1. What are the computer games and what is your experience in finding them relevant to the proposed work?

Neurofeedback equipment comes with pre-designed computer games, like PackMan and SpaceRace, that reinforce patterns of brain activity. In NF training, the subjects’ own neural activity is recorded from scalp electrodes in a computer, and is fed back in real time to subjects. The subjects’ own brain wave activity guides what happens in the game. If their brains produce the desired configuration, the game proceeds; when their brain produces activity that is associated with anxiety, distraction, depression, etc, the game slows down—space ships may move in the wrong direction, the music may stop playing, etc. In this way NF is thought to change behavior by changing neuronal connectivity patterns in the central nervous system (CNS) via operant conditioning.

In previous studies, we mainly used EEGer games. We started with “island and highway” because the child could visually see (on the screen) the activity of the brain activity that is being trained. Then, depending on the child, other games were introduced, such as packman. Once the child’s engagement with the EEGer games waned, we introduced Zukor games. These games are more complex (for example, flight simulator or carnival) and children were highly responsive to these games. As each child has difference game preferences, we give them a choice which game they wish to play—all of them are based on the same reinforcement patterns.

2. Are all the children with adoptive parents, and if yes, are you screening for how long they have been with them?

A large portion of our sample will be children living with adoptive parents. In the context of assessing the child’s background, we gather information on placement history and length of current placement. We do not control for length of time of placement—though it needs to have been stable for at least three months. This study targets out of control behavior.

In our previous child Neurofeedback study, the majority of children resided in adoptive homes: 28 out of 37 participants were adopted, 3 were with kinship care and 6 children were in the custody of the biological parent(s). All children that were adopted lived with their adoptive parents for several years (average length of placement: 5.5 years).

3. Do you anticipate engaging children who are still with their abusive parents?

No. One of the criteria for the participants of this study is that the child is in a stable and safe living situation and that the child has been in the placement for a minimum of 3 months. We specifically are selecting youth who have caregivers that are providing them with safety and stability, both of which are necessary components for being able to attend and make use of NFT.

All staff and research assistants are well versed in Massachusetts child protection laws. Any and all information provided by the child and / or other caregiving system (such as adoptive family, Department of Children and Families, service providers such as outside therapists, etc.) will be documented; and any information indicating that harm was or is coming to the child will be reported to the appropriate entities in accordance with Massachusetts law.
However, we hope that the emerging research (such as the proposed study – and to our knowledge nobody else, aside from close colleagues in Sydney Australia) will eventually allow NFT to be made available to children who are still in acute distress, i.e., children living in homes that are unsafe. But that hurdle can only be overcome if solid research proves its efficacy in dysregulated children who currently live in safe conditions, and where objectively safe conditions are insufficient to help the child to actually feel safe.

4. Are you screening in any way for economic class, gender, race, baseline IQ, other?

No. This study will not exclude participants based on their socioeconomic status, gender, race, intellectual functioning, disability, sexual orientation, etc. As identified in the methods section, we are excluding participants who have underlying seizure disorder etc. due to effort to avoid negative reactions to NFT.

We will, however, be collecting demographic data on all participants.

Based on previous experience, we anticipate some homogeneity based on our requirements that youth live in a stable, structured home and with caregivers that are able and willing to provide transportation to NFT sessions twice per week.

5. How would you explain neurofeedback to a non-scientist who had never heard the word?

This is what we say on the Trauma Center Website (www.traumacenter.org):

Neurofeedback is the first therapy that takes what we have learned about brain function in the past three decades and uses this new knowledge to change the way the brain processes information. Neurofeedback is a research-supported treatment to sharpen attention, relieve anxiety, enhance mood, and improve learning and behavior—without medication. Neurofeedback makes use of the brain’s natural capacity to change by reshaping brain networks. Although we are all born with “hard wiring” – networks of neurons and connecting fibers – our brains are constantly being shaped by experience. Repeated experience results in increased connections among neurons and in greater strength in the existing connections. Small changes that are repeatedly reinforced lead to changes in how our brains work.

Neurofeedback involves monitoring and analyzing brain signals picked up by surface electrodes placed on the scalp. We can visualize these electrical changes in the form of brainwaves, as recorded on an electroencephalogram (EEG).

In neurofeedback, a person is effectively playing video games with his or her brain. Eventually the brainwave activity is “shaped” toward more desirable, more regulated performance. The frequencies we target, and the specific locations on the scalp where we listen in on the brain, are specific to the individual and determined by an analysis of their quantitative EEG (qEEG).

