REVIEW ARTICLE

The Mental Health from the Self-Regulation Perspective; What Research on Heart Rate Variability Revealed about the Interaction between Self-Regulation and Executive Attention Dysfunction In Acute Kidney Injury And Sex-Specific Implications

Author:

Gewnhi Park

Author's affiliation:

Department of Psychology, Azusa Pacific University, Azusa, California, USA. Email: gpark@apu.edu

ABSTRACT

Dysfunctional self-regulation has been proposed to be the hallmark of almost all types of poor mental health. Although many prominent researchers have emphasized the role that executive attention control plays in self-regulation, the link between the two in mental health has been less apparent. According to the neurovisceral integration model, cardiac vagal tone, which refers to the parasympathetic influence on the heart at rest, can indicate the functional integrity of selfregulatory systems. A series of recent experiments demonstrate how individual differences in cardiac vagal tone indexed by heart rate variability (HRV) were associated with a varying degree of attentional control to emotional stimuli. The current paper reviewed recent research findings that showed how HRV modulated key components of executive control. These new findings provide evidence linking self-regulatory capacity and executive control, which may play an important role in supporting healthy mental health.

American Psychiatric Association defines mental illnesses as "health conditions involving changes in emotion, thinking or behavior (or a combination of these). Mental illnesses are associated with distress and/or problems functioning in social, work or family activities." ² Unfortunately, the number of people affected by mental illness is staggering and increasing at an alarming rate. According to the American Psychiatric Association ², nearly one in five (19 percent) U.S. adults experience some form of mental illness in a given year. One in 24 (4.1 percent) percent of individuals are being diagnosed with debilitating mental illnesses such as schizophrenia, bipolar disorder, or major depression and one in 12 (8.5 percent) with a substance use disorder.

There is a growing body of literature showing that dysfunctional self-regulation is one of the important contributing factors of the etiology and maintenance of various mental illness. ^{1, 2-6} Self-regulation refers to the ability to regulate cognition, emotion, and behavior to make an adaptive response to meet constantly changing environmental demands, which has been recognized as a key concept that helps understand human development and psychopathologies. ^{1, 7-9, 10-11} Of particular interest is the link between attention and self-regulation. Attention involves selecting and focusing on information, which shapes and guides thoughts and actions. ^{10, 12-13} Also, attention plays a critical role in producing self-regulatory responses not only by selecting and focusing on stimuli in the physical environment but also by internally modulating cognitive processes of different information processing. ¹⁰

1. Self-regulation and Executive Attention: Extensive research has identified three major attentional systems, which are alerting, orienting, and executive control. ¹⁰ Alerting describes the condition of one's wakefulness and arousal; orienting refers to one's ability to select sensory information from a physical environment; and executive control refers to one's ability to resolve conflict to perform goal-directed behavior while delaying or inhibiting ^{10, 14} Particularly, default responses. research has highlighted the roles that executive control, which refers to volitional and controlled control of the attentional system, plays in making self-regulatory responses. 10-11

Evidence self-regulation linking to executive emerged from control developmental research on temperamental 10-11 in effortful control. differences Research with children has shown that executive control was positively related to guilt/shame, empathy and but was negatively related to personal distress and negative affect such as anger. ¹⁵⁻¹⁶ Children with high executive control handled anger by using non-hostile verbal methods than

overt aggressive methods.¹⁷ As such, executive attention plays a critical role in developing self-regulatory behaviors, rather than reinforcing reactive responses to positive and negative events. ¹¹ Researchers proposed that executive attention contributes to the development of selfby providing regulation attentional flexibility that enables people to regulate negative affect. to consider moral consequences of actions, and to exert voluntary attention. ¹¹ Recent research on individual differences in cardiac vagal tone provided evidence linking self-regulation and executive attention.

The Neurovisceral Integration 2. **Model:** Previous research has shown that there are several neural networks mediating self-regulation, including various parts of the brain, such as the anterior cingulate, the insula, the ventromedial prefrontal cortices, the central nucleus of the amygdala, the paraventricular and related nuclei of the hypothalamus, the periaqueductal gray matter, the parabrachial nucleus, the nucleus of the solitary tract (NTS), the nucleus ambiguous, the ventrolateral medulla, the ventromedial medulla, and the

medullary tegmental field, among others.^{8,} 18 These self-regulatory networks are implicated in making adaptive visceromotor. neuroendocrine, and behavioral responses for various environmental demands. 1, 8, 18-19

