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SPECIAL ISSUE

Treating Postconcussion Syndrome with LORETA *Z*-Score Neurofeedback and Heart Rate Variability Biofeedback: Neuroanatomical/Neurophysiological Rationale, Methods, and Case Examples

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Media attention has highlighted the critical problem of concussion injuries in sport and the challenge of treating and rehabilitating individuals with traumatic brain injury. The authors present a framework for the treatment of traumatic brain injury, using low-resolution electromagnetic tomography Z-score based neurofeedback and heart rate–variability biofeedback. The article advocates a comprehensive assessment process including the use of a 19-channel quantitative electroencephalogram, a heart rate variability baseline, and symptom severity questionnaires for attention deficit/hyperactivity disorder, depression, and anxiety. The initial medical assessment, neuropsychological assessment, and evoked potential studies also have potential for a more precise assessment of deficits in brain activation patterns, which assists the targeting of neurofeedback training.

Introduction

In the last few years, thanks largely to greater awareness through articles in the media, concussion in sport has gone from being seen as an accepted part of many games to being regarded as an injury with potentially serious consequences. Previously a concussion might even confer macho bragging rights, with phrases like "had my bell rung" or "saw stars" suggesting a tough guy had played a hard game. Now that the brains of former National Football League players are being donated for autopsy and almost 80% of those brains (121/128) showed signs of chronic traumatic encephalopathy (CTE; Breslow, 2014), attitudes are rapidly changing. (For a scholarly explication of CTE, see McKee et al., 2009. McKee is head of the Department of Veterans Affairs brain repository at Boston University in Bedford, MA.) This publicity means that there is not only more emphasis on accurate diagnosis, but also enormous interest in the best ways to manage the injury and promote full recovery after a concussion.

With respect to both diagnosis and treatment, the field of biofeedback has a great deal to offer people who have suffered a traumatic brain injury (TBI). Results have been particularly gratifying in people who have suffered for years from postconcussion syndrome. We always combine neurofeedback (NFB; either single channel, and/or the latest iteration, low-resolution electromagnetic tomography [LORETA] *Z*-score neurofeedback [LNFB]) with heart rate variability (HRV) training because when you hit your head, it also affects cardiac function. This is due to heart–brain connections discussed later. These connections have been known and trained for years in the biofeedback community. More recently, the director of the Mayo Clinic Concussion Program has presented on heart measures being an effective way to evaluate TBI (Dodick, 2013).

Definitions

According to the Consensus Statement from the Fourth International Conference on Concussion in Sport held in Zurich in November of 2012 (McCrory et al., 2013), concussion is a subset of mild TBI (mTBI) involving low-velocity injury that causes brain "shaking," resulting in clinical symptoms that are not necessarily related to pathological injury. Concussion is defined as a complex pathophysiological process affecting the brain, induced by biomechanical forces.

Concussion can be caused by any significant blunt force trauma to the head, jaw, or neck or by sudden deceleration that causes the soft brain tissue to hit the hard skull and then rebound and hit the opposite side of the skull, which is the classic coup–contrecoup injury. There can be rotational forces within the skull that cause the twisting of neurons'

axons and dendrites. As well, there is the stretching or even tearing of axons that occurs because gray matter (unmyelinated fibers) and white matter (myelinated fibers) have different densities and will thus move at different speeds with sudden deceleration, as when a football player is tackled or a hockey player receives a hard check. People do not have to hit their heads to suffer a concussion. Nor is lack of consciousness a prerequisite for diagnosing concussion; indeed, 95% of concussions in sport do not involve the person being knocked out (Tator, 2013). After a first concussion, most symptoms resolve in a week to 10 days if the athlete rests both physically and mentally. When symptoms persist, as is often the case if there were prior concussions or the injury was severe and involved a period of unconsciousness or coma, the patient will often continue to suffer symptoms. Then the patient is said to have postconcussion syndrome. Those people can still be helped with a combination of NFB and HRV training even many years postinjury.

Case Example

The longest time elapsed between injury and successful recovery among our clients was over 50 years. This man came to the ADD Centre with the goal of improving his concentration, explaining that he was 60 years old but knew he would have to work for many more years because he could not afford to retire. He was self-diagnosed with attention deficit/hyperactivity disorder (ADHD) and said to keep working, he needed to focus better. He had started work at age 16 in construction, worked as a bricklayer and then as a truck driver. For the past 6 years he had been employed as a dispatcher for a taxi company, but he only took night shift work so there would be minimal distractions and no supervisor. In asking about ADHD symptoms in childhood, the second author (L.T.) learned that he had always felt in a fog at school and things got even worse after his mother died when he was 11. By age 14 he was in reform school. He did not read a book until he was 20 and it was a biography of Martin Luther King, Jr. Thereafter he became a regular user of the library. He said that he was not close to his family, did not have friends, and had never married: Books allowed him an escape from his everyday existence. The most important part of his story, however, concerned a TBI he suffered in childhood. At age 4, while he was playing in front of his farmhouse near the road, a car lost control on newly laid gravel and struck a hydro pole that toppled and struck him. He did not recall the accident (doubtless he suffered retrograde amnesia), but he did recall awakening in a hospital with both legs in traction and being very frightened and upset. His family had emigrated when he was 2 years old but English was not spoken at home and he had not started school, so he did not understand what anyone said to him and had no idea what had happened or where he was. His parents, when told he was out of coma, thought that his survival was a miracle. It seems they never connected his subsequent problems with learning and behavior in school with his accident, nor had he until we discussed the long-term effects of head injuries during his intake assessment. He had done some therapy as an adult in the 1970s regarding the emotional trauma of awakening in hospital and being frightened and disoriented and unable to communicate in English but he had not realized that being a "slow learner," having a short fuse, getting into trouble with the law, suffering mood swings, and leading a solitary life with no close friends could be related to his early head injury. It was a revelation to him that he was probably not inherently a "stupid kid" or a "bad kid" (labels he recalled from childhood) but, rather, a child who had suffered brain damage. With hope that he might discover who he really was if NFB could heal his brain, he embarked on training that combined NFB and biofeedback.

We did recordings at Cz and determined initial training parameters to improve his concentration (his stated goal) by reducing his excessive slow wave activity and increasing sensorimotor rhythm. Cz, also called the vertex, is the central reference point in the International 10-20 system for localizing scalp placement of electrodes. Cz is the midpoint between the nasion and inion, and is also the midpoint between the left and right preauricular points. We also put an inhibit on "busy-brain frequencies" in the 23–35 Hz range to help even out his mood. For biofeedback we initially did some finger temperature training for relaxation and then had him practice achieving respiratory sinus arrhythmia, getting his diaphragmatic breathing in synchrony with his heart rate changes. Today we would be doing LNFB plus HRV training, but this was a few years ago before we had those capabilities. Stay tuned for his results at the end of this paper.