During a session, people sit in a chair and listen to sounds and/or play a video game on a computer screen using their brain to direct the action. When the desired brain wave state is achieved, the game continues and points are accumulated. Nothing is being put into your brain—we are simply “listening” to your brain wave activity through sensors. You get instantaneous feedback about changes in your brain’s electrical activity by comparing your brain activity to a desired goal for change. When you meet that goal, you receive an auditory and/or visual signal.
and “reward.” In neurofeedback, we provide positive feedback to increase desired brain activity to teach self-regulation of brain function. Self-regulation is fundamental to healthy psychological functioning. New patterns of neuronal communication tend to result in changes in thinking, emotions, and behavior. Over time, these changes can endure without continued use of an instrument.

6. The proposal language was geared to someone familiar with trauma research and brain science. Could you restate briefly in layman’s terms what effect trauma has on the brain, how those effects are currently treated and how neuro feedback differs from traditional approaches?

Maybe the best explanation of this may be found in Dr. Van der Kolk’s NYT best selling book: the Body keeps the Score. To summarize this very complex topic simply: The brain develops in a systematic fashion, in which a combination of genetic predisposition and actual life experiences shape connections within the brain. When children experience significant trauma their brains shift into “danger” mode, where the natural instinct to survive takes precedence over other types of learning. For example, when a child is in real or perceived danger, he or she will focus on surviving, making use of the fight / flight / freeze / submit response. When this alarm system is engaged, everything else (like learning in school, picking up on social cues) is irrelevant. When children live in continuously stressful situations, such as being in a home with significant domestic violence, the child’s brain will habitually focus on survival.

This habitual orientation interferes with being able to learn new information, pay attention to non-threat related cues, and safely engage with others. Thus, their brain organization prevents them from being able to develop into mature adults who can keep calm, even under stress, wait their turn, listen to other people’s point of view, consider different perspectives, and appreciate the consequences of their actions.

The specific systems that are most impacted are the ability to understand and regulate their emotions, executive functions (e.g., starting and stopping tasks, organizing information, etc.), and learning social competencies. In addition, trauma also impacts a child’s natural development of a sense of self, where many children who have experienced significant trauma see themselves as incurably damaged and other people as a persistent threat.

In the past thirty years brain imaging studies have shown that terrifying early attachment experiences often result in impaired functioning of brain areas devoted to self-reflection (the medial prefrontal cortex), being able to distinguish dangerous from safe or pleasurable stimuli (the amygdala), being aware of the consequences one’s actions over time, and realizing that feelings have a beginning, middle and end (the dorsolateral prefrontal cortex), the capacity to filter out relevant from irrelevant stimuli (the anterior cingulate), as well as having an integrated relationship to the demands, warnings, and comfort of one’s bodily sensations (the insula)². When learning new skills, the brain requires the biological structures as well as experience to be able to support mastery and learning. Thus, brain development relies on both nature and nurture / experience.

Trauma-informed care requires comprehension of the full extent to which chronic stress impacts the brain. Large-scale trainings, easily accessible publications, and visual depictions of brain development in the context of child abuse and neglect will expand the scope of informed professionals which, in turn, will advance more accurate diagnoses and improve the potential for cross-disciplinary trauma-informed care.
Traditional approaches to trauma treatment rely heavily on the use of verbal communication and the ability to use the pre-frontal cortex (the “control center” of the brain). This means that treatments are reliant on the individual having understood and processed their experiences while having a basic command of language (excluding “pre-verbal trauma,” meaning trauma that occurs prior to an individual’s development of language) and that they have some access to executive functioning skills (use of pre-frontal cortex). However, many children who have experienced pre-verbal trauma and chronic early exposure to adversity may not have these basic pre-requisites for engaging in “traditional” treatments, i.e., “talk therapy.” Neurofeedback is different from the “traditional” ways of treating trauma in that it does not rely on the child’s ability to independently “calm” their brains enough to be able to take in information that will then be used to change child’s brain. Instead, NFT skips the use of words to be able to affect brain functioning and neural connectivity, and directly effects a calming of brain activity.

References:
Van der Kolk BA The Body keeps the Score: Brain, mind and body in the healing of Trauma. MY, Viking Press, 2015.

7. What neuro feedback software will you be using (vendor and release)? What QEEG software?

ERP and qEEG will be collected with Mitsar-EEG 201 amplifier by MITSAR Brain Diagnostic Solutions. The NFB training will be performed with a Spectrum2 by J&J Engineering amplifier.
8. **How will the qEEG'S be analyzed, by computer or by a human being? How will treatment protocols be chosen?**

The qEEG will be analyzed in several steps:
(a) The first step includes artifact rejection - will be performed by a human using Neuroguide and/or HBI software.
(b) Individual level brain maps will be created by HBI and Neuroguide databases.
(c) A group analysis will be performed by using Neuroguide.
(d) Sophisticated mathematical techniques from modern machine learning algorithms such as optimization, cluster techniques, neuronal networks will be used to classify qEEG patterns and to find correlations between qEEG and other variables such as symptoms, type of trauma, age of trauma, gender.

Treatment protocols will be chosen based on the individual brain mapping (i.e., qEEG) that are then informed by the state of the current literature, research, and clinical experience.

