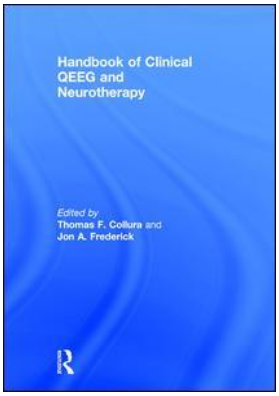

Handbook of Clinical QEEG and Neurotherapy

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An Integrative Approach to Optimizing Neural Function

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AN INTEGRATIVE APPROACH TO OPTIMIZING NEURAL FUNCTION

Exploring the Brain–Gut Connection

Nancy E. White and Leonard M. Richards

Abstract

Neuroscience, as with most of the life sciences, continues its advance toward a more systemic approach to both research and treatment, one that is slowly displacing the linear thinking that has long prevailed with a paradigm that is impacting how we might evaluate, diagnose and treat brain function. This new thinking urges us to go beyond symptom toward cause, thereby plunging us into a web of intricate and sometimes mind-boggling interactions between the brain and the physical system-of-systems that we call the body. One important interaction is called the *Brain–Gut Axis* and a growing body of literature describes the nature, functioning and relevance of this complex bidirectional signaling process mediated by the Autonomic Nervous System. How the messages coursing this communication system impact brain function and ultimately affect mood and behavior involves many participants, such as the massive colony of mainly friendly bacteria that manage how the gut works, and the intricate nerve pathways that deliver the messages back and forth between gut and brain. The quality and type of nutrients that travel through the digestive system and how those nutrients are processed also affect brain function, while chronic stress not only affects brain function directly, but indirectly by its effect on gut function. Tools are available to assess the condition of the brain–gut relationship and treat to normalize its impact on brain function and behavior. By describing an integrative neuroregulation practice, the reader can get an idea of how to broaden the scope of a practice to include the use of these tools.

Introduction

Neuroscience today provides us with many more labels and far more detailed descriptions of the brain and its functions than our predecessors had; we know much more about how the brain works, have plumbed more of its secrets and have begun to decipher more of its relationships with other systems of the human body. One important relationship has given rise to the relatively new field of *Neurogastroenterology*, which explores the complex, symbiotic communications between the gut, which feeds the brain both nutrients and information, and the brain, which affects gut response and, at another level, seeks to modulate gut activity. The intricate system of pathways that carries these communications has come to be known as the *brain–gut axis* and the road to explaining it continues under construction. Still, science today can tell us a lot about how highly integrated are the gut and the brain, showing us more almost every day of the intricate bidirectional pathways by which such

communication occurs. It becomes possible to see from these discoveries that if the gut isn't happy the brain can't be happy either and that by extension the reverse is true. Even popular books, such as Dr. David Perlmutter's *Brain Maker* (Perlmutter, 2015), can now describe for laypersons, with adequate scientific reference, what neural disorders can arise from chronic gut problems and what one can do about them.

Furthermore, the still-developing field of Neuroregulation, a name we can give to the emerging integration of Neurofeedback, Transcranial Stimulation, Deep Brain Stimulation—and perhaps other as yet uncovered approaches—is being swept up in a paradigm shift, along with elements of medicine, psychology, physics and even religion, away from reductionist thinking and isolated treatments toward a systems approach, based on an emerging understanding of how things interconnect and influence each other.

Given all this, perhaps it makes sense to seriously consider the impact this ongoing, intimate interaction between gut and brain has, not only on problems of brain function that the field traditionally encounters, but on protocols to which the field has traditionally turned in addressing them, if for no other reason than to reduce the potential for gut-based problems to sabotage neuroregulation's outcomes.

So, in this chapter we start by locating and identifying major brain structures and physical systems responsible for bidirectional pathways along which brain–gut intercommunications move, indicating the impact brain–gut intercommunication can have on neural development, mood, and behavior. This opens up some significant implications for treating problems of brain function and provides grounds for a rationale that advocates a more integrative approach to treatment on the part of practitioners. To help the practitioner actualize a way that such a treatment approach might look, we characterize this rationale in the form of a Neurotherapy practice that has integrated what science and technology currently offer into a more comprehensive neurobehavioral treatment model.

