The Growing Role of Neurofeedback in Integrative Medicine

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We are at the threshold of revolutionary change in our approach to mental dysfunctions as they come to be seen primarily in the frame of neural network relations. To date the recovery of brain function has been approached mainly in the frame of neurochemical models, but even this principally involves neurochemistry in the service of neural communication. The medications in common use for mental dysfunctions by and large target the neuromodulator systems that regulate synaptic excitability. But there is another aspect to the problem. Information transport via the action potential mechanism is subject to tight timing constraints, and this represents a major potential failure mechanism for the brain under duress. This is a particular issue following physical or emotional trauma, or when the brain has been diverted from its proper developmental pathway early in life. In these cases there may be little or no evidence of structural injury to the brain. The deficits must lie almost entirely in the functional realm, and therefore should be accessible to a functional remedy. And yet we know that pharmacotherapy is largely ineffective in application to these conditions. The deficits are more easily understood in the bioelectrical domain of timing and frequency. And when remedies emerge based on an appeal to neural network functioning in the frequency domain, the case for a new departure in understanding mental dysfunctions is consolidated. This is where we now find ourselves.

Progress in brain imaging over the last two decades has brought these issues to the fore. At first we had to make do with the static imagery of PET and SPECT, but this already drew our attentions back to the intact, functioning brain, and elevated our gaze from brain slices in petri dishes and the firing patterns of individual neurons. Such a divide-and-conquer strategy gave us no hope of ever fully understanding the living brain. A complementary systems-level perspective was missing. With the emergence of functional magnetic resonance imaging in the early nineties we had our first opportunity to witness brain dynamics, albeit with very poor time resolution as the process being monitored was glucose uptake. This led in time to the identification of our core connectivity networks, which constitute the foundation of a hierarchy of functional organization in cortex.[1] Follow-on studies revealed that identifications could be made between various mental disorders and dysfunctions in our intrinsic connectivity networks (ICNs).[2] On that basis, Menon proposed that much of psychopathology could be grounded in the failure of our core control networks to coordinate properly. Evidence was cited for several conditions, including schizophrenia, depression, anxiety, dementia, and autism. But the mechanism undoubtedly has more general applicability.[3] Yet other studies demonstrated that conditioning experiments targeting localized features of the fMRI could elicit functional improvement.[4] As an example, deCharms demonstrated benefit for Complex Regional Pain Syndrome (CRPS1), yet another relatively intractable condition that does not yield to pharmacotherapy.[5] Jointly these findings implicate functional connectivity of the core networks as a basic failure mechanism in mental disorders. The full exploitation of these new findings call for an integrative, systems-level perspective on brain function, one that takes both perspectives---the neurochemical and the bio-electrical domains---into account. And on the clinical side that implies the need for an integrative approach to remediation as well.

Very few scientific novelties burst upon the scene without obvious antecedents, and the same holds true here. Much of what is now being proved out in fMRI-based neurofeedback has been previously demonstrated using feedback with the EEG as a training variable. For example, just two years after the publication by deCharms a similar report was published using EEG-based training with CRPS1, and the results were comparable, if not better.[6] The method used was just one year old at the time. It was infra-low frequency training, the principal topic of this paper. However, the antecedents of this method go back more than thirty years.

The EEG was our first non-invasive technique for studying brain dynamics, but its complexity limited its clinical utilization, so the world moved on. It has taken new developments in mathematical analysis and in data acquisition to restore the EEG to its proper place in research. This is also having beneficial fallout for clinical practice, with innovation increasingly occurring at the pace of software development. The history of EEG biofeedback, now commonly termed neurofeedback, is elaborated in a book just published by Taylor and Francis, titled “Restoring the Brain: Neurofeedback as an Integrative Approach to Health.” The book covers recent developments, with particular focus on the rapidly emerging technique of infra-low frequency training. The case is made for neurofeedback to play a complementary role in integrative medicine.[7]

