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THE EFFECTS OF NEUROFEEDBACK TRAINING IN THE COGNITIVE DIVISION OF THE ANTERIOR CINGULATE GYRUS

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This study examines the efficacy of neurofeedback training in the cognitive division of the anterior cingulate gyrus and describes its relationship with cortical regions known to be involved in executive functions. This study was conducted with eight non-clinical students, four male and four female, with a mean age of twenty-two. Learning occurred in the ACcd at significant levels over sessions and in the anterior regions that receive projections from the AC. There appears to be a multidimensional executive circuit that increases in the same frequency in apparent synchrony with the AC and it may be possible to train this sub-cortical region using LNFB.

Keywords anterior cingulate gyrus, attention, cognition, electroencephalography, executive function, LORETA, neurofeedback

INTRODUCTION

The anterior cingulate gyrus (AC) is a subject of intense interest and has been the focus of numerous studies over the past decade. Studies report involvement of the AC during a wide variety of cognitive, mnemonic and emotional tasks (Cabeza & Nyberg, 2000; Cannon et al., 2005; Markela-Lerenc et al., 2004; Devinsky et al., 1995). In a review, Devinsky et al. (1995) sum the processes of the AC as: crucial in initiation, motivation, and goal directed behaviors, emotion and motor functions, attention, direct control of skeletal and visceromotor systems, response selection, cognitively demanding processing devoid of movement and possible reclamation from short-term memory. Attentional processes are probably the most investigated function of the AC (Pardo et al., 1990; Bench et al., 1993; Posner & Petersen, 1990). Activation of the prefrontal cortex (PFC), AC, bilateral parietal cortex and occipital areas is reported in functional magnetic resonance imaging (fMRI) experiments involving sustained attention and counting (Ortuño et al., 2001). Studies report significant activation of the supplementary motor area (SMA) during attentional tasks and suggest that the SMA, dorsolateral PFC, inferior parietal lobes and the AC would be related to attentional effort as a general factor (Carr, 1992). Posner and Peterson (1990) suggest an anterior attention system that involves the AC and portions of the SMA and a posterior attention system that involves parietal regions and sub-cortical structures. Positron Emission Tomography (PET) studies report bilateral metabolic reductions in the hippocampal formation, thalamus, AC, and frontal basal cortex, which support the contribution of the AC in a network involving memory (Fazio et al., 1992). One prominent theory proposes that the AC detects the need for executive control and signals the PFC to execute the control (Markela-Lerenc et al., 2004). Executive functions are suggested to be an enveloping process that involves all cognitive processes associated with goal completion, anticipation, goal selection, planning, and initiation of activity, self-regulation, monitoring, and use of feedback (Sohlberg & Mateer, 1989). This suggests that executive functions are not only instrumental in cognitive processes but also crucial in attentional effort and maintenance.

It has been demonstrated that humans can acquire a certain degree of control over the electrical activity of their own AC, coupling the low-resolution electromagnetic tomography (LORETA) with the neurofeedback technique (Congedo, 2003; Congedo et al., 2004), yielding a non-invasive technique known as LORETA Neurofeedback (LNFB). In these preliminary studies, only the changes in the AC have been evaluated. However, it has been established that executive processes are mediated by the frontal lobes and in particular by the projections from the AC to the prefrontal and parietal cortices (Kondo et al., 2003; Heyder et al., 2004; Duncan & Owen, 2000), namely, the bilateral Q2 dorsolateral prefrontal cortex, left (LPFC) and right (RPFC), the right post-central gyrus (RPCG), the bilateral supramarginal gyri (RSMG, LSMG), and the cuneus. Hence, based on current information, this study sought to define the correlational structure of cortical regions directly involved in the self-regulation of the electrical activity of the AC. Particularly, the study investigated the efficacy of the LNFB training within the cognitive division of the AC (ACcd) and its effect in these connected regions. Following Congedo, Lubar, and Joffe (2004) the study aimed at improving attentional processes, thus individuals were trained to increase 14–18 Hz (low-beta) power activity in a seven-voxel cluster defining the ACcd, within the Brodmann Area (BA) 32 with center coordinates at $X = -3$, $Y = 31$, $Z = 29$. The definition of the region of interest (ROI) followed indications of Devinsky et al. (1995). The effect of the training was assessed by means of a number of pre–post and learning electrophysiological measures. On the other hand, the efficacy of the training was assessed by means of pre–post training psychometric testing using subtests of the Weschler Adult Intelligence Scale—Third Edition (WAIS—III).

