland responds to GnRH. Increased stress leads to elevated testosterone levels in individuals. Stress also shortens the menstrual cycle duration but does not affect other aspects of the cycle (Shirtcliff et al., 2015; Tarter et al., 2013). Cortisol, the HPA system's end product, is often measured with reliability from blood, saliva, and urine (Tarter et al., 2013). The signals that cause the production of cortisol from the anterior pituitary glands is the release of corticotrophin-releasing hormone (CRH) at the hypothalamus (Tarter et al., 2013). A meta-analysis of 208 research studies revealed the stress situations and social communication that most consistently caused a rise in cortisol (Tarter et al., 2013; Wirth et al., 2011). Although cortisol is sometimes referred to as the "stress hormone, " contrary to what the term "stress" may imply, cortisol elevations do not always correlate with unpleasant emotions (Wirth et al., 2011). Instead, intellectually challenging and vigorous tasks that promote approach behavior might cause cortisol levels to rise (Wirth et al., 2011). To quantify the impacts of stress better, distinguishing "positive stress" from "negative stress" and developing a composite index across biological systems would be helpful.

The primary stress systems widely acknowledged are physical, social, cognitive, and biological stresses (Dziechciaż and Filip, 2014; Shirtcliff et al., 2015; Tarter et al., 2013; Wirth et al., 2011; Smith and Vale, 2006; Sandi and Pinelo-Nava, 2007; Epel et al., 2018; Tan and Yip, 2018). Psychological stress is the emotional and mental stress that people go through in response to many life occurrences and circumstances, such as job-related stress, financial hardships, or relationship issues (Dziechciaż and Filip, 2014; Shirtcliff et al., 2015; Tarter et al., 2013; Wirth et al., 2011; Smith and Vale, 2006; Sandi and Pinelo-Nava, 2007; Epel et al., 2018; Tan and Yip, 2018). Physical stress refers to the stress the body feels due to physical exertion or exposure to environmental variables, such as temperature extremes or toxins (Dziechciaż and Filip, 2014; Shirtcliff et al., 2015; Tarter et al., 2013; Wirth et al., 2011; Smith and Vale, 2006; Sandi and Pinelo-Nava, 2007; Epel et al., 2018; Tan and Yip, 2018). Social stress is the stress people encounter in their connections, such as family members, friends, coworkers, and strangers (Dziechciaż and Filip, 2014; Shirtcliff et al., 2015; Tarter et al., 2013; Wirth et al., 2011; Smith and Vale, 2006; Sandi and Pinelo-Nava, 2007; Epel et al., 2018; Tan and Yip, 2018). Cognitive stress is pressure from excessive mental demands, such as multitasking, making decisions, or solving problems. Finally, biological stress describes the physiological reactions in the body in response to various stressors, such as the production of stress hormones or changes in heart rate and blood pressure (Dziechciaż and Filip, 2014; Shirtcliff et al., 2015; Tarter et al., 2013; Wirth et al., 2011; Smith and Vale, 2006; Sandi and Pinelo-Nava, 2007; Epel et al., 2018; Tan and Yip, 2018).

Hans Selye, a scientist widely regarded as the father of stress research, introduced the idea of positive stress, a favorable outcome resulting from environmental stressors while negative stress can cause severe mental and physical health issues (Tan and Yip, 2018). He suggested examining catabolic and anabolic hormones in response to stress as part of a thorough stress strategy (Shirtcliff et al., 2015; Tarter et al., 2013; Demling, 2005; Kraemer et al., 2020). When under stress, the body releases catabolic hormones like cortisol and adrenaline, which encourage the breakdown of complex molecules to produce energy (Shirtcliff et al., 2015; Tarter et al., 2013; Demling, 2005; Kraemer et al., 2020). However, persistent activation of the catabolic stress response can harm the body, impairing immunological response, lowering bone density, and raising the risk of cardiovascular disease, among other adverse effects. Contrarily, anabolic hormones encourage the body's creation and storage of complex substances, including glycogen, insulin, growth hormone, and testosterone (Shirtcliff et al., 2015; Tarter et al., 2013; Demling, 2005; Kraemer et al., 2020). These hormones assist bodily tissue growth, development, regrowth, and repair. Therefore, analyzing the ratio of catabolic to anabolic hormones in the body's response to stress is vital to a thorough stress strategy. Persistent stimulation of the catabolic stress response can decrease the activity of the anabolic hormones, which can cause an imbalance between these hormones (Anker et al., 1997). However, the balance between catabolic and anabolic hormones can be restored through stress-reduction tactics, such as mindfulness exercises and relaxation techniques, thus enhancing general health and well-being (Demling, 2005; Kraemer et al., 2020; Anker et al., 1997).