Of particular importance is the roles that the inhibitory prefrontal-subcortical circuits play in self-regulation.²⁰ One of the important functions of the prefrontal cortex is to identify safety signals from the environment and to exert the inhibitory control over subcortical circuits, including the central nucleus of the amygdala, which produces the fight or flight response. ^{18, 20} This inhibitory regulation of the prefrontal cortex over the subcortical structures serves an important role in making optimal selfregulatory responses to meet various 18-19 Indeed, environmental demands. extensive research has demonstrated that the inhibitory prefrontal-subcortical circuits support various regulatory behaviors, including appetite, attitudes, and prejudice. ²⁰ The dysfunction of the circuits, which results in reduced prefrontal inhibition and hyperactive subcortical activity, may lead to not only physiological deterioration but also prolonged activation of defensive behavior mechanisms, such as hyper-vigilance and perseverative cognition (e.g., worry or rumination), which eventually leads to mental and emotional problems. ¹⁸⁻¹⁹ The disruption of the prefrontal-subcortical circuits has been observed in various psychopathologies, including depression, anxiety, schizophrenia, and addictive behavior. 21-25

According to the neurovisceral integration model, the inhibitory prefrontal-subcortical circuits are linked to the heart via the vagus nerve. ^{1, 8, 26-27} For example, when the orbital and medial prefrontal cortices were temporarily inactivated by using the Wada test in which participants were infused with sodium amobarbital, there was an increase in HR and a decreased in HRV. 28 The demonstrated experiment that the inactivation of the prefrontal cortex leading to the failure of suppressing subcortical circuits, which resulted in an increase in HR and a decrease in HRV. Also, the greater reduction of HRV after the inactivation of the right hemisphere was consistent with previous findings showing that vagal nerves from the right hemisphere were more closely associated with to chronotropic control than those from the left hemisphere. Furthermore, evidence from a positron emission tomography method has identified that the superior medial prefrontal cortex and left posterior orbitofrontal and anterior insular cortices were correlated with HRV in response to emotional stimuli, but the right inferior frontal cortex and brain stem (inferior pontine tegmentum) were correlated with HRV in response to neutral stimuli.²⁹

As a result of the physiological link between the self-regulatory neural network and cardiac vagal control, cardiac vagal tone can serve as a physiological correlate of self-regulation. ^{1, 8} Cardiac vagal tone can be indexed by heart rate variability (HRV) that refers to the differences in beatto-beat alterations in heart rate. 1, 27-30 According to the neurovisceral integration model, higher resting HRV is associated with the highly functional self-regulatory system whereas lower HRV is associated with the poor self-regulatory system and

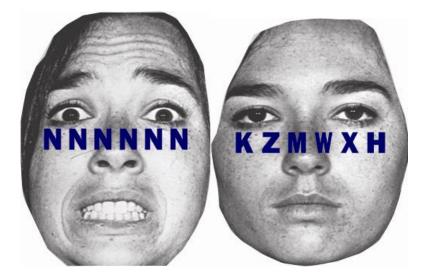
rigid neurovisceral integration. ^{1, 8, 18} In fact, it has been well documented that lower HRV was associated with poor mental health such as a higher incidence of psychiatric disorders (e.g., generalized anxiety disorder, panic disorder, depression, bipolar disorder, and schizophrenia). ³¹⁻³⁶ Also, healthy individuals with lower resting HRV showed greater activations of the middle occipital gyrus and the cuneus in response to emotional and neutral stimuli, which are typically observed in people with high risk of psychosis.^{8, 37} As such, these data may suggest that lower HRV may be a predisposing factor for greater susceptibility of developing emotional and psychiatric problems.^{8,37}

Furthermore, it has been suggested that increased phasic HRV-HRV reactivityindicates the exertion of greater selfregulatory effort. ^{1, 9, 38-39} For example, alcoholics with good impulse control demonstrated greater phasic HRV in response to alcoholic cues. ³⁸ Similarly, when participants demonstrated greater phasic HRV when placed in a situation that required greater self-regulatory exertion (e.g., when instructed to eat only carrots) than in a situation that did not require the exertion of self-regulatory effort (e.g., when instructed to eat only cookies). ⁹ Also, participants who engaged in emotion suppression and reappraisal emotion regulation demonstrated greater phasic HRV. 40 As such, not only trait HRV but also phasic HRV can indicate the functioning of self-regulation.

Recent research has demonstrated that individual differences in HRV reflecting one's ability to control the self-regulatory system are related to a varying degree of executive control in response to emotional stimuli. More specifically, previous research has demonstrated that individual differences in HRV predicted cognitive tasks that allowed for assessing three functions of executive control that play an important role in self-regulation, which are (1) conscious detection, (2) inhibition and (3) conflict resolution. The present paper will review these studies that may shed light on the nature of the relationship between self-regulation and executive control, which plays an important role in mental health.