The EEG gives us insight into the brain’s regulatory activities and how these are organized both spatially and temporally. The argument briefly goes as follows: Cortex is organized for massive parallel processing in the service of pattern recognition. The organization of such patterns must be supported by neuronal assemblies of macroscopic spatial scale, and these must be organized for simultaneity in processing. The principle that ‘simultaneity defines belonging’ is known as *time binding*.[8] Seen in its simplest mathematical terms, the neuron is organized for coincidence detection—on the timescale of milliseconds---by the nature of the action potential mechanism. Coincidence at the level of the neuron in turn supports simultaneity at the level of the neuronal assembly. Since action potentials are perishable entities that are not self-replicating, the persistence of states must be explicitly organized through repetition. Refresh is supported via a recursive cerebral architecture, thus generating a periodicity that maintains continuity. Simultaneity of action at the level of the neuronal assembly, in combination with periodicity, translates to local synchrony at the level of the EEG. Communication between cortical sites is reflected in synchronous (or at least coherent) activity at those sites. Thus, the regulatory role of neuronal assemblies is reflected in frequency-based organization of sufficient magnitude to become discernible to us in the EEG, giving us exquisite insight into timing relationships at the network level. Hence the EEG distills for us the aspect of neuronal activity that is involved in neuronal regulation (as opposed to information transfer). We don't get to see the text, but rather only the context.

We know that the brain is a highly competent, if not over-eager, correlation detector, and in feedback this quality is put to good use. If the brain is allowed to witness selected features of its own EEG, it has no difficulty recognizing its own agency with respect to that signal. Once that loop is closed, the brain inevitably also takes responsibility for the signal and tries to control it. This process is analogous to the brain taking responsibility for keeping the bicycle properly balanced and the car properly pointed down the freeway. The rider or the driver doesn't have to be engaged on these matters. They can be left to the brain to handle in background. The same principle holds in the case EEG feedback and fMRI feedback. The process does not necessarily involve conscious mediation. All that is required is that the process not be interfered with. Distraction is the bane of the bicyclist, of the driver, and of the neurofeedback trainee.

When the brain is involved in feedback under conditions in which it is allowed to exercise its discretion, there is a bias in the direction of better regulation. Left to its own devices, but with the benefit of physiologically relevant information, the brain tends to move toward calmer, better-controlled states. It is residence in calm, de-stressed states that presents the therapeutic opportunity for the functional reorganization of the core networks. The brain is entirely in charge of the recovery process that follows. We have simply arranged to provide a propitious context. The client is usually aware of nothing more than the feeling of migration to a state of calmness with which he may not have been previously acquainted. (Even squirrely autistic children may adopt a quiescent, meditative pose while undergoing the training.) The client may also remark about a state of alertness that does not seem congruent with such a state of placid calmness.

What has been described above is the typical experience of someone undergoing neurofeedback in the infra-low frequency region of the EEG. There are many other ways of doing neurofeedback, however, and some history needs to be reviewed to provide context for the discussion to follow. EEG biofeedback got its start in the 1960's with the training of the cortical resting rhythms, principally the famous alpha band at nominally 10 Hz,[9] and the sensorimotor rhythm at nominally 13 Hz.[10] The alpha band signal at the occiput could be regarded as the resting rhythm of the visual system, and the sensorimotor rhythm (SMR) could be understood as the resting rhythm of the motor system. Since the activity in these bands has an episodic, bursting character, it was trained in an operant conditioning paradigm of challenge (with respect to a threshold) and reward. In both instances, the objective was to move the trainee toward lower levels of arousal, i.e. toward calmer states, and toward improved levels of regulation. In the case of the alpha training, this was found to be ameliorative of anxiety states, [11] and the SMR-training was found to be stabilizing against motor seizures and even temporal-lobe seizures, among others.[12] These initial findings were vigorously challenged at the time, but they have been amply validated since.[13, 14] A meta-analysis of the work with epilepsy has also been published.[15]

The research on SMR-training for seizure management became the springboard for application to hyperkinesis, which later became ADHD.[16,17] All but one of the ADHD studies that also tracked IQ found significant improvements in IQ score with the training. A 20-point IQ improvement was observed in two 8-year-old mildly mentally retarded twins. The results were published after five years of follow-up, over which time the gains held but no further improvements could be elicited.[18] The work with SMR-beta training led to much broader application to psychopathology by the early 1990s.[19] It emerged that the challenge to a single dominant rhythm of the EEG in a training paradigm sufficed to evoke broad functional reorganization of the cerebrum.