Assessment Procedures

Today when there is a history of brain injury, we always do a full brain map in addition to doing a single-channel assessment at Cz. With 20 min of data collection using the eVox system manufactured and distributed by Evoke Neuroscience (New York, NY) we have four things: 19-channel electroencephalogram (EEG) data; HRV measures to guide HRV training; event-related potentials (ERPs) to assess brain speed; and responses to questionnaires that tell about severity of symptoms. The 19-channel data is needed

to guide LNFB *z*-score training. We have quantitative EEG (QEEG), HRV, and ERP results interpreted by Evoke Neuroscience in New York. The first author (M.T.) also does an "in-house" QEEG interpretation using NeuroGuide. Based on those findings and the rest of the assessment procedures, we design a customized intervention for each client. Often we do a combination of LORETA and single-channel NFB. There is always HRV training. HRV training is the update to the respiratory sinus arrhythmia training we have done since the 1990s. It allows us to determine a person's resonance frequency for breathing and to track statistics such as the standard deviation of the normalized (after correcting for artifacts) beat-to-beat interval (SDNN) and power, as discussed later in this paper.

Our standard intake measures also include questionnaires: ADHD inventories and social-emotional self-reports that, for adults, include the Beck Depression Checklist (Beck, Steer, & Brown, 1996) and the Beck Anxiety Inventory (Beck, 1993). Adults additionally complete an online neuropsychological battery from CNS Vital Signs (Morrisville, NC) at home. In our office there is administration of the Intermediate Visual Auditory (IVA [IVA+Plus CPT Test v 4.6]; BrainTrain, Inc., Richmond, VA) and Test of Variables of Attention (T.O.V.A.; The TOVA Company, www.tovatest.com) continuous performance tests. There is review of previous assessments and report cards, if available. Also, of course, there is an extensive interview covering reason for assessment, history, current situation, medical factors, medications, lifestyle factors (diet, sleep exercise), and goals. Finally, there is the low-tech, high-yield measure called Draw-a-Person. This is not scored in a formal way and certainly artistic merit is not the important factor, but there are nearly always telling changes in human figure drawings after NFB training. The initial drawing produces hypotheses about emotional functioning, as distinct from intellectual, academic, or vocational functioning.

Assessment using 19-channel QEEG, ERPs, HRV measures, biomedical analysis (done with an outside service if deemed necessary), and neuropsychological testing gives comprehensive information. Having additional measures of balance would be desirable, but we have not acquired equipment, such as a force plate, to make those measurements. In his doctoral dissertation at Pennsylvania State University, Thompson (2007) developed a new combined metric for assessing concussion in varsity athletes. He used QEEG, ERPs, balance, and virtual reality with a sway test, as well as the traditional self-report data and symptoms checklist. He clearly established that multimodal assessment is more accurate than any single measure and that self-reporting was not very accurate for detecting dysfunction beyond a week. It was also clear that resolution of self-reported symptoms did not mean there had been resolution of the injury (Thompson, 2007; Thompson & Hagedorn, 2012).

Intervention based on the multimodal assessment will also be multimodal. At the ADD Centre it will include some combination of the following: single-channel NFB, LNFB, HRV training, coaching involving metacognitive strategies, and counseling regarding diet and supplements, sleep hygiene, and exercise. To encourage clients to be active, we are currently "prescribing" for home viewing the YouTube video "23 ½ Hours," produced by a Toronto physician (Evans, 2012) who reviewed the positive effects of exercise. For selected patients, transcranial direct current stimulation, hemoencephalography, and peripheral biofeedback are used. For some clients there is the addition of counseling, usually a half-hour, done after their NFB session.

Concussion Symptoms and Their Frequency

The following list, based on the review done by Charles Tator (2013), is rated according to frequency of reported symptoms, as follows:

- Symptom reported by >65% of patients (1)
- Symptom reported by 40%–65% of patients (2)
- Symptom reported by <40% of patients (3)

Emotional and Cognitive Symptoms:

- Irritability (1)
- Poor memory, forgetfulness (1)
- Impatience, frustration (1)
- Cognitive, attention, and concentration difficulties (1)
- Anxiety (1)
- Depression or tearfulness (2)
- Restlessness (3)

Physical and Sensory Symptoms:

- Sensitivity, particularly to noise and light (2)
- Insomnia (2)
- Fatigue and sleep problems (2)
- Headache (2)
- Poor balance, dizziness (2)
- Blurred or double vision (3)
- Inability to stay warm (3)
- Nausea and vomiting (3)

Note that a number of these symptoms can occur in people who have not suffered concussions. A lack of objective pathognomonic signs of concussion means that a physician's diagnosis often rests, for the most part, on the patient's report of subjective symptoms, such as headaches, that are also common in the nonconcussed population and known to vary day to day. Common presenting symptoms include fatigue, irritability, cognitive difficulties, and balance deficits. The cognitive problems include slowed processing speed, poor sustained attention, poor concentration, word finding and comprehension difficulties, impaired short-term and long-term memory, and learning problems (Dockree et al., 2004; Van Zomeren & Brouwer, 1987).

After a concussion, a person is 3 times more likely to develop depression. In some cases, family and friends notice a major personality change while the person is not aware of how difficult he or she has become because lack of self-awareness can be a symptom, especially when structures in the default mode have been affected. (The default mode becomes activated when a person is not engaged in any particular cognitive or motor task. It reflects awareness of self and self-in-the-world—how one relates to the physical and social world.) An interesting example of concussion affecting default network functioning came from a recent assessment. The woman said that after her head injury, when she was not doing something, her head was "just empty." It took many months for that absence-of-thought phenomenon to be gradually replaced by self-awareness and inner dialogue that felt normal.

In a vulnerable person, such as someone who has not fully recovered from a previous TBI, even a mild head injury, such as whiplash without loss of consciousness, can result in profound memory, cognitive, and interpersonal relationship difficulties that do not spontaneously resolve with rest. For purposes of assessing the question of previous brain injury, keep in mind that people who deal with emotional trauma and post traumatic stress disorder report that the brain effects and the brain's vulnerability after emotional trauma is equivalent to having suffered a TBI. In other words, a prior emotional trauma equals a previous concussion in terms of the brain's vulnerability to subsequent head injuries.