Neurofeedback techniques have been utilized in clinical and research settings for treatment of epilepsy (Sterman, 2000, 2001), attentional disorders (Lubar & Lubar, 1999), alcoholism, and posttraumatic stress disorders (Peniston & Kulkosky, 1989–1991), and continue to be a focal point of development for possible treatments for psychological disorders. A recent fMRI study reports neurofeedback techniques initiating blood oxygenated level dependent (BOLD) changes in the AC, caudate and substantia nigra in ADHD children (Levesque et al., 2006). LNFB and spatial-specific training offer the possibility to influence regions deep in the medial temporal lobes, limbic regions, and regions at the base of the brain, such as the insular cortex, parahippocampal, lingual, fusiform, and orbital-frontal gyri, which contribution to surface EEG is poor. As compared to the effects of traditional neurofeedback, which is spatially unspecific (Congedo, 2003), LNFB may target a relatively small neuronal population. This study focused on those regions of the cortex that change in low-beta activity as a possible function of or in synchrony with the AC over approximately 30 sessions of LNFB training. To date, no study has investigated the simultaneous changes that occur in several regions of the cortex as a consequence of either traditional or spatial-specific neurofeedback training.

METHOD

Participants

This study was conducted with eight participants, four male and four female non-clinical students at the University of Tennessee, Knoxville. The mean age was 22, with standard deviation 1.92 and range 20–26. Seven of the participants were right handed and one was ambidextrous. All participants read and signed an informed consent to protocol approved by the University of Tennessee Institutional Review Board. All received extra course credit for participating in this study. Exclusionary criteria for participation included previous head trauma, history of seizures, drug or alcohol use, and any previous psychiatric diagnosis.

Procedures

Participants were prepared for EEG recording using a measure of the distance between the nasion and inion to determine the appropriate cap size for recording (Electrocap, Inc; Blom & Anneveldt, 1982). The head was measured and marked prior to each session to maintain consistency. The ears and forehead were cleaned for recording with a mild abrasive gel to remove any oil and dirt from the skin. After fitting the caps, each electrode site was injected with electrogel and prepared so that impedances between individual electrodes and each ear were <6 KΩ. The LNFB training was conducted using the 19-leads standard international 10/20 system (FP1, FP2, F3, F4, Fz, F7, F8, C3, C4, Cz, T3, T4, T5, T6, P3, P4, Pz, O1, and O2). The data was collected and stored with a band pass set at 0.5–64 Hz at a rate of 256 samples per second. All recordings and sessions were carried out in a comfortably lit, sound attenuated room in the Neuropsychology and Brain Research Laboratory at the University of Tennessee, Knoxville. Lighting and temperature were held constant for the duration of the experiment. Each session required approximately 40 min to complete.

Intracranial Current Density Estimation

LORETA (Pascual-Marqui, 1995, 1999; Pascual-Marqui et al., 1994; Pascual-Marqui, 2002) was used to estimate in real-time current density in the ACcd. In conventional neurofeedback, electroencephalographic (EEG) activity is recorded at a particular scalp location. The physiological measurements are extrapolated from the signal and converted into auditory stimuli or visual objects that animatedly co-vary with the magnitude of a specified brain frequency or frequency band. Similarly, LNFB correlates the physiological signal with a continuous feedback signal; however, the physiological signal is defined as the current density in a specified ROI. This allows the continuous feedback signal to become a function of the intracranial current density and to covary with it. LORETA is a widespread linear, discrete, instantaneous, full-volume inverse solution for brain electromagnetic measurements (for review see Pascual-Marqui et al., 2002a, 2002b). Whereas EEG is a measure of electric potential variations, LORETA estimates the current density that results in the potential divergence on the scalp. Using realistic electrode coordinates (Towle et al., 1993) for a three-concentric-shell spherical head model co-registered on a standardized MRI atlas (Talairach & Tournoux, 1988); anatomical labeling of the reconstructed neo-cortical volume is possible (Lancaster et al., 1997, 2000). This study used the three-shell concentric spherical head model implementation made available from the Key Institute for Brain-Mind Research, Zurich, Switzerland. In this implementation, the current density is mapped for 2394 voxels of dimension 7 × 7 × 7 mm covering the entire neocortex plus the AC and hippocampus.

