



Infra-Slow Fluctuation Training: On the Down-Low in Neuromodulation

Mark Llewellyn Smith, LCSW, BCN

Infra-slow fluctuation (ISF) training focuses on the lowest frequencies the brain produces. It is performed with Ag/AgCl or Silver/Silver Chloride electrodes and a direct current (DC) coupled amplifier. Why a DC encoder? Because a DC amplifier is better suited to image the low frequencies. The integration of the lower, direct current (DC), and higher, alternating current (AC), energies produces enough “bounce” in the low alternating current domain to filter and train the frequencies that researchers Satu and Matias Palva (Palva & Palva 2012) have named the Ultradian (<0.01) and Infra-Slow Fluctuations (ISF) (0.01-0.1), with more clarity and less noise in the signal.

What follows is a discussion of the technical, historical, and clinical circumstances that led to the development of ISF training and its current clinical application. Among researchers, there is no precise definition of the frequencies that determine the bottom end of the infra-slow regime. However, there is at least an agreement among most researchers that the low frequency band begins at 0.1 hertz. The terms used to describe this band in research and in clinical work are Infra-Slow Fluctuation (ISF), Infra-Slow Frequencies (ISF), Infra-Slow Oscillations (ISO), and Infra-Low Frequency (ILF). These terms will be used interchangeably to denote the energy below 0.1 hertz. All human EEG contains AC and DC current unless one is filtered out. DC was eliminated by the introduction of a high pass filter on most EEG amplifiers. The high pass filter acts like a gate and allows the faster frequencies to “pass” and cuts off or attenuates the lower ones.

The advent of the built-in high pass filter on AC amplifiers with a “corner” or cut off frequency of approximately 0.5 hertz, is more than half-a-century old.

These AC amplifiers produced signals that allowed researchers and neurofeedback practitioners to focus on the faster oscillations, considered the most salient features in the human EEG at that time. Before that time, attempts to record slow events produced electrode drifts that tended to saturate the amplifiers and so hastened the initiation of high pass filtering on all amplifiers. The consequence of the ubiquitous installation of high pass filtering was a loss of all infra-slow dynamics whether artifactual or physiological. All human EEG contains AC and DC current unless one is filtered out. DC was eliminated by the introduction of a high pass filter on most EEG amplifiers. The high pass filter acts like a gate and allows the faster frequencies to “pass” and cuts off or attenuates the lower ones.

The first human direct current recordings became possible with the introduction of chopper-stabilized amplifiers in the 1950’s. A lack of stable electrodes and the need to manually cancel offset voltages prevented the widespread use of the technology (Tallgren 2006). As DC equipment improved, researchers began to describe the observed phenomena at frequencies below the conventional limits. One definition proposed that EEG in the frequency range below 0.5 hertz consisted of a standing potential (SP) and a slowly changing potential (SCP) (Manaka & Sano 1979).

In the following decades, DC-coupled amplifiers became more common. The terms changed from standing potential to “DC potential shifts” and slowly changing potential to “slow cortical potentials” (Birbaumer et al. 1990, Elbert et al. 1980). DC potential shifts are non-oscillatory fluctuations in amplitude measured in millivolts (Collura 2009).

Until very recently, AC amplifiers

capable of training higher frequencies but less proficient with the lower ones, were the only amplifiers available to neurofeedback clinicians. Amplifier designs that led to the elimination of lower frequencies determined the scope of neurofeedback training. Led by practitioners and researchers, largely in Europe, that began to change in the last three decades. The proliferation of DC-coupled amplifiers led to a focus on the energy below the cut off frequencies in AC amplifiers. This in turn steered practitioners toward the development of Slow Cortical Potential (SCP) training.

This was a precipitous event for ISF training. Infra-Low Training (ILF), the precursor to the development of ISF, was implemented on an AC platform, the BrainMaster 2E amplifier, with a typical cut-off frequency 0.5 hertz. As the targeted frequencies of ILF training moved lower and lower, challenges presented by this AC amplifier became more apparent. A noisy signal, saturated amplifiers, and infrequent rewards were the obstacles of equipment not optimized to filter infra-slow oscillations. The availability of DC-coupled amplifiers led to an exploration of the DC-coupled platform with ILF training in 2006. It was immediately clear that the inclusion of direct current in the training paradigm minimized the obstacles presented by alternating current amplifiers. The inclusion of DC clarified minute changes in the ISF signal. Frequencies that had been obscured by noise were now illuminated with more subtlety. Small changes in the ISO that had previously been hidden in AC amplifier limitations were now available for feedback. Small vicissitudes of current that appeared as a singular bump in AC mediated training amplitude became rendered as a series or wave of amplitude

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is determined through multiple factors, including “in session” feedback from the client, observation of physiological responses (skin tone, pupil dilation and body temperature changes), and 24 hour “post session” reporting. Like other modalities, the most significant issues are tracked to assess frequency effectiveness and sensor placements. Most of my ASD clients cannot self-report during a session, making observation of physiological changes and the 24-hour report a more critical component of care. Sensor placements include T4-P4 for sensory calming, T4-T6 to enhance empathy and facial recognition, T4-F8 to enhance speech production, and T4-FP2 to enhance emotional control.

