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Clinical Neurofeedback: Training Brain Behavior

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The clinical practice of brain training through neurofeedback has developed within the field of medicine mostly in the domain of Behavioral Medicine. Its rapid growth in recent years as a form of complementary medicine and its emphasis on a direct engagement with brain physiology urge its more formal appraisal within the realm of Neurology. The immature central nervous system is especially suited for this form of targeted brain training, as the developing brain is tasked with integrating regulatory and modulatory pathways that orchestrate emergent neuronal function.

The practice of neurofeedback, which is effectively electroencephalographic (EEG) operant conditioning, has recently been extended to the infra-low region of EEG frequencies (below 0.1 Hz).[1] These slower frequencies, routinely filtered out from the clinical practice of electroencephalography, have historically been ignored. Interest in this frequency region has grown in recent years because of work in functional magnetic resonance imaging (fMRI) of the brain, which disclosed that fluctuations in cortical baseline metabolic activity were directly reflected in the EEG-recordable Slow Cortical Potential.[2] Conditioned reinforcement of EEG-derived infra-low brain frequency activity engages directly with core regulatory functions of the central nervous system (CNS).[3] This has broad therapeutic implications for clinical conditions reflecting a state of CNS dysregulation.

The current work describes the evolution of the method of infra-low frequency brain training. To illustrate its clinical effectiveness, we report on the comprehensive recovery of a case of adult posttraumatic stress disorder (PTSD), an example of a multi-symptom complex or syndromic disorder reflecting CNS dysregulation. Many adult intractable medical conditions such as irritable bowel, migraine, and PTSD are traceable to precursor conditions that prevailed in childhood, in particular physical abuse[4] and emotional abuse or trauma.[5] Earlier intervention to exploit available neuroplasticity in the remediation of some of the most serious challenges facing us in pediatrics enhances the life prospects of children with respect to their risk for significant health issues later in life.

Introduction

Brain training with neurofeedback utilizes the brain's EEG as an "information channel" to its own physiologic regulation. Neurofeedback has been used in a variety of pediatric applications, including attention deficit hyperactivity disorder (ADHD),[6] epilepsy,[7] and autism.[8] The most immediate clinical objective is the regulation of central arousal states and enhancement of CNS stability. The training can be thought of as "brain exercise" in which the feedback reinforcement alters the prevailing state of the brain, compelling the brain's response to the perturbation so as to restore its optimal state. It is as though an internal conflict is set up and the brain's subconscious regulatory mechanisms are engaged in the resolution. This exercises the regulatory circuits and over time alters the set-point of baseline arousal, thereby also enhancing CNS stability.

In application to traumatic brain injury and hypoxic-ischemic injuries such as near-drowning, brain training with neurofeedback can be seen as a rehabilitative technique that exploits available brain plasticity.[9] In this context, brain plasticity is generally thought of in terms of gradual cortical reassignments. The rate of recovery seen with neurofeedback

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supports the view that the dominant mechanism of recuperation primarily involves the readjustment of timing relationships, or re-regulation within existing brain networks that were disrupted or dysregulated by the trauma. This is the dominant mechanism in spontaneous recovery[10] as well as for EEG operant conditioning after spontaneous recovery has plateaued. We see the evidence for this in the rapid restoration of more normal band magnitudes and spectral coherence relationships, particularly when brain EEG coherence anomalies and hemispheric asynchrony are targeted directly in the training.[11]

The quality of brain function is a matter of both structural and functional connectivity. Central nervous system (CNS) regulation entails multiple-network signaling through intra-cortical pathways, inter-hemispheric commissures and hierarchically organized regulatory circuits from brainstem to cortex and back. Notably, the autonomic and limbic nervous systems are critically correlated. Optimal brain performance is the result of successful signal coordination and integration effecting a highly orchestrated regulation of cortical and subcortical functional entities. Clearly the basis for this success is a matter of timing, with a temporal sensitivity prescribed by the action potential mechanism itself. Well-timed signalling allows for coordination among functional subsystems, to which an orchestrated musical performance may be a good analogy.