The Brain–Gut Axis

The brain and the gut communicate in a bidirectional manner largely by means of the Autonomic Nervous System (ANS) and the Hypothalamic–Pituitary–Adrenal (HPA) Axis. A growing body of literature outlines the nature and functioning of this specialized bidirectional signaling system between the brain and the gut and is mapping both the ways in which multiple neurochemicals act mainly on nerve pathways of the ANS and how secretions of the HPA Axis act, mainly via the bloodstream, to transmit information back and forth (Jones, Dilley, Drossman & Crowell, 2006; Mayer, Knight, Mazmanian, Cryan & Tillisch, 2014).

The Role of the Autonomic Nervous System

Like a route map through a maze of public highways and local roads, the brain–gut axis is defined by those pathways that the gut and the brain generally use to get information back and forth to each other. Like a long distance traveler, brain–gut messages use all three parts of the autonomic nervous system:

1. the sympathetic nervous system (SNS), via a network of nerves emanating first from the thoracic spine then through ganglia that combine and reroute their messages to individual sites (Elankov et al., 2000);
2. the parasympathetic nervous system (PNS), specifically the visceromotor component of the Vagus nerve which runs from the brain stem all the way through the abdomen and the viscera (Leanage, 2014). The full Vagus nerve serves as the main neural pathway between the brain and the organs of the body, including the esophagus, heart, and lungs which lie along its path to the

gut (Bergland, 2014). About 80–90% of the vagal nerve fibers relay information *to* the brain, including messages from the enteric nervous system, informing the brain of visceral feelings and gut instincts (Hadhazy, 2014);

3. the enteric nervous system (ENS), an intricate neural network that manages the gut. The enteric nervous system consists of sheaths of neurons—approximately 100 million of them—embedded within the walls of our some 28-foot-long alimentary canal (Hadhazy, 2014). Accordingly, it is sometimes termed "the second brain" because of its innate ability to manage much of the digestive process independent of direct Vagus input (Bergland, 2014).

All these systems are connected and, again like an interstate highway system, the messages they transport seem to know exactly which exits to take in order to connect locally with their intended target organs (Bergland, 2014). Various non-site specific neurotransmitters guide the bidirectional traffic along neural highways, influencing not only gastrointestinal, endocrine and immune function, but human behavior and emotional states as well (Mulak & Bonaz, 2004).

Research increasingly demonstrates that brain–gut interactions are the mechanisms of both gastrointestinal function and human mood and behavior. Disturbances at every level of the brain's connection with the gastrointestinal tract can have a modulating effect on gut function, including both the perception of, and response to, visceral events. Alternatively, studies show that information from the gut to the brain by way of the Vagus nerve has a modulating effect on mood and "distinct forms of anxiety and fear" (Klarer et al., 2014, p. 7067).

The Role of Intestinal Bacteria

There is another important, even critical, participant in the brain–gut conversation. Recent research has shown that a principal source of the visceral events and related gut instincts relayed to the brain lies not just with the alimentary canal itself, but with a community of microbes, or commensal *microbiota*, that inhabit mainly the lower gut, creating an environment called the *gut microbiome* (Mulak & Bonaz, 2004). The human gut contains between 400 and 1,000 different bacterial species that make up an intricate network of cohabiting organisms (Collins, Surette & Bercik, 2012). This colony of trillions lives in symbiosis with its human host and takes an active role in digestion and metabolism, in fact determining in large part the ability of the gut to function well. Colonization of the gastrointestinal tract, mainly the colon, begins at birth, continues during early development and remains throughout life. While each person's microbial profile is distinct, certain phylotypes seem to be similar among healthy individuals, which has offered a broad-based way of inducing a healthier gut for most of those in need of one (Rhee, Pothoulakis & Mayer, 2009).

The state of the microbiome is passed to the brain from nerve endings embedded along the intestine, then through the enteric nerve to the Vagus nerve, providing a continuous information flow (Rhee et al., 2009). The brain affects gut microbiota indirectly by initiating changes in gastrointestinal motility and secretion and directly by means of signaling molecules released into the gut from cells in the intestinal wall (Forsythe, Bienenstock & Kunze, 2014), thus establishing effective two-way communication between the microbiome and the brain.