Summary

Among the many neuromodulation approaches used at the Crossroads Center of NJ, the Infra-Slow Fluctuation approach has taken a prominent role. While I employ qEEG-based neurofeedback and still sporadically utilize Z-score, S-Loreta, LENS, HEG, TDCS, NeuroField, and traditional symptom-based neurofeedback approaches, all my clients receive Infra-Slow Fluctuation neurofeedback. The improvements clients experience are surprisingly fast and positive. It is the modality of choice for children with developmental delays and with people experiencing chronic illness; it has also been highly effective with traumatic brain injuries.

Jackie de Vries, MS, is the director of the Crossroads Center of NJ (www.crossroadscenterofnj.com), located in Ridge-wood, NJ.

Sheryl Leventhal, MD is the Medical Director at Crossroads and provides functional medicine consults at Hudson Valley Functional Medicine (www.hudsonvalleyfunctionalmedicine.com), located in Valley Cottage, NY. Crossroads specializes in neurofeedback to support recovery from medically related conditions.

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fluctuations measured in tenths of microvolts with the inclusion of DC.

As our spectral displays improved, the relationship between DC shifts in amplitude, measured in millivolts, and the infra-slow frequencies, measured in microvolts, became illuminated. The rise and fall of the large amplitude of the DC potential shift was observed to be correlated with the smaller energy of the frequency domain measured in microvolts. We see this in spectral displays in our current training screens when both the DC and ISF signal are imaged simultaneously (Figure 1).

It is this interaction between DC shifts and frequencies that directed the name change from Infra-low frequency to Infra-slow fluctuation training. The DC shifts were observed to impact microvolt fluctuations in the slow frequency regime and offer a target for feedback.

Small, recurrent amplitude changes of the ISF signal are the focus of reinforcement, not the return of the slow oscillation itself. We do not reinforce an oscillation that takes scores of seconds or minutes to complete its cycle, a common misconception. During the cycle of a .01 hertz frequency, a frequency that takes 1 minute and 24 seconds to fully oscillate, DC shifts in amplitude much more frequently and induces the ISF signal

to rise and fall in very small amplitude increments. The amplitude change is often a fraction of one microvolt. It is this minute rise and fall in amplitude that ISF training targets.

Reinforcing this slow signal has produced rapid and profound behavioral changes in a multitude of presentations as measured by qEEG and pre/post treatment behavioral scales. Autism, reactive attachment disorder, generalized anxiety disorder, panic disorder, and ADHD are a few of the many presentations treated by clinicians using ISF training over the last six years.

The clinical results presented in this article are typical within the ISF provider network and resonant with the fifty years of research that has been executed involving the frequencies below .1 hertz.

The infra-slow rhythm was first identified by Russian researchers nearly sixty years ago (Aladjalova 1957, Aladjalova 1964). Scientists at the Institute of Biophysics in Moscow implanted electrodes in the brains of rabbits. The infra slow band was observed to increase in amplitude and frequency when animals were subjected to stress producing stimuli. They theorized that the increase in amplitude of the infra slow oscillations reflected the hypothalamus’s reparative, parasympathetic response. Supporting a role for the



Figure 1: ISF signal in the top box with both green (damped ISF signal) and white (Undamped Signal measured in microvolts: .37 uV). DC in bottom box measured in millivolts; white line (here approximately 11 mV). The DC shift amplitude in the bottom panel is more than a thousand times greater than the ISF fluctuation in the top panel. Notice the similarity of the amplitude fluctuations as imaged by the morphology of the white lines.

ISO in the function of the neuroendocrine system, Marshall (Marshall et al. 2000) discovered an association between ISOs and hypothalamic-pituitary secretory activity. An increase in the amplitude of the infra-slow periodicities was coupled with the onset of the pulse of the luteinizing hormone. This hormone is released by the hypothalamus and triggers ovulation in females and stimulates the production of testosterone in males.