The most serious consequence of having a second concussion before recovery from the first one is complete involves acute swelling in the brain that can lead to death or serious lasting impairment. This is called second impact syndrome and accounts for one or two deaths per year in the USA in football alone, often in young players under the age of 18. Adolescents and women appear to be more vulnerable to the effects of a concussion, perhaps because the strength and girth of their necks is less, so that injuries like whiplash or from taking headers in soccer are greater (Tator, 2013).

Initial Medical Assessment

In the emergency department the experienced physician will use the Sport Concussion Assessment Tool, the SCAT 3 (Guskiewicz, et al., 2013), and the Glasgow Coma Scale (Teasdale & Jennett, 1974). The reader can get reprints of the SCAT3 from http://journals.bmj.com/cgi/reprintform. You can download the scale from http://bjsm.bmj.com. It was published in the *British Journal of Sports Medicine* (Guskiewicz et al., 2013). The emergency room physician may also do further neurological assessment or order brain scans. They know that MRI and CT scans show only structural damage and do not detect the pathophysiology involved in concussion, so they only rarely order those tests and usually only if they suspect a bleed. If there is subdural bleeding, then the person will require acute medical care or even neurosurgery. Usually a person who has not suffered loss of consciousness is sent home with instructions to rest from both physical and mental activity for a week or until symptoms have resolved. A relative or friend will be told to check the patient's pupils for any changes in the next few hours and days and to watch out for signs of grogginess or loss of balance that could indicate bleeding in the brain. Rest is the only universally agreed upon "intervention" after a head injury, and even that is becoming a bit controversial in terms of how long a period of rest is required before one can start gentle exercise, such as going for a short walk wearing sunglasses. Something that can be done immediately (but is not always mentioned by physicians) is taking supplements, in particular, a fish oil supplement so that there is a sufficient supply of omega-3 essential fatty acids to provide the building blocks for myelin production and repair.

Pathophysiological Changes following TBI

There is a complex cascade of neurochemical and neurometabolic changes that occur after a head injury. These were reviewed in detail in an article entitled "Managing TBI" that was published in this journal in 2013 (Thompson, Thompson, Reid-Chung, & Thompson, 2013). The processes of secondary injury to neurons following a concussion can affect neurological functioning so that a person can actually become worse in the days and weeks after the injury than they were immediately after the TBI. This is because the diffuse axonal injury caused by the tearing and stretching and twisting of axons disrupts communication between neurons. Cell death can occur from extensive glutamate release and the sequelae of

inflammation. Essentially, there is an energy crisis within the cell after the flood of glutamate depolarizes cortical neurons with a huge influx of sodium and calcium (Giza & Hovda, 2001.) The neurons could survive if they had sufficient adenosine triphosphate energy production within the cell, but at the same time that energy demands increase, there is vasoconstriction caused by the release of potassium from the cell, and this limits the supply of oxygen and nutrients to the cell just when they are needed most (DeWitt, Jenkins, Wei, Lutz, Becker, & Kontos, 1986). Thus the high-energy demand, restricted blood flow, and oxygen debt all combine to create an energy crisis that exhausts the neurons and may lead to their death. This will inevitably lead to symptoms such as mental confusion and failed memory, symptoms commonly seen in people who have had a concussion.

The brain will take varying amounts of time to recover. The time to restore the chemical balance will vary among people and will depend on variables including age, general health, history of previous head injuries, and many other factors, such as nutrition. With injury, long-term potentiation is decreased, long-term depression is increased, and membrane excitability is reduced. These changes must be normalized for full recovery to occur. NFB, of course, enhances long-term potentiation through the repeated stimulation of particular neuronal connections in the brain.

Role of QEEG in Assessment

The helpful thing about QEEG data combined with knowledge of symptoms is that you can develop hypotheses about what networks are affected in a particular client and then design interventions to improve network functioning. Many networks can be affected by a concussion. These include the executive networks (attention, deductive and inductive reasoning networks, cognitive processing functions, verbal comprehension, and word finding); the affect networks, (including the autonomic nervous system functioning), the vestibular networks, and aspects of memory. Disruptions in memory, emotions, and cognitive functioning can persist for months to years after a concussion. Persistent EEG changes can include slowing, decreased power, episodic discharges, and changes in coherence. A slowed peak frequency (also termed the dominant frequency or peak alpha) that drops below the usual 10 Hz in adults is a common finding, and with training, the peak frequency (eyes closed) increases. A dominant frequency below 8 Hz in an adult is considered abnormal. The most consistent power findings after a concussion are reduced power in the higher frequency bands (8–40 Hz), and increased slow waves (1–4 Hz) (Haneef, Levin, Frost, & Mizrahi, 2013; Slobounov, Sebastianelli, & Simon, 2002; Thatcher, 2009). There are long-term changes associated with an increase in the 1–4 Hz/8–12 Hz ratio (Korn, Golan, Melamed, Pascual-Marqui, & Friedman, 2005; Slobounov, Cao, & Sebastianelli, 2009). In particular there is an initial increase in low alpha, 8–10 Hz, but a decrease in fast alpha, 10.5–13.5 Hz and fast beta 20–35 Hz (Haneef et al., 2013). A change (increase) in this 1–4 Hz/8–12 Hz ratio activity is negatively correlated with patient outcome 6 months postinjury (Leon-Carrion et al., 2009).

Early research by Thatcher, Walker, Gerson, and Geisler (1989) demonstrated that increased frontal and temporal coherence and decreased phase, increased anterior-posterior amplitude difference, and reduced posterior power could discriminate normals from post-TBI patients. His Neuroguide program includes a TBI discriminant analysis that is helpful for tracking progress in training, though it cannot be used diagnostically. Thatcher et al. (2001) has suggested that power changes in the EEG following concussion result from dysfunctional ionic channels of neuronal membranes (e.g. Na+, K+, Ca++) and reduced average current flux. Decreased and/or increased coherence is a common finding. Coherence reflects communication between different sites in the brain and represents the amount of phase-locked activity in a particular frequency band. TBI will disrupt coherence. The most common finding is a decrease in coherence that is colloquially called a "disconnect." Diffuse axonal injury has also been shown in other studies to be associated with disturbances in connectivity between different areas of the brain (Meythaler, Peduzzi, Eleftheriou, & Novack, 2001). A less frequent but important finding may be episodic discharges. Despite all these QEEG findings, the practioner should also look for brief high-amplitude bursts of any frequency and do single-point analysis (available using LORETA in the Neuroguide program) of these isolated bursts. If their source correlates with the patient's symptoms, then these can be targeted for training when doing LNFB. An example is shown in Figure 1. The blue vertical line can be moved through a short horizontal distance to different points on the high amplitude wave in the frequency band you are interested in. In this case we told the program to look at high beta in the 25–30 Hz range.