Accumulated research findings, such as those by Borre, Moloney, Clarke, Dinan, and Cryan (2014) and Cryan and Dinan (2012), indicate that changes in the gut microbiome affect not only endocrine and immune conditions, but by means of this two-way communication network they influence brain function and behavior as well. Studies involving germ-free animals, as well as animals exposed both to various pathogens and to probiotics, indicate that the gut microbiota play a role in regulation of anxiety, mood, cognition and pain (Cryan & Dinan, 2012). Additionally, studies support the idea that normal gut microbiota can help maintain normal brain development and behavioral functions (Borre

et al., 2014; Heijtz et al., 2011). Alternatively, dysfunction of the microbiome has been implicated as an important factor in the development of stress-related disorders such as depression, anxiety and irritable bowel syndrome as well as neurodevelopmental disorders such as autism (Borre et al., 2014; Heijtz et al., 2011).

The Role of the HPA Axis

The Hypothalamic–Pituitary–Adrenal Axis (HPA), important in the integration of adaptive responses to stress, also has a significant impact on gut function. Both physical and psychological stressors can affect the composition and metabolic activity of the gut microbiota (Elenkov et al., 2000). Further, experimental changes to the gut microbiome have been shown to affect emotional behavior and related brain systems. Exposure to psychological stress in particular activates the HPA Axis by means of a chemical cascade described in some detail by Chrousos (1992), Gold and Chrousos (2002) and Tsigos and Chrousos (2002), leading to altered intestinal barrier function and disruption of the gut microbiome which, when relayed back to the brain, can have, as shown earlier, significant effects on mood and behavior.

By way of orientation, the Hypothalamus, together with the Thalamus and part of the Pineal, is part of the *Diencephalon*, located just posterior to the forebrain and immediately in front of the midbrain, just above the brain stem. The Pituitary is positioned directly below the Hypothalamus, connected to it by a short tubule (The Diencephalon, n.d.). The Hypothalamus controls the autonomic nervous system, among other things, and links the nervous system to the endocrine system by way of the Pituitary, which it governs (Boundless, 2014)

Under ordinary, non-stressful conditions the Hypothalamus manages a regular, well-documented chemical cascade, via the Pituitary, ending with the adrenals secreting mainly cortisol in a pulsative circadian cycle. Under conditions of excessive stress such as may originate from physiological and psychosocial sources, a variety of brain nuclei spur the HPA Axis to initiate what Hans Selye (1936) termed a "general adaptation syndrome" the result of which is the release of additional stress hormones including cortisol, epinephrine and norepinephrine in an attempt to help the brain–body system regain overall balance (Tsigos & Chrousos, 2002).

The disruptive effects of stress hormones on gut sensation, motility and secretion, when fed back to the brain, are compounded by messages from the Hypothalamus activating other brain structures that respond to stress, creating a measurable effect on pain perception, mood and behavior, such as melancholic depression and anxiety-causing memories (Tsigos & Chrousos, 2002). Chronic stress can make these conditions worse because the Hypothalamus tends to be hyperactive in depression, leading to excessive secretion of such chemicals as vasopression, which can increase suicide risk, and oxytocin, which can fuel eating disorders. In chronic stress these and other factors affecting the brain's responses have been shown ultimately to induce severe physical problems, progression of which can have their own effects on mood and behavior (Jones et al., 2006; Tache, Martinez, Million & Rivier, 1999; Tsigos & Chrousos, 2002).

The Role of Nutrition

Most Neurofeedback practitioners are aware of recommended dietary strategies for conditions they usually treat. A number of well-known experts, including Harvard Medical School (Harvard Mental Health Letter, 2009) and Daniel Amen MD (2013), are clear that most forms of ADHD are helped by a diet high in protein, low glycemic carbohydrates and a sufficient amount of healthy fats. In addition, many ADHD children and a preponderance of persons on the autistic spectrum require gluten free—if not fully grain-free—menus (Celiac disease defined, n.d.) or casein-free diets (Casien Allergy Overview, n.d.). These researchers and others see sugar as generally bad.

