Follow-Up Study of Learning-Disabled Children Treated With Neurofeedback or Placebo

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ABSTRACT

This report is a 2-year follow-up to a previous study describing positive behavioral changes and a spurt of EEG maturation with theta/alpha neurofeedback (NFB) training in a group of Learning Disabled (LD) children. In a control paired group, treated with placebo, behavioral changes were not observed and the smaller maturational EEG changes observed were easily explained by increased age.

Two years later, the EEG maturational lag in Control Group children increased, reaching abnormally high theta Relative Power values; the absence of positive behavioral changes continued and the neurological diagnosis remained LD. In contrast, after 2 years EEG maturation did continue in children who belonged to the Experimental Group with previous neurofeedback training; this was accompanied by positive behavioral changes, which were reflected in remission of LD symptoms.

INTRODUCTION

NFB is an operant conditioning procedure, whereby an individual can learn to modify the electrical activity of his or her own brain.[1] The aim of neurofeedback training is to redress any EEG abnormality, resulting in a concomitant improvement in behavioral and/or cognitive performance.[2]

LD are one of the most frequent problems that afflict children in elementary school.[3] LD are diagnosed when an individual's achievement on individually administered, standardized tests in reading, mathematics, or written expression is substantially below that expected for age, schooling, and level of intelligence. LD are classified as "specific" (reading disorder, mathematics disorder, or disorder of written expression) or "learning disorder not otherwise specified," which might include problems in all three areas.[3] Children included in this study belonged to the latter group. Although LD children often have some deficit in attentional processes and there is a high comorbidity between LD and Attention Deficit /Hyperactivity Disorder (ADHD), children in our study didn't satisfy the criteria to be classified as ADHD.[3]

The EEG of LD children is characterized by more slow activity, principally in the theta range, and less alpha than normal children of the same age[4-10]; therefore an adequate NFB protocol could be to reward the reduction of theta/alpha ratio in the region with highest ratio.

Two years ago, we applied this NFB treatment to an Experimental Group (n = 5) of LD children who had abnormally high theta/alpha ratios, and we applied a placebo treatment to a paired Control Group.[11] All changes observed exclusively in the Experimental Group indicated better cognitive performance and the presence of greater EEG maturation in the Experimental Group than in the Control Group, which suggested that changes were due not only to development but also to NFB treatment.[11]

In this paper we present the results of a 2 year follow-up study of LD children treated 2 years ago, except for one child from Control Group who left the school, and he did not want to participate in the experiment anymore.

Some reports exist about follow-up studies in NFB, principally in epilepsy,[12-16] alcoholism[17-20] and ADHD.[21-25] But not many of them are controlled studies[12,15,18,20,23,24] making it difficult to separate the effects of NFB from the influence of both maturation effects and effects caused by the therapist's care. To our knowledge, there are no follow-up studies of pathologies such as schizophrenia, affective disorders and LD. Thus, at present the evidence for the long-term efficacy of NFB for these pathologies remains equivocal. In this paper we present the first report of a controlled follow-up study in LD children.

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METHODS

Subjects

Two years ago, we selected 10 children (7-11 years old, 2 female) out of more than 80 children who presented academic problems in order to carry out the experiment described above.[11] At that time, they had the following characteristics: no neurological or psychiatric disorders except for the presence of LD not otherwise specified; no important alterations in their brain Computed Tomography; their IQ scores were at least 70, and they did not have severe sociocultural disadvantages. All of them had an abnormally high EEG theta/alpha ratio for their age, at least in one lead, and no paroxysmal activity in the alpha frequency range. All children were volunteers; parents' informed consent was obtained in all cases.

