The Autonomic Nervous System, Assessment, Evaluation

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Disclosure

In the spirit of full disclosure I acknowledge that I currently serve on the President of Creative Cybernetics, Inc and on the Scientific Advisory Board of Biocom Technologies (unpaid) and own a small percentage of the company stock.
human brain

100 000 000 000 neurons (& other cells)

100 000 000 000 000 synaptic connections

Dendrite

Spine

pre-synaptic neuron

synapse

post-synaptic neuron

(Cajal 1928)

Purkinje Neuron

adapted from Sanes and Lichtman (1999)
Lateral view of brain with 10 different areas (such as primary auditory area and primary motor area) labelled and differentiated by colors
Brain Stem

- Lateral view of brainstem
- Cut edge of ascending tracts to cerebrum
- Thalamus
- Optic tract
- Midbrain
- Pons
- Cranial nerves
- Cut edges of tracts leading to cerebellum
- Medulla oblongata
- Spinal cord
Autonomic Nervous System

• **Definition:** a motor system that innervates the heart, smooth muscle, and glands. Sensory is NOT part of the system

• **Autonomic pathway organization:** primary visceral sensory neuron in peripheral ganglia secondary order visceral sensory relay that projects locally and to the thalamus visceral motor neurons. All autonomic cell groups are regulated by neurons above the level of the spinal cord and brainstem
Autonomic Nervous System

• **Basic unit**: two-neuron chain that consists of:

• **Preganglionic** – cell body is located in the gray matter of the spinal cord or brainstem. Axon projects out of the CNS onto the postganglionic neuron

• **Postganglionic** – cell body is located in a ganglion outside the CNS. Axon projects onto an end organ (heart, smooth muscle, or gland).
Autonomic Nervous System

- **Central and reflex control:** The basic two neuron autonomic effector does not operate autonomously. Activity of the preganglionic neuron is modulated reflexively and/or by specific centers in the brain (i.e. medulla, pons, hypothalamus, cerebral cortex)
- **3 divisions:** Sympathetic, Parasympathetic, and Enteric
Sympathetic (thoracolumbar) nervous system

• Preganglionic neuron – cell body in the intermediolateral cell column of spinal cord segments T1 to L2,3. Axons are myelinated (termed white rami), pass out of the spinal ventral root, enter chain root ganglia and synapse with postganglionic neurons (connections converge and diverge) in ganglia of peripheral nervous system.
Sympathetic Nervous System

Postganglionic neuron – unmyelinated; innervate heart, smooth muscle, and glands. Emerge as gray rami innervates blood vessels (vasomotor), hair (pilomotor), and sweat glands (sudomotor). Cell bodies located in 2 types of ganglia.
Parasympathetic (craniosacral) nervous system

Preganglionic: Associated with cranial nerves: III (oculomotor), VII (facial), IX (glossopharyngeal), X (Vagus)

Innervates smooth muscle and glands of head, heart, and abdomen

X (Vagus) is most important, since it supplies all thoracic and abdominal viscera; motorneurons are found in dorsal motor nucleus (contains parasympathetic only) and nucleus ambiguus. Unmyelinated and long (synapse with ganglia close to end organ, in contrast to sympathetic, which have chain ganglia)

Sacral location: intermediolateral gray segments S2-S4 form the pelvic nerve innervates pelvic viscera

Postganglionic: short and unmyelinated (cell body in ganglia next to end organ), Cranial ganglia (ciliary, otic, submaxillary)
The Brain in Your Gut

The gut’s brain, known as the enteric nervous system, is located in sheaths of tissue lining the esophagus, stomach, small intestine and colon.

**Small Intestine Cross Section**

**Submucosal plexus**
Layer contains sensory cells that communicate with the myenteric plexus and motor fibers that stimulate the secretion of fluids into the lumen.

**Myenteric plexus**
Layer contains the neurons responsible for regulating the enzyme output of adjacent organs.

**Lumen**
No nerves actually enter this area, where digestion occurs. The brains in the head and gut have to monitor conditions in the lumen across the lining of the bowel.

**Mesentery**
Attaches the bowel to the body wall and contains major arteries, veins, lymphatics and external nerves.

Source: Dr. Michael D. Gershon, Columbia University
Enteric Nervous System
With a coronal view, regions of cortical control of the autonomic nervous system are visible on magnetic resonance imaging.

C = cingulate cortex; PF = prefrontal cortex; I = insular cortex; HT = hypothalamus; A = amygdala
Examples of magnetic resonance imaging susceptibility to motion artifacts before and after filtering in an electrocardiogram and a photoplethysmogram.
Magnetic resonance imaging in a patient with Shy-Drager (left) is normal; a “hot cross buns” sign may be evident in patients with multiple-system atrophy (right).
A review of four fMRI studies of stressor-evoked blood pressure reactivity demonstrated activation in corticolimbic areas, including the cingulate cortex, insula, amygdala, and cortical and subcortical areas that are involved in hemodynamic and metabolic support for stress-related behavioral responses.

**TABLE**

<table>
<thead>
<tr>
<th>Cortical region</th>
<th>Effect of electrical stimulation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Heart rate</td>
</tr>
<tr>
<td>Cingulate</td>
<td></td>
</tr>
<tr>
<td>Prefrontal</td>
<td></td>
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<tr>
<td>Insula</td>
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<tr>
<td>Right</td>
<td>+</td>
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<tr>
<td>Left</td>
<td></td>
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<tr>
<td>Amygdala</td>
<td>±</td>
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<tr>
<td>Hypothalamus</td>
<td></td>
</tr>
<tr>
<td>Lateral</td>
<td></td>
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<tr>
<td>Ventromedial</td>
<td>+</td>
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</tbody>
</table>

— = decrease; + = increase
Despite the difficulty of visualizing brainstem areas that govern autonomic response, functional magnetic resonance imaging and electrocardiographic data demonstrated brainstem regions that correlated with autonomic involvement during a handgrip task.16
Functional MRI of heart-brain interactions has strong potential for normal subjects, in whom the BOLD effect is small, within the limits of motion and susceptibility artifacts. Typically, such applications require averaging results over multiple subjects. Its potential utility in disease states is less significant because of the additional limitations of MRI with sick patients (the MRI environment, blunting of autonomic response in disease, possible impairment of BOLD), but continued investigation is warranted.

Jones, S. Imaging for autonomic dysfunction Cleveland Clinic Journal of Medicine, August 2011 vol. 78 Suppl 1 S69-S74 doi: 10.3949/ccjm.78.s1.12
“It is not the strongest of the species that survive, nor the most intelligent, but the one most responsive to change.”

-Charles Darwin
Body’s Response to Stress

The Defense/Defeat Model

- fight or flight
- immune system suppression

*Folkow (1993)
STRESS RESPONSE SYSTEM

HPA AXIS—the interplay among the hypothalamus, the pituitary and the adrenal glands—is a central component of the brain’s neuroendocrine response to stress. The hypothalamus, when stimulated, secretes corticotropin-releasing hormone (CRH) into the hypophyseal portal system, which supplies blood to the anterior pituitary. CRH stimulates the pituitary [red arrows show stimulatory pathways] to secrete adrenocorticotropic hormone (ACTH) into the bloodstream. ACTH causes the adrenal glands to release cortisol, the classic stress hormone that arouses the body to meet a challenging situation. But cortisol then modulates the stress response [blue arrows indicate inhibitory effects] by acting on the hypothalamus to inhibit the continued release of CRH. Also, a potent immunoregulator, cortisol acts on many parts of the immune system to prevent it from overreacting and harming healthy cells and tissue.
BRAIN AND IMMUNE SYSTEM can either stimulate (red arrows) or inhibit (blue arrows) each other. Immune cells produce cytokines (chemical signals) that stimulate the hypothalamus through the bloodstream or via nerves elsewhere in the body. The hormone CRH, produced in the hypothalamus, activates the HPA axis. The release of cortisol tunes down the immune system. CRH, acting on the brain stem, stimulates the sympathetic nervous system, which innervates immune organs and regulates inflammatory responses throughout the body. Disruption of these communications in any way leads to greater susceptibility to disease and immune complications.
### 11β-HSD1 in Innate Immunity

<table>
<thead>
<tr>
<th>Monocytes/Macrophages</th>
<th>Glomerular Mesangial Cells</th>
<th>Dendritic Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑ Expression with differentiation promotes neutrophil phagocytosis</td>
<td>↑ Expression with TNFα</td>
<td>↑ Expression with differentiation</td>
</tr>
<tr>
<td>↑ Expression with TLR signalling</td>
<td>↓ Expression with antigenic stimulation</td>
<td></td>
</tr>
</tbody>
</table>

### 11β-HSD1 in Adaptive Immunity

<table>
<thead>
<tr>
<th>T-Lymphocytes</th>
<th>B-Lymphocytes</th>
<th>Thymocytes</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑ Expression with activation and Th1/Th2 polarisation</td>
<td>Detectable expression (less than T-Lymphocytes)</td>
<td>↑ Expression with burn injury and TNFα/IL-1β</td>
</tr>
<tr>
<td>↑ Activity with age Can ↓ inflammatory cytokine secretion</td>
<td></td>
<td>↑ Thymocyte apoptosis</td>
</tr>
</tbody>
</table>

### 11β-HSD1 in Tissue Response to Inflammation

<table>
<thead>
<tr>
<th>Synovial/Skin/Spleen/Fibroblasts</th>
<th>Osteoblasts/Adipocytes/Myoblasts</th>
<th>Vascular Smooth Muscle Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑ Expression with TNFα/IL-1β Can ↓ decrease with IL-6 synthesis Activity correlates with ESR in RA</td>
<td>↑ Expression with TNFα/IL-1β</td>
<td>↑ Expression with IL-4/IL-13</td>
</tr>
</tbody>
</table>
Interactions between epinephrine, ascending vagal fibers, and central noradrenergic systems in modulating memory for emotionally arousing events

C. C. Chen and C. L. Williams

It is well-established that exposure to emotionally laden events initiates secretion of the arousal-related hormone epinephrine in the periphery. These neuroendocrine changes and the subsequent increase in peripheral physiological output play an integral role in modulating brain systems involved in memory formation. The imparissimality of the blood-brain barrier to epinephrine represents an important obstacle in understanding how peripheral hormones initiate neurochemical changes in the brain that lead to effective memory formation. This obstacle necessitated the identity of a putative pathway capable of conveying physiological changes produced by epinephrine to limbic structures that incorporate arousal and affect related information into memory. A major theme of the proposed studies is that ascending fibers of the vagus nerve may represent such a mechanism. This hypothesis was tested by evaluating the contribution of ascending vagal fibers in modulating memory for responses learned under behavioral conditions that routinely emotional arousal by manipulation sensitive stimuli. A combination of electrophysiological recording of vagal afferent fibers and in vivo microdialysis was employed in a second study to simultaneously assess how elevations in peripheral levels of epinephrine affect vagal nerve discharge and the subsequent potentiation of norepinephrine release in the basolateral amygdala. The final study used double immunohistochemistry labeling of c-fos and dopamine beta hyroxyase (DBH), the enzyme in the synthesis to determine if epinephrine administration alone or stimulation of the vagus nerve at an intensity identical to that which improved memory in Experiment 1 produces similar patterns of neuronal activity in brain areas involved in processing memory for emotional events. Findings emerging from this collection of studies establish the importance of ascending fibers of the vagus nerve as an essential pathway for conveying the peripheral consequences of physiological arousal on brain systems that encode new information into memory storage.

Keywords: amygdala, emotional arousal, epinephrine, learning, memory, vagus nerve

INTRODUCTION

An extensive number of findings reveal that the emotional nature of learning experiences contributes to the strength of novel events that are encoded and stored into memory. The influence of highly arousing events on memory is attributed to the impact salient stimuli have in initiating and maintaining heightened levels of neural activity in the amygdala (Cahill and McGaugh, 1995; Gerra et al., 1996; Canli et al., 2002; Chang et al., 2005; Pelletier et al., 2005). Emotional experiences influence the amygdala and regulate how effective new events are converted into memory by their capacity to evoke epinephrine secretion from the adrenal glands (McCory and Gold, 1981) which in turn initiates a long-lasting and sustained release of norepinephrine in the amygdala (Williams et al., 1998; O’Carroll et al., 1995; Hurlemann et al., 2005). The contribution of norepinephrine activation of the amygdala to memory processing is revealed by studies showing that infusion of this transmitter or beta-noradrenergic agonists into the basolateral amygdala selectively improve memory for responses acquired in inhibitory avoidance (Ferry et al., 1990), contextual fear conditioning (Lalumiere et al., 2003; Huth et al., 2006), or spatial learning tasks (Hatfield and McGaugh, 1999).

Although a great deal of attention has been devoted to understanding how activation of the amygdala modulates neuronal functioning in other limbic structures during memory formation, less emphasis has been placed on identifying how changes in peripheral autonomic activity produced by adrenal hormones, feedback to the brain to influence noradrenergic activation of the amygdala during this important process.

Liberation of the mechanisms underlying these interactions will provide a more comprehensive understanding of memory formation since they have circumstantial effects on how effective new events are represented in memory. For example, the uniform enhancement in memory observed following heightened states of arousal produced by epinephrine release is abolished by...
Central Autonomic Network
(Thayer & Brosschot, 2005)

- The central nervous system that regulates the ANS balance is called the central autonomic network (CAN). The CAN work with networks to regulate the following functions:
  - Executive
  - Social
  - Affective
  - Attentional
  - Motivational
<table>
<thead>
<tr>
<th>CAN</th>
<th>(Thayer &amp; Brosschot, 2005)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Autonomic, cognitive, and affective function assist humans maintain balance in the face of environmental challenges.</td>
<td></td>
</tr>
<tr>
<td>Inhibitory or negative processes or feedback circuits that permit behavior and redeploy resources needed elsewhere.</td>
<td></td>
</tr>
<tr>
<td>When negative circuits are compromised positive circuits develop and result in hypervigilance. The symptoms can be devastating and if not ameliorated can develop into permanent conditions.</td>
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</tbody>
</table>
A common subcortico neural system regulates defensive behavior including autonomic, emotional and cognition.

When prefrontal cortex is taken “offline” for whatever reason parasympathetic inhibitory action is withdrawn and relative sympathetic dominance associated with defensive occurs.

This can be measured by assessing parasympathetic contribution to overall HRV.
Hypervigilance

• Growing evidence supports the use of HRV as a predictor of hypervigilance and inefficient allocation of attentional and cognitive resources (Thayer & Brosschot, 2005)
PTSD and the ANS

- Inescapable Shock
- Autonomic Nervous System
- Sympathetic
- Parasympathetic
- Defense Defeat Model
Suicide and Cortisol
Psychosomatics and Psychopathology
Thayer & Brosschot, 2005, p. 1053

• “Autonomic Imbalance and Decreased Parasympathetic Tone in particular may be the final common pathway linking negative affective states and dispositions, including the indirect effects via poor lifestyles, to numerous diseases and conditions as well as increased mortality, and it may also be implicated in psychopathological conditions”.
THE ANATOMY OF ANXIETY

WHAT TRIGGERS IT...
When the senses pick up a threat—a loud noise, a scary sight, a creepy feeling—the information takes two different routes through the brain.

A. THE SHORTCUT
When startled, the brain automatically engages an emergency hot line to its front center, the amygdala. Once activated, the amygdala sends the equivalent of an all-points bulletin that alerts other brain structures. The result is the classic fear response: sweaty palms, rapid heartbeat, increased blood pressure, and a burst of adrenaline. All this happens before the mind is conscious of having smelled or touched anything. Before you know you’re afraid, you are.

B. THE HIGH ROAD
Only after the fear response is activated does the conscious mind take over. Some sensory information, rather than traveling directly to the amygdala, takes a more circuitous route, stopping first at the thalamus—the processing hub for sensory cues—and then the cortex—the outer layer of brain cells. The cortex analyzes the data streaming in through the senses and decides whether they require a fear response. If they do, the cortex signals the amygdala, and the body stays on alert.

...AND HOW THE BODY RESPONDS
By putting the brain on alert, the amygdala triggers a series of changes in brain chemicals and hormones that puts the entire body in anxiety mode.

1. Auditory and visual stimuli
Sights and sounds are processed first by the thalamus, which filters the incoming cues and shunts them either directly to the amygdala or to the appropriate parts of the cortex.

2. Olfactory and tactile stimuli
Smells and touch sensations bypass the thalamus altogether, taking a shortcut directly to the amygdala. Smells, therefore, often evoke stronger memories or feelings than do sights or sounds.

3. Thalamus
The hub for sights and sounds, the thalamus breaks down incoming visual cues by size, shape, and color, and auditory cues by volume and dissonance, and then signals the appropriate parts of the cortex.

4. Cortex
It gives rise to feelings and sounds meaning, enabling the brain to become conscious of what it is seeing or hearing. One region, the primate cortex, may be vital to turning off the anxiety response once a threat has passed.

5. Amygdala
The emotional core of the brain, the amygdala has the primary role of triggering the fear response. Information that passes through the amygdala is tagged with emotional significance.

6. Bed nucleus of the stria terminalis
Unlike the amygdala, which sets off an immediate burst of fear, the BNST perpetuates the fear response, causing the longer-term unease typical of anxiety.

7. Locus ceruleus
It receives signals from the amygdala and is responsible for initiating many of the classic anxiety responses: rapid heartbeat, perspiration, and dizziness.

8. Hippocampus
This is the memory center. It’s responsible for storing the raw information coming from the amygdala along with the context, along with the events, and the emotions attached to the data during their trip through the amygdala.

STRESS-HORMONE BOOST
Responding to signals from the hypothalamus, the amygdala triggers the adrenal glands to pump out high levels of the stress hormone cortisol. Too much cortisol signals the cells in the hippocampus, making it difficult to organize the memory of a trauma or stressful experience. Memories lose their context and become fragmented.

RACING HEARTBEAT
The body’s sympathetic nervous system is responsible for heart rate, breathing, and shifting into overdrive. The heart beats faster, blood pressure rises, and the lungs hyperventilate. Sweat increases and gets the hair ending of the skin stingle into action, creating goose bumps.

FIGHT, FLIGHT OR FRIGHT
The sense of danger becomes hyperalert, drinking in every detail of the surroundings and looking for potential new threats. Adrenaline80s to the muscles, preparing the body to fight or flee.

DIGESTION SHUTDOWN
The brain stops thinking about things that bring pleasure, shifting its focus instead to identifying potential dangers. To ensure that energy wasted on digestion, the body will sometimes respond by emptying the digestive tract through intestinal vomiting, urination or defecation.
ANS Dysfunction

• Sympathetic Dominance can produce:
  – muscle bracing, bruxism, ocular divergence, tachycardia, diaphoresis, pallor, tremor, startle, hypervigilance, panic rage and constipation
ANS Dysfunction

- Symptoms of palpitations, nausea, dizziness, indigestion, abdominal cramps, diarrhea, and incontinence

- Self perpetuating symptoms causing continued dysregulation “free falling”

“The syndrome of trauma has now literally taken control of the body”
ANS and Disease

• The ANS plays an important role in the development and maintenance of a wide range of somatic and mental diseases.

• In general autonomic imbalance and decreased parasympathetic tone may be the final common pathway linking negative affective states and ill health (Thayer & Brosschot, 2005).
Measuring the ANS
Low Heart Rate Variability
(parasympathetic withdrawal)

- Low HRV is associated with the following conditions
- Cardiac symptoms of panic attack
- Poor attentional control
- Poor emotional regulation
- Behavior inflexibility

- Friedman and Thayer, 1998
Low Heart Rate Variability (parasympathetic withdrawal)

- Depression (Thayer et al., 1998)
- Generalized anxiety disorders (Thayer et al., 1998)
- PTSD (Cohen et al., 1999)
- Cardiovascular morbidity and mortality
- Diabetes (Ziegler et al., 2001)
Low Heart Rate Variability (parasympathetic withdrawal)

- Immune deficiency and inflammation contributing to:
  - Aging
  - CVD
  - Osteoporosis
  - Arthritis
  - Alzheimer’s
  - Periodontal disease
  - Certain types of cancers as well as muscle decline increased frailty and disability
Extreme Biological Rhythms

- Exposure of rhythmic environments to chemical or behavioral stressors can result in increases and decreases in the response (Antleman (1996, 1997))

- Possible innate biological function designed to reset the rhythm
The amygdala mediates many of the behavioral and autonomic aspects of the reaction to both unconditioned (e.g. shock) and conditioned (e.g. light that has been paired with shock) stimuli. It is believed that an associative process takes place in the amygdala, which then projects to hypothalamic and brain stem targets in order to mediate the various symptoms of fear.

<table>
<thead>
<tr>
<th>Inputs</th>
<th>Outputs</th>
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<tbody>
<tr>
<td></td>
<td>ANATOMICAL TARGET</td>
</tr>
<tr>
<td>Condensed fear stimulus</td>
<td>Hypothalamus: Sympathetic activation ➔ Rapid heartbeat, galvanic skin response, paleness, pupil dilation, blood pressure elevation.</td>
</tr>
<tr>
<td>Sensory thalamus</td>
<td>Parabrachial nucleus/Solitarius: Increased respiration ➔ Panting, respiratory distress.</td>
</tr>
<tr>
<td>Polymodal sensory cortex</td>
<td>Ventral tegmental area: Activation of dopamine, norepinephrine, and acetylcholine ➔ Behavioral and EEG arousal, increased vigilance.</td>
</tr>
<tr>
<td>Hippocampus</td>
<td>Locus coeruleus: Cessation of behavior ➔ Freezing, conditioned emotional response, social interaction.</td>
</tr>
<tr>
<td>Brain stem reticular formation</td>
<td>Central (Periaqueductal) grey (different cells than SPA): Increased reflexes ➔ Increased startle.</td>
</tr>
<tr>
<td>Trigeminal and facial motor nerves</td>
<td>Mouth open, jaw movements ➔ Facial expressions of fear.</td>
</tr>
<tr>
<td>Paraventricular nucleus (hypothalamus)</td>
<td>ACTH release ➔ Corticosteroid release (&quot;stress response&quot;).</td>
</tr>
</tbody>
</table>

The central nucleus of the amygdala makes direct connections with a variety of target areas in the brain that express the various symptoms of fear.
PTSD

• http://www.youtube.com/watch?v=jeGKuTZtkpg
Biochemical Measurements

Hypothalamus/Pituitary/Adrenal (HPA) Profile
The HPA profile provides measurement of 6 primary urinary neurotransmitters: Serotonin, GABA, Glutamate, Dopamine, Norepinephrine, Epinephrine. Salivary Adrenal Hormones are also measured: 4 timed Cortisols and 2 DHEAs are also included in this profile. Neurotransmitters are measured from a single urine sample, while cortisol (X4) and DHEA (X2) are measured from four saliva samples, the first taken between 7:00 and 8:00 am and then one every five hours thereafter for the remaining three samples.

Measuring Stress Related Biochemical Change

- **Cortisol is elevated in response to real and perceived stressors.**
- **Salivary Alpha Amylase reflects autonomic nervous system involvement.**
- **GABA helps with relaxation and sedation.**

Cortisol
Cortisol is a hormone that can be used to measure the plasticity of the hypothalamic pituitary axis as high morning and lower afternoon and evening values have been consistently reported. Cortisol stimulates fat accumulation and is elevated by perceived and physiological stress. Cortisol is considered an indicator of endocrine, metabolic, and circulatory health with chronic high levels associated with central obesity in adults and a variety of chronic diseases such as diabetes. In a preliminary study, involving twenty male and female alcoholic subjects (10 matched controls), ages 18-45, the question was asked whether three types of recreational activities, classified according to the amount of oxygen required to perform them, could decrease cortisol. The findings indicated that cortisol levels were significantly lower after participation in board game recreational activities (p<.05). A number of studies have demonstrated a correlation between salivary cortisol and serum cortisol.

Gamma-Aminobutyric Acid (GABA)
Gamma-aminobutyric acid is a neurotransmitter that mediates muscle activation at synapses between nerves. The GABA system is located in the hippocampus and is involved with memory formation. Low plasma GABA has been reported in some depressed patients and, in fact, may be a useful trait marker for mood disorders. More specifically, melancholic and psychotic patients demonstrate low occipital GABA. Electroconvulsive treatment and antidepressants are effective because they increase GABA and suggest a cause and effect relationship. It may be possible that other factors, including participation in pleasurable activities can also increase GABA.

Protein Alpha-Amylase A
It has recently been discovered that a specific protein reflective of acute stress can be detected and quantified in human saliva. Salivary Alpha-Amylase (sAA) is an indicator of sympathoadrenal medullar activity and is a good biochemical predictor of sympathetic and parasympathetic activity. A number of studies have since verified that sympathetic activity increases sAA secretion while parasympathetic activity increases salivary flow rate. Increases in sAA have been consistently recorded after both physical stress (i.e. exercise) and to a lesser extent psychosocial stress. It is hypothesized that the experimental group will exhibit greater decreases in sAA that the control group.
Purpose

• The overall goal of the ECU Wounded Warrior Program is to increase performance and promote functional independence.
Good Early Indications

• Preliminary clinical data collected so far indicate decreases in ANS hyperarousal and increases in parasympathetic activity. Reports on PHQ-SF 36 indicated positive changes in physical symptoms, and decreases in depression panic attack and anxiety.
• Possible bipolar effect with parasympathetic becoming dominant and then sympathetic rather than rhythmic
Outcome Indicators

• Heart rate variability training changes
• Neurofeedback
• The Posttraumatic Stress Checklist (PCL)
• Deployment and Resilience
• Patient Health Questionnaire short form (PHQ SF-36)
• Profile of Mood States
• Salivary alpha-amylase (sAA) changes.
• Behavioral questionnaire assessing alcohol, drug, nicotine use, nutrition habits etc.
• Self satisfaction inventory
Heart Rate Variability

• HR variability can demonstrate energetic supply of any activities, physical, mental, or emotional

• There is generally agreed, that all activities followed by increased sympathetic influence involves an increase of HR frequency and a decrease of HR variability (HRV)

• HRV can be used for evaluation of quality of work for both mental or physical work loads
Heart Rate Variability (HRV) also is a Measure of Adaptive Capacity

- **Higher HRV**
  - Youth (age <40)
  - Aerobic fitness
  - Exercise/altitude tolerance
  - Better neurocognitive executive function

- **Lower HRV**
  - Heart failure
  - Death after heart attack
  - Diabetic cardiovascular disease
  - Depression, anxiety, stress
  - Most diseases
Performance: Cognitive or Mental Effort

• Heart Rate Variability
  – Increasingly becoming a popular measure of effort.
  – Provides an indication of sympathetic and parasympathetic activity as relates to resource demand.
High HRV associated with better performance on tasks involving executive function

Fig. 1. Number of true positive responses to WMT (Error bars = S.E.).

(Hansen, Johnsen, & Thayer, 2003)
Training effect and HRV

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Age (y)</th>
<th>Sympathetic</th>
<th>Parasympathetic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arai et al.[127]</td>
<td>43</td>
<td>25–69</td>
<td>No change</td>
<td>Withdrawal</td>
</tr>
<tr>
<td>Brenner et al.[130]</td>
<td></td>
<td></td>
<td>Increase at onset</td>
<td>Withdrawal</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Later on attenuated increase due to higher temperature</td>
<td></td>
</tr>
<tr>
<td>Kamath et al.[131]</td>
<td>19</td>
<td>20–32</td>
<td>Decrease</td>
<td></td>
</tr>
<tr>
<td>Maciel et al.[132]</td>
<td>23</td>
<td>25–35</td>
<td>No change</td>
<td>Withdrawal</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Increase at higher activity level</td>
<td></td>
</tr>
<tr>
<td>Perini et al.[126]</td>
<td>7</td>
<td>23.7 ± 0.5(^a)</td>
<td>No change at low intensity; decrease at higher</td>
<td>No change at low intensity</td>
</tr>
<tr>
<td>Shin et al.[133,134]</td>
<td>5</td>
<td>17–21</td>
<td>Decrease</td>
<td>Decrease</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>21–40</td>
<td>Decrease</td>
<td>Decrease</td>
</tr>
</tbody>
</table>

\(^a\) Mean ± SD.

AR = autoregressive model; FFT = fast Fourier transform.

(Aubert et al., 2003)
Acute Physical Activity on Cognitive Function: A Heart Rate Variability Examination

Nicholas P. Murray · Carmen Russoniello

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Abstract The purpose of this study was to examine the relationship of physical activity and cognitive function (as determined by reaction time and the trail-making test) in active versus non-active participants. Participants were divided into one of four groups: active experimental, active control, non-active experimental and non-active control. All groups completed a complex cognitive task (the trail-making test) as well as a set of reaction time tasks both before and after the experimental session. The experimental groups completed a 30-min exercise session while the control groups monitored the physical activity of the experimental group. In addition to the measures of cognitive function, heart rate variability was recorded during the pre- and post-tests. There was significant cognitive performance improvement in tasks with a higher cognitive and perceptual component. Heart rate variability data indicated that a moderate level of arousal based on sympathetic nervous system activity post exercise was associated with an increase in cognitive performance. The findings are discussed in light of the inverted U hypothesis.

Keywords Cognition · Acute exercise · Executive control · Heart Rate Variability · HRV

McMorris and Graydon 1997; or Tomporowski 2003 for reviews) assessing the effects of exercise on cognitive function. However, even with considerable evidence that acute exercise improves cognitive performance, there is still a lack of consensus of the precise relationship. For some studies in which physically fit participants were compared to sedentary ones, there was an increase following an acute bout of exercise in perceptual speed, reasoning and working memory for the fit participants (e.g., Arcelin et al. 1998; Hancock and McNaughton 1986). Other studies (e.g., Bard and Fleury 1978; Cote et al. 1992; Luft et al. 2009; Magnie et al. 2000) found no significant differences between fit groups and unfit groups on cognitive tests.

Many authors (Etner et al. 1997; Etner et al. 2006; Hall et al. 2001; Tomporowski and Ellis 1986) have described methodological problems that could explain these divergent findings. For instance, there are large differences in duration and intensity of exercise as well as differences in the type of cognitive tasks and the timing of these tasks (relative to the exercise bout) that contribute to the difficulty in comparing results. For example, if the exercise session was too short or too long, it may lead to poorer performance on a cognitive task due to a participant
Other HRV Applications

- Adult Pre Screening for Preventive and Health Evaluation
- Diabetic Neuropathy Assessment
- Pre Condition Cardiac Health Screening
- Post-MI risk assessment and evaluation
- Medical research
- Drug studies, dose relationships to ANS function, for example risk of trip and fall in elderly
- Stress measurement, physical or emotional, for example ADHD children
Other HRV Applications

• The American and world populations are living with chronic medical conditions, such as cardiac conditions, diabetes, hypertension, respiratory disease, sleep apnea and other chronic stress related conditions. These chronic maladies are on the rise and are reflective of our overstressed and overworked society.
• Disease Management Tele-medicine
• Patient Monitoring Home and Mobile
• Personal Health Systems
• Clinical Research
The Utility of Autonomic Testing
Mayo Clinic

Points to remember

Autonomic testing helps to determine the presence, severity, distribution, and localization of autonomic dysfunction.

Symptoms and conditions that can benefit from autonomic testing include syncope, flushing, bladder and bowel dysfunction, dizziness, endocrine dysfunction, Parkinson's-like symptoms, gastrointestinal tract distress, painful feet, orthostatic intolerance, extreme fatigue, tachycardia, cognitive dysfunction, anhidrosis, and hyperhidrosis.

Routine reimbursable autonomic evaluation includes tests of sudomotor, cardiovagal, and adrenergic function. Autonomic testing can distinguish primary from secondary autonomic disorders, true autonomic neuropathy from conditions that mimic it, and psychogenic from organic conditions. It can also help to differentiate progressive diseases and serve as a means of monitoring disease progression and response to treatment.
Quantitative Sudomotor Axon Reflex Test (QSART)
(also called Quantitative Sudomotor Autonomic Reflex Testing)

What is it?
The quantitative sudomotor axon reflex test (QSART) is used to assess the small nerve fibers, which are linked to the sweat glands.

Why do it?
QSART is used to diagnose:
- Painful, small fiber neuropathy when nerve conduction test results are normal
- Disturbances of the autonomic nervous system, which controls the sweat glands, heart, digestive system, other organs, and blood pressure
- Complex pain disorders

How is it performed?
The test has three parts and measures resting skin temperature, resting sweat output, and stimulated sweat output. Measurements are typically taken on arms, legs or both. A small plastic cup is placed on the skin and the temperature and amounts of sweat under the skin are measured. To stimulate sweat a chemical is delivered electrically through the skin to a sweat gland, but the patient will only feel warmth. A computer is used to analyze the data to determine how well the nerves and sweat glands are functioning.

How will it feel?
The patient will experience little or no discomfort, but the test could take two or three hours to complete.
The Effects of Casual Video Games on Depression, Anxiety & Cognition

Psychophysiology and Biofeedback Lab

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Heart Rate Variability and Biological Age: Implications for Health and Gaming

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Abstract

Accurate and inexpensive psychophysiological equipment and software are needed to measure and monitor the autonomic nervous system for gaming and therapeutic purposes. The purpose of this study was to determine whether heart rate variability (HRV) derived from photoplethysmography (PPG) technology was predictive of autonomic nervous system (ANS) aging or biological age. Second, we sought to determine which HRV variable was most predictive of ANS change and aging. To test our hypotheses, we first conducted a criterion related validity study by comparing parameters of a 5 minute resting HRV test obtained from electrocardiography (ECG), the current “gold standard,” with PPG technologies, and found them to be significantly correlated \((r \geq 0.92)\) on all parameters during a resting state. PPG was strongly correlated to ECG on all HRV parameters during a paced six breaths per minute deep breathing test \((r \geq 0.98)\). Further analysis revealed that maximum variation of heart rate had the highest negative correlation \((r = -0.67)\) with age. We conclude that PPG is comparable to ECG in accuracy, and maximum variation of heart rate derived from a paced breathing test can be considered a marker of biological aging. Therapeutic interventions and games designed to reduce dysfunction in the ANS can now be developed using accurate physiological data.
References

References

References

• Lombardi F, Sandrone G, Mortara A et al. Linear and nonlinear dynamics of heart rate variability after acute myocardial infarction with normal and reduced left ventricular ejection fraction. *Am J Cardiol* 1996;77:1283–1288[CrossRef][ISI][Medline]
References

Task Force of the European Society of Cardiology and the
North American Society of Pacing and Electrophysiology, *Circulation*,
18, 165–171.
Mainardi, L., Hankala, Y., Korhonen, I., Signorini, M. G., Bianchi, A. M., Takala, J., Nieminen, K. and Cerutti, S.,
205–217.
References

D. Narayana Dutt†,* and S. M. Krishnan Computer processing of heart rate variability signals for detection of patient status in cardiac care units. *CURRENT SCIENCE*, VOL. 78, NO. 7, 10 APRIL 2000