While most people can easily get the connection between nutritional deficiencies and physical illness, relatively few people are aware of the connection between nutrition and mood disorders such as depression and anxiety (Gold & Chrousos, 2002). Yet emerging scientific evidence indicates that carefully administered dietary supplements have a positive impact on the most common mental disorders (Lakhan & Vieira, 2008). For example, mental health professionals typically think of depression as emotionally-rooted or biochemically-based, while Neurofeedback therapists may look for well-known neural patterns indicating a particular condition. However, both may tend to overlook "easily noticeable eating patterns that can play a key role in the onset as well as severity and duration of depression" (Sathyanarayana Rao, Asha, Ramesh & Jagannatha Rao, 2008, p. 77). Similarly, in a systematic review of 24 studies, Lakhan and Vieira (2010, p. 1) concluded that: "Based on the available evidence, it appears that nutritional and herbal supplementation is an effective method for treating anxiety and anxiety-related conditions without risk of serious side effects," benefits of which, they add, may include placebo effects.

Emerging evidence also tells us that front-line communication to the brain about the effects on the gut of a person's food and supplement intake comes from the extensive community of bacteria in the intestine, the microbiota, which, as we have shown, evokes brain responses that include modulation of behavior, such as depression and anxiety, making the gut microbiota an essential part of a network of relationships that govern homeostasis (Cryan & O'Mahony, 2011). It follows, then, that a decrease in, or a chronic major imbalance of, desirable gastrointestinal bacteria is likely to lead to a deterioration in gastrointestinal, neuroendocrine or immune conditions that ultimately can lead to disease (Cryan & O'Mahony, 2011)

A pro-inflammatory diet, such as one overly concentrated on red meat, carbohydrates and sugar, especially in conjunction with ongoing excessive stress, has been shown to disrupt the normal process by which the gut sloughs off and renews its mucus lining and the normal process by which it renews intestinal epithelial cells. Disruption of this process, known as *apoptosis* (programmed normal cell turnover), can lead to *leaky gut syndrome*, gut inflammation, *irritable bowel syndrome* and intestinal cell *necrosis* (excessive, non-programmed cell death) with a potentially more lasting negative impact on brain development, mood and behavior (Ramachandran, Madesh & Balasubramanian, 2000).

The literature is increasingly clear regarding pro-inflammatory substances in foods generally considered healthy, such as whole grains and dairy products, and most practitioners are aware of the need to have patients be examined for gluten and casein sensitivity, especially in cases of ADHD and Autism Spectrum Disorder (Amen, 2013), so they are simply mentioned here as elements to be included in the mix rather than examined in detail. Similarly, artificial sweeteners and food colorings, about which numerous articles relate a litany of adverse neural events—and which many Neurofeedback practitioners have observed in their own patients—is a complicated area where the body of formal research gives us little help. With respect to Aspartame in particular, there is a multitude of practitioner reports describing adverse events (Martini, n.d.), while a survey of the formal research through 1998 showed that 100% of industry-funded studies deemed the sweetener safe, while 92% of independently funded studies showed it to be a problem (Walton, n.d.).

At the same time, a reliable body of neurochemical research has identified a number of specific nutrients that the brain requires in order to maintain normal functioning, such as the Vitamin B group—elements of which are important to neurotransmitter biosynthesis and insufficiencies of which have been linked to neurological problems—as well as trace minerals such as zinc, copper and selenium, which have been shown to have a vital role in maintaining normal brain function (Gibson & Blass, 1999).

The brain is sensitive to diet, dependent on a continuous supply of nutrients, some of which cannot be synthesized by other organs for use by the brain, but have to be furnished by what we eat. Our food can alter brain function in the short run by altering neurotransmitters and neuronal firing and can actually alter membrane structure in the longer run (Gibson & Blass, 1999). On the other hand,

development of a diet and nutritional program based on sound neurochemical and valid scientific observations can be a rational way to deal with imbalances in brain-related problems. This has been further demonstrated in recent research studies conducted by Bravo et al. (2011) and Smith et al. (2014) which gave increased recognition to the benefits of probiotics as adjunctive therapy for conditions such as depression, anxiety, ADHD and even autism.