Use of ERPs

As reviewed in the previous paper (Thompson et al., 2013) information from evoked potentials, also called event related potentials (ERPs) because they are time-locked to a specific event (sight or sound or even touch), can be used

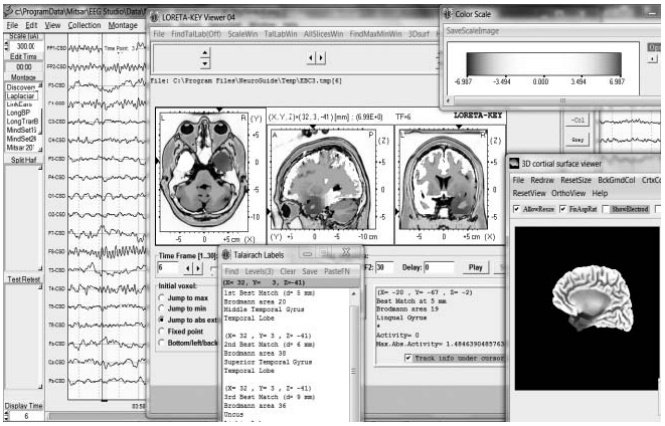

Figure 1. A.N., male, age 35. Single-point analysis of spindling beta (25–30-Hz band) observed at F8 shows right uncus as source (from *The Neurofeedback Book*, Second Edition, Thompson & Thompson, in press).

following concussion to determine the intactness of cortical pathways and speed of processing within these pathways (De Beaument et al., 2009; Dupuis et al., 2000). ERPs have been shown to be resistant to practice effects and are therefore a hearty diagnostic assessment tool (Mendez et al., 2005) that can be repeated as often as necessary. People who have suffered a TBI demonstrate reduced amplitudes for the P3 components (P3a and P3b) of their ERPs. *P* refers to positive-going waves and *N* to negative-going waves. The number, such as 300 (sometimes shortened to just 3), refers to the number of milliseconds after the stimulus when you expect the response to occur. Thus P300 is a positive-going wave that occurs 300 ms or more after a stimulus. It essentially marks when the conscious processing of the stimulus begins, whereas earlier components indicate automatic processing by the brain as it receives a signal. Reduced amplitude after TBI can indicate diminished attention because the amplitude of the P3 has been shown to be related to the amount of attention allocated to information processing (Bernstein, 2002; Duncan et al., 2004, 2005). P3 can be broken down to P3a and P3b. P3a is an attention orienting frontal component (measured at Fz) while P3b reflects sustained attention and monitoring and is more central-parietal with the largest amplitude being observed at Pz (see Polich, 2007, for a detailed explanation of ERPs). He is a renowned researcher who acted as the consultant for the Go/No-Go task used during the eVox assessment to measure ERPs. In general terms, after TBI the pattern is "low and slow"; that is, lower amplitude and longer latency of the P3 response. In our experience, patients with TBI generally have early (automatic) sensory components (P1 and N2) that are longer latency and lower amplitude compared to people who have not suffered a TBI. Figure 2 shows information on the P3a and the P3b

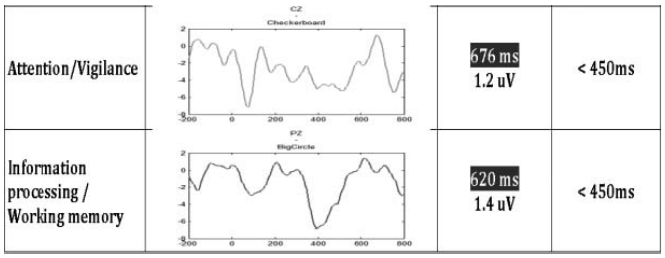

Figure 2. Example of ERPs from a 21-year-old woman with presenting symptoms of motor dysfunction, memory complaints, and cognitive impairment, copied from an Evoke Neuroscience report. In this example the P300 after a concussion is low (amplitude) and slow (latency).

components of the evoked potential of a 21-year-old female who presented with postconcussion symptoms.

Neuropsychological Testing

As mentioned above, we most often use computerized neuropsychological testing for baseline and to track changes over time. This is much more time and cost efficient than administering the appropriate Wechsler Intelligence Scale, though the latter yields a great deal of clinical information as well as IQ scores. The Wechsler Intelligence Scales include the Wechsler Adult Intelligence Scale-IV for adults, the Wechsler Intelligence Scale for Children-V (for children ages 6 to 16), and the Wechsler Preschool and Primary Intelligence Scale-IV (for children 4 to 6½ years), each available from www.pearsonclinical.com. The test battery we use from CNS Vital Signs, coordinated through Evoke Neuroscience, can be done cheaply, rapidly, and frequently to follow progress. It takes an hour or less for the client to complete. You can customize your own battery of tests through the company CNS Vital Signs. We include objective tests of attention and memory in addition to standard well-researched questionnaires.

Notes Concerning HRV

HRV is severely affected by concussion with marked decreases evident in SDNN and power. In a healthy person, there will be high variability above 50 ms. Our hearts do not operate like metronomes; rather, there is a constant interplay of heart rate changes that correlate with changes in blood pressure (BP) with a slight increase in heart rate followed by a decrease in heart rate so the time between each beat changes. (Note that SDNN does decrease with age, so in the elderly it will not necessarily be as high as 50 ms.) HRV training is proving to be an important component of treatment in TBI. We have postulated that NFB combined with biofeedback could be expected to help patients more than either modality alone. In a clinical setting we must use both and cannot remove either

modality from a patient's treatment for research reasons. The reasoning behind our assumption that the combination should be effective is partially based on the observation that the areas of the brain that can affect HRVs involve neuroanatomical structures and networks that are influenced by both NFB applied through scalp electrodes and HRV training that uses diaphragmatic breathing techniques. The areas of the brain and brain stem that are central to these systems and networks are neuroanatomically linked. Figure 3 illustrates these connections.

Note in the figure shown above that the amygdala innervates the hypothalamic nuclei. It also innervates the parabrachial nucleus, which controls respiratory rate, and the locus coeruleus, which produces norepinephrine and can thus influence the increase in BP found in conjunction with anxiety. The central nucleus of the amygdala can be important in responses to anxiety and fear. This may be particularly true when it is not sufficiently inhibited by the medial prefrontal cortex (Thayer, Åhs, Fredrikson, Sollers, & Wager, 2012) and the fusiform and superior temporal areas (Porges, 2007). Using LORETA we often see this area identified as being outside data base norms in postconcussion patients.