Neurofeedback Protocol

Thirty-three training sessions composed of four 4-min rounds were conducted three times per week. Following Congedo, Lubar, and Joffe (2004), this study aimed at improving attentional processes, thus individuals were trained to increase 14–18 Hz (low-beta) power activity in a seven-voxel cluster defining the ACcd, within the Brodmann Area (BA) 32 with center coordinates at $X = -3$, $Y = 31$, $Z = 29$. The definition of the region of interest (ROI) followed indications of Devinsky et al. (1995). In a preliminary session, the participants were instructed to control tongue and eye movements, eye-blinks, and muscle activity from forehead, neck, and jaws. This enabled the subjects to minimize the production of extra-cranial artifacts (EMG, EOG, etc.) during the sessions. At the end of the preliminary session, they were informed of the inhibitory and reward aspects of the training. Thresholds were then set and maintained for each participant. The protocol used was:

A. Electro-oculogram (EOG) < 15.0 (Microvolts); SUPPRESS
B. Electromyogram (EMG) < 6.0 (Microvolts); SUPPRESS
C. Region of Interest (ROI) > 5.0 (Current Density); ENHANCE

The participants were provided visual and auditory feedback and points were achieved when they were able to simultaneously

A. Decrease 1–3 Hz activity in a linear combination of six frontal channels: FP1, FP2, F3, F4, F7, F8 and
B. Decrease 35–55 Hz activity in a linear combination of six temporal and occipital channels: T3, T4, T5, T6, O1, and O2, while
C. Increasing current source density (14–18 Hz) in the ROI.

Maintaining the condition for 0.75 s achieved one point. Following Congedo, Lubar, and Joffe (2004), this study made use of both auditory and visual feedback. The auditory stimuli provided both positive and negative reinforcement, an unpleasant splat sound when the conditions were not met and a pleasant tone when they were. Similarly, the visual stimuli were activated when the criteria were being met, for example, a car or a spaceship driving faster and straighter. Alternatively, a slower car, driving in the wrong lane or the spaceship flying slow and crooked occurred when the criteria were not being met. The score for meeting the criteria was also seen by the participants in a small window of the game screen.

Data Collection

Three-minute eyes-opened and eyes-closed baselines were collected before and after the neurofeedback training for pre–post brain imaging comparison. Likewise, three-minute eyes opened baseline recordings were collected before and after each session. In contrast with studies on traditional neurofeedback, the whole-head EEG data was continuously stored during the sessions. In addition, the participants in this study provided a written record of their experience, strategies, and mental processes employed to obtain points for each session during this training.

Data Pre-Processing

All EEG data were processed with particular attention given to the frontal and temporal leads. All episodic eye blinks, eye movements, teeth clenching, jaw tension, body movements, and possible EKG (Electrocardiogram) were removed from the EEG stream. Fourier cross-spectral matrices were computed and averaged over 75% overlapping 4-s artifact-free epochs, which resulted in one cross-spectral matrix for each subject and for each discrete frequency.

Psychometric Pre-Training Measures

The Weschler Adult Intelligence Scale—Third Edition (WAIS—III) was administered for a pre-training measure. The mean Full Scale Index Score (FSIQ) is 124, range (118–139), SD $= 6.79$. The authors selected the Working Memory Index (WMI) and Processing Speed Index (PSI) scores for post training comparison. The mean pre WMI score is 118, range (94–141), $SD = 5.81$. The mean pre PSI score is 107, range (88–120), $SD = 3.93$. The WMI score consists of the sum of scaled scores in the Arithmetic (A), Digit Span (DS), and Letter-number sequencing (LN) subtests. The PSI score consists of the sum of scaled scores in Digit-symbol Coding (CD) and Symbol Search (SS). These combinations of subtest scores were used following indication of Sattler (2001).

Data Statistical Analysis

This study focused on seven ROIs, of which one is the *active ROI* (ACcd) and the other six, the *secondary ROIs,* have been found to be functionally associated to it (see Introduction). Table 1 lists the name of the ROIs, the number of voxels

Table 1. The specific regions of the cortex, the number of voxels assigned to the region by LORETA, the X, Y, Z Talairach Coordinates, and the region of the brain

ROI	# of Voxels[3]	X, Y, Z Talairach coordinates	Brain region
Anterior Cingulate Gyrus	7	(−3, 31, 22) (−3, 24, 29) (−10, 31, 29) (−3, 31, 29) (−4, 31, 29) (−3, 38, 29) (−3, 31, 26)	Brodmann area 32, anterior cingulate gyrus, limbic lobe
Left Dorsolateral Prefrontal Cortex	3	(−38, 31, 36) (−38, 31, 43) (−31, 31, 43)	Brodmann area 8, middle frontal gyrus, frontal lobe
Right Dorsolateral Prefrontal cortex	4	(39, 31, 36) (39, 24, 43) (32, 31, 43) (39, 31, 43)	Brodmann area 8, middle frontal gyrus, frontal lobe
Right Post-central gyrus	5	(46, −25, 43) (53, −25, 43) (60, −25, 43) (53, −18, 43) (53, −25, 50)	Brodmann area 3, post-central gyrus, parietal lobe
Left supramarginal gyrus	5	(−59, −53, 15) (−59, −60, 22) (−59, −53, 22) (−59, −46, 22) (−59, −53, 29)	Brodmann area 40, supramarginal gyrus, temporal lobe
Right supramarginal gyrus	6	(60, −53, 15) (60, −60, 22) (53, −53, 22) (60, −53, 22) (60, −46, 22) (60, −53, 29)	Brodmann area 40, supramarginal gyrus, temporal lobe
Cuneus	7	(−3, −67, 22) (−3, −74, 29) (−10, −67, 29) (−3, −67, 29) (4, −67, 29) (−3, −60, 29) (−3, −67, 36)	Brodmann area 7, Cuneus, occipital lobe

