An EEG Biofeedback Protocol for Affective Disorders

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**Introduction**

Despite our own older work which showed that biofeedback with somatosensory evoked EEG potentials can have profound effects on pain perception in rats and people (Dowman & Rosenfeld, 1985; Rosenfeld, Silvia, Weitkunat, & Dowman, 1985; Rosenfeld, 1990), it seemed to us quite a leap to think that an application of EEG biofeedback could be effective in treatment of depression and other affective disorders. Yet the logic of developing such an intervention would be no different than that which we used in our work in the pain modality: In that work, we were aware of a sizeable literature documenting evoked EEG potential (EP) correlates of pain (e.g., Rosenfeld, Diaz-Clark, & Olson, 1983; Buchsbaum, Davis, Coppola, & Naber, 1981a, 1981b; Carmon, Dotan, & Sarne, 1978; Chapman, Chen, & Harkins, 1979). We reasoned simply that if a large value of a particular EP component accompanied intense pain, whereas a smaller value accompanied no pain or analgesia, then if one could train individuals to reduce the particular EP, one ought to see reductions in perceived pain. This approach yielded very promising results (reviewed by Rosenfeld, 1990). Thus it seemed to us that if we could find a reliable EEG index of affect, then we would be in a position to develop an EEG biofeedback protocol for depression.

However, until the relatively recent publication of work from R. Davidson’s laboratory (reviewed by Davidson, 1995), there were no documented reliable indices of affect in the waking EEG. Based on evidence from the neurology literature, Davidson and associates hypothesized that the right frontal cortex contained a neural system mediating negative emotion and avoidance behavior, whereas, in contrast, the left frontal cortex contained a neural system mediating positive affect and approach behavior. An active cortex is known to show higher (13-30 Hz) “Beta” frequencies in a low amplitude, desynchronized EEG, whereas an idling or inactive
cortex is known to show lower (8-12) “Alpha” frequencies of synchronous (sinusoidal) higher amplitude activity. Davidson and colleagues thus hypothesized that positive emotion should correlate with high beta and low alpha activity in the left frontal cortex and with low beta and high alpha activity in the right frontal cortex. Negative emotion would correlate with the reverse pattern of cortical activity: high left frontal alpha, low left frontal beta, high right frontal beta, and low right frontal alpha. Because there are harmonics of electromyographic activity reaching down to the beta range (which could be therefore mistaken as beta), many researchers have focused on the alpha (inverse) indices of emotion. (It is possible to utilize beta, but it requires added steps to correct for electromyographic artifact.)

In a series of ingenious, original experiments, Davidson and colleagues provided a strong set of evidence that cortical activation asymmetry (as inversely indexed by alpha power or magnitude) was a reliable correlate of positive and negative emotion. The asymmetry metric developed by the Davidson group will be referred to here as the asymmetry score $A_1 = \log R - \log L$ where $R$ is alpha power at cortical site $F_4$ and $L$ is alpha power at cortical site $F_3$. It is also possible to define an asymmetry score as $A_2 = (R-L)/(R+L)$. Although $A_1$ and $A_2$ are not mathematically equivalent, they correlate very highly ($\geq .98$; Baehr, Rosenfeld, Baehr, & Earnest, 1998). What has been generally found is that a higher $A_1$ or $A_2$ scores go with positive affect and lower $A_1$ or $A_2$ scores go with negative affect. (Hereafter, I will sometimes use the unsubscripted term “A-score” to refer to generic alpha asymmetry indexed by either $A_1$ or $A_2$).

The former condition means relatively greater left frontal activation; the latter means relatively greater right frontal activation. I use the term “relatively” because in any individual case, one cannot say from an A-score whether the critical effects are in the left versus right cortex (or both) since A-scores combine $R$ and $L$. 
Davidson and colleagues (Davidson, 1995) did a variety of studies to support their hypothesis. For example, they showed that a person’s resting frontal alpha asymmetry predicted their affective responses to emotionally positive and negative film clips (Tomarken, Davidson, & Henriques, 1990). They also showed that rewards and punishments led to differential asymmetry responses (Sobotka, Davidson, & Senulis, 1992). They also showed that facial expressions of emotion were systematically related to asymmetry scores (Ekman, Davidson, & Freisen, 1990). Many other examples are reviewed in Davidson, 1995.)