Note also that the insula (or insulae, plural because there is a right insula and a left insula) are central in the diagram. This should be no surprise because the infolding of cortex in each of the two hemispheres, called the insula, has direct control over HRV. In many of our TBI assessments, LORETA indicates involvement of the insula (BA 13) and these areas (right insula, left insula) have been among the targets in our work using LNFB. Interestingly, research has demonstrated that injury, as from a stroke, to the right insula has dramatic effects on autonomic balance and heart functioning (Nagai, Hoshide, & Kario, 2010; Shah, Klumpp, Angstadt, Nathan, & Phan, 2009). Stroke affecting the right insula can result in low values for standard deviation of the corrected R-R interval (SDNN). It can also alter values for the ratio of the amplitude of low to high frequency spectral power in HRV, in addition to resulting in symptoms of nonsustained ventricular tachycardia and premature ventricular contractions. There may also be an increase in nocturnal BP and higher norepinephrine levels. Patients with left insular cortex involvement have decreased baroreceptor sensitivity (BRS).

The insulae are important regulators of autonomic balance. The right insula predominately affects the sympathetic and the left the parasympathetic nervous system, in part through connections to the nucleus accumbens, which has a role in balancing the sympathetic and parasympathetic systems (Nagai et al., 2010). The

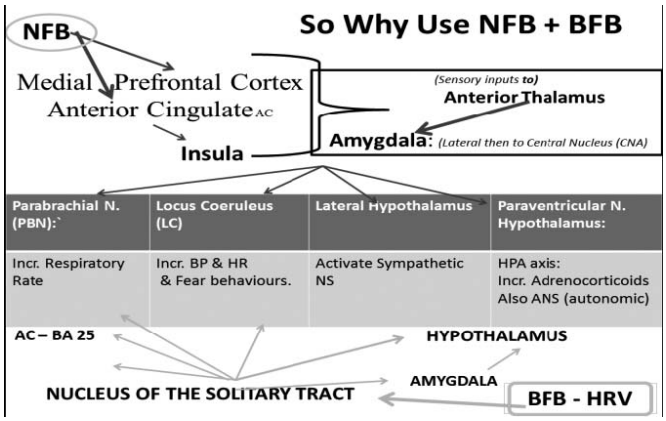

Figure 3. Relevant brain systems and networks (from *The Neurofeedback Book*, Thompson & Thompson, in press).

insular cortex has reciprocal connections with the anterior cingulate gyrus, amygdala, entorhinal cortex, orbitofrontal cortex, and the temporal pole, which are all involved in the affect and default networks and may also be implicated in executive functioning. It has afferent connections with the hippocampal formation. Additionally, the insular cortex has dense reciprocal connections with subcortical autonomic core centers including the hypothalamic paraventricular nuclei. The paraventricular nuclei can control the hypothalamic-pituitary-adrenal axis, and it is the only nucleus to have both afferent and efferent connections to parasympathetic and sympathetic aspects of the autonomic nervous system. These nuclei also have important connections to the lateral hypothalamic area (sympathetic system), nucleus tractus solitarius (HRV control), and parabrachial nucleus (respiratory control), and all of these centers are also reciprocally connected to each other.

Nagai et al. (2010) review goes on to state that using amobarbitol to inactivate either right or left hemispheres has shown that the right hemispheric inactivation can induce a significant decrease of BP and an increase in high-frequency amplitude, and that left inactivation can induce an increase in HR, BP, and low-frequency amplitude. It can also result in a decrease of BRS by nearly 30%. (For a more complete description of techniques for the measurement of BRS, see review by La Rovere, Pinna, & Raczak, 2008).

Summary of Why We Combine NFB and HRV

The above explication of heart–brain connections gives convincing evidence of the logic behind combining brain and heart training. Since LORETA allows the practitioner to find the source of different frequencies deep within the cortex, and because the Neuroguide database allows one to calculate which frequencies are deviant, decisions can be made regarding target areas that can be influenced by LNFB

training. This information, when combined with the practitioner's knowledge of the major functions of different Brodmann Areas and their relationship to neural networks, can assist the practitioner in deciding whether a specific frequency at that site, or coherence and phase abnormalities that involve that site, could correlate with a patient's symptoms. This can help the clinician decide whether or not a pattern correlates with a cognitive, motor, sensory, or affect problem for a specific patient, which, in turn, determines what to target for training.

Using QEEG and LORETA differences from databases, norms are found even a number of years after they have suffered from one or more concussions. These areas and networks are usually observed to be functionally related to their presenting symptoms. Brain areas that may be directly influenced by HRV training and, in particular, by the influence of this training on the solitary nucleus, do have connections to the same regions that we are training in the cortex. The solitary nucleus has connections to cortical areas that are central to affect, executive, and default networks, which, in turn, are central to our work with NFB.

Due to these connections we have decided that training to simultaneously improve HRV and EEG variables will be an effective means to improve the patient's thinking, feeling, and behavior by influencing the same cortical and subcortical structures.

Biochemical Rationale for HRV Training Postconcussion

In addition to the neuroanatomical connections that may be influenced by HRV, part of the reason for our opinion that we should combine NFB and HRV comes from our knowledge of the inflammatory response that occurs after a TBI. Unfortunately, evidence of inflammation can remain even many years after a concussion (Johnson et al., 2013). Johnson et al. (2013) found extensive, densely packed, reactive microglia up to 18 years posttrauma. There was also a reduction in white matter volume with a thinner corpus collosum. Their work, which constituted an 18-year follow-up of patients first seen for the Glasgow Coma Study, is published in the journal *Brain* and makes fascinating reading.

Within minutes of a traumatic impact, a robust inflammatory response is elicited in the injured brain. Inflammation is a stereotyped response that is a protective attempt by the organism to remove the injurious stimuli and to initiate the healing process. There is an activation of glial cells, microglia, and astrocytes, and the infiltration of blood leukocytes.