composing it, the Talairach coordinates of all voxels within the ROI, and its Brodmann area/anatomical labeling.

The data analysis for this study included four stages. First (stage I), to assess the covariance of the ROIs within the linear increase over session and rounds the authors conducted an ANOVA. The within-subjects experimental design required an accommodation for the violation of the assumption of independent observations, which is typical of neurofeedback because each session is dependent on the previous sessions as are the rounds within each session. The General Linear Mixed Models method was utilized (Barry, 2003; Schabenberger & Pierce, 2002), PROC MIXED in SAS, version 9.1. The study used the REML (Residual Maximum Likelihood) estimation method (Kackar & Harville, 1984; Rao, 1972) for the Prasad–Rao–Jeske–Kackar–Harville (1990) fixed effects model and the Kenward–Roger (1997) adjustment for degrees of freedom. The experiment wise error rate was maintained at 0.05 using Tukey methodology (Westfall et al., 1999).

Second (stage II), after averaging across the four rounds within each session, the authors conducted a Pearson correlation analysis to assess a linear upward or downward trend of the current density changes in the seven ROIs of Table 1. Threshold of significance for the correlation coefficients r was set to $\text{abs}(r) = 0.01$. This stage was conceived to individuate those ROIs in which current density amplitude tends to increase (positive correlation) or decrease (negative correlation) as a function of the neurofeedback learning process.

Third (stage III), in order to assess the electrophysiological differences between pre and post training baselines over the entire neo-cortex, the authors conducted all voxel-by-voxel t-tests setting the threshold to abs $(t) = 4.0$.

Finally (stage IV), the pre and post psychometric scores were analyzed using an ANOVA. This analysis tests whether the spatial-specific training of low-beta activity in the ACcd results in a positive influence in cognitive performance related to attention and executive processes in normal subjects.

RESULTS

Learning Curves

Table 2 shows the results of the mixed model analysis of the learning curves (stage I). The model defines the variance-covariance and mean parameters for the fixed effects of each ROI with the ACcd, that is, the main effect of learning in each region for rounds, sessions, and rounds by sessions. There is a significant learning effect in the ACcd, LPFC, RPFC, RPCG, and RSMG. The cuneus and LSMG show no learning effect in the trained frequency. The session, round,

Table 2. ANOVA table and the Type III test of fixed effects from the mixed models analysis

ROI session round	Num *df*	Den *df*	*F* Value	*p*
ACcd	7	25	4.82	.0015
LPFC	1	1202	250.48	<. 0001
RPFC	1	1214	144.96	<. 0001
RPCG	1	1219	9.41	0.0022
RSMG	1	1221	5.23	0.0224
LSMG	1	1212	0.10	0.7556
CUN	1	1195	0.04	0.8502
Rounds	5	44.4	1.42	0.2371
Session	32	198	0.78	0.7943
Ses∗rnds	160	995	1.10	0.2125

Table 3. Pearson correlation matrix of the seven ROIs in the trained (14–18 Hz) frequency

	ACcd	LPFC	RPFC	RPCG	RSMG	LSMG
LPFC	.732*	—	—	—	—	—
RPFC	.625*	.783*	—	—	—	—
RPCG	.454*	.614*	.749*	—	—	—
RSMG	.101	−.024	.101	.120	—	—
LSMG	−.038	.014	.078	−.023	.257	—
Cuneus	.127	−.019	−.092	.033	.471*	−.638*

*$p < 0.01$.

and session by round effects are not of significance; in this model this is an expected result because these items are defined as a covariance structure rather than a main effect within the model.

Correlation Analysis

Table 3 shows the degree to which neuronal populations in the extracted anterior regions of interest share a relationship with each other (stage II). The relationship between the ACcd, bilateral dorsolateral prefrontal cortex, and right post-central gyrus is significant. The anterior and posterior regions do not appear to be correlated. It is interesting that the left supramarginal gyrus is negatively correlated with the cuneus whereas the right is positive.