The biological variables—such as resting systolic and diastolic blood pressure, body mass index (BMI), glycated hemoglobin (HbA1c), albumin, creatinine clearance, triglycerides, C-reactive protein (CRP), homocysteine, and total cholesterol—can be used to create a composite stress score (Lateef et al., 2020; Crews, 2007). For instance, psychosocial stress, including perceived and life event stress, was positively associated with weight gain but not weight loss. The found relationships were shaped in part by age, smoking, obesity, and other stresses. Although some evidence suggests a connection, the exact nature of the association between stress and HbA1c in diabetes outcomes is still unclear. People dealing with high levels of stress as a result of their type 2 diabetes may find that exercise helps them manage their disease (Lateef et al., 2020; Crews, 2007). Therefore, an individual's general health status, and the impact of stress on different physiological systems can be assessed more thoroughly when using a composite stress score through the mentioned biological variables (Lateef et al., 2020; Crews, 2007). Each biological parameter used to calculate the composite score offers data on various facets of a person's health, including blood pressure, glucose control, renal function, and inflammation. Each parameter is given a weighted score based on its relative significance in predicting health outcomes, which is used to calculate the composite score (Lateef et al., 2020; Crews, 2007; Dennis, 2010; Gyurak et al., 2011; McDuff et al., 2020). A total composite score is created by adding the weighted scores, and thus it can be used to evaluate a person's general health and risk of developing chronic conditions (Lateef et al., 2020; Crews, 2007; Dennis, 2010; Gyurak et al., 2011; McDuff et al., 2020). Thus, a composite stress score offers a more thorough assessment of the influence of stress on physiological functioning, and can be particularly helpful in research investigations looking at the association between stress and health outcomes (Lateef et al., 2020; Crews, 2007; Dennis, 2010; Gyurak et al., 2011; McDuff et al., 2020).

Additionally, it can be a helpful instrument for physicians in determining a person's risk for developing chronic illnesses and creating individualized treatment regimens with advancing age (Lateef et al., 2020; Crews, 2007; Dennis, 2010; Gyurak et al., 2011; McDuff et al., 2020; Gaffey et al., 2016). Chronic stress can raise oxidative stress, cellular damage, and inflammation, which can hasten the onset of age-related illnesses like cardiovascular disease, diabetes, and cognitive decline (Lateef et al., 2020; Crews, 2007; Dennis, 2010; Gyurak et al., 2011; McDuff et al., 2020; Gaffey et al., 2016). An individual's risk for acquiring these age-related diseases can be determined by a composite stress score considering variables including blood pressure, BMI, HbA1c, and CRP (Lateef et al., 2020; Gaffey et al., 2016). For instance, elevated levels of HbA1c links to an increased risk of diabetes, whereas high levels of CRP links to an increased risk of cardiovascular diseases (Lateef et al., 2020; Gaffey et al., 2016). In addition, variations in the stress response system, such as changes in cortisol levels and SNS activity, have been linked to age-related reductions in cognitive function and exercising ability (Lateef et al., 2020; Crews, 2007; Dennis, 2010; Gyurak et al., 2011; McDuff et al., 2020; Gaffey et al., 2016). Overall, a composite stress score can be a valuable tool for determining how stress affects aging and age-related health consequences, and researchers and healthcare practitioners can create targeted therapies to promote healthy aging.

On the other hand, stress at work may shorten telomeres, which are located at the ends of chromosomes and are essential for preserving the genome's stability, in people who are becoming older (Epel et al., 2004; Victorelli and Passos, 2017). As cells proliferate, telomeres naturally shorten with aging, and shorter telomeres have been linked to some age-related diseases and health issues (Epel et al., 2004).