Most relevant to this chapter, (1) Henriques & Davidson (1990) showed that currently depressed persons have left frontal hypoactivation (lower $A_1$ scores) in comparison with never depressed persons; (2) Henriques & Davidson (1991) showed that previously depressed but now remitted persons show also a relative left frontal hypoactivation in comparison with never depressed persons. We (Gotlib, Ranganath, & Rosenfeld, 1998) replicated and extended this finding by comparing (in one study) three groups: currently depressed, formerly depressed, and never depressed persons. We found that both the currently depressed and remitted patients had comparably low levels of left frontal activation (reduced $A_1$ scores) in comparison with the never-depressed controls. From one perspective, the significance of these findings was that the activation asymmetry seen was apparently a trait marker, since the current state of depression (or remission) did not predict the $A_1$-score. The implication was that a pathological activation asymmetry indicated the ubiquitous vulnerability to depressive reactions to stressful events. Remitted depressives may be currently not depressed, but are always vulnerable to depression as indexed by their putatively chronic left frontal hypoactivation.

When we first learned of the bare outlines of Davidson’s work, we were encouraged about a possible biofeedback application for depression because we now had (in the A-score) a possible reliable neural correlate of affect to train. However, the notion that the A-score indexed an innate vulnerability, a constitutional trait, suggested that the picture was less promising: It did not seem intuitively reasonable to contemplate modification of an innate physiological tendency. On the other hand, the reports of Henriques & Davidson (1990, 1991) and Gotlib et al (1998) were consistent with, but did not prove the trait hypothesis: The data were also consistent with the view that no one shows a pathological activation asymmetry until his/her first bout of depression, which then imposes the pattern on a more or less permanent basis. The pattern could thus be seen as a consequence of, rather than a necessary antecedent condition for depressive reactions.

In any case, it seemed for us that the best approach to seeing if activation asymmetry was modifiable would be to try to modify it. Thus, in two experiments, each using a different method of extracting alpha energy in the EEG, we trained 13 normal subjects to increase A-scores (Rosenfeld, Cha, Blair, & Gotlib, 1995) over a period of just three training days. (Details of the training protocol as used for patients are given below.) The results were that nine of the 13 subjects doubled their rates of $A_1$-scores reaching an a priori hit criterion equal to the pretraining mean $A_1$ value plus .85 standard deviations. The other four subjects were unsuccessful. However, since most modern EEG biofeedback applications call for 40 or more training days, we were extremely encouraged by our first data set.

These results in no way suggested that the EEG biofeedback protocol utilized would affect emotion, even in the normal subjects utilized in the experiment. This is because no measures of
emotion were studied in this first exploratory experiment. However, these results certainly suggested that in the next study, emotion should be measured in conjunction with EEG. The results also suggested that those sources of variance in frontal cortical activation asymmetry which were operantly conditionable were state variables: Although the A-score might be a trait indicator in part, as indicated by earlier studies discussed above, it was also subject to the influence of phasic psychological states under a subject’s self-control.

Another of our studies also suggested that the A-score was a state indicator as well as a possible trait indicator: Rosenfeld, Baehr, Baehr, Gotlib, & Ranganath (1996) utilized a clinical population of depressed out-patients in therapy sessions to track day-to-day fluctuations in A2-scores, and their relationship to affect changes. We found that the A2-score obtained in the beginning of a therapy session correlated significantly and as highly as Pearson r > .5 with the change in affect seen during the therapy session. Thus, day-to-day fluctuations in A2-score predicted whether affect would improve or become negative in response to the therapy session. Here was further evidence of the lability of activation asymmetry in conjunction with affect.