The three following subsections detail results of the learning curves in the ACcd, anterior regions and posterior regions.

Anterior Cingulate Gyrus. Figure 1A shows the within session group results at the ACcd. The plot is obtained averaging current density across all subjects and sessions. On the average, rounds one and two decrease within sessions as compared to the beginning baseline (BB). Then there is a linear increase in current density in rounds three and four and the ending baseline (EB). Figure 1B shows the average current density in the ACcd for all subjects for all rounds combined over sessions. In this particular training, the current density in neuronal populations within the ACcd shows an increase over sessions at significant levels (Table 2).

Anterior Regions. Figure 1C shows the average current density in the extracted anterior regions of the cortex over sessions. The cluster of three voxels in the LPFC for all subjects averaged a linear increase significantly

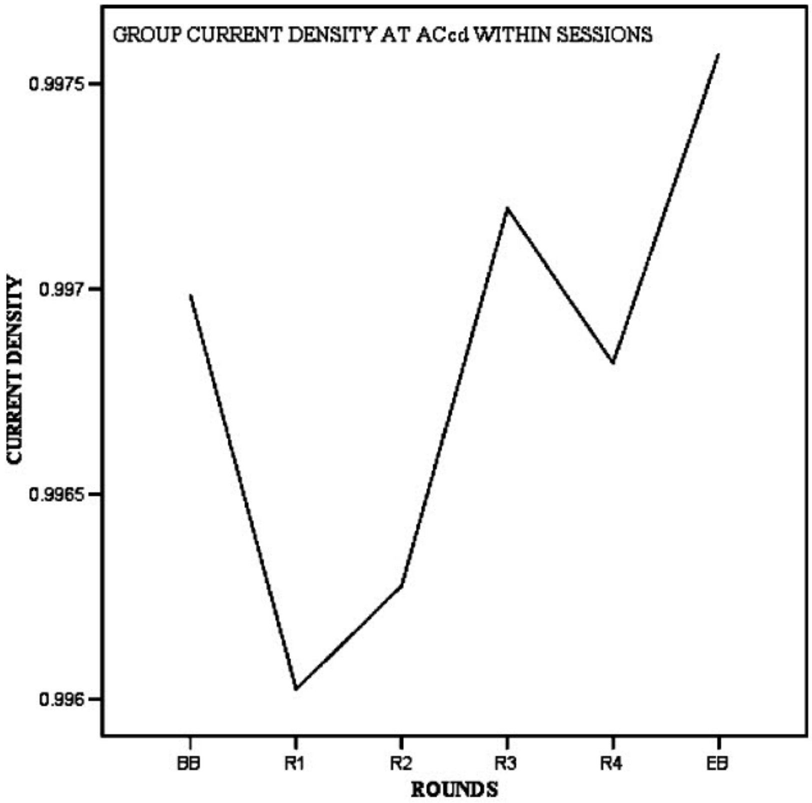

Figure 1A. Group means for current density averaged across sessions for each round and mean current density for pre (BB: beginning baseline) and post (EB: ending baseline) baseline measurements.

higher than the current density produced in the ACcd. The cluster of four voxels in the right dorsolateral prefrontal cortex increases in current density at an average rate higher than the ACcd for all rounds combined over sessions; however, lower than the LPFC in the same respect. The current density in the five-voxel cluster in the RPCG also increases over sessions. The activity in this cluster correlates significantly with the right dorsolateral prefrontal cortex (.749). Note that the frontal and parietal lobes are typically divided into two functional areas, immediately rostral and caudal to the Rolandic fissure, the anterior region including BA 1, 2, 3, and the posterior area that includes BA 5 and 7.

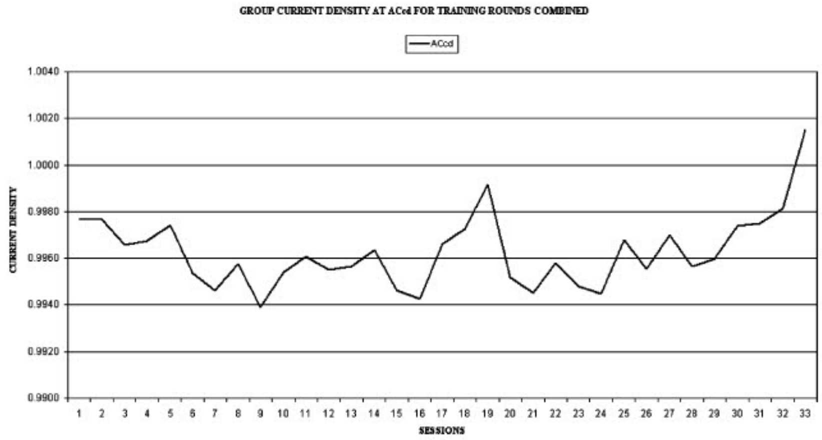

Figure 1B. Group average current density in the ACcd for the combined rounds of training over sessions. The trend is positive and significant (see Table 2).