The functional connectivity of the brain is accessible to us through the EEG.[12] Spectral decomposition shows the EEG to be highly organized into collective rhythmic activities at frequencies that densely cover the entire EEG spectrum. Collective neuronal activity is always regulatory in character. It does not serve an information transfer function directly. Hence we can use the EEG to distill the information at particular frequencies that is relevant for the enhancement of regulatory control. In neurofeedback raw EEG is recorded from specified scalp site locations, digitized, and segregated into frequency bands with software-defined filters. The amplitude of a selected EEG frequency band is then made available to the brain in feedback, providing a window into the time course of site-to-site communication. This in turn reflects the modulation of functional connectivity as the brain undergoes endogenous state change or meets exigent demands. Just as the whole brain participates in the generation of the raw EEG, the whole brain participates in the response to the reinforcement to effect its own self-regulation.

The objective in neurofeedback is to enhance brain regulation; any CNS dysregulated state is theoretically amenable to this form of neurotherapy. This makes for a significant shift in the way a clinician views a patient's complaints. Whereas the traditional medical objective addresses specific diagnoses – for example insomnia, migraine, or depression – by undertaking an intervention for each diagnosis, in neurofeedback the focus is on the enhancement of overall CNS function, and the observed "dysfunctions" (diagnoses) serve as measures of progress. The analogy to preparations for a symphony concert may be helpful here. The conductor is concerned with all aspects of the orchestra's performance; the focus is on enhancing performance by practice rather than on obliterating discord. This approach is particularly appropriate in Pediatrics, where minor dysregulations in early childhood may be consolidating a trajectory toward major dysfunction later in life. The ACE (Adverse Childhood Event) study demonstrates this with respect to a number of factors that do not directly contribute to organic dysfunction or disease; the mediator is an acquired or learned central dysregulation.[5]

Evolution of Infra-low Frequency Training

The promotion of CNS stability is the first objective of brain training. The unstable brain is also more sensitive to the specifics of reinforcement. This mandated an individualized training strategy in which reinforcement parameters, in particular the reinforcement frequency, had to be optimized for each individual. The optimization procedure was aided by the fact that patients reacted strongly to any deviation from their optimum reinforcement frequency (ORF). At the same time, the training furnished growing evidence of a similarity in response to neurofeedback among the various instabilities. By and large, all patients with instabilities responded to a small set of inter-hemispheric bipolar electrode placements, with the vast majority responding to a single such placement, namely T3-T4 (standard 10-20 nomenclature for electrode placement at the left and right mid-temporal lobes). If a patient complained of more than one kind of instability – migraine and asthma, for example – both would respond to the same reinforcement frequency. This augured for the proposition that stability itself was being promoted, that CNS stability was the target rather than the seizure, the migraine, or the sleep disorder specifically.[13]

A basic uniformity in approach was adopted for all instabilities, and since all prominent central nervous system instabilities such as epilepsy, migraine, night terrors and episodic dyscontrol trained similarly, an appraisal of the cumulative distribution of optimum reward frequencies was justified. In fact all diagnostic distinctions were ignored in this compilation because patients responded favorably at their ORF across all symptom categories (such as mood disorders, executive function deficits, insomnia), not just the instabilities (such as migraine headaches, seizures, irritable bowel syndrome). A clear trend toward the lower EEG frequencies was observed in the distribution of ORFs. Early results dating back to 2006 are shown in Figure 1. By 2006, a gradual trend toward lower reward frequencies had already been underway for some five years. The training of mid-range EEG frequencies had mandated the use of a 3-Hz signal bandwidth, and with this limitation the lowest available setting of the filters was 0-3 Hz, for a center frequency of 1.5 Hz. As shown in Figure 1, the distribution was essentially flat, which actually means that the modal value was 1.5 Hz (as the single frequency within the lowest band). These