There was yet one more study (Quinn, 1998) performed in my laboratory that provided strong support for the lability rather than or in addition to the trait-like fixedness of the A-score: It has been long-known that humans have a nasal cycle in which one or the other nostrils is dominant. That is, every few hours, the blood vessels in the walls of one of the two nostrils will become engorged (under autonomic control), and the other nostril then passes more air to the lungs. The consequence is that since the sensation of air passing through the nostril is relayed contralaterally (via the trigeminal nerve) to the cortex, the left and right cortices should show alternating activation in phase with the nasal cycle, and this effect should result in alternating positive and negative affect. To test this hypothesis, Quinn (1998) tested nostril dominance of
subjects as they entered our lab, and then immediately tested A₂-scores and affect scores in both males and females. The result in males was exactly as expected (as it was in females, but not significantly so). Those entering the lab with dominant right nostrils showed left frontal cortical activation and higher positive affect than those with left nostril dominance. Clearly, the A-score was not simply a constant trait indicator since it varied with the nasal cycle. All these results strongly suggested that a biofeedback study be undertaken, with affect scores tracked along with A-scores.

Allen & Cavender (1996) were the first to replicate and extend our work (Rosenfeld et al., 1995) by utilizing affect measures along with biofeedback of A₁-scores: In two groups of subjects, one trained to increase, the other to decrease A₁-scores, it was seen that the uptrained subjects increased their A₁-scores whereas the downtrainers decreased these scores. Moreover, the direction of training was related to subsequent affective responses to emotionally evocative film clips: Subjects trained to increase A₁-scores showed greater positive affect to happy and neutral films than did subjects trained to decrease A₁-scores. This was exactly what would have been predicted from Davidson’s earlier results and formulations.

Clinical EEG Asymmetry Studies

While the results just described were exciting for us—it is always gratifying to be replicated and extended by an independent research team—they did not involve clinical effects of EEG biofeedback in a clinical population. Such results were eventually provided by Baehr, Rosenfeld & Baehr, (1997), and are extended and reviewed by Baehr, Rosenfeld, & Baehr (1999).

In all our clinical training sessions with patients, we use the following protocol: Prior to EEG biofeedback training sessions, patients are trained for 15-30 minutes to breath
diaphragmatically and warm their hands to a 95°F criterion. These relaxation procedures help minimize artifacts. In EEG training, patients sit in a recliner with elevated feet. The EEG biofeedback sessions, twice per week, consist of 50% biofeedback followed by 50% psychotherapy including discussion of feelings during and about biofeedback. For EEG biofeedback, F3 and F4, both referenced to Cz, are recorded. Impedances are maintained below 5kohms. EEG for both right and left sites are derived via FFT with Blackman-Harris windowed analog signals over one second epochs. The calculated index for each epoch is $A_2$ as defined earlier in this chapter, \((F4-F3)/(F4+F3)\). When this value exceeds zero, a clarinet tone signals the patient of a successful trial, and its pitch varies with the $A_2$ value. No sound is heard when $A_2<0$. Patients are told to try to keep the sound on and to try to continuously raise its pitch.

Patients receive EEG biofeedback training for 30-60 sessions.

In Baehr, Rosenfeld & Baehr (1997), two case studies from the clinical out-patient practice of Elsa and Rufus Baehr were presented. In one of these cases, the $A_2$-score averaged over the first nine sessions was about +4.3. For the last nine (of 36 total) sessions, the average $A_2$-score approached +8.0, an almost 100% increase. The objective depression index used in that study was the D-scale of the MMPI, which changed from >60 to <40 from before to after training. As detailed in Baehr et al. (1997), there was also a correlated improvement in the clinical picture. In the second case, the $A_2$-score improved from +4.7 to +7.2 in comparing the $A_2$ averages of the first eight and last 10 days of training. In this case, there was also a reduction of the D-scale of the MMPI from about 64 to about 47, and a clear clinical improvement as assessed by psychiatric evaluation. The rather remarkable feature of this case was that the person had been the patient of Elsa Baehr for 12 years, during which time a variety of other interventions were tried, including pharmacotherapy, and other EEG biofeedback protocols. It was only after the
EEG frontal alpha asymmetry protocol was applied that major, stable clinical improvements were documented, and the patient discontinued Paxil during sessions 25-34. This is the only dataset (based on the asymmetry protocol) we know of in which some control for non-specific effects is present. Of course it remains possible that simple passage of time mediated a spontaneous remission. It is clear that in all this kind of work (including work from other chapters in this issue), good control studies are essential, yet largely absent, in order to allow attribution of clinical benefits specifically to the EEG biofeedback protocol. Such systematic data are also lacking with respect to the asymmetry protocol; we are trying to collect them with various clinical collaborators from around the country, however it has been an unfortunately elusive goal to set up control conditions (described below) within the constraints imposed by private clinical practices. So far, the second case described above is the closest thing to a control study that we have.