Posterior Regions. The supramarginal gyri, along with the angular gyrus are referred to as the inferior parietal lobes, and are suggested being involved with the cuneus in higher order visual processing. Figure 1D shows the average current density in the posterior regions of the cortex for all training rounds combined over sessions. The cluster of six voxels in the right supramarginal gyrus decreases in the trained frequency over sessions, as does the five-voxel cluster in the left supramarginal gyrus and the seven-voxel cluster in the cuneus.

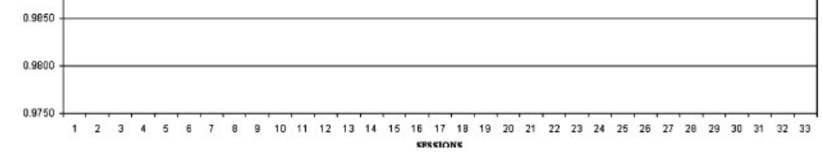

Figure 1C. Group average current density in the anterior regions of the cortex for the combined rounds over sessions. These regions increased at significant levels (see Table 2).

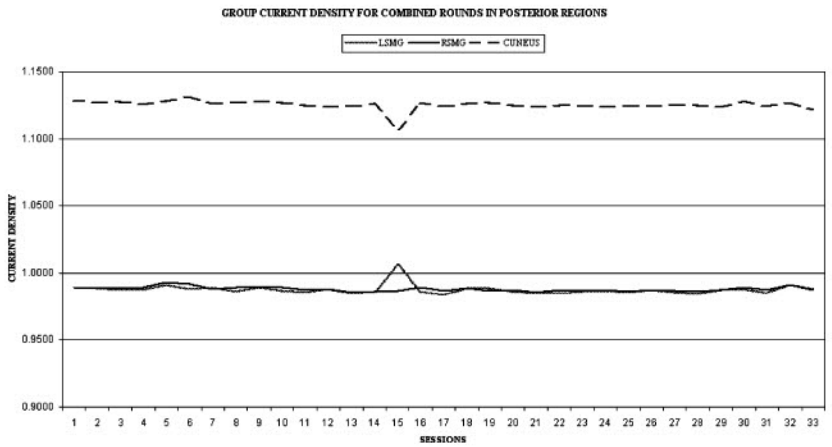

Figure 1D. Group average current density in the posterior regions of the cortex for the combined rounds over sessions. The activity in these regions decrease over sessions in the trained frequency (see Table 2).

Pre–Post Comparisons. Pre and post eyes-closed and eyes-opened baseline recordings were evaluated for significance (stage III). The resulting images plot only the significant *t*-values for the comparison, with the t-value maximum threshold set at >4.0. Figure 2A shows the significant differences between pre and post eyes-closed baselines pointing at the ACcd. The maximum increase is in the right inferior temporal region, whereas the maximum decrease is in the left parietal and temporal cortices. Also of significant increase are the superior frontal gyrus, the orbital, rectal and medial frontal gyri, the right post central gyrus and temporal regions. Figure 2B shows the significant increase in the ACcd in an eyes-opened recording. The maximum increase assigned by LORETA is in the right inferior temporal region and the maximum decrease is in the left parietal and temporal cortices, right parietal and occipital regions, including the cuneus and posterior cingulate. Of particular interest is the increased activation in the right inferior temporal cortex and how it relates to the region of interest, ventral portions of the AC and its role in visual processing.

Psychometric Post Measures

The post psychometric measures for all subjects were taken at session 30, which was one week prior to the end of the spring semester. This time was to opted for

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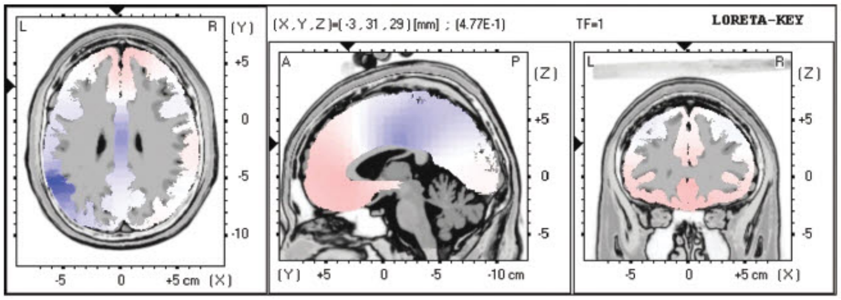