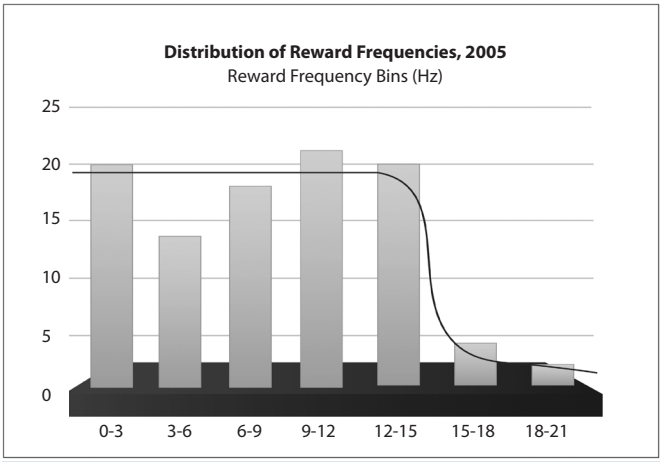

Figure 1. Distribution of optimum reinforcement frequencies in 2006, just prior to the inclusion of infra-low frequencies. A fairly flat distribution prevails for frequencies in the alpha range and below.

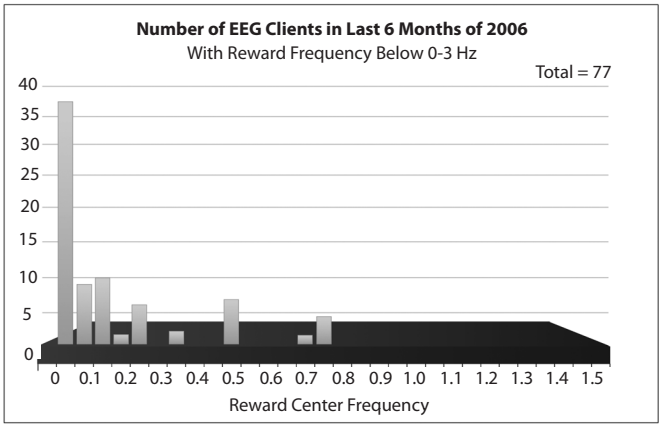

Figure 2. Initial distribution of optimum reinforcement frequencies with the range extended to 0.05 Hz.

data motivated the extension of the available range to yet lower values of target frequency for the ORF, which was accomplished by limiting the signal bandwidth further. An additional incentive was provided by the clinical impression that the lowest frequency used for training was associated with the most positive results in symptom relief from the patient's point of view.

Routine clinical EEG evaluations typically extend only down to 0.5 Hz, and the same has held true in research by and large. This limit is typically hardware-based. In order to extend the range of ORFs to lower frequencies, that band limit had to first be extended to lower frequencies. The ORF range was extended initially to 0.05 Hz, and as more clinical data were acquired, ultimately to 0.01 Hz, then to 0.001 Hz, and finally to 0.0001 Hz, or 0.1 milliHertz (mHz).

While the results of this progression to lower target frequencies is succinctly summarized here, it covered a number of years in practice and involved close to a thousand patients in just the single clinic that spear-headed this development. The extension to 0.05 Hz occurred in June of 2006, and over the first six months 52% of clients trained at the lowest frequency. This is shown in Figure 2, which presents a sharp contrast to the trend in Figure 1 by virtue of the dominance of the lowest available reinforcement frequency. Over the next six months, this dominance increased further to 66% as more familiarity was gained with the low-frequency training. More than 250 patients were involved during this phase. With the extension of the reward frequency range to 0.01 Hz in 2008, matters stayed in pattern: 65% trained optimally at the lowest available frequency. With the further extension to 0.001 Hz soon thereafter, the percentage training at the lowest frequency rose to 77% over a period of time as clinical skills were honed. The range was further extended to 0.1 mHz (0.0001 Hz) in March of 2010, and over time more than 85% of patients ended up at the lowest reward frequency within their first few sessions. It appeared that the lowest frequency was the best tolerated as well as the most effective. Notably, with each extension of the range to a lower limit, the clinical reach extended to complex clinical presentations that had not responded well earlier, and outcomes systematically improved.

Why the effects of the reinforcement should become stronger and of more inclusive clinical reach even as the rate of information flow to the brain is reduced at lower target frequencies remains to be explained. Either the low-frequency signal is more recognizable to the brain, or it is more salient, or both. All the above constrains any potential theoretical model for the mechanisms that underlie neurofeedback in the infra-low frequency range. One theoretical model will be presented shortly.