The reason it has been difficult to run a solid control study in a clinical setting is quite easily appreciated upon consideration of what ideal experimental and control treatment groups should look like. What the groups look like, in turn, depends upon what inferences one wants to draw from the study. The most extreme inference would be that the EEG biofeedback component of the protocol is necessary and sufficient to effect change in mood of clinical significance. To make this statement, one would put one (experimental) group through EEG asymmetry training only; (i.e., no concomitant psychotherapy, pharmacotherapy, etc.). The control group would receive another form of EEG biofeedback which trains an EEG variable not associated with affect, e.g., increased sensorimotor rhythm. Control and experimental subjects would be randomly assigned to groups and drawn from the same population. A neutral technician would run the subjects who, along with the trainer, would be blind to which protocol
was being used. It would be necessary to show that both groups reach similar training levels in terms of hit rate, but that only the experimental group showed significant changes in EEG asymmetry and affect. (A more scientifically perfect but ethically impossible study would train one group in increased asymmetry and another in decreased asymmetry. The former group should improve clinically, the latter group should get worse!)

A more feasible control study would utilize randomly assigned patients, drawn from the same population, however these patients might all have other concommittant treatments. It would be necessary for medication levels to remain constant throughout the training. Again, experimental subjects would receive asymmetry training, control subjects would receive some other EEG biofeedback protocol unrelated to affect. Again it would be best for the study to be run in a double-blind fashion. If there were clinical differences between groups, one could infer that the EEG asymmetry component of the treatment package was a necessary component; one would conclude nothing about sufficiency. This would, nevertheless, be a significant addition to knowledge.

During the Baehr et al. (1997) study, it was also seen that the course of training was not always smooth. One patient in particular received some serious bad news during training, and her A2-scores promptly regressed, before ultimately recovering and progressing further in a positive direction. This observation has two important implications: 1) the protocol training effects may be influenced by life’s vicissitudes, which should temper unrealistic enthusiasm about the protocol which, may have positive but not perfect effects, and 2) it is clear that frontal alpha asymmetry is more than a trait index, since it changes with life events.

More supporting clinical data are being collected by independent clinicians and by ourselves. These data will be shortly presented, but since they use an index of alpha asymmetry
not yet explained here, it will be introduced now: The average A-score (whether $A_1$ or $A_2$) as a summary statistic for a session is easily influenced by occasionally very high (or low) samples, and is thus quite variable. Baehr, Rosenfeld, Baehr, & Earnest (1998) reasoned that an index based on percent of time when the A-score exceeds some criterion (e.g., zero) might be a less variable, summary asymmetry index for a session since it is not influenced by occasional extreme values. For example, both small and large departures from threshold would count the same. We tested this notion by comparing depressed and normal patients on both session average $A_2$-scores, as well as on PCT scores = percentage of time in a session during which the $A_2$ score was greater than zero (by any amount). It was found that indeed the PCT score was a significantly better diagnostic index than the $A_2$-score. Obviously, the moment-to-moment A-score must still be used with a reinforcement criterion during a training session. However, the PCT-score is not only a better summary discriminator for the entire session, it is also easier to define for patients during review of their progress with them during the course of treatment. Its lower variability also allows the patient to more readily appreciate progress.