Figure 2A. This is a *t*-statistical image for the difference between pre and post eyes-closed baseline comparison. This is a horizontal, sagittal, and coronal view of the region of interest from left to right. The red in the image indicates regions of significant increase in activation, whereas the blue indicates significant decreases. The maximum increase given is at (X = 53, Y = 3, Z = −41) Brodmann area 21, Middle Temporal Gyrus, Temporal Lobe. In addition, as much of the data presents, the ACcd and ventral portions of the AC are also of significance. The maximum decrease is at (X = −59, Y = −53, Z = 22) Brodmann area 40, Supramarginal Gyrus, Temporal Lobe.

avoid the possible confounding effects of the stress and anxiety associated with finals. Table 4 shows the results for the analysis of the pre and post obtained subtests; WMI and PSI scores (stage IV). Included in the table are the pre and post subtest scaled scores, the mean, standard deviation, 95% confidence intervals (lower–upper), the difference between the pre and post subtests, the

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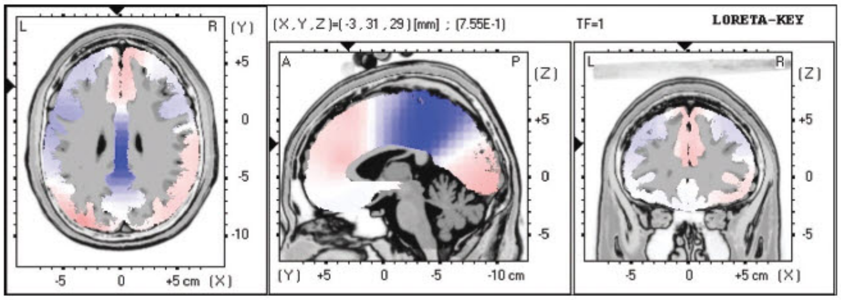

Figure 2B. This is a *t*-statistical image for the differences between pre and post eyes-opened baseline comparisons. This is a horizontal, sagittal, and coronal view of the region of interest from left to right. The red in the image indicates regions of significant increase in activation, whereas the blue indicates significant decrease. The voxel of maximum increase in activation is at (X = 67, Y = −32, Z = −13) Brodmann area 21, Middle Temporal Gyrus, Temporal Lobe. The ACcd and right post central gyrus are of significant increase. The maximum decrease is at (X = −24, Y = −53, Z = 64) Brodmann area 7, Superior Parietal Lobule, Parietal Lobe.

Table 4. Results for the pre and post psychometric measures. There was no change in arithmetic and an insignificant change in LN sequencing. The differences in the other scores are of significance

Group Pre-Post WAIS III Subtest and Index scores							
Subtest *Index	Mean	SD	95% Upper-Lower	Diff	*df*	F	*p*
Pre C	11	2.77	(8.67–13.32)				
Post C	13	3.20	(10.31–15.68)	+2	1,6	51.32	0.0004
Pre A	13	3.02	(11.09–16.05)				
Post A	13	1.99	(11.95–15.29)	0	1,6	2.83	0.1438
Pre DS	12	2.99	(10.36–15.38)				
Post DS	15	4.36	(11.59–18.90)	+3	1,6	11.48	0.0147
Pre SS	11	1.84	(9.83–12.91)				
Post SS	13	2.66	(11.14–15.60)	+2	1,6	14.01	0.0096
Pre LN	12	3.70	(9.53–15.71)				
Post LN	14	2.54	(12.61–16.88)	+2	1,6	4.89	0.0691
*Pre WMI	117	16.44	(103–131)				
*Post WMI	128	17.64	(114–143)	+11	1,6	45.12	0.0005
*Pre PSI	106	11.13	(97–115)				
*Post PSI	117	14.17	(105–129)	+11	1,6	23.93	0.0027

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degrees of freedom, the *F* value and the probability of *F*. In psychometric testing, there is the consideration of practice effect and test–retest reliability. For the WAIS—III, the test–retest gains and losses for the age group 16–29 are reported as: Coding (+1.2), $p < .001$, Arithmetic (+0.6), $p < .001$, Digit Span (+0.5), $p < .05$, Symbol Search (+1.0), $p < .001$, Letter-Number Sequencing (+0.1), $p > 0.05$, Working Memory Index (+2.9), $p < .01$, Processing Speed Index (+6.0), $p < .001$ (Sattler, 2001). The differences between the pre and post measure scores are significantly higher in the present group than in the test–retest group in all subtests, except in the Arithmetic and Letter-Number sequencing scores, where differences still are in the desired direction.