After the Test Of Variables of Attention (TOVA)[26] in its visual version was applied to all children, they were classified in two groups, which did not differ in averages of age, sex, IQ, ADHD score from TOVA, and per capita income in the family. One group, the Experimental Group (n = 5), received NFB treatment, and the other group, Control Group (n = 5), received a placebo treatment. On the basis of the EEG activity at the most abnormal lead, NFB or placebo treatment was applied, depending on the group to which the child belonged. At that time, 2 years ago, NFB was conducted using an NFB program adapted to the MEDICID IV recording system and software. EEG recordings were obtained from a lead situated at the place with the most abnormal theta/alpha ratio, relative to linked earlobes. The threshold level was selected every 3 minutes so that the subject obtained the reward (a 500 Hz tone) between 60% and 80% of the time. Throughout the recording, the ratio was computed for 20 milliseconds every 5 milliseconds and compared with the threshold. If the ratio was lower than the threshold, the reward was given. Subjects were told to maintain the tone as much as possible because it meant that their brain was working well. In the placebo treatment all conditions were exactly as in NFB, except that in this case the reward and its duration were random, non-contingent with EEG activity. Each child received 20 sessions of training (each of which lasted 30 min) at a rate of 2 per week over a period of 10 to 12 weeks.

The current follow-up study was carried out 2 years after the end of the NFB or placebo treatment. In order to analyze the EEG and behavioral changes that had occurred during these 2 last years, the following studies were applied again: TOVA, WISC-R, parental interview, neurological exam, and EEG recording.

EEG recording and analysis

Subjects were seated in a comfortable chair in a dimly lit room with acoustic isolation. EEG was recorded in 19 leads from the International 10-20 System using linked ear lobes as reference. A1A2 reference was used in order to have the same conditions as in normative data. The amplifier bandwidth was set between 0.5 and 30 Hz. The EEG was sampled every 5 milliseconds using a MEDICID 3E System and edited off-line. An expert electroencephalographer using visual editing selected twenty-four artifact-free segments of 2.56 sec for quantitative analysis, as in the normative database.

Analysis was done off-line. The Fast Fourier Transform was conducted over EEG segments of 2.56 sec, and the cross-spectral matrices were calculated every 0.39 Hz. The following measures were obtained for each referential lead: the absolute (AP) and relative (RP) powers in each of four frequency bands: delta (0.5-3.5 Hz), theta (3.6-7.5 Hz), alpha (7.6-12.5 Hz), and beta (12.6-19 Hz). The ranges of these bands were selected according to normative data[27] provided by MEDICID 3E. Also, Z-score values for AP and RP were computed as follows: $Z = (x-\mu)/\sigma$ where μ and σ are respectively the mean value and the standard deviation, respectively, of the normative sample[25] of the same age as the subject.

Statistical analysis

Sample sizes are very small and normal distribution is not warranted, so parametric analyses are not appropriate. The statistical significance of the differences between behavioral and EEG data before and after treatment was assessed by a multivariate non-parametric permutational test[28] for dependent variables. The analysis was made for each group separately. In each group, one measure or a group of measures in two different conditions were compared using the t-Student statistic for dependent samples. In each comparison two types of hypotheses are tested: a global hypothesis, that takes into account all variables included, and as many marginal hypothesis as variables were considered. For EEG data, we performed separate analyses for each band (delta, theta, alpha, beta) and each measurement (zAP and zRP). For example, if we compared the theta AP before and 2 years after of NFB treatment, the global null hypothesis tested the equality between theta AP recorded before and 2 years after NFB treatment in all leads (19), and the 19 marginal null hypothesis tested the equality of the theta AP at a particular lead. This procedure computes the exact probabilities, which we considered as being significant at the level of $p < 0.05$. This multivariate non-parametric permutational test[28] had been used in some previous works of our group with very good results.[11,29,30-32]

Multivariate statistics can be used to summarize and test differences between two conditions obtained from the maximum value of all the univariate statistics. This may also be the maximum of the t distributions calculated between the two sets of data, *tmax*, for all frequencies and across all the leads. The distribution estimated by permutation techniques for *tmax* can then be used to set significance levels that control the experiment-wise error for the simultaneous univariate comparisons, avoiding the inflation of type I error.[33,34]