This research is resonant with our treatment outcomes, in that it suggests that ISF training may impact hypothalamic/pituitary/adrenal activity. ISF training routinely reduces anxiety, promotes relaxation, regulates sleep architecture, and results in behavioral scales that make observations of arousal reduction, affective regulation, and attention promotion among trainees (See our Child Behavior Check List (CBCL) results with children in a special needs educational setting, in the final section of this paper, following).

We consistently observe within-session indications of autonomic regulation. Typically, ISF training produces in-session state changes associated with parasympathetic functioning. Increases in peripheral body temperature, as measured with a simple stress thermometer, often reflect temperature increases of ten degrees or more. Increases in coherence of heart rate variability measures reflected by the HeartMath instrument: EmWaves have been reported within the ISF clinical network. Capnography instruments measuring End Tidal CO2 have revealed normalization of CO2 with increased diaphragmatic breathing accompanied by reductions in the number of breaths per minute. Routine clinician observations of client pupil restriction and client reports of tingling in peripheral body parts are all suggestive of increased relaxation and parasympathetic response.

The organization of autonomic regulation so characteristic of ISF training may reflect the centrality of these slower frequencies in the control of cortical excitation. Cross frequency correlations be-

tween ISOs and faster frequencies have been observed in research for the last two decades (Keković et al. 2012, Nir et al. 2008, Pfurtscheller et al. 2012, Vanhatalo et al. 2004, Zschocke & J. 1993).

Our post hoc treatment analysis is consistent with this research outcome. Strong cross frequency correlations between our ISF training band and faster frequencies were identified across all bands. The strongest correlations were observed in the delta, theta, and gamma bands as evidenced by the cross frequency correlation coefficient graph illustrated in Figure 2.

Vanhatalo and co-workers (Vanhatalo et al. 2004) proposed a role for the infra-slow frequencies in determining cortical excitability. They found that the phase of ISOs modulate gross cortical excitation as evidenced by their association with interictal-epileptiform events, high amplitude paroxysmal activity in cortex and K complexes, the largest event in

the human EEG, linked with suppressing cortical arousal in the sleeping brain, and promoting memory consolidation.

ISFs reflect the centrality of these slower frequencies in cortical network control. Recent research revealed that the default mode network (DMN) is characterized by high gamma band coherence that is modulated at infra-slow frequencies (Ko et al. 2011). According to Ko and workers, this coherence modulation forms the neurophysiological basis of the DMN. During goal-oriented activity, the DMN is deactivated and another network, the task-positive network (TPN) is activated. Recent research in the USA and England identified coherent low frequency oscillations that are attenuated in the DMN during task positive activities (Broyd et al. 2009). This resting brain network is anti-correlated with the task positive network. The ISF reflects a toggling mechanism that switches between the DMN, the network of introspective

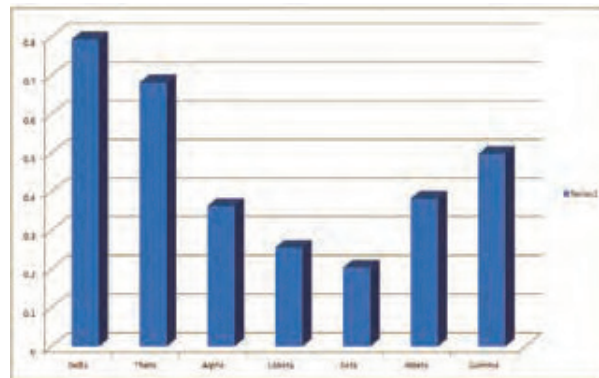


Figure 2: With Thomas Collura Cancun 2012. Correlation Coefficients of ISF and traditional frequency bands

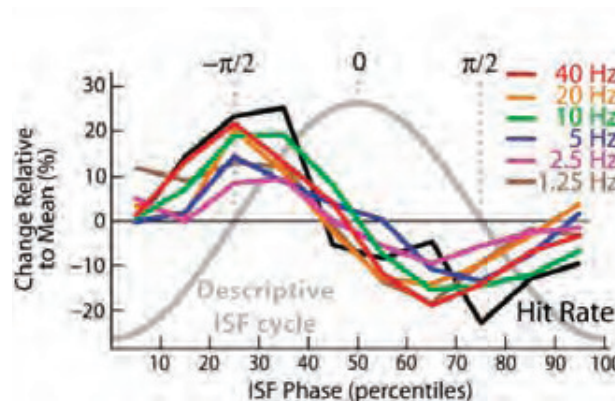


Figure 3: EEG ISFs are salient in awake human EEG. A. Large amplitude ISFs are readily observable in raw full-band EEG data (gray line: phase, unfiltered, black line amplitude: band-pass filtering from 0.01 to 0.1 Hz. Amplitudes of 1–40 Hz oscillations are correlated with the ISF phase. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.) Adapted with permission from (Monto et al. 2008)

and self-referential thought, and the TPN, that responds to extrospective stimuli.