Brain Training at Infra-low Frequencies: The Clinical Method

The very earliest EEG feedback was done with the alpha rhythm, which typically dominates the EEG spectrum under eyes-closed conditions.[14] The usual training objective was to increase the alpha amplitude in the interest of deepening a state of relaxation and/or to decrease anxiety levels. The technical task then lay in tracking the amplitude of the alpha-band activity and feeding it back with minimal delay.

The techniques used at the time carry over to the modern day. Electronics involve a differential amplifier to detect the extremely small brain signal in the presence of probable and often substantial electrical interference. Frequency-selection is typically done with narrow-band filtering to achieve band-limiting of real-time brain activity that is to be presented back to the client in a feedback loop by way of some visual, auditory, and/or tactile medium. Strategically, the relatively uninteresting visual feedback signal has been imbedded in material of greater visual interest, such as a movie or video game. The process involves brain training

exclusively, and makes no appeal to the cognitive or intentional involvement of the trainee.

With the objective of training band amplitude in conventional EEG feedback, the reference side of the differential amplifier was customarily placed on the ear lobe or other neutral non-scalp site ("referential" recording). Alternatively, the practice used with routine clinical EEG in which signals are typically derived differentially between scalp sites (the standard sequential derivation), was also used, referred to as a "bipolar" montage. Bipolar placement gives equal weight to both scalp sites and renders the net signal sensitive to the phase relationship prevailing between the two sites at the target frequency. Because the objective in brain training is to challenge the brain in its timing relationships, the phase prevailing between the selected scalp sites is the more relevant measure to train. It must be kept in mind, however, that the amplitude of the net output signal drives the feedback, irrespective of whether one is using referential or bipolar montage. However, this net amplitude is directly governed by the prevailing phase difference between the two active sites. For the above reasons, bipolar montage became the standard placement in all of the work. This choice was soon validated in that the various brain instabilities presenting in the trainee responded more immediately and more strongly to training with bipolar montage than with the customary referential placement in traditional neurofeedback. This in turn made the choice of the target reinforcement frequency more critical, further compelling the schema of frequency optimization toward the infra-low range, as detailed above.

At conventional EEG frequencies (0.5 to 40 Hz), band amplitudes are obtained from the narrow-band filtered signals by rectification and smoothing with appropriate time constants. In the classic instrumental conditioning paradigm, a threshold is then applied which triggers appropriate rewards whenever a positive threshold crossing occurs. In the infra-low frequency region (where the time course to complete a full cycle at the ORF may extend over hours) one has no choice but to abandon that approach and move simply to signal-following. The neurofeedback trainee just observes the evolving time course of the differentially amplified slow cortical potential. There is no threshold, and there are no discrete rewards. The process is no longer one of operant conditioning as generally understood. In the case of infra-low frequency training, the differentially amplified signal undulates between positive and negative phases, and one is not more virtuous than the other in the process of the brain engaging with the signal. The brain interprets the signal in terms of its own internal activities through a continuous process of correlation. None of the elements of this process are perfect, including in particular our own abstraction of the signal. There is a compelling urge for the clinical neurophysiologist to get caught up with the signal, what it actually represents, and in some way to exert external controls and interpretations based on past learning, habitual thought and practice. This tendency must remit in current neurofeedback practice, even while the interest in the signal remains compelling in the perspective of clinical research.

Wherein then lies the challenge for the brain? It must be inherent in the correlation process itself. To make this reasonable, one must see the brain as an active agent directing its own affairs rather than as a passive recipient of information from the environment. This means regarding the brain as a forecasting entity. The brain's internal states are made "visible" or "mirrored" to itself in neurofeedback, which the brain finds compelling and even riveting. As soon as the brain recognizes its authorship of the signal it takes charge of it as well. The brain is then engaged in a continuous optimization procedure in which the actual is played off against the imagined ideal or the intended objective. Closure is never attained in this process. A discrepancy always remains, and therein lies the perpetual challenge. What we have here is closely analogous to the manner in which the brain navigates through life generally. We have simply tightened the control loop by going to the EEG as the correlate or analogue of brain behavior.