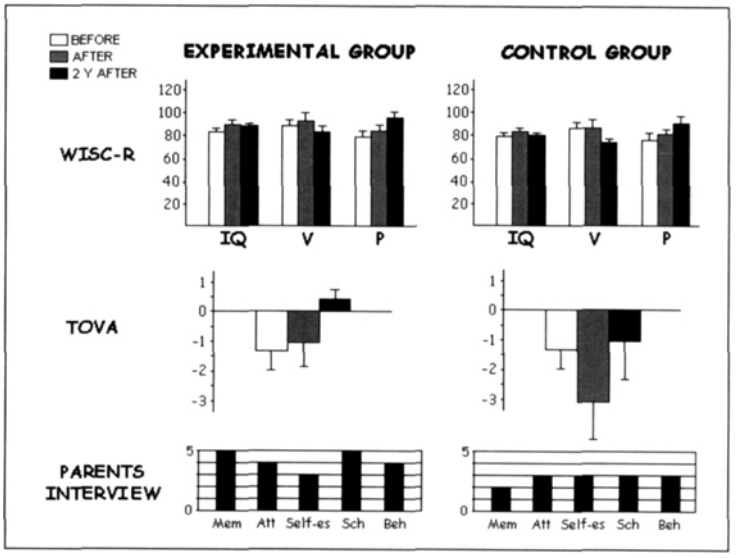

Figure 1.
Behavioral changes for both groups in WISC-R and TOVA in three different periods: before (white), after (gray) and 2 years after (black) the Experimental Group's NFB treatment. IQ=total IQ, V=verbal IQ, and P=performance IQ. On the bottom, behavioral changes reported by parents. On X-axis the principal variables of the interview are represented: memory (Mem), attention (Att), self-esteem (Self-es), school achievement (Sch), and behavior (Beh). On Y-axis the number of children who showed some positive change is represented.

Due to the elapsed interval of 2 years, only variables corrected for age were used in this study in order to eliminate the effect of age: ADHD score from TOVA, global IQ and verbal and performance scales from WISC-R, and Z-score values for AP (zAP) and RP (zRP) from the EEG. An exception was made for the results of the parental interview; although they were not corrected for age, they were taken into account because we considered that parents' opinion was important. The comparisons between groups were exclusively qualitative.

In the previous paper[11] we compared the results of "before" vs. "after" NFB treatment. Therefore, in this paper we will present the results of the other two comparisons: "before" vs. "2 years after" and "after" vs. "2 years after".

RESULTS

Two years after NFB treatment, the Experimental Group was composed of the same 5 children (F = 1, M = 4), with ages ranging between 9.08 and 12.58 (11.2 ± 1.4) years, and the Control Group was composed of 4 of the 5 control children (F ▪ 1, M = 3) with ages ranging between 10.33 and 14.33 (12.1 ± 1.6). The other child, who had received placebo treatment, left the school one year prior to the current study and declined to participate in the tests. No significant differences between groups exist in age, IQ, and ADHD score in any of the three time periods: before, after, and 2 years after NFB treatment. In the Experimental Group the IQ was, on average, 83.2 ± 17.2 before NFB, 88.4 ± 17.8 after NFB, and 87.2 ± 6.6 2 years after NFB; while ADHD score from TOVA was -1.2 ± 2.2 before NFB, -1.0 ± 2.1 after NFB, and 0.48 ± 1.3 2 years after NFB. In the Control Group the IQ was, on average, 79.7 ± 9.8 before, 83.0 ± 7.8 after, and 80.5 ± 5.1 2 years after the NFB study; while ADHD score from TOVA was -1.3 ± 1.2 before, -3.0 ± 2.5 after, and -0.96 ± 2.6 two years after the NFB study.

Behavioral and cognitive results

In Figure 1 results from WISC-R, TOVA and parental interview of Experimental and Control Groups at the three times (before, after, and 2 years after) are shown. In the Control Group there were no significant differences between any time comparisons nor in WISC-R or in ADHD scores from TOVA. In the Experimental Group, the global IQ ($p = 0.04$) and the performance scores increased significantly ($p < 0.05$), but the verbal scores decreased in the last 2 years with respect to both before and after NFB treatment. In the Experimental Group, the ADHD score from TOVA also increased significantly 2 years after as compared to the scores both before and after NFB treatment.

In the Control Group only 3 out of 4 children who wanted to participate in the study improved their attention, self-esteem, behavior, school attitude and scholastic achievement, and only 2 improved their memory in the opinion of their parents. One child did not show any change. In contrast, in the Experimental Group 3 out of 5 children improved their self-esteem, 4 improved their attention and behavior, and all children improved their memory, school attitude and scholastic achievement.