3. Conscious detection: Conscious detection refers to the ability to select a target from distractors and process it further. 10-11 Recently, it has been shown that individual differences in HRV predicted task performance of a letter detection task with the emotional distractor. ^{8, 19} Participants were instructed to detect a target letter, either X or N, among letter strings superimposed on either fearful or neutral distractor faces. In half of the trials. letter strings consisted of six target letters, which made the target detection easier. However, in the other half the trials, letter strings consisted of one target letter and five non-target letters, which made target detection difficult (see Figure 1). When target detection was easy, there was no individual difference in HRV. When the task was difficult, people with higher resting HRV showed faster target detection in trials with neutral distractors compared to fearful distractor. However, people with lower resting HRV demonstrated slower target detection with both fearful and neutral distractors. ¹⁹ These results indicated that people with higher resting HRV demonstrated efficient conscious detection, which is the capacity of selecting targets while ignoring neutral distractors in difficult trials where fewer cognitive resources were available. In contrast, people with low resting HRV demonstrated the difficulty in exerting conscious detection by showing slow responses to detect targets in the presence of both neutral and fearful distractors.

Figure 1. Example stimuli from Park et al. (2013, 2014). A string of six letters was superimposed on fearful and neutral facial emotions. In the low cognitive load condition, the letter string consisted of six X's or six N's (left). In the high cognitive load condition, letter strings consisted of one target letter and five non-target letters (H, K, M, W, or Z) arranged in random order (right).



Furthermore, people with high and low resting HRV demonstrated different autonomic responses to neutral and fearful responses in easy and difficult trials. For example, people with higher resting HRV showed phasic HRV enhancement in response to fearful distractors when the task was easy, suggesting the exertion of selfregulatory effort in response to fearful distractors when more cognitive resources were available. Conversely, people with lower resting HRV showed phasic HRV suppression, which suggested an autonomic stress response, in the conditions with

fearful distractor faces under both low and high load. ⁴¹ There are other studies linking lower resting HRV to the phasic HRV suppression, an autonomic stress response. ^{9, 40, 42} This hyper-vigilant autonomic stress response will activate and prolong biological and behavioral defensive responses, which eventually wear and tear down systems.^{8, 41} Indeed, low resting HRV has been associated with various physical problems, such as hypertension, diabetes, high cholesterol, obesity, arthritis, and some cancers.⁸ Therefore, the failure in executive control associated with poor selfregulation affects physical as well as mental health. 8

4. Inhibition: Cognitive inhibition has been defined as an automatic or conscious influence to slow down or to reduce the chance of a certain mental process to occur. ⁴³ Inhibitory mechanisms are widely involved in attention, memory and language processes. ¹¹ Recent research has shown that individual differences in resting HRV could predict the functioning of inhibition in memory as well as attention. ⁴⁴⁻⁴⁶

Inhibitory attentional mechanism. The relationship between HRV and inhibitory attentional mechanisms has been studied using the inhibition of return paradigm. The inhibition of return (IOR) refers to the inhibitory attentional mechanism that inhibits one's attention from going back to previously examined locations, which facilitates an efficient search. ⁴⁶⁻⁴⁸ People direct their attention to the location where a stimulus is presented, but they divert their attention to a new location when previously attended locations are no longer relevant to a task at hand, and there is time to explore new areas. ⁴⁶ Previous research has shown that there are at least two separate neural mechanisms of IOR: (a) collicular (retinotectal) and (b) cortical mechanisms. Our group examined whether individual differences in HRV would predict the inhibition of return to emotional and neutral face cues. 46

Furthermore, we explored whether the relationship between HRV and IOR to emotional stimuli depended on different neural pathways of IOR by utilizing different spatial frequency information.