In the evolution of the infra-low-frequency training technique over the last six years, the basic training approach remained essentially the same except for the progressive movement of target frequency (the ORF) towards the infra-low frequency region of the EEG. There was also some refinement of the clinical decision tree with respect to scalp placements to address specific clinical neurophysiological objectives.

Rationale: Illustrative Case

The training history of a veteran with PTSD is illustrated in Figure 3, where symptom-tracking data are shown for the dominant complaints. PTSD is chosen because the symptoms are largely those of central dysregulation. An adult case is presented here because the symptoms are more clearly elaborated. In this case, as in all others, a wide-ranging initial clinical interview established the critical issues for this person. These are quantified here in terms of severity on a Likert scale of 0-10. (The initial symptom list included several hundred items, of which some 60 are commonly reported in PTSD. Twenty-five of the more significant symptoms in this case are shown in the illustration.)

The impression given by the results of brain training over time is one of joint resolution across the seemingly disparate symptom categories. The similarity in learning curves is more clearly reflected in Figure 4, which just replots the same data. It is noteworthy that this list includes such varied symptoms as depression, bruxism, migraine, irritable bowel, addictive behaviors, and chronic constipation. All move jointly toward clinical insignificance over the period of forty training sessions. This pattern is a common observation.[15] All this was accomplished with essentially four

electrode placements: right parietal training for physical calming; right frontal training for emotional calming and control; inter-hemispheric training for brain stability; and left frontal training for recovery of executive function. A more specific description of the actual clinical approach may be found in the Protocol Guide by Susan Othmer.[16]

Clinical experience testifies to the fact that the brain usually moves in the desired direction of calmer and more controlled states. However, the training is not without its hazards. The neurofeedback challenge also accelerates the shifts in state through state space. State change may be rapidly induced with respect to arousal level and the local activation of specific subsystems (such as the motor system). When this process is undertaken with a highly dysregulated brain, an acceleration through state space occurs, which increases the risks of encountering adverse or unstable states such as migraines, nausea, or pain. This concern is implicitly supported by observations within clinical neurology: seizure susceptibility is known to be greatest during the process of waking or of falling asleep, times when the arousal level is undergoing a rapid shift. This necessitates the in-depth training of educationally pre-qualified clinicians interested in offering neurofeedback in their clinical practice.

A Theoretical Model

If one accepts, for the sake of continuing the discussion, that the above case is broadly representative of clinical experience, then the following propositions must be explained by any putative theoretical model:
1) Many symptoms that have been relatively refractory to standard medical intervention yield to a regular brain training remedy;
2) Remediation is often so prompt and so complete that the conditions should be regarded as disorders of a primary brain dysregulation;
3) Uniformity in learning curves among disparate symptom categories implicates a single dominant failure mechanism; 4) Relatively quick recovery (which is often seen) demonstrates that a modest set of electrode placements is sufficient to effect a remedy across the entire range of symptoms of dysregulation at issue.