All children were initially diagnosed as LD in the neurological exam because it was an inclusion criterion. Two years after treatment, children in Control Group continued presenting LD, but 4 out of 5 children in the Experimental Group had a normal diagnosis.

EEG results

Figure 2 shows the leads in which NFB had a significant effect on Z-score values of EEG, AP and RP. In both groups zAP increased in almost all leads in which there was a significant change, both in "before NFB vs. 2 years after NFB" and "after vs. 2 years after" comparisons. In general, the increase occurred from negative values to values

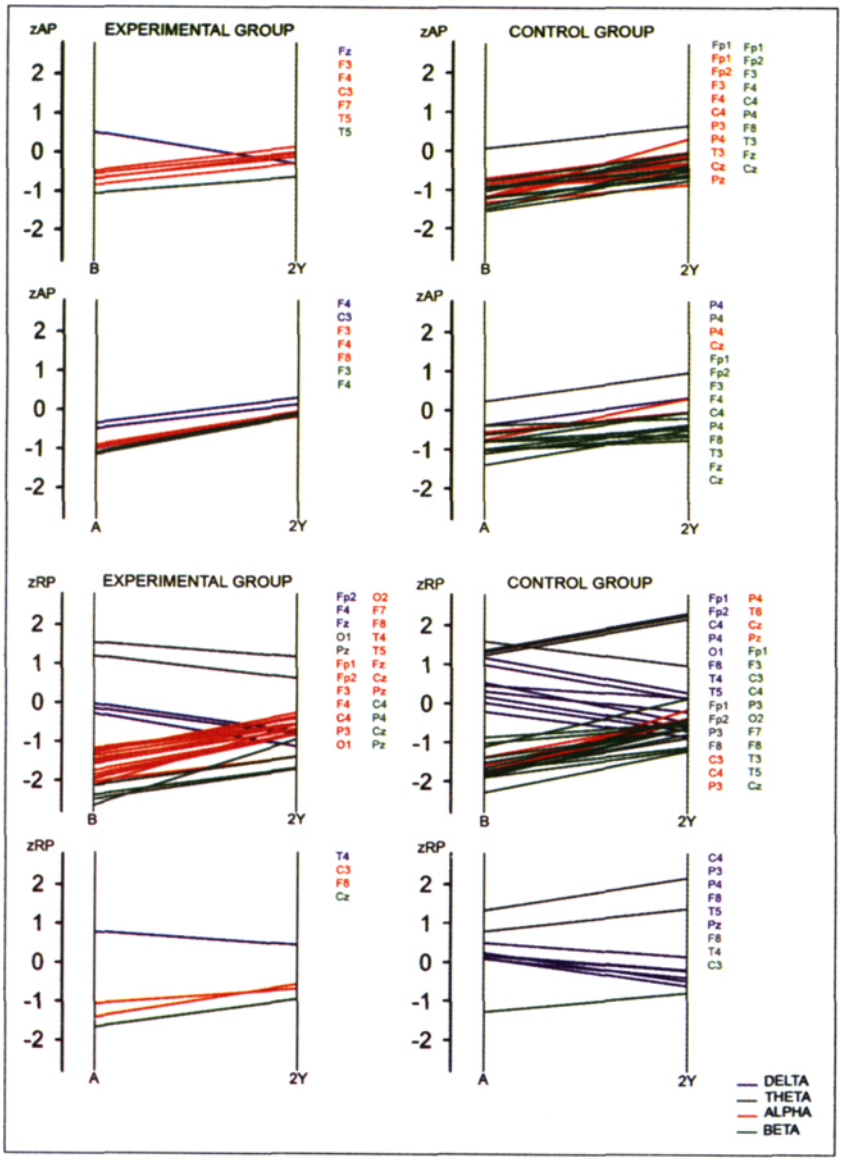

Figure 2.
NFB effect on zAP and zRP. Figures in the first and third lines show the "before (B) vs. 2 years after (2Y)" comparison for both groups; figures in the second and fourth lines show the "after (A) vs. 2 years after (2Y)" comparison. Each line represents a lead in which a significant difference was observed. Line color represents the frequency band: delta (blue), theta (gray), alpha (red), and beta (green).

close to zero. The single exception was that in the Experimental Group, delta zAP in Fz decreased with respect to the value before NFB from a positive value to a negative value close to zero. In both groups all values were within normal limits, and the changes were toward normalization, which is represented by zero.