Subjective Reports

In an attempt to control for the subjective state of the individual during the task, which is seldom done in brain imaging studies, this process were utilized in order to maintain a record of the mental activities the subjects engaged in during the LNFB sessions. These reports will be analyzed with the EEG data and presented in a future work. The written reports included attention to muscle and eye movement, the visual characteristics of the game, the pleasant tone and making the unpleasant splat stop, working memory, long- and short-term memory, counting, mental verbalization (talking to the game, themselves, or singing songs), thoughts of daily stresses, frustration relating to performance, sexual imagery, and breathing or visualization techniques.

CONCLUSION AND DISCUSSION

This study sought to determine the efficacy of LNFB in training nonclinical subjects to activate a subcortical region and to describe the nature of the relationship between these seven groups of neuronal populations within cortical regions that are identified in the literature as being active in tasks involving attention, mnemonic, cognitive, and executive processes (Cabeza et al., 2003; Carr, 1992; Heyder et al., 2004; Kondo et al., 2004; Ortuño et al., 2001; Tzourio et al., 1997). The obtained data suggest that LNFB may be an efficacious methodology for neurofeedback training in the AC. The linear measures of learning are significant in the AC and the anterior and parietal regions of interest. There are significant, positive linear associations between neuronal populations within the ACcd, LPFC, RPFC, and RPCG, which offers further support to the specificity of these regions in executive functions; moreover, it supports the suggested domination of a fronto-parietal right hemispheric network in attentional processes. The regions of interest in the dorsolateral prefrontal cortex (RPFC, LPFC) and the right post central gyrus (RPCG) show significant learning effects relative to the AC. Of considerable interest is how these regions improve to a greater degree than the AC in the trained frequency. This increase is possibly attributed to the AC's centralization to the aforementioned fronto-parietal network and its possible regulation of tasks involving selective attention, concentration, motor control, spatial information, controlling muscle activity, attention to surroundings, the game itself, visual and auditory stimuli, and using cognition, attention, and mnemonic, that is, executive processes as goal-directed behaviors.

Q5

It is suggested that several independent circuits operate to control attention, cognition, memory, and executive functions. Alternatively, executive functions are suggested to include all the processes of attention, cognition, memory, initiation and drive, response inhibition, task persistence, organization, generative thinking, and awareness (Sohlberg & Mateer, 2001). It is the authors speculation that the data obtained in this study offers support to this second suggestion, and maps a plausible circuit of executive function involving these *ROIs* and the AC. If the AC is indeed a gating mechanism, as suggested by

Q6

Pizzagalli et al. (2003), then sustained activity in this particular cluster of voxels may represent a ceiling effect and initiate facilitation of cortical areas that are known to receive projections from the AC. This appears to be reinforced by the differences in learning curves achieved in the secondary *ROIs*. The AC remains a focal point for study, due in part to its location in the brain and its projections throughout the cortex and to sub-cortical structures. The data obtained in this study suggests that this circuit is activated and developed in the trained frequency over sessions and the individuals in this study learned to activate this circuit through feedback about the electrical activity of their own ACcd.

The posterior parietal regions of interest (LSMG, RSMG, and Cuneus) appear less sensitive to the influence of the AC in the trained frequency. They do, however, increase in higher beta activity 20–32 Hz, which is possibly attributed to the focus on the auditory and visual aspects of the training and reported techniques utilized by the subjects to obtain points. The differences between these posterior and anterior *ROI*s offer the possibility of frequency-specific activity, rather than two separate systems. The psychometric results offer support to the increase of higher beta activity in the occipital and higher order visual processing regions. The increase in PSI scores suggests that the neurofeedback training positively influenced processes involving visual motor coordination, attention, concentration, visual acuity, visual scanning and tracking and short-term memory for learning new tasks. Similarly, the increased WMI index score suggests a positive influence in short-term memory, auditory memory, and attentional processes, which would be aided by the LPFC and ACcd. The results imply that LNFB training positively influenced both working memory and processing speed tasks.

Two limitations of the neurofeedback method based on inverse solutions as implemented in this research should be kept in mind. First, the actual region trained does not correspond exactly to the ACcd due to approximated head model used. Second, the spatial specificity of LORETA with 19 electrodes is in the order of several cm^3, therefore the activity of brain regions close to the regions monitored could have influenced the results. The first limitation can be resolved by constructing realistic head models based on magnetic resonance imaging information. The second has been the object of a recent investigation (Congedo, *in press*). **Q7**

It would have been beneficial to this study to include a control group for excluding confounding effects and this is planned for future research, which will also involve training individuals to activate the clusters of neuronal populations in the dorsolateral prefrontal cortex to be compared to the AC.

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