Subsequent to the early research, alpha training evolved in three directions. One aimed toward optimum functioning through the broadening of the attentional repertoire via the promotion of whole-brain alpha synchrony.[20] Another used intensive alpha synchrony training in support of psychotherapy and personal transformation.[21] The third and most common application was oriented toward the promotion of deep, internally focused states that facilitated the resolution of traumas and a reprieve from addictive propensities. This came to be known as Alpha-Theta training once theta-band reinforcement was added to the protocol.[22,23,24]

The next major thrust in the technology was toward the individualization of what came to be known as SMR-beta training (because reinforcement of the slightly higher-frequency beta 1 band (15-18 Hz) was also commonly included in the protocol). The personalization of the training took two forms. The first of these followed immediately upon the availability of affordable full-brain mapping capability on PCs in the early nineties. This allowed the transient excursions into dysregulation to be detected wherever they occurred on cortex, and the training strategy to be adapted to focus on such excursions. The training brain was cued with respect to such excursions in what was referred to as inhibit-based training. This involved nothing more than the transient withholding of rewards. Brain activity was not actually being inhibited. The other thrust, for which our own group was responsible, consisted of the individualization of the reward frequency, which began after 1995. It was observed that sensitive and unstable brains were differentially responsive to different EEG frequencies, and that for optimal outcomes the target frequency sometimes had to be tuned to within 0.5 Hz or even less.

Such frequency specificity could be readily confirmed because of its repeatability. In the highly responsive individuals at issue here, we were dealing with demonstrable real-time control of their physiological state. For instance, one person might feel hungry at one frequency, and yet experience satiety at a nearby frequency. The therapist could toggle the frequency back and forth and reliably reproduce these feeling states. Another person might feel tearful at one frequency (without having any basis for being teary), and yet feel placid or even upbeat at an adjacent frequency. The transition period could be as little as a minute or two. Yet another person might feel the onset of a migraine aura at one frequency, and observe its subsidence at an adjacent frequency. Again this held true reproducibly. Unsurprisingly, bipolar individuals are particularly responsive, and in some cases can be actively moved between depressive and manic states within a period of minutes with a slight shift in reward frequency. In between these two frequencies lies the optimal target frequency at which the brain can train itself toward stability simply by virtue of lingering there for a number of training sessions. This gives the neural networks the opportunity to consolidate the new configuration.

The implications of this responsiveness are huge. We were in fact effecting real-time alteration of physiological state in the general case. Trainees mainly differed in their awareness of such state shifts. Those with the most sensitive, unstable, or reactive brains were the best reporters on their own state as well as being the most sensitive to the choice of target frequency. For both of these reasons, such sensitive individuals were the canaries that guided further development of the method. In the event, we were led to provide training at ever lower frequencies to accommodate them. By 2006, after several years of gradual migration to lower frequencies, this trend caused us to enter the infra-low frequency region. Training was performed at frequencies of 0.1Hz and below, the very region in which the intrinsic connectivity networks were first identified using fMRI. In the following, this will be referred to as ILF training.

At such low frequencies, threshold-based training was out of the question. The cycling time was too slow. We had to resort to signal-following, in which the brain is simply exposed to the exceedingly slow undulations of the signal. The brain's interest was captured by the continuity of information flow, and the whole training exercise became more effective than it had ever been before. For the first time, the brain was being trained in accord with its own preferences rather than being regimented like one of B.F. Skinner's pigeons. The brain was in charge of its own journey, based on its own assignment of meaning to the signal it was observing. (The reader's indulgence is requested for the use of such anthropomorphic language with reference to the brain as an autonomous agent.) The results were so dramatic—and so parametrically specific—that we promptly issued a Protocol Guide to our practitioner network.[25]

What, then, can we accomplish with techniques such as this at our disposal? In order to organize the full range of clinical findings it is useful to have in mind the hierarchy of the brain's regulatory obligations. Considering the brain in its role as a control system, its principal burden is to assure its own unconditional stability. The method is very effective with brain instabilities such as migraines, panic attacks, asthma episodes, seizures, vertigo, night terrors, and even Bipolar Disorder. The training has been relatively ineffective to date for narcolepsy and sleep apnea, although it can be very helpful in isolated cases.