Monto and co-workers (Monto et al. 2008; see Figure 3, page 43) discovered that behavioral performance, in the form of a somatosensory detection task, was robustly correlated with the phase of the infra-slow fluctuations band passed between 0.1 and 0.01 hertz. Stimulus detection was greatest during the rising phase of the ISF amplitude. Moreover, these researchers observed the amplitudes 1–40 hertz nested in the phase of the ISF: amplitudes of faster frequencies were largest in the rising phase of the ISF. As with the Broyd study above, this research correlates performance, the ISF, and overall cortical excitation.

Palva and Palva (Palva & Palva 2012) make a demarcation between the infra-slow (0.01-0.1) and the Ultradian rhythm (<0.01) and refer to the former as infra-slow fluctuations. They point out in their research that the blood-oxygenation-level-dependent (BOLD) signals are correlated with constellations of brain regions that are very similar to networks that are correlated with the ISF signal. They note the direct association between ISFs in amplitude with ISFs in the BOLD signal. The researchers conclude that ISFs arise from local cellular level mechanisms in neurons and glia, as well as blood, and reflect the same underlying physiological phenomena: a superstructure of interrelating ISFs that regulates the integration within and decoupling between active neuronal networks.

We propose that ISF neurofeedback addresses this superstructure of interrelating neuronal networks. We submit that our pre/post qEEGs reveal profound changes in activation measures, but especially in network dynamics, as reflected by the coherence metric. The modification of information sharing between cortical areas produced by ISF training is consistent with research that demonstrates a role for the ISF in the regulation of neuronal networks. Addressing the integration of networks responsible for

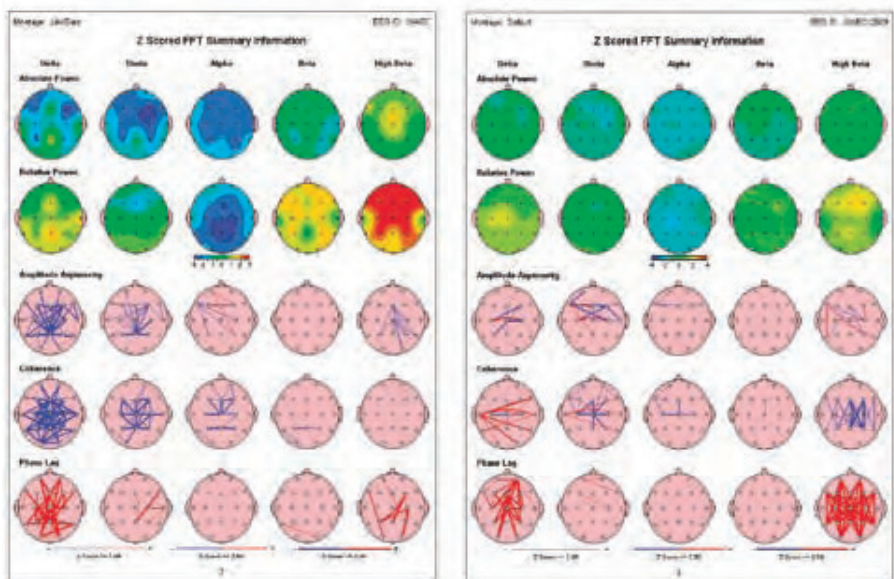
memory, affective response, autonomic regulation, and attention, to mention a few, may account for the reduction in symptom severity among our clients.

One clear demarcation between ISF practitioners and others in the area of slow-frequency training is the regular use of qEEG in treatment. As with any symptom-based approach, qEEG is not necessary to train effectively with ISF. However, it is taking a more central role in the application of the intervention, as it proves helpful with determining a variety of treatment parameters. From separating potential treatment responders from mixed-responders and determining beginning ten/twenty placements, to defining inhibit strategies and shaping treatment course, it continues to take a more principal role in ISF training. The use of qEEG has inevitably led to the use of multiple channel assessments during training. With Ag/AgCl 19-channel caps and two-channel electrode arrays, ISF clinicians become capable of assessments while simultaneously training in the traditional bipolar montage. This has allowed us a window on connectivity and activation unavailable to the simple one-channel bipolar mon-

tage. It has also allowed us to implement varieties of training that combine referential and bipolar montages, permitting simultaneous ISF and Z-score training or ISF and sLORETA training. We are exploring a substitution of Z-scores for the traditional broadband inhibit strategy of slow frequency training. Our analysis capability has suggested that a “one size fits all” inhibit strategy may not be optimal for all clients. Rewarding transients both high and low, as Z-score training does, may be a better overall strategy than the unidirectional training of traditional inhibits. Moreover, inhibiting low voltage EEG when it is present in any individual frequency band may not be optimal. QEEG makes these determinations readily available, and multiple-channel training allows for the implementation of a precise ISF protocol tailored to the specific neuronal needs of an individual client.