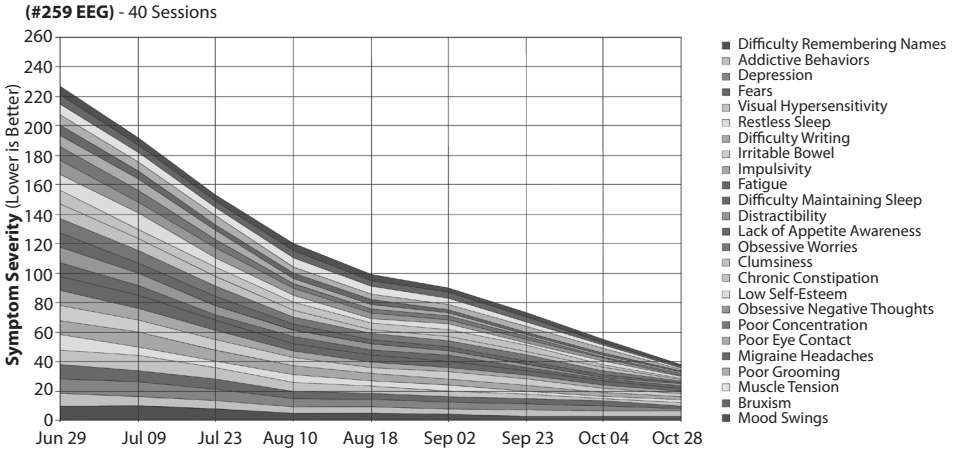

Figure 3. Symptom tracking data for a case of adult PTSD. 25 symptom categories are tracked with a Likert scale of 0-10. Symptom severity declines in a common pattern over some forty training sessions, to the point of clinical insignificance for nearly all symptoms.

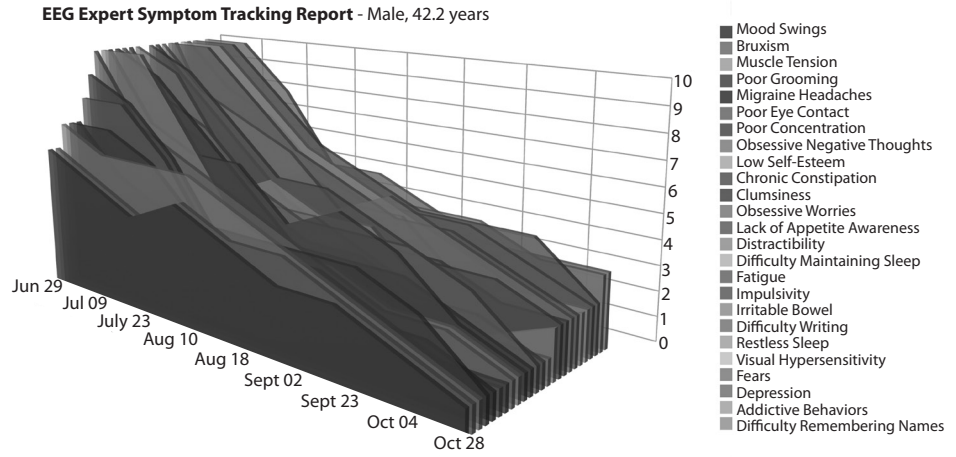

Figure 4. Learning curves for all 25 symptoms are shown, revealing an essential similarity in learning curves even for disparate symptom categories. This is strongly suggestive of a common underlying failure mechanism.

It is the discovery and elaboration of the brain's resting state networks through functional magnetic resonance imaging that has provided the most appealing model in which all of the above can make sense.[17] Over the last decade the organization of neuronal network activity in baseline states has been described in terms of a set of core networks that maintain stable conformations across waking and sleeping states, and even through anesthesia.[18] Such stability is observed in the temporal correlations between BOLD (Brain Oxygen-Level Dependent) signals among the spatially distributed constituents of a particular resting state network.[12] The role of resting state dysregulation in mental disorders has also been addressed.[19] A recent study implicates three of the principal resting state networks.[20] Affecting the connectivity relationships within any two parts of such a network is likely to

have consequences throughout the network. If the integrity of resting state networks is the key to the brain's functional competences, then even a simple challenge to network functional connectivity is expected to have broad clinical effects across a variety of functional domains.

Discussion

Adopting a systems approach to the understanding of healthy CNS functional organization, and of its dysfunction or dysregulation, holds profound implications for the practice of neurology, and perhaps especially for developmental pediatrics and pediatric neurology. Individualized brain training with neurofeedback may have particular relevance for the pediatric population where brain plasticity is a natural therapeutically to be recruited before it has served perversely to consolidate dysfunction. The emergence of neurofeedback as a potent remedial strategy to reconstituting CNS regulatory control provides an important noninvasive and non-pharmacological option. There is, first of all, the reality that the available medical arsenal offers no good remedies for the emotional problems of childhood, which we now know to lay the basis for physiological dysfunction later in life.[5] There are certainly no good medical remedies for the dysregulation of sleep, that is so common in childhood and adolescence. There are no adequate remedies for the lingering symptoms of minor head trauma, commonplace in childhood. Left un-remediated, an even minor head injury sets the stage for heightened susceptibility to subsequent brain insults.[21] There are no good remedies for persistent head pain and stomach pain. There are no good remedies for chronic constipation, which is commonplace among autistic children. There are not even good medical remedies for ADHD; follow-up data on the NIH multi-site study identified no benefit of stimulant medication after three years.[22]