In Summary

We now know that diet has the potential to alter brain health and cognition, influencing cognition in particular by acting on cellular processes vital to maintaining cognitive functioning, and it should be clear from a growing body of research that gut condition, and especially inflammation, has a significant influence on neural process and associated behaviors so that:

- we can no longer view neural function as fully distinct from and independent of most physical disorders;
- it is increasingly evident that nearly all degenerative diseases, including those of the brain, have similar biochemical etiologies; and
- whatever the etiology of a disorder, neural function is likely to be affected, answering a cogent question Seaman (1987) raised years earlier.

The brain is now seen as being in direct communication with the immune and endocrine systems, which means that systemic inflammatory reactions and responses can influence brain function. In that respect, research, such as that by Wilson, Finch and Cohen (2002) has been actively exploring ways that inflammatory *cytokines*—a group of low molecular weight amino acids with specific receptors that mediate cellular intercommunication by various means—cross the blood-brain barrier to induce changes in the brain that affect cognition and contribute to the development of neurodegenerative diseases.

The literature indicates that giving due attention to gut–brain interaction can support, and potentially enhance, the outcomes of Neurofeedback and Neuromodulation protocols, even though the specific impact of such attention has yet to be determined. Nonetheless, it still follows that reducing systemic inflammation and improving gut health should be considered an integral part of treating for a more functional brain.

A Brain–Body Model

This conclusion brings up several potentially unsettling questions for a practitioner, like what does it take for a practitioner to put such a program together, how affordable is it and how disruptive to an existing practice—and its income stream—may be the changes implied by the inclusion of a gut health regimen in what has, to date, been a rather straightforward system of diagnosis and treatment. In that respect the field has changed relatively little, fundamentally, over the years, even with increasingly sophisticated equipment and software based on rapid advances in technology and neuroscientific research.

The changes implied by broadening a practice to include a brain-gut-microbiome model, thus moving it toward a systems approach to treatment, shouldn't alter significantly the fundamental clinical work of evaluation, testing and diagnosis; rather, it requires incorporation of what else in the human mega-system is shown to have a significant impact on neuroregulation outcomes. Specifically, since the condition of the gut is shown to have a demonstrable effect on brain function and behavior, and that effective means exist to evaluate gut condition and reregulate the microbiome, a practitioner can feel confident about using such means to support and augment treatment outcomes.

The practitioner would be dealing with, first, a shift in the scope of testing and evaluation to find out what a patient needs to move gut condition toward active support of neural treatment; second, a cost-effective and reliable way for the patient to get done the required testing and results; and third, a way the practitioner can receive the testing results to incorporate in his/her evaluation, treatment plan and monitoring program.

Two other important questions a practitioner is bound to ask are: if I am to go through all this adjustment, how do I know it will make a real difference for the patient and if so, how much of a difference would it make? The answers are: we don't know that it will make a significant difference for everyone and we don't know exactly how much of any improvement can be attributed solely to treating gut function. What we *do* know is: the literature demonstrates clearly that problems of the gut and its microbiome adversely affect mood, behavior and brain function, that treating the brain with those problems present is like swimming against the tide and that a practice which includes a gut function module as part of its program seems likely to achieve better results than it did before. Bottom line, if the practitioner's job is to deliver the patient measurably improved neural functioning in a lasting way, then it would be well for him/her to include gut function in the process of evaluation and treatment.

A Brain–Body Model in Practice

What follows is the profile of a neuroregulation practice with a well-established brain–body model in place. This practice has broadened its scope of treatment by:

- including in its intake package a questionnaire specifically designed to indicate physical problems impinging on neural function;
- linking with a functional medicine doctor to order necessary testing, interpret results and recommend dietary and supplement regimens to treat indicated problems; and
- providing a range of advanced Neurofeedback, Neuromodulation and adjunctive modalities to increase treatment options.

Most patients coming into this practice follow a fairly conventional treatment path:

- Initial interview
- Testing and interpretation of results
- Evaluation, diagnosis and treatment plan
    - Evaluation outline from the assembled results
    - Detailed consultation with patient and caregivers
    - Treatment orders
- Ongoing evaluation of progress
- Follow-up evaluation and next steps
    - Follow-up testing
    - Consultation
    - Ongoing dietary and supplement program
    - Referrals to further treatment as indicated

Initial Interview, Testing and Interpretation

The importance of an initial interview, in addition to letting new patients sense that they've been heard, is to ask cogent questions around their presenting problems that include diet and lifestyle habits and to garner other information that may be of value in reviewing test results.

