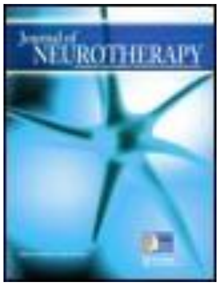


Journal of Neurotherapy: Investigations in Neuromodulation, Neurofeedback and Applied Neuroscience

Changes in Lateralized Memory Performance in Subjects with Epilepsy Following Neurofeedback Training

M