This is followed by the secretion of immune mediators called cytokines. Cytokines are small, short-lived proteins produced by blood leukocytes and glial cells. They are quickly released in response to TBI. Cytokines that initiate or propagate an inflammatory response are said to be pro-inflammatory, while cytokines that inhibit the inflammatory response are called anti-inflammatory. While Interleukin-10 is regarded to be primarily an anti-inflammatory cytokine, Intrleukin-6 (IL-6) is a cytokine related to inflammation. It is produced by microglia and astrocytes. A 100-fold increase in IL-6 can be measured in serum following TBI (Woodcock & Morganti-Kossmann, 2013). IL-6 regulates inflammation, immunity, bone metabolism, hematopoiesis (formation of blood cellular components), and neural development and is implicated in aging, osteoporosis, autoimmune disease, Alzheimer's disease, and brain injury. Gevirtz (2013) noted that heart rate resonance training could influence the parasympathetic cytokine control system that modulates immunity through interleukins and interferons. Gevirtz (2013) stated that the efferent vagus nerve inhibits the release of pro-inflammatory cytokine and protects against systemic inflammation, calling this vagal function the "cholinergic anti-inflammatory pathway." In making these statements Gevirtz (2013) is citing Pavlov and Tracey (2005) who did original research on Il-6 and inflammation and stated, "activation of the vagus nerve through either electrical stimulation, or biofeedback seems to be a promising therapy." Important for biofeedback practitioners, this pro-inflammatory cytokine should be reduced by HRV training. HRV training has been paired with NFB for nearly every client at our centers and these findings provide one more reason to do so.

Neurophysiological Approach to Effective Treatment

We state in the second edition of *The Neurofeedback Book* that basic rehabilitation procedures—as are carried out in hospital settings and rehabilitation settings—should be adhered to. However, though necessary, these are often not sufficient for full recovery. The NFB/biofeedback practitioner and nutritionists have important techniques to apply that are now being demonstrated to be significant and life changing.

Normalizing the QEEG deviations from a normal database is a first step. This intervention must be designed while keeping in mind that not all deviations will correspond to symptoms. This training, which addresses shifting functioning toward what is expected for the person's age, is often done using LNFB. Nevertheless, we must note that we have had excellent results using single-

channel training in past years. As with other disorders, we also do HRV training during each training session. HRV is severely affected by concussion with marked decreases evident in SDNN and power. HRV training is proving to be an important component of treatment in TBI. As previously noted, part of the reason for this opinion comes from our knowledge of the inflammatory response that occurs after a TBI.

How Do You Combine HRV training with NFB and LNFB?

There are a number of instruments that allow one to simultaneously do biofeedback and NFB. Our first experience combining neuro- and biofeedback was with the Focused Technology F1000 equipment (Focused Technology, Prescott, AZ) in the 1990s and then we moved on to the Biograph program and the Infiniti instrument (Thought Technology, Montreal West, Quebec, Canada). The Biograph program has screens that give feedback for EEG parameters, such as decreasing the amplitude of slow waves (theta) and high-frequency beta waves while increasing the amplitude of sensorimotor rhythm (SMR) or beta frequencies below 20 Hz. The eight-channel Infiniti can simultaneously do EEG biofeedback at the same time as it also shows other biofeedback variables on the screen. This is particularly important for monitoring when a person achieves synchrony between breathing and the changes in heart rate as NFB is simultaneously done.

When doing LNFB, the HRV training is done while the trainer is putting on the 19-channel electro-cap. It can also be done, as appropriate, during the session by shifting attention from the screen attached to the LNFB equipment to the screen attached to the Biograph Infiniti equipment. There is one monitor and computer showing an HRV training screen that is linked to the Biograph-Infiniti system and another screen is linked to the 19-channel equipment. We use both Mitsar (Nova Tech EEG, Mesa, AZ) equipment and also the system from Evoke Neuroscience (Evoke Neuroscience, Inc., New York, NY) for the LNFB.

Published case studies also support the effectiveness of NFB for individuals with TBI to improve learning and memory (Reddy, Jamuna, Indira Devi, & Thennarasu, 2009). Researchers have seen improvements in functioning in small case series of people who had suffered brain injuries (Ibric, Dragomirescu, & Hudspeth, 2009). At the ADD Centre, LNFB is now done from the beginning with people who present with postconcussion syndrome. Sometimes we alternate one regular NFB session and one LNFB session each week. Both regular and LNFB are combined with HRV training. The initial assessment using LORETA in the majority of patients who have suffered a TBI typically shows both positive and negative deviations (>2 *SD*) at multiple sites, often in central midline areas. Those deviations are accompanied by both coherence and phase differences compared to data base norms. LNFB allows the practitioner to address many parameters simultaneously, correcting the activity at various sites at the same time for amplitude and/or coherence and/or phase deviations.

Do Patients Recover?

At the time of writing we have had more than 50 patients with postconcussion symptoms treated with a combination of NFB + HRV. These were usually patients who came a considerable time after all spontaneous recovery had plateaued. Often they came with other complaints related to poor regulation of attention or emotions, and the TBI was then disclosed during the initial interview, as was the case with the man mentioned at the beginning of this article who came because he wanted to improve his concentration and better deal with his self-diagnosed ADHD symptoms. And how did things turn out for him?

When we did our progress testing, which we always do at no charge after 40 sessions are completed in order to have pre- and postdata for our own tracking purposes and also to provide a bonus to the client for completing that amount of training, he was a transformed individual. The standard measures of TOVA, IVA, and questionnaire data were all in the normal (nonADHD) range. The reduction in anxiety symptoms was particularly marked. His single-channel EEG showed a reduction in busy brain activity above 20 Hz and his busy-brain/SMR ratio was fine. The 9-Hz peak that had been the most extreme deviation in his single-channel EEG profile was now just a very slight blip up and the theta/beta ratio was fine. No longer working at night as a taxi dispatcher in order to avoid interaction with people, he was now a friendly and gregarious person who was running his own small moving business. He was not only exercising regularly, which was already a good habit upon intake, he was now passionate about doing volunteer work to bring fitness to the elderly. He had been to Europe to visit relatives for the first time in his life and had taken along a copy of his ADD Centre Initial Assessment report so that his aunts, uncles, and cousins could read it and understand how his childhood injury had led to him being so reclusive for so many decades. He even thoughtfully brought back souvenirs for the staff who had worked with him. At the age of 61 he was no longer experiencing depression or social anxiety and was, in fact, feeling that the best years of his life were ahead of him. He decided to do a further 20

sessions on a once-a-week basis as an optimal performance client.

Most of our clients with postconcussion syndrome take more than the standard 40 sessions that constitute our usual intervention for people with ADHD. Clients seen more recently with whom we did LORETA training from the outset are, however, seeing excellent results after just 40 sessions of training, so our impression is that the work is going faster. (Though the gentleman above also showed remarkable success with just 40 sessions of NFB and biofeedback.) This success occurs despite having less awareness of their mental state during training as the brain is being asked to simultaneously change so many more parameters. There is also less time spent on coaching in metacognition because the client is typically watching a DVD for LORETA feedback and not doing part of each training session on task the way they do with regular NFB. The tasks were what we hypothesized would activate, and thus exercise, different brain networks. Now the LORETA selection specifies the networks.