Therefore, to better assess the effects of stress on older adults, it would be advantageous to distinguish between "positive stress" and "negative stress" that may occur with advancing age and to develop a composite index for those individuals that includes all biological systems.

2.6. Relations of social factors with brain neurobiology

Social factors (e.g., social engagement) and personality traits (e.g., optimism, bonding, compassion) can modulate cardiac vagal responses (Geisler et al., 2013). Sociocultural factors can substantially alter how motivation is perceived and valued and how this impacts the neurobiology of the brain (Kim, 2013). Cultural norms and expectations can influence how individuals perceive and value motivation, thereby influencing the brain mechanisms that underlie motivation and reward processing (Hinsz et al., 2019; Valori et al., 2022). For instance, ships carry goods for most countries with ports and access to maritime routes. However, the captain can hail from Saudi Arabia, the chief engineer from Italy, the main chef from Canada, and the deck officers from Panama and Spain. Several conditions must be satisfied for this multicultural crew to transport their goods securely and on time. Members are expected to complete their respective jobs, collaborate, and address any challenges that may arise due to diversity. Members will have to learn new things and how to deal with other cultures because of all the demands placed on them (Hinsz et al., 2019; Valori et al., 2022). For example, cultural ideals of success and achievement can influence how individuals perceive and evaluate motivation for success. People may value motivated behavior more and experience greater neural reward responses when they achieve their objectives and/or in cultures emphasizing achievement and success (Corker et al., 2013). In other cultures, collectivist beliefs may place greater importance on interpersonal connections than individual success, influencing how individuals perceive and value motivated behavior (Triandis, 2001). Sociocultural factors may also affect how individuals respond to stress and adversity, influencing motivation and the neural systems that regulate it (Ozbay et al., 2007; Telzer et al., 2021). The functioning of the brain systems that regulate motivation and reward processing may be affected, for example, by discrimination or social marginalization, resulting in increased stress and decreased motivation in specific individuals (Kim, 2013; Hinsz et al., 2019; Valori et al., 2022; Corker et al., 2013; Triandis, 2001; Ozbay et al., 2007; Telzer et al., 2021). Consequently, it is essential to consider the diverse cultural contexts in which people live and work when designing interventions and therapies.

A growing body of evidence suggests that social factors such as social support, socioeconomic status, and education may substantially affect brain neurobiology and aging (Chan et al., 2018b). According to studies (Chan et al., 2018b; Chen et al., 2019), those with a higher level of education have a superior cognitive function and are less likely to experience cognitive decline as they age. This may be due to the correlation between education and cognitive reserve or the brain's capacity to adapt to injury or illness. Comparing individuals with higher socioeconomic status to those with lower socioeconomic status, it is common to discover that those with higher socioeconomic status have larger brain volumes and superior cognitive function (Yu et al., 2018). Therefore, when treating various chronic diseases and geriatric issues, it is essential to consider the sociocultural factors and personality traits.

3. Conclusions

The aging of the ANS can have complex and variable effects on physiological functions and health outcomes. Besides regulating blood pressure, heart rate, respiration, and digestion, the ANS regulates motivation and behavior. Age-related ANS dysregulation modifies the capacity of the ANS to respond to physiological stimuli. It causes chronic and geriatric conditions that pose serious risks to older adults' autonomy, health, and well-being. A comprehensive strategy consisting of healthcare services, therapy, assistive technology, lifestyle modifications, and social support is required to address these challenges and assist older adults in maintaining their independence and quality of life. Researchers continue to examine these alterations to determine how they influence aging and how to control or mitigate them to promote healthy aging. Multiple limitations to this review require careful thought as causal links cannot be established in a narrative review, and the data used in this study comes from some earlier studies that used very tiny sample sizes. More comprehensive studies are required to confirm the findings. Further research is also needed to explore cardiac stimulation to address early-stage autonomic imbalance in healthy elderly adults by monitoring heart rate variability, as recent studies show. It would be wise to contribute to further research in this sector.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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