The following pre/post treatment qEEGs (figures 4 and 5) are taken from a 50-year-old a male with PTSD. His history included a fractured skull, witness to violence in his family of origin, and substance abuse in remission. He suf-

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Figures 4 & 5: Figure 4 on the left is the pre-treatment qEEG. Figure 5 on the right is the post treatment qEEG. Results include vivid improvements in absolute power and amplitude asymmetry, and dramatic changes in network information sharing as assessed by the coherence metric.

ferred with acute anxiety and depression before treatment. The client reported that he slept with a rifle to manage his fear of nighttime attack. The client had 31 sessions of ISF training in bilateral temporal

neurofeedback program. Fourteen of the 16 students had a positive response that involved either: a significant reduction of tantruming behavior; reduction/elimination of psychotropic medication; and/or

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lobes, parietal, and pre-frontal regions.

Post treatment results included reduced anxiety, depression, and improved sleep. He reported that he no longer sleeps with a rifle. Notice the dramatic changes in absolute power, amplitude asymmetry, and coherence.

ISF Neurofeedback Program in a Special Needs School in New York City

With John Ferrera, PhD, an ISF treatment program was established at a special needs school in New York City. The school has developed a curriculum and programs for special needs children with a variety of issues, including autism, ADHD, and reactive attachment disorder. In the first year we had a total of 16 students in the

improved ability to sustain attention, resulting in academic progress. The improvement was assessed with the Child Behavior Check List.

The Child Behavior Check List is a commonly used method of assessing problem behavior in children. Developed by Thomas M. Achenbach, it is a module of the Achenbach System of Empirically Based Assessment. The school-age checklist consists of 120 questions that are asked of a parent or caregiver who knows the child well. Responses are recorded on a Likert scale.

Mark Llewellyn Smith LCSW, BCN, is a licensed clinical social worker whose early career was established in the world

of work as the director of clinical services to nurses, doctors, and staff of NYU Medical Center and Downtown Hospital in New York City. In private practice since 2000, Mark is a leading developer, teacher, and clinician of neurofeedback interventions for a variety of disorders. He was an early adopter and developer of Z-score and infra-slow fluctuation training, both now primary interventions in EEG-biofeedback therapy. Currently, he is developing sLORETA training with Thomas Collura and others. Mark has taught neurofeedback and qEEG on four continents and continues to educate and train neurofeedback providers in international workshops and conferences. Mark was the founder and Clinical Supervisor of the Child School's Neurofeedback Program. The program provided neuromodulation interventions in a special needs school setting. He is the founder and clinical director of Neurofeedback Services of New York, PC, neurofeedbackservicesny.com.



References are available in the supplement at: <http://isnr.org/neurofeedback-info/neuroconnections-newsletters.cfm>.

Mary St. Clair—Still a Part of Us

Mary St. Clair died peacefully on Tuesday, July 23, 2013, surrounded by her family. She was born June 8, 1953, and practiced in West Bloomfield, Michigan. Mary was a leading light in the Neurofeedback Society. Many practitioners have written about Mary and these are some of those thoughts: Gretchen wrote that Mary's infectious passion for neurofeedback led to her influencing a healthy growth of neurofeedback practitioners in Michigan. She was instrumental in founding and growing what is now the Midwest Society for Biofeedback and Behavioral Medicine, was an active participant in the TLC community, and on the list-serve. Mostly, Mary was a kind and generous person as well as a gifted healer. She was wise, patient, and very giving of her time and knowledge. We have missed her vigorous participation since her illness and now feel deeper loss with her passing. Sara Harper wrote, "Mary fought for life every day these past five years. She pursued traditional and non-traditional treatments. She lived to see her precious daughter married to a wonderful man. She lived to see the birth of a grandchild. When these goals were accomplished, only then did she let go." Diane Stoler shared, "What we have once enjoyed we can never lose. All that we love deeply becomes a part of us. ~Helen Keller" Mary St. Clair was and still is a part of us.