Remarkably all of the above conditions respond well to a single protocol, which makes it plain that we are remediating a core vulnerability rather than specific conditions. The placement of choice is T3-T4 (in the International 10-20 system), which indicates that the functional deficit relates to the coordination between the two hemispheres. However, no claim of uniqueness is implied. The above conditions respond to a variety of other protocols as well. For example, a 90% favorable response for migraines was observed by Walker using QEEG-based methods.[26] So the T3-T4 training is usually sufficient for the purpose, but it is not obligatory.

Remediating brain instabilities had been our strong suit from the moment we first adopted the inter-hemispheric placement of T3-T4 in 1999. Up to that time we were using lateralized placements to target migraines that were typically also lateralized. When a particular migraine simply migrated to the other hemisphere when it was directly targeted, the inter-hemispheric placement was tried, and the migraine dissipated promptly. The inter-hemispheric placement soon became standard. It was the brain instabilities that mandated such a precise targeting in terms of frequency, and thus drove the agenda to ever lower frequencies.[27]

Next in the hierarchy is the issue of tonic state regulation, and within this broad category we have a hierarchy as well, one that conforms to our developmental sequence. Foundational in this hierarchy is the regulation of tonic arousal, which is in turn intimately connected with affect regulation, autonomic regulation, and interoception. This is the developmental priority in infancy and early childhood, and it is the primary target in ILF neurofeedback. Fortunately the deficits in these domains lie largely in the functional realm, quite irrespective of how intractable they may appear behaviorally. They are therefore accessible to us for remediation with neurofeedback.

Within the category of arousal regulation we include insomnia, agitation and hypervigilance, as well as general over-arousal. Within the domain of affect regulation we include the anxiety-depression spectrum, the capacity for attachment and empathy, and the personality disorders. Within the domain of autonomic regulation we include dysautonomia, sympathetic/parasympathetic balance, regulation of blood pressure, heart rate, and vasoconstriction; peripheral temperature, galvanic skin response, and even gastric secretions (in connection with reflux). With respect to autonomic regulation there is a substantial correspondence with traditional biofeedback utilizing measures of peripheral physiology.

Within the general category of state regulation we also encounter transient dyscontrol (quite possibly externally mediated) that is subsumed in the general category of behavioral disinhibition. It needs to be distinguished from brain instabilities. This category includes impulsivity, obsessive and/or compulsive behaviors, Tourette Syndrome, bruxism, and rage behavior. Among these Tourette Syndrome and OCD present the greatest challenges to neurofeedback in its present state of maturity. Impulsivity, on the other hand, responds more consistently and is more completely resolved than the other conditions. In large group evaluations of ILF training for a general clinical population (5,746 participants), the effect size was ~0.75 and the post-training distribution in impulsivity was found to exceed the norm. These data have been presented in a professional forum, but have yet to be published. They are shown in Figure 1.