9. **What NF protocols were used in the Phase 1, 2 and 3 studies? What were the electrode placements and reward/inhibit frequencies? Were the protocols the same for all subjects or were they customized?**

**Study 1:** The pilot study (Gapen et al., 2016) showed that NFT significantly reduced the PTSD symptoms of adults with chronic trauma (n=17). The participants were randomly assigned to one of the two bipolar protocols: T4-P4 or T3-T4, with a reward of low beta (12-15Hz) and inhibition of both theta (4-8Hz) and high beta (22-36Hz). The reward was adjusted based on participants’ after-session feedbacks of over or under-arousal symptom questionnaire. The participants underwent 40 biweekly NFT sessions. Training time was between 12 to 21 minutes. Multilevel Growth Curve Modeling (GCM) results of pre-post assessments showed that NFT statistically significantly reduced the PTSD symptoms (Davidson Trauma Scale) and improved affect regulation (Inventory of Altered Self Capacities-Affect Dysregulation). Training at T4-P4 showed a larger impact than at T3-T4 but was not statistically significant.

**Study 2:** The main study (van der Kolk et al., 2016), showed that NFB statistically significantly reduces PTSD symptoms of adults with chronic PTSD. The study included 52 individuals with chronic PTSD, who were randomly assigned to the active NFB study (n=28) or to the waiting list-control group (n=24). The NFT was performed twice a week for 24 sessions. The training protocol was a bipolar T4-P4, with a reward starting at 10-13Hz and inhibition of 2-6Hz and 22-36Hz. Training time was 30 minutes. Multilevel GCM of pre-post assessments results showed that only 27.3% of the individuals in the active NFT group continued to meet PTSD diagnosis compared to 68.2% among the control group. PTSD diagnosis was based on Clinician Administered PTSD scale (CAPS).

**Study 3:** See answer to question 10.

10. **How many NF sessions were provided in the Phase 3 study? When will preliminary results be available? Can we see a copy?**
The impedance of all electrodes (gold electrodes) were kept under 10 kΩ. All electrodes were placed according to the international 10/20 system. All participants started with a bipolar protocol of T4 as the active site, P4 as the reference site, and the left ear A1 as the ground. The inhibition was 2-4Hz, 4--7Hz, and 22--36Hz with thresholds of 35%, 35% and 25% respectively. The reward band was individualized and based on the individual Posterior Dominant Rhythm (PDR). The PDR was calculated as the 3Hz band from 1Hz below PDR to 1Hz above PDR. PDR was measured at PZ with eyes closed. The threshold for the reward band was initially set for 65%. This protocol is based on the results of the previous studies (Gapen et al., 2016 & van der Kolk et al., 2016), scientific knowledge about the impact of trauma on the brain (Teicher & Samson, 2015) and clinical experience.

Adjustments to the protocol were based on the caregiver and/or child reports, NFT Symptom Checklist reports and clinical judgment. For example, if the caregiver reported significant symptoms worsening for two consecutive sessions, and these changes were not attributed to an external source, the reward band was adjusted by 0.5 or 1Hz. Changes in the electrodes’ location were in situations that the adjustments of the reward band had not improved the symptom(s).

NFT consisted of 24 sessions, twice a week for 12 weeks. The training time for each session was 6-18 minutes. During the session, the electrical activity of the brain was recorded, while the participants played a computer game. Participants were informed that audio and visual rewards are good signs and that no specific effort on their part is required since the learning process is mostly unconscious. If the power of the recorded brain signals at the specific frequencies (bands) were met, i.e. above the threshold for the reward band and below the threshold for the inhibition bands, then participants were rewarded with the audio and visual rewards.

The results of PTSD diagnosis as measured by responses on the K-SADS measurement showed that at baseline, the majority of participants in each group met the criteria for PTSD, and there was not a significant difference between participants in the WL (13/17, 76.5%) and NF (19/20, 95.0%) conditions meeting PTSD criteria, χ² (1, n = 37) = 2.70, p = .100. At the midpoint assessment, a higher proportion of WL participants (11/16, 68.8%) met criteria for PTSD than NF participants (6/17, 35.3%), χ² (1, n=33) = 3.694, p = .055. At the endpoint assessment, there was significant difference between the two groups; a higher proportion of WL participants (10/16, 62.5%) met criteria for PTSD than NF participants (4/16, 25%), χ² (1, n=32) = 4.571, p = .033. At the follow-up assessment, equal number of WL participants met the criteria for PTSD compared to those who did not meet criteria (7/14, 50%) and more NF participants did not meet the criteria for PTSD than those who didn’t (10/15, 66.7%) although these differences were not significant between the two groups χ² (1, n=29) = 8.29, p = .362.

*We anticipate that the manuscript with the data will be ready in the next several weeks, at which point we will send you a copy.*