Here is an example of results using HRV and LNFB only. Of course there was also a supportive trainer working with the client each session (often the third author, A.R.-C.) and the trainer often offered practical suggestions and advice as well as enthusiastic coaching concerning the feedback. In January 2015 we completed a 1-year follow-up on this young woman, who had virtually complete remission of symptoms after she did 40 sessions of LORETA plus HRV training, even though there were still some deviations compared to QEEG database norms. Not only did her anxiety, brain fog, daily headaches, balance problems, and difficulties reading or writing anything complex resolve, the blurred vision and need for bifocals that had occurred after her motor vehicle accident also resolved. Her ophthalmologist was astonished that her prescription was actually less strong for distance vision than it had been pre-accident. A year after she finished training she had maintained her gains on T.O.V.A. and IVA and had improved further on questionnaire ratings related to anxiety, depression and ADHD symptoms. Six months ago she married the man who stood by her during the 16 months postTBI and preNFB period when she was unable to work and could barely manage grocery shopping, cooking, and a bit of aquafit exercise. For the past year she has been employed full time at an interesting job that relates to the master's degree she was completing just prior to the head injury. She is considering going on to do a PhD degree because she is not finding the work that challenging. She is a huge fan of the power of NFB and has referred other clients.

It is hard to predict at the outset how much training will be required, so we still talk about progress testing after 40 sessions to measure gains and gather data to fine tune any further training that may be required. Sometimes, too, client goals change and then more training is appropriate. One would-be author who could not compose a paragraph when initially assessed 2 years after a motor vehicle accident said she just wanted to be able to write the book she was beginning at the time she became disabled by her injuries. She has subsequently authored six books, one of them entitled *Concussion is Brain Injury* (Jeejeebhoy, 2012). Her name is used with permission because she is happy to share her story of recovery and we are happy to promote her book. She returned for further training a year after "graduating" because she had been reading about gamma brainwaves and wanted to try to enhance her gamma through NFB. So we designed an optimal performance training for her that emphasized enhancement of Sheer rhythm, the frequencies around 40 Hz (but that is a topic for another article).

The addition of HRV training to the NFB is important because clients report that using their effortless diaphragmatic breathing is helpful in everyday life as a stress management tool. We regularly hear stories of breathing being effectively used before tests and examinations, before job interviews, to aid in falling asleep, and to stay calm when having conversations that are emotionally charged. By practicing on HRV screens during every session and also using diaphragmatic breathing in everyday life for short periods each day, it becomes an overlearned response that can be utilized even under stress.

Even though these techniques are not yet validated by controlled research, it is clear from clinical experience that the combination of HRV and NFB are powerful tools that can be used not just to help people recover from head injuries but to truly set clients up for success.

References

Beck, A. (1993). Beck Anxiety Inventory. Beck Institute for Cognitive Therapy. Available at http://www.pearsonclinical.com.

Beck, A., Steer, R. A., & Brown, G. K. (1996). Beck Depression Inventory - II. Beck Institute for Cognitive Therapy. Available at http://www.pearsonclinical.com.

Bernstein, D. M. (2002). Information processing difficulty long after self-reported concussion. *Journal of the International Neuropsychological Society*, *8*(5), 673–682.

Breslow, J. (2014, September 30). 76 of 79 deceased NFL players found to have brain disease. *Frontline*. Available at http://www.pbs.org/wgbh/pages/frontline/concussion-watch/

De Beaumont, L., Theoret, H., Mongeon, D., Messler, J., Leclerc, S., Tremblay, S., & Lassonde, M. (2009). Brain function decline in healthy retired athletes who sustained their last sports concussion in early adulthood. *Brain, 132*(Pt 3), 695–708.

DeWitt, D. S., Jenkins, L. W., Wei, E. P., Lutz, H., Becker, D. P., & Kontos, H. A. (1986). Effects of fluid-percussion brain injury on regional cerebral blood flow and pial arteriolar diameter. *Journal of Neurosurgery, 64*(5), 787–794.

Dockree, P. M., Kelly, S. P., Roche, R. A., Hogan, M. J., Reilly, R. B., & Robertson, I. H. (2004). Behavioural and physiological impairments of sustained attention after traumatic brain injury. *Cognitive Brain Research, 20*(3), 403–414.

Dodick, D. (2013, March). *ANS testing to diagnose TBI*. Presentation at the Annual Meeting of the American Academy of Neurology, San Diego, CA.

Duncan, C. C., Kosmidis, M. H., & Mirsky, A. F. (2005). Closed head injury-related information processing deficits: an event-related potential analysis. *International Journal of Psychophysiology, 58*(2-3), 133–157.

Dupuis, F., Johnston, K. M., Lavoie, M., Lepore, F., & Lassonde, M. (2000). Concussions in athletes produce brain dysfunction as revealed by event-related potentials. *Neuroreport, 11*(18), 4087–4092.

Evans, M. (2012). 24 hour fitness - 23½ hours. YouTube video produced by 24 Hour Fitness with Michael Evans. Available at https://www.youtube.com/watch?v=3FSly9JQao.

Gevirtz, R. (2013). The nerve of that disease: The vagus nerve and cardiac rehabilitation. *Biofeedback, 41*(1), 32–38.

Giza, C. C., & Hovda, D. A. (2001). The neurometabolic cascade of concussion. *Journal of Athletic Training, 36*(3), 228–235.

Guskiewicz, K. M., Register-Mihalik, J., McCrory, P., McCrea, M., Johnston, K., Makdissi, M., Dvorák, J., et. al. (2013). Evidence-based approach to revising the SCAT2: Introducing the SCAT3. *British Journal of Sports Medicine, 47*(5), 289–293.

Haneef, Z., Levin, H. S., Frost, J. D., & Mizrahi, E. M. (2013). Electroencephalography and quantitative electroencephalography in mild traumatic brain injury. *Journal of Neurotrauma, 30*(8), 653–656.

Ibric, V. L., Dragomirescu, L. G., & Hudspeth, W. J. (2009). Real-time changes in connectivities during neurofeedback. *Journal of Neurotherapy, 13*(3), 156–165.

Jeejeebhoy, S. (2012). *Concussion is brain injury*. Toronto: Iguana Press.