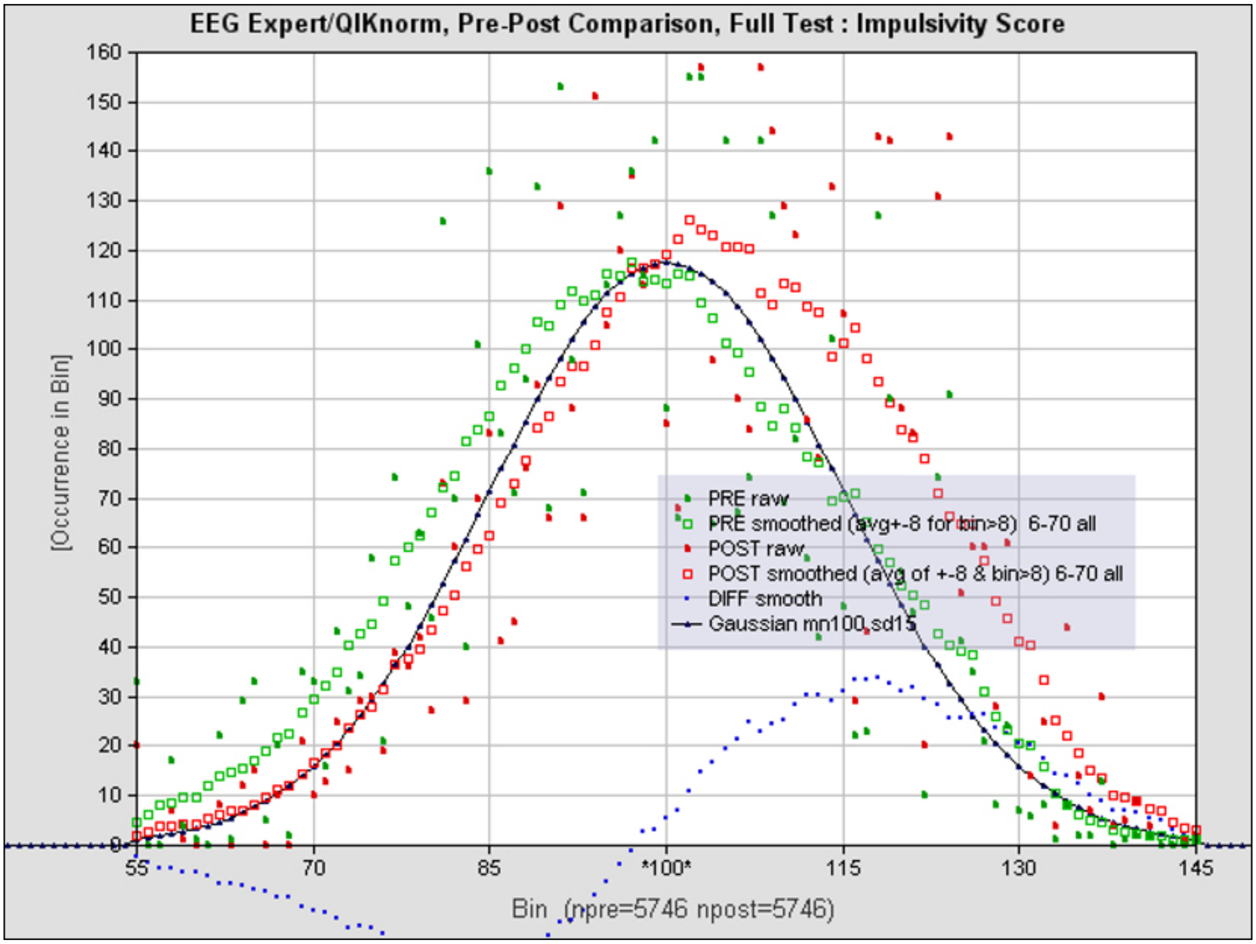

Figure 1: The plots show the distribution of impulsivity in terms of standard scores for a clinical population of 5746. The population is unselected, consisting of everyone in the customer base who had done the QIKtest both before and after twenty session of neurofeedback training. The training was offered for a variety of indications. The black curve shows the Gaussian distribution for the norming pool. The green curve illustrates the distribution prior to training; the red curve, post-training. The data have been subjected to near-neighbor averaging for clarity. Improvement by nominally 0.75 standard deviations with training is indicated. The likelihood of scoring two standard deviations above the norm was doubled. The data are not naturally Gaussian-distributed. Non-parametric statistics were used throughout. Conversion from percentile scores to standard scores was performed for ease of interpretation.

The above observation illustrates that this kind of training is best regarded in the frame of training toward optimum brain function rather than as a technique to expunge dysfunction. The latter objective is accomplished by virtue of the former. That explains why the approach can rely on a modest number of electrode placements for all trainees. It is basic regulatory mechanisms common to us all that are being targeted in the training, not one or another specific deficit.

Beyond state regulation issues we have the third category of regulatory burden, namely responsiveness to the environment both on the input and on the output side. This category includes sensory processing issues, learning disabilities, maintenance of vigilance, attentional faculties, and working memory. It also includes motor planning and motor function such as speech articulation.

