NONPHARMACOLOGIC MANAGEMENT OF EPILEPSY COMORBIDITIES

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Rationale

Neurofeedback (NF) has been used effectively in the treatment of closed head injury[1], insomnia[2], migraine, depression[3], ADHD[4], and posttraumatic stress disorder[5]. A recent meta-analysis review concluded epilepsy was positively impacted by clinical neurofeedback ($p = 0.001$).[6] We therefore hypothesized that NF could serve as a therapeutic modality for epilepsy patients with refractory comorbidities. In the present study we applied a NF protocol to two male patients with well controlled seizures but with medically refractory comorbidities: insomnia, intractable headaches and ADHD in Patient A, and episodic dyscontrol (self-banging/ mutilating episodes) in Patient B.

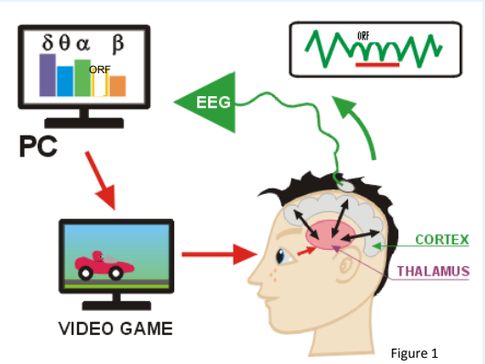


Figure 1

Introduction

Neurofeedback is in essence EEG operant conditioning.[1] The individual receiving neurofeedback is given a computerized visual program to watch, the content of which is mostly driven by real-time EEG "behavior" at examiner-selected EEG frequencies. Along these lines, the individual is cued with respect to the presence of excessive excursions in EEG amplitudes that may arise from paroxysmal activity and other physiologic noncephalic factors (Figure 1.)

In neurofeedback the individual is "trained," "reinforced," or "exercised" to remain within specific parameter ranges with respect to frequency, net amplitude, or phase (which are selectively fed to control the video) that are assessed to reflect his or her optimal level of functioning.[7] The resulting induced state shift may be subjectively felt somewhat immediately, and may last for days. Over the course of about 20 training sessions the individual's central nervous system (CNS) is likely to have "learned" enhanced control of state, and the capacity to maintain state regulation in the face of challenges leading to CNS stress.

Study Subject Profiles

Patient A is a 19 years old male with intractable epilepsy managed by vagus nerve stimulation and three anticonvulsants, zonisamide, oxcarbazepine, and rufinamide, who also suffered comorbidities of insomnia, depression, chronic daily migraine type headaches with intermittent exacerbations, and attention deficit hyperactivity disorder. Prior to initiating neurofeedback these comorbidities were managed by Halcion, Seroquel, amitryptyline, Zoloft, Lomital, Metadate, and Lortab prn. He would also present for unanticipated clinic visits at least weekly to receive acute headache management in the form of intravenous nubain with phenergan. Patient A's past EEGs revealed a potential for primary generalized or rapid secondarily generalized seizures.

Patient B is a 6 year old male with cerebral palsy, clinical autism and remote symptomatic epilepsy controlled by topiramate. A distressing symptom of Patient B was intermittent aggressive self-stimulation in the form of repetitively hitting himself in the head with his fists to the point of bruising and bleeding. He was also a chronic insomniac. He failed sequential trials on sertraline, risperidone, fluoxetine, and clonidine to control these injurious behaviors. Patient B's prior EEG revealed a multifocal epileptic encephalopathy with maximum spike activity and slowing at T5 and P3 (standard 10-20 nomenclature).

Methods

We obtained consent for NF therapy promoting central nervous system (CNS) self-regulation. Baseline performance tests (symptom profiles, TOVA[8], QEEGs, and observer evaluations) were to be repeated after 21 sessions to compare results to pre-treatment baseline. Procedures were performed under physician direction and supervision (one of the authors). Patient A's implanted vagus nerve stimulator (VNS) device was temporarily inactivated for all his NF sessions. Initial NF trials sought an optimal reinforcement frequency (ORF) for each patient reflecting his optimal arousal state, based on subjective reporting by the patient as well as observer ratings of behavioral alertness. The ORF was established using bipolar training at T3-T4 (the ORF being within the clinical EEG band, particularly the infra-low region < = 0.1 – 1.5 Hz).[9, 10] The T3-T4 bipolar recording was used to maximize the reward-based frequency feedback signal without promoting hemispheric coherence (of concern in individuals with seizures). Subsequently, each patient was scheduled to receive 21 separate 30-minute NF sessions (Othmer protocol[7]) over a period of four weeks. The computer system used for clinical neurofeedback was Cygnet™ neurofeedback software, integrated with Somatic Vision videogames, run via Windows (XP or Vista) operating system utilizing standard PC desktops and high-resolution monitors.