People with lower resting HRV IOR demonstrated reduced effect, indicating reduced inhibitory function. In contrast, people with higher resting HRV demonstrated a typical IOR effect, which was even more pronounced in response to fearful faces at a high spatial frequency that tapped into the cortical based IOR. ⁴⁸ These findings demonstrate that individual differences in HRV demonstrated varying degrees of inhibitory attention, such that people with higher resting HRV are capable of controlling inhibitory attention, whereas people with low resting HRV are less capable of controlling it. 46

Inhibitory memory mechanism. The relationship between HRV and inhibitory mechanisms in memory has been studied by using a thought suppression paradigm and a think/no-think paradigm. 44 In the think/nothink paradigm, participants studied a list of word pairs (e.g., Tape-Radio). Participants were then repeatedly presented with the cue word (Tape). In the think trials, participants were instructed to think of the corresponding response word with which a cue word was presented (Radio). In the nothink trials, participants were instructed to pay full attention to cue words to prevent the recall of corresponding response words. A wealth of evidence suggested that people showed significantly reduced recall of nothink items, demonstrating the ability to inhibit retrieval of unwanted memory. Recent research has shown that individuals with higher resting HRV showed lower recall of no-think items, demonstrating the superior ability to inhibit the retrieval of unwanted memory. ⁴⁴ Furthermore, people with higher resting HRV reported the fewer occurrence of intrusive thoughts in the thought suppression task in which participants were instructed to indicate the number of occurrences of a target by pressing a computer keyboard. ⁴⁴ As such, there is accumulating empirical evidence suggesting that individual differences in HRV are associated with varying degrees of inhibitory capacity in attention and memory.

5. Conflict Resolution: Resolving conflicts involves selecting responses in the presence of highly compatible alternatives. ⁵⁰ For example, in Posner's spatial cueing paradigm ^{10, 51}, participants were presented with a cue that followed by a target; cue can

indicate the location of a target accurately (*valid*) or inaccurately (*invalid*; see Figure 2). 10, 51-52 In the valid trials, selecting the location of a target is facilitated by accurate prediction of a target. However, in the invalid trials, participants have to select a target presented in a location opposite to what a cue points out, which requires voluntary attention to resolve the conflict. Some empirical studies have reported that when emotional stimuli (e.g., fearful faces) are presented as cues in the task, people showed slower reaction times to disengage attention away from cues in invalid trials (slower attentional disengagement).

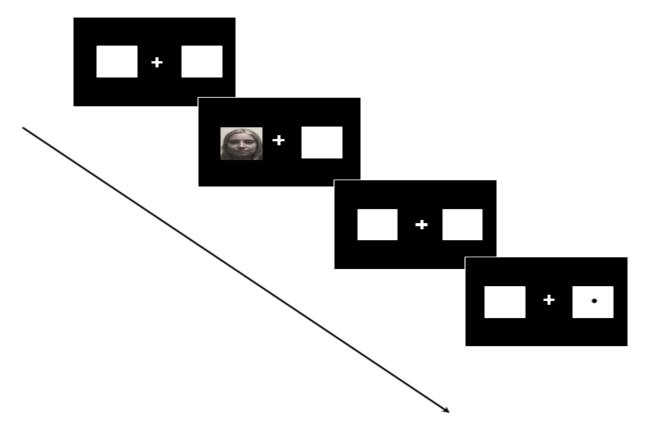


Figure 2. Sample trial in the spatial cuing task. Either fearful or neutral face cues created at broad, high, and low spatial frequency, appeared for 250 ms. After a 50 ms delay with the initial fixation display, a target circle appeared in the center of the left or right box until the participant responded (or until 2,000 ms elapsed). Stimuli are not drawn to scale.

However, slower disengagement from emotionally negative cues is maladaptive disengagement indicates because the difficulty in exerting voluntary attention to disengage attention away from emotionally negative stimuli. 53-54 Neuroimaging studies have revealed that attentional disengagement from fearful face cues in invalid trials is associated with increased activity of the ventromedial prefrontal cortex, including the rostral anterior cingulate cortex. ⁵⁵ Extensive research has shown that people with high anxiety exhibit slower attentional disengagement from threatening stimuli compared to healthy 56-57 controls. Recent research that examined individual differences in HRV has shown that people with lower resting HRV showed significantly slower attentional disengagement from fearful faces relative to people with higher resting HRV, suggesting the difficulty in resolving the conflict between the cue indication and accurate target location. These findings provide initial evidence that individual differences in resting HRV are associated with top-down and bottom-up emotional attention.

6. Conclusions: The current review presented evidence of an underlying interaction between individual differences in cardiac vagal tone—a physiological proxy of self-regulatory capacity—were associated with different components of executive control, which plays an important role in emotional well-being and mental health. These studies provide evidence that higher resting HRV is associated with highly effective exertion of executive

control that serves functional selfregulation, eventually leading to good mental health. In contrast, lower resting HRV is associated with difficulty in exerting and controlling executive control that may be detrimental to self-regulation and eventually to mental health, which might explain the link between lower HRV and a wide range of poor mental and physical health. This line of research demonstrated how self-regulation is linked attentional control. which then to contributes to mental health.

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