Prior to the initial interview the prospective patient fills out a detailed individual and family history, including dietary and lifestyle information, current and past medication history and family patterns of behavior and disease. They also fill out an extensive questionnaire, in person or online, that offers insight into neurophysiologic symptoms for which testing may be indicated in addition to a Quantitative EEG—administered to every incoming patient—and a TOVA or IVA as indicated.

The questionnaire used by this particular practice includes the self-ranking of specific symptoms in a number of categories on a 0–3 Likert Scale (nonexistent to severe). Inquiries include symptoms such as gas, bloating, bowel movement frequency, antibiotic and prescription drug use, ringing in ears, ankle swelling, frequent drowsiness, and questions around such conditions as sleep, stress, diet and lifestyle. Results are collated and symptom categories are arranged for the respondent in order of apparent importance. A questionnaire such as this can give the practitioner important information regarding factors impinging on brain function and provide a focus for functional medicine testing.

This practice has found the questionnaire form of inquiry to be highly informative. For example, in a sample of 48 current and recent patients presenting at this clinic (ages 14 to mid-70s, mixed gender) the five most frequent symptom categories revealed by their questionnaires, along with the percent of respondents who scored in the particular category, were:

- Heavy metals (lead, mercury, cadmium, etc.) = 81%
- Adrenal, Hypothalamus, Pituitary (chronic stress, HPA Axis activation) = 67%
- Liver-gallbladder (toxicity: pollution, pesticides, hair and skin products) = 63%
- Thyroid (secondary to stress, toxicity, HPA Axis dysregulation) = 60%
- Gastrointestinal system (inflammation, Dysbiosis, leaky gut) = 58%

The value of this sample is that it's made up of a diverse group of individuals coming off today's streets looking for enhancement of brain function. The percentages indicate that most respondents had several of these categories among their top five. The take-home point of this exercise is that today's assaults on functional health from lifestyle, diet and the environment are affecting how our brains work—mine, yours and theirs—and, by extension, are likely to impact the effectiveness of Neurofeedback and Neuromodulation protocols, regardless of their sophistication.

Only one other symptom category shows up in more than 50% of responses: nutritional deficiencies at 56%. These six categories as a group indicate a general symptomology arising from toxicity, chronic stress and gut problems, all of which have been shown previously to have an adverse impact on brain function, mood and behavior.

A Note on Heavy Metals

This paper has focused mainly on gut-biome dysregulation and activation of the HPA Axis and ways these dynamics can affect brain function. These conditions usually can be corrected with appropriate supplements and changes in diet and lifestyle. On the other hand, toxic levels of heavy metals, while fairly easily tested for, are much more difficult to correct.

Research, well-summarized by Clarkson (1987), shows that both inorganic and organic compounds of such metals as aluminum, lead and mercury tend to target the nervous system and are demonstrated to be neurotoxic. Chang (1990) demonstrated that toxic levels of the organic compounds of lead and mercury have a generally adverse effect on neural function and selectively damaging effects on neurons. If heavy metals ranks among the top symptom categories in this practice's questionnaire, a heavy metals test, which can be either blood-based or urine-based, is ordered. If toxic levels are found, the functional medicine doctor can order chelation therapy in intravenous, oral or rectal form.

Balancing Neurotransmitters to Enhance Neuroregulation Protocols

Neurotransmitter testing is generally ordered for depression, anxiety and chronic stress because much of the symptomology arising from toxicity, mood disorders, chronic stress and gut problems, including those resulting from poor diet and nutrition, is likely to be reflected in neurotransmitter imbalances. The literature indicates, and intuitively it makes sense, that rebalancing neurotransmitter activity tends to improve overall mood and behavior and to quiet the HPA Axis, reflecting an overall improvement in brain function (Wells, n.d.). Neurotransmitter testing may be blood-based or urine-based (Neuroscience Inc., n.d.) and specially formulated corrective amino acid and dietary supplements are generally recommended based on test results. This practice found that urine-based testing is generally better for young children and those averse to needles. The practitioner can monitor patient supplements during the treatment process and initiate retesting if he/she sees a need for it.