When we analyzed zRP changes, in both groups zRP decreased in the delta band and increased in alpha and beta bands, converging to normalization in almost all cases. In the Experimental Group, theta zRP values (O1, Pz) diminished, also converging to zero; but in the Control Group, theta zRP values increased in Fp1, Fp2, and F8 with respect to before, and in F8, and T4 with respect to after placebo training. These changes in the theta band in the Control Group were from a less positive value to a higher positive value, reaching abnormally high values.

When we compared the zAP results with the zRP results, we observed that there is a greater number of significant changes in zRP than in zAP, principally in the "before" vs. "2 years after" NFB comparisons. Also, more changes were observed in the Control than in the Experimental group.

DISCUSSION

Many follow-up studies of NFB training have been carried out,[10-25] but none has been in children with LD. Furthermore, very few studies have included a Control

Group in the follow-up.[12,15,18,20,23] In this paper we report a 2 year follow-up study of one Experimental Group that received NFB treatment, and of one Control placebo group.

In the previous report[11] behavioral changes were observed only in the Experimental Group, both in WISC and in ADHD score from TOVA. In both cases they represent a behavioral improvement, which was not observed in the Control Group. In the last 2 years the behavioral improvement continued in the Experimental Group; however, the verbal scores decreased in the last 2 years with respect to both before and after NFB treatment. Apparently, there was no improvement with age in the verbal score, probably due to the low sociocultural level of the children.

In the previous report[11] of the same subjects, EEG changes were observed after the NFB study in both groups. Those changes were compatible with changes produced by age increase; however, the Experimental Group showed a greater number of regions with significant changes, and these changes were greater in magnitude. Two years later the number of leads with significant changes was greater in the Control than in the Experimental Group. One explanation is that children in the Experimental Group had had an important spurt in EEG maturation as a consequence of theta/alpha NFB treatment. Children in the Control Group did not present this phenomenon, but they had the EEG improvement described by Harmony et al.[31] as a consequence of adolescence (although no significant statistical differences in age exist between groups, on average, the children in the Control Group are older than children in Experimental Group).

The most important EEG difference between groups was that in the Control Group theta zRP increased in frontal regions with respect to before NFB, and in right temporal regions with respect to after the Experimental Group's NFB training, reaching abnormally high values. It is important to point out that theta RP is the measurement that best distinguishes between LD and normal children.[4-8] Therefore, in Control Group children, there was evidence that the EEG maturational lag increased in the 2 years following the NFB treatment study; these children did not present positive behavioral changes, and, as a consequence, their neurological diagnosis continued to be LD. In contrast, EEG maturation continued in the children who belonged to the Experimental Group in the 2 years following NFB treatment. This was related to positive behavioral changes, which were reflected in remission of LD symptoms: 2 years after NFB treatment, the neurological diagnosis was normal in 4 out of 5 children.

In clinical practice, most NFB treatments include 40-60 sessions. Rossiter and La Vaque[36] demonstrated that 20 sessions of an NFB program significantly reduce the cognitive and behavioral symptoms of ADHD, and we have demonstrated the same in LD children with abnormal values of the theta/alpha ratio. These results may be explained by the theory of operant conditioning in relation to the characteristics of the reinforcement given: learning is more efficient if the stimulus used for reinforcement is simpler. On the other hand, it should not be forgotten that LD children present perceptual deficits, and that a complex stimulus may prolong the time required for its analysis, thus reducing the stimulus efficiency to induce NFB. However, it may be speculated that greater improvements may have been seen if the treatment had consisted of more sessions.

CONCLUSION

This work shows that NFB can be an efficient treatment for children with LD who present an EEG maturational lag. The beneficial effects are attained not only soon after NFB, but also after a longer period, producing in most of our patients a total remission of LD symptoms after 2 years.

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The Bioethics Committee of the Neurobiology Institute, National Autonomous University of Mexico, approved the experimental protocol.

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