It was executive function that received most of the attention in neurofeedback in the early decades, mainly because this conformed to the interests of cognitive neuroscience. For the same reason, the training for the ADHD spectrum targeted the left hemisphere exclusively because that was the only one for which a cartography was available. The right hemisphere remained terra incognita; there was no point in even showing it in the textbooks (with the exception of the sensorimotor strip).

And yet clinical demands had driven us ever more toward lower frequencies and toward a right-hemisphere priority. Just as the left hemisphere has priority with respect to executive function, the right hemisphere has priority with respect to the foundational regulatory concerns of arousal, affect, and autonomic regulation. The right insula has a very different life experience from that of the left, so to speak. Since it was our most challenging clients that drove us ever lower in training frequency and ever more firmly onto the right hemisphere, it follows that the most intractable conditions encountered in mental health relate to vulnerabilities of right-hemisphere function first and foremost.[28] Further, since we are driven to attend to the earliest developmental priorities of the developing infant, it follows that we are targeting the residual sequelae of early childhood trauma in much of our work.

Throughout the evolution of the training protocol schema over the last two decades a remarkable consistency has been observed. The frequency at which right-hemisphere training optimizes for any individual differs systematically from that of the left. In the infra-low frequency range, the left hemisphere training optimizes at twice the frequency of the right. In biological systems it is the lowest frequency that sets the tone, and higher frequencies coordinate with the basic rhythm. A harmonic relationship is not unexpected. Within the conventional EEG frequency range, the right hemisphere optimizes at two Hz lower than the left. Here it is likely that the left hemisphere is taking the lead and the right hemisphere is the follower. The division of labor seems appropriate: The right hemisphere is in charge of our state of being, of our vegetative and our core or intrinsic self; the left hemisphere is in the lead when it comes to reacting to and engaging with the world. This view has recently received support from an evaluation of information flow within microstates.[29]

The implications for brain training are that we should understand the infra-low frequency training principally in terms of right-hemisphere priorities, and we should understand training in the conventional EEG range in terms of left-hemisphere priorities. That is indeed how matters have unfolded over the years. The crossover between these two realms is at the only place that it can be, namely at two Hz on the right hemisphere, which corresponds to four Hz on the left in both the high frequency and the low frequency perspectives. The frequency relationships are illustrated in Figure 2.