Therefore, we present in Fig. 1, the PCT scores, MMPI-T scores (on D-scale), and Beck Depression (BDI) scores, before and after training for four patients. (The details of these and two other cases are in Baehr et al., in press.) It is clear that as PCT increases, the BDI and MMPI-T scores decline. These kind of results have now also been replicated by an independent single case report from another clinician (Earnest, 1999). This report extended our results also by demonstrating the success of the protocol for the first time with an adolescent patient suffering with depression.
Conclusions and Remaining Problems:

The clinical story, to date, has been most promising, but we do need control data, as noted above. We should also note that our protocol has been unsuccessful with two bipolar patients. However, there have been recent problems regarding the original empirical foundation of the asymmetry protocol: For example, in comparing adolescent suicide attempters with normals in cortical asymmetry, Graae, Tenke, Bruder, et al. (1996) found differences, but the non-depressed attempters (vs. depressed attempters) accounted for the preponderance of asymmetry effects particularly in posterior (vs. frontal) regions. This is not what the Davidson group might have predicted, since their major effects are more often seen frontally. However, it is noted that the Graae et. al. (1996) group utilized a nose reference for EEG recording, which the Davidson group does not. That the choice of referencing montage can have a profound effect on EEG recording has long been known. Indeed, the effects cited above by Quinn (1998) regarding nasal cycle and asymmetry were obtained only when referencing F3 and F4 to Cz, as the Davidson group did in early studies. (More recently, they have used other montages, however the asymmetry effects reported were usually obtained with all montages.) Recently, Reid, Duke, & Allen (1998) also failed to replicate the typical early findings of the Davidson group, and likewise noted differential effects of montage. They too found key effects to occur parietally rather than frontally. Likewise, Hagemann, Naumann, Becker, Maier, & Bartussek (1998) reported that analysis procedure and referencing montage affected outcome, such that one could replicate or fail to replicate the early Davidson group findings depending on the reference used. However Hagemann et. al. did replicate the typical frontal asymmetry association with affect only when they used a Cz referencing montage along with appropriate other procedures. This agrees with findings in our lab (Gotlib et. al., 1998; Quinn, 1998), however as discussed by
Hagemann et al., the use of a Cz reference for lateral leads could imply that asymmetries discovered are in **phase** rather than **amplitude** of alpha. They could not replicate the typical findings using other referencing schemes which are theoretically and empirically better for demonstration of any EEG asymmetry.

The implications of these conundrums for our clinical program are minimal: we still have a viable EEG protocol in need of further support via controlled studies. However the interpretation (conceptual foundation) of these effects will have to be changed should it turn out that alpha phase asymmetry, rather than amplitude (activation) asymmetry underlies the correlation of the Cz referenced A-score and affect. (Davidson, 1998, has also addressed these concerns).
Table 1: Abbreviated Patient Descriptions:

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age</th>
<th>DSM-IV Diagnosis</th>
<th>Prior and Concomitant Other Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F.</td>
<td>65</td>
<td>296.32</td>
<td>Psychotherapy 12 yrs, Paxil, 20 mg/day at start of asymmetry training; discontinued 30 days later.</td>
</tr>
<tr>
<td>2</td>
<td>M.</td>
<td>37</td>
<td>300.4</td>
<td>Psychotherapy 1yr., Zoloft, 75 mg/day 5 mos. prior to asymmetry treatment, discontinued during treatment.</td>
</tr>
<tr>
<td>3</td>
<td>F.</td>
<td>34</td>
<td>296.21</td>
<td>Psychotherapy, Prozac, 20 mg/day 15 mos. prior to EEG training, discontinued after 6 weeks of training.</td>
</tr>
<tr>
<td>4</td>
<td>F.</td>
<td>40</td>
<td>300.4</td>
<td>Psychotherapy, Paxil, 20 mg/day 2 yrs. prior to treatment, continued during treatment.</td>
</tr>
</tbody>
</table>
References


Figure Legend

Fig 1. Each pair of black bars in a graph gives for 4 cases, one per row, the scores before (left bar) and after (right bar) EEG Biofeedback training. The first column (PCT) gives the percent of time the Activation Asymmetry or A-score > 0. (See text regarding A-Scores.) The second column gives the Beck Depression score (BDI), and the third column gives the T-score on the Minnesota Multiphasic Personality Inventory (MMPI).