Another means of treating neurotransmitter imbalance, and one used by this practice, is to introduce Nexalin™ Advanced Therapy at the front end of treatment. Nexalin™ uses a FDA-cleared form of Transcranial Electrical Stimulation (TES) pulse wave at a specific frequency to stimulate the Hypothalamus, which helps balance neurochemistry and can begin to quiet the HPA Axis (Marshall & Binder, 2013; Reato, Rahman, Bikson & Parra, 2013). Both supplementation and transcranial stimulation have achieved satisfactory improvements in neurochemistry at this practice, although transcranial stimulation appears to work more quickly and with good persistence. In several cases the practice has found it beneficial to use the two methods together.

Several other tests relating to functional medicine may be ordered during the evaluation and testing process as indicated by patient responses at the initial interview either on the intake form or in the questionnaire:

- *Minnesota Multiphasic Personality Inventory (MMPI-2 RC) and/or Millon Clinical Multiaxial Inventory (MCMI III)*: where psychological assessment and intervention may be indicated (Sellbom, Graham & Schenk, 2006).
- *Hormone testing*: may be indicated as a factor in neurochemical imbalance affecting cognition, depending on gender and age (Barth, Villringer & Sacher, 2015; Drake et al., 2000).
- *Micronutrient testing*: assessment of vitamin, mineral and essential nutrients shown to have an effect on brain function (Gómez-Pinilla, 2008).
- *Food sensitivities testing*: an assessment of which fruits, vegetables, meats, dairy, grains, nuts and other foods are likely to cause or increase a patient's gut inflammation, with potential inflammatory effects on the brain (Klein, 2013).

With respect to psychological testing, results are generally considered as information for the practitioner to use in optimizing the patient treatment plan and the practitioner has to be careful about what he/she shares with the patient and how what's shared is presented.

In the wake of micronutrient testing and a survey of food sensitivities, as was discussed earlier in this paper, a patient may be prescribed a gluten-free, casein-free or grain-free diet, along with a vitamin and probiotic regimen, to heal gut issues and support outcomes of neuroregulation treatments.

Of all the factors that influence inflammation, we have seen that diet may have the most direct impact. A number of nutrient-dense foods with specific anti-inflammatory qualities, such as green vegetables, sprouted grains, legumes and healthy fats, are shown to support brain health and cognitive function. On the other hand, junk foods high in sugars and trans-fats fuel inflammation and impair cognitive function. Worse, insulin dysfunction—usually related to chronically elevated blood sugar from an unhealthy diet—is a major longer term risk factor in dementia and cognitive decline (Eliaz, 2013).

Evaluation, Diagnosis and Treatment Plan

These results and recommendations are added to results of Quantitative EEG and TOVA, or IVA, testing to provide a basis for the practitioner to develop a treatment plan and to outline what he/she considers important to explain to the patient and caregivers during an extended consultation.

This practice emphasizes the value of an extended consultation that brings together all the facets of the patient's condition, those overseen by the functional medicine doctor as well as those to be treated within the practice. This is an extended conversation designed to support the diagnosis, demonstrate the value of a comprehensive treatment plan and make certain that all the patient's questions are addressed. This consultation also provides the practitioner, the patient and his/her caregivers a basis for ongoing check-ins to improve compliance with the treatment program and communicate progress.