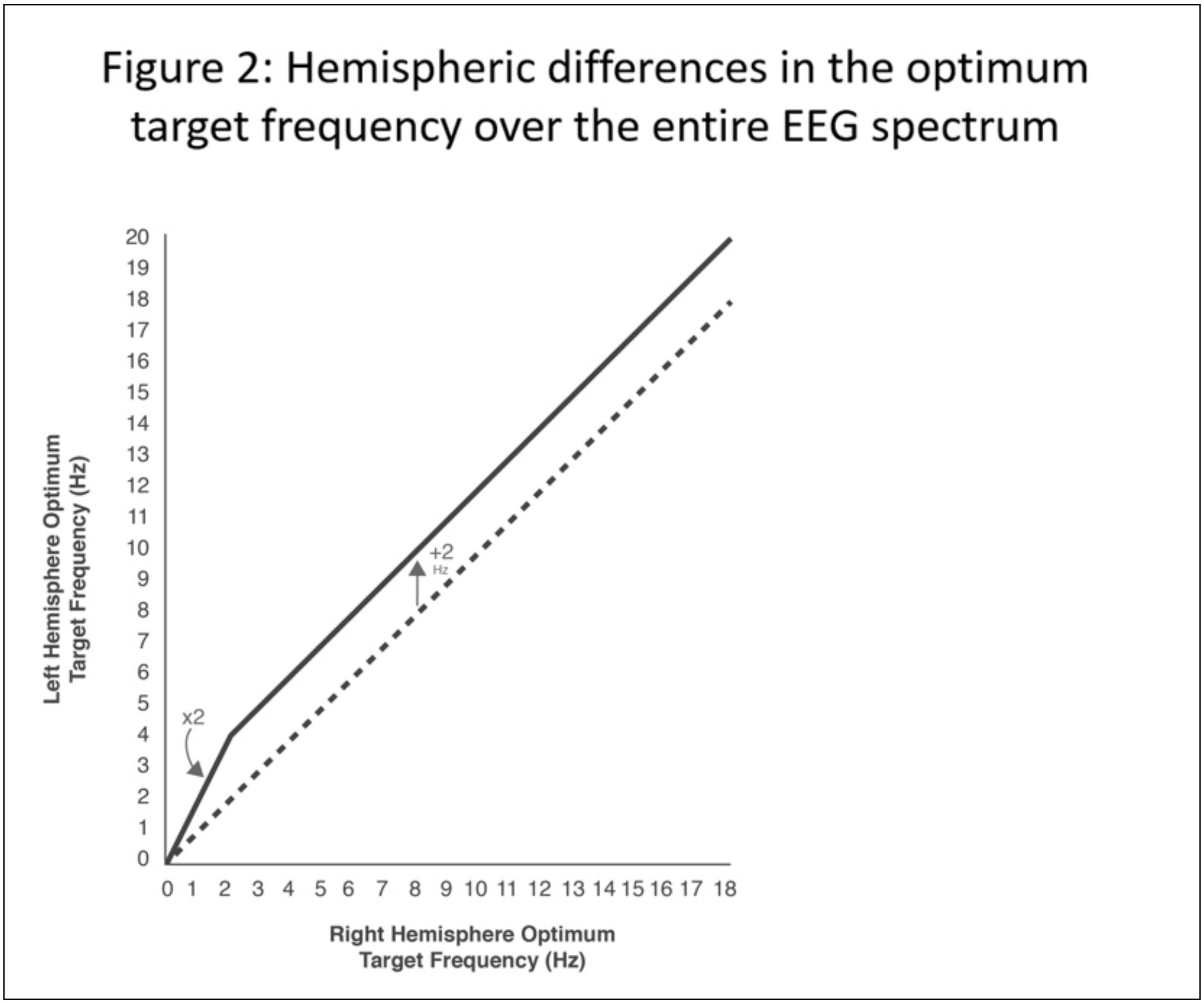

Figure 2: A fixed relationship prevails between the optimum response (target) frequencies in the left and right hemispheres. In the EEG range above two Hz, the left hemisphere training optimizes at two Hertz higher than the right. Below two Hz, the relationship is harmonic. The left hemisphere training optimizes at twice the frequency of the right. This relationship holds throughout the infra-low frequency region.

Fleshing out this model are frequency rules that relate inter-hemispheric training in the frontal and pre-frontal region to training on the central strip, and those that relate the parietal and occipital inter-hemispheric training to that on the central strip. Collectively this model testifies to the specificity---as well as the subtlety---with which brain dynamics are organized on the large scale. It supports the presumption that the integrity of timing and frequency relationships are foundational to the harmonious functioning of the brain.

It should be observed in passing that the sole evidence for the above frequency rules consists of the collective subjective reports of trainees that allow the determination of the optimum training frequency in each case. No independent evidence for these frequency rules yet exists. There is not even any objective evidence for the existence of the optimum response frequency. So on the one hand, the findings fail to meet conventional research standards in terms of objective evidence, and on the other hand the posited relationships are likely among the most firmly established rules governing the dynamic organization of our neuronal networks. The frequency rules have been observed to hold consistently by thousands of clinicians who use them to guide their work. They hold over the entire range of frequencies that has been characterized, some four orders of magnitude.

The current status of neurofeedback in health care

Collectively we are still near the beginning of the journey of exploiting techniques such as neurofeedback for physical and mental health. But already much has been well established and the outlines of what is possible are becoming clear. All neurofeedback methods have their more specific and their more general effects, in that every brain challenge affects not only the specific mechanism being engaged but with it the whole brain as well. The particularity of the different methods means that no single one can be expected to satisfy all of the clinical objectives.