There is an understandable reluctance to medicate children aggressively. Given the noninvasive non-pharmacologic approach described here, there is less reluctance from the parents' perspective to train their children's nervous systems towards self-regulation. One would ordinarily not medicate a child who has just experienced a first seizure episode, and yet statistically we know that such a child is vulnerable to subsequent seizures.[23] This could and perhaps should lead to a recommendation of prophylactic neurofeedback. Stimulant medication should be seen as a temporary measure to allow the child with attentional issues to obtain neurofeedback for what is essentially a disorder of CNS dysregulation. Neurofeedback is particularly helpful for the behavioral penumbra of ADHD of oppositionality, conduct problems, and rage, where stimulant medication offers no reprieve.[24]

With regard to sleep dysregulation, neurofeedback can be profoundly helpful with bedwetting, with sleep walking, with night terrors, and with nocturnal bruxism.[25] Neurofeedback can be substantially effective with headaches, including migraines,[26] and it can potentiate the recovery from minor traumatic brain injury.[9,11] Neurofeedback can retrain the anxious or depressed nervous system[27] and alleviate accompanying physical symptoms. Even for conditions where medical remedies exist, neurofeedback training offers advantages. Asthma susceptibility (the episodic type) is a case in point. With ILF neurofeedback training, the risk of an asthma episode can be substantially reduced (personal observations).

The benefits offered by neurofeedback are most apparent in those cases where medical interventions are not restorative, as is the case with varied forms of developmental delay, developmental trauma, the autism spectrum and minor traumatic brain injury. It also shows benefit in more severe brain insults such as near-drowning, cerebral palsy, fetal alcohol syndrome, and severe emotional trauma. Training with neurofeedback may also modify significant deficits in specific modes of sensory processing. The list is by no means all-inclusive; for example, the response of patients with movement disorders to neurofeedback has been less than remarkable to date.

It is the authors' combined clinical experience that the introduction of infra-low frequency training has improved patient outcomes across the board and extended the clinical reach to conditions considered refractory to medical intervention. It is in the areas of the greatest neurological deficits that infra-low frequency (ILF) neurofeedback training has particularly distinguished itself. The ILF training imposes no substantial cognitive burden on the trainee, allowing for brain-training even in cases of diminished conscious awareness (coma states) as well as in early infancy. The training can also be done in background, while the child is otherwise engaged. This resolves the issue of boredom, on the one hand, and allows the training to be integrated into a child's life in a variety of ways in those cases where long-term training is indicated.

Summary and Conclusion

Infra-low frequency training with EEG feedback has developed over the past several years as a general process of specific brain exercises to optimize functioning in the compromised central nervous system. This is presumed to occur through a challenge to the functional connectivity of the brain's resting state networks. Since resting state activity endures throughout the range of functional demands on brain networks it is foundational to the preservation of quality nervous system functioning in all domains of function. Hence the neurofeedback challenge should be appraised in a systems perspective. This makes all symptoms of CNS dysregulation an objective for relief, on the one hand, and an index to progress, on the other. Whereas the target of this form of neurotherapy is the enhancement of CNS function, the measure of success is the abatement of maladaptive symptoms attributable to jointly or severally malfunctioning core regulatory networks.

A prediction of the systems perspective is that infra-low frequency neurofeedback training should distinguish itself particularly in application to the most universal of central nervous system failures, such as are seen in pervasive developmental delay, in traumatic brain injury, in the autism spectrum, and in developmental trauma. It should also distinguish itself with respect to the principal nervous system instabilities such as seizures, migraines and panic disorder. Clinical evidence is beginning to bear this out, but at this stage the findings remain to be confirmed in formal studies. Awareness of neurofeedback in pediatric practice should be broadly helpful both to the children who may potentially benefit and to practicing pediatricians and developmental subspecialists.

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