Results

Table 1.

Patient Baseline Assessment and Response to Neurofeedback Therapy

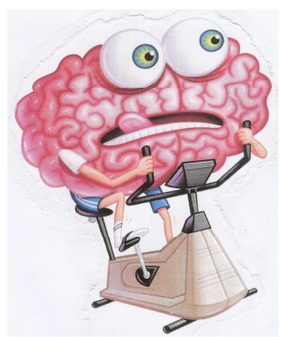
Patient	Sex	Age yrs	Tests: TOVA*	QEEG**	Observer Ratings	Medications	Othmer Protocol sites trained	ORF
A	male	19			no seizures since VNS implanted 6 months ago		T3-T4 C3-C4	1.5Hz
Pre-NF			SIGNIFICANT FOR ADHD PLUS DISINHIBITION	F7/T3/T4 F3/ F4 T4/T6/O2 excessive low frequencies	4 - **Anxiety Score** (lowresult) 0 - **OCD Score** headache rating 8-10 weekly stat clinic visits for IV nubain/ phenergan sleep difficulty rating 10	Halcion Seroquel Lortab prn Amitryptyline Lomital Zoloft Metadate Trileptal Banzel Zonegran IV Nubain/ Phenergan STAT prn		
Post-NF 43 sessions *patient discontinued due to financial hardship		not done	not done	not done	headache rating 4-6 (a 2 after sessions) not one stat clinic visit for IV meds sleep difficulty 6	Trileptal (oxcarbazepine) Banzel (rufinamide) Zonegran (zonisamide) Halcion prn		
B	male	6			**autism profile score**		T3-T4 C3-C4	0.001 Hz
Pre-NF				dilture theta frontal delta	59	Zoloft Clonidine Topamax Risperdal Prozac	T4-F4 T4-Fp2	
*continuing sessions Post-NF 29 sessions			not done (financial hardship)		22	Topamax (topiramate) Clonidine prn		

*Test of Variable Attention
**The QEEG did not guide therapy protocol

(Table 1.) Patient A completed only 13 sessions (discontinuing for financial reasons). Nevertheless Patient A's medications for insomnia, headache, and ADHD were progressively discontinued and he remained seizure free on his original three antiepileptic drugs (oxcarbazepine, rufinamide, and zonisamide). Patient B's symptom profile was reduced 62.7% following 21 NF sessions; his seizures remained well-controlled on monotherapy (topiramate).

Discussion

It is likely that the mechanisms for epilepsy in both individuals were also favorably impacted, given that their comorbidities improved and because of supportive literature in this regard. [6, 11] Many epilepsy comorbidities are syndromic expressions of the same CNS dysregulation that gives rise to seizures. Significantly, Patient A's VNS was inactivated during NF sessions before positive subjective effects were reported. Vagus nerve stimulation may be considered an exogenous regulator of the central nervous system and might interfere with the process of clinical neurofeedback (endogenously derived regulation). Current diagnostic classification for neurological disorders is descriptive, aids in specific choice of therapy for each disease category, and is also potentially redundant when considering that epilepsy and its comorbidities together reflect one centrally dysregulated state.



Neurofeedback as "Brain Exercise" to enhance CNS self-regulation

Conclusions

Early results support the hypothesis that clinical neurofeedback is a useful therapeutic modality for managing epilepsy comorbidities without compromising seizure control. Furthermore, NF treatment can allow medications other than AEDs to be discontinued, thereby averting potential adverse effects arising from multiple drug interactions. The success of neurofeedback in this regard, fully researched and better understood, may lead to a more integrative understanding of the multi-level mechanisms underlying epilepsy and its comorbidities. Not least, because of reported adverse effects on the developing brain by commonly prescribed antiepileptic drugs [12, 13] this modality offers a nonpharmacologic intervention that is preferable especially in pediatric populations, in view of the fact that many childhood epilepsies resolve with maturation in any event.

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