Among the principal approaches, infra-low frequency training likely has the most comprehensive clinical footprint. The particular strength of the infra-low frequency training is in application to the various trauma syndromes that afflict core state regulation, which must be the clinical priority.[30] This includes in particular developmental trauma and the autism spectrum, where systematic remedies have clearly been lacking. It also includes the adult manifestations of early trauma such as Dissociative Identity Disorder, Borderline Personality Disorder, other personality disorders, and chronic pain syndromes. A case series for pediatric epilepsy utilizing ILF training has been published.[31]

The largest documented experience base exists for PTSD among recent combat veterans.[32] In a survey of some 300 trainees in the 2009-11 timeframe, about 25% recovered within twenty training sessions. Another 50% recovered within 40 sessions. The remaining 25% either took even longer, or recovered only partially. Recovery meant that symptom severity fell below clinical significance. Some 75 symptoms of dysregulation were tracked. 90% reported recovery from migraines. In 80% of those suffering from depression, scores were cut in half within two weeks, or less than ten sessions. The same was found for anxiety. There was nominally 75% response for most symptom categories. The least responsive symptom was tinnitus, at 50%. These results were presented at a professional meeting but have not been published.

The ILF training can be profoundly helpful for the degenerative conditions, the dementias and Parkinson's, but a broad distribution in outcomes is to be expected. In all these cases, training has to be maintained at some level to retain gains. The training can be helpful with schizophrenia as well. In one astounding case, the trainee (who was also a 20-year veteran with PTSD) lost his interest in smoking by the fourth session, a signature of progress with respect to the schizophrenia and the nicotine dependency. He had had no intention of quitting when he came for training.

The most commonly used neurofeedback method at the present time is very likely to be a variant of the Sterman/Lubar SMR-beta training, since that has the largest research base behind it, and the largest trained practitioner community. We ourselves taught that method to several thousand clinicians for about ten years starting in 1990. This protocol has been shown in six formal studies to match stimulant medication, as judged by a continuous performance test. The application is mainly to the ADHD spectrum, likely the largest category of referrals for neurofeedback. A meta-analysis covering this work has been published, [33, 34] and an update that also covers the research history was published four years later.

The specific virtue of QEEG-based training is to target brain dynamics in the conventional EEG range of frequencies using mainly inhibit-based training protocols. Remarkable results have been published for application to schizophrenia and Down Syndrome.[35, 36] QEEG-based training can also be very helpful for the localized deficits that may be found in traumatic brain injury and in CVAs.[37, 38]

Multi-site alpha band training serves to improve attentional function. It induces states similar to those achieved in meditation, and thus may be used in support of meditation. Alpha-Theta training is used very effectively in addictions treatment, and it also plays a role in recovery from PTSD. Long-term outcomes are very favorable with this method in comparison to standard treatments.[39]

Infra-low frequency training is not the only technique that relies on the slow cortical potential for training. In Europe a challenge-based method has been under development since the eighties. It is called Slow Cortical Potential (SCP) training and involves challenging the trainee to alter the slow cortical potential at Cz by several microvolts within a period of eight sessions. The objective is to train the mechanisms of cortical activation.[40,41]

It is estimated that currently some 20,000 practitioners of neurofeedback are active in some fifty countries. Over fifty professional licenses are engaged in the practice of neurofeedback, and the work has been published in over 275 different refereed journals. In the United States most of the services are on a self-pay basis because third-party reimbursement remains marginal. The cost burden can be moderated in cases of long-term training by means of supervised home training by parents who have received a modicum of instruction in the method. Clinical decision-making remains in professional hands. Application to sports performance and to the performing arts is a growing interest, one that is not constrained by the bounds of licensure.

One can already project that in their mature implementation neurofeedback technologies will impact significantly on the mental health status of the population, and that it will at the same time decrease the overall medical cost burden, much of which is secondary to brain-based disorders.

Supportive Materials and Additional Reading:

Those who wish to see more specifics on the above treatment may find the following publication helpful:

> **Endogenous Neuromodulation at Infra-Low Frequencies**
> **Siegfried Othmer, Susan F. Othmer, David A. Kaiser, John Putman**
> ***Seminars in Pediatric Neurology, 20(4): 246-260 (2013)***

See also the following web-accessible monograph:
http://www.eeginfo.com/research/researchpapers/A-Rationale-for-InfraLow-Frequency-Neurofeedback-Training.pdf

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