Elements of the Treatment Program

1. The practitioner oversees compliance with the supplementation and dietary recommendations of the functional medicine doctor to get as much mileage as possible from the neuroregulatory program indicated by the Quantitative EEG.
2. Transcranial Electrical Stimulation (TES) may be introduced early in the treatment regimen. The extensive research behind TES and its effectiveness was reviewed by Gilula and Kirsch (2005), who concluded: "The results suggest there is sufficient data to show that CES technology has equal or greater efficacy for the treatment of depression compared to antidepressant medications, with fewer side effects" (p. 7). The effectiveness of TES continued to be shown by Kadosh (2013) and by Krause and Kadosh (2013), indicating promise for TES modalities to help enhance cognition. The normal protocol used in this practice is designed to move neurotransmitter levels more toward normal, thus quieting anxiety and improving mood. It consists of ten 40-minute sessions over two weeks, initially five consecutive days on and two days off followed by five more consecutive days of treatment. Additional sessions may be indicated, administered on a more flexible schedule.
3. EEG Neurofeedback protocols. At the clinician's discretion, after several Nexalin™ treatments, EEG Neurofeedback can be started. This clinic uses several configurations of EEG Neurofeedback, depending on the objectives of treatment. Most of the practice's training protocols are Z-score based.
4. Adjunctive treatments:
    a. Transcranial Magnetic Stimulation (rTMS) using a variety of frequency-based protocols. This modality provides a diffuse cortical stimulation used mainly to support and amplify the effects of Neurofeedback (Fitzgerald & Daskalakis, 2013; George et al., 1995).
    b. Syntonic Phototherapy. This modality uses a system that sends specific colors of light from a specially developed source into the eyes at a given flash rate to stimulate the brain through both the optical pathways and a secondary nerve pathway that runs from the eye to deep brain structures. The system has been shown to help not only with sight, but with depression, phobias and reading disabilities (Liberman, 1991; Mischio, 2012)
5. Interim Abbreviated Quantitative EEGs, administered as indicated during the treatment program to assess progress and adjust the treatment program as necessary.

Post-Testing and Consultation

This practice finds it helpful in most cases to have a post-treatment Quantitative EEG and IVA to compare with the initial QEEG and IVA. This gives both the practitioner and the patient a tangible representation of progress and supports a conversation that offers either closure or a better understanding of what next steps might be indicated. Follow-up testing on brain-gut issues addressed at the

beginning of treatment should be included in this conversation to clarify issues around continuation of dietary and supplementation programs. The practitioner should make clear, both to the patient and to any caregivers, how important it is to maintain the improvements they have taken the time and expense to obtain.

Putting It Together in Practice

Making a shift toward the more integrative brain-gut-biome model for enhancing brain function in a lasting way is, as with most things, easier said than done. While it need not be prohibitively expensive to shift the practice in that direction, the practitioner is likely to face an extensive amount of change in assessment and testing procedures, along with possibly significant problems of finding a good functional medicine practitioner to work with. The patient path is altered significantly and the degree of direct control the practitioner has over it may be diluted by the presence of another practitioner with a substantial role to play. Moreover, there is a learning curve involved in understanding what is being tested, what the interpretations mean and what that implies regarding treatment. Last, but hardly least, the patient is asked to take on additional expense if a significant amount of additional testing is indicated. While most aspects of the testing mentioned above may be covered in whole or in part by insurance, there usually will be some out-of-pocket cost for supplements.

Ultimately, the shift is dependent on the successful negotiation of five major hurdles:

- Finding and creating a satisfactory working relationship with a functional medicine doctor. If there is no one in the immediate town or area of the practice, then arrangements could be made with the laboratories, and with a local phlebotomist, to acquire and submit samples directly from the practice. Laboratory reports could be sent both to the practitioner and to the non-local doctor who could consult by visual software, Skype or email.
    - Considering financial arrangements: who charges for what and how much to charge. Some health insurers and related services publish a periodic survey of charges for many procedures. This can provide a guideline.
- Learning what results of the expanded testing means, how to discuss it in the patient consultation and how to monitor patient compliance with ongoing mini-consults.
- What additional treatment equipment or software upgrades might be required to optimally carry out a more advanced treatment plan.
- How to maintain a satisfactory patient flow into the integrative practice, marketing to potential patients and other professionals.

Worries attached to owning and managing a professional practice are not reduced, but patient outcomes are likely to be better, with concomitant patient satisfaction and potential for increased referrals.

If the reader takes away nothing more from this paper than the sense that he/she is actually dealing with a nonlinear, far-reaching and broadly interactive system when working with the brain, the authors' point will have been made. If the information provided here actually prompts more practitioners to work from a wider, more systemic point of view, then that would be terrific. Either way, the march of applied neuroscience puts the future on the side of integrative treatment.

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