Johnson, V. E., Stewart, J. E., Begbie, F. D., Trojanowski, J. Q., Smith, D. H., & Stewart, W. (2013). Inflammation and white matter degeneration persist for years after a single traumatic brain injury. *Brain, 136*, 28–42.

Korn, A., Golan, H., Melamed, I., Pascual-Marqui, R., & Friedman, A. (2005). Focal cortical dysfunction and blood-brain barrier disruption in patients with postconcussion syndrome. *Journal of Clinical Neurophysiology, 22*(1), 1–9.

La Rovere, M. T., Pinna, D. G., & Raczak, G. (2008). Baroreflex sensitivity: Measurement and clinical implications. *Annals of Noninvasive Electrocardiology, 13*(2), 191–207.

Leon-Carrion, J., Martin-Rodriguez, J. F., Damas-Lopez, J., Barroso y Martin, J. M., & Dominguez-Morales, M. R. (2008). Delta–alpha ratio correlates with level of recovery after neurorehabilitation in patients with acquired brain injury. *Clinical Neurophysiology, 120*(6), 1039–1045.

McCrory, P., Meeuwisse, W. H., Aubry, M., Cantu, R. C., Dvořák, J., Echemendia, R. J., Engebretsen, L., et al. (2013). Consensus statement on concussion in sport: 4th International Conference on Concussion in Sport held in Zurich, November 2012. *British Journal of Sports Medicine, 47*, 250–258.

McKee, A. C., Cantu, B. C., Nowinski, C. J., Hedley-Whyte, E. T., Gavett, B. E., Budson, A. E., Santini, V. E., et al. (2009). Chronic traumatic encephalopathy in athletes: Progressive tauopathy following repetitive head injury. *Journal of Neuropathology and Experimental Neurology, 68*(7), 709–735.

Mendez, C. V., Hurley, R. A., Lassonde, M., Zhang, L., & Taber, K. H. (2005). Mild traumatic brain injury: Neuroimaging of sports-related concussion. *The Journal of Neuropsychiatry and Clinical Neurosciences, 17*(3), 297–303.

Meythaler, J. M., Peduzzi, J. D., Eleftheriou, E., & Novak, T. A. (2001). Current concepts: Diffuse axonal injury-associated traumatic brain injury. *Archives of Physical Medicine and Rehabilitation, 82*, 1461–1471.

Nagai, M., Hoshide, S., & Kario, K. (2010). The insular cortex and cardiovascular system: A new insight into the brain-heart axis. *Journal of the American Society of Hypertension 4*(4), 174–182.

Pavlov, V. A., & Tracey, K. J. (2005). The cholinergic anti-inflammatory pathway. *Brain, Behavior, and Immunity, 19*, 493–499.

Polich, J. (2007). Updating P300: An integrative theory of P3a and P3b. *Clinical Neurophysiology, 118*(10), 2128–2148.

Porges, S. W. (2007). The polyvagal perspective. *Biological Psychiatry, 74*, 116–143.

Reddy, R. P., Jamuna, N., Indira Devi, B., & Thennarasu, K. (2009). Neurofeedback training to enhance learning and memory in patient with traumatic brain injury: A single case study. *Indian Journal of Neurotrauma, 6*(1), 87–90.

Shah, S. G., Klumpp, H., Angstadt, M., Nathan, P. J., & Phan, K. L. (2009). Amygdala and insula response to emotional images in patients with generalized anxiety disorder. *Journal of Psychiatry and Neuroscience, 34*(4), 296–302.

Slobounov, S., Cao, C., & Sebastianelli, W. (2009). Differential effect of first versus second concussive episodes on wavelet information quality of EEG. *Clinical Neurophysiology, 120*(5), 862–867.

Slobounov, S., Sebastianelli, W., & Simon, R. (2002). Neurophysiological and behavioral concomitants of mild brain injury in collegiate athletes. *Clinical Neurophysiology, 113*(2), 185–193.

Teasdale, G., & Jennett, B. (1974). Assessment of coma and impaired consciousness. A practical scale. *Lancet, 13*(2), 81–84.

Tator, C. H. (2013). Concussions and their consequences. *Canadian Medical Association Journal, 185*(11), 975–979.

Thatcher, R. W. (2009). *EEG evaluation of traumatic brain injury and EEG biofeedback treatment*. In T. Budzynski, H. Budzynski, J. Evans, & A. Abarbanell (Eds.), *Introduction to quantitative EEG and neurofeedback* (2nd ed., pp. 269–294). San Diego: Elsevier.

Thatcher, R. W., Biver, C., Gomez, J. F., North, D., Curtin, R., Walker, R. A., & Salazar, A. (2001). Estimation of the EEG power spectrum using MRI T2 relaxation time in traumatic brain injury. *Clinical Neurophysiology, 112*(9), 1729–1745.

Thatcher, R. W., Walker, R. A., Gerson, I., & Geisler, F. H. (1989). EEG discriminant analysis of mild head trauma. *Electroencephalography and Clinical Neurophysiology, 73*(2), 94–106.

Thayer, J. F., Åhs, F., Fredrikson, M., Sollers, J. J., III, & Wager, T. D. (2012). A meta-analysis of heart rate variability and neuroimaging studies: Implications for heart rate variability as a marker of stress and health. *Neuroscience and Biobehavioral Reviews*, *36*(2), 747–756.

Thompson, J. (2007). *Concussion in sport: Investigation of assessment measures, mechanisms, and functional deficits* (Doctoral dissertation). Pennsylvania State University, State College, PA.

Thompson, J., & Hagedorn, D. (2012). Multimodal analysis: New approaches to the concussion conundrum. *Journal of Clinical Sport Psychology*, *6*, 22–46.

Thompson, M., Thompson, L., Reid-Chung, A., & Thompson, J. (2013). Managing TBI: Appropriate assessment and a rationale for using neurofeedback and biofeedback to enhance recovery in post-concussion syndrome. *Biofeedback*, *41*(4), 158–173.

Thompson, M., & Thompson, L. (in press). *The neurofeedback book: An introduction to basic concepts in applied psychophysiology* (2nd ed.). Wheat Ridge, CO: Association for Applied Psychophysiology.

Van Zomeren, A. H., & Brouwer, W. H. (1987). Head injury and concepts of attention. *Neurobehavioral recovery from head injury* (pp. 398–415). New York: Oxford University.

Woodcock, T., & Morganti-Kossmann, M. C. (2013). The role of markers of inflammation in traumatic brain injury. *Frontiers in Neurology, 4*(18). DOI: 10.3389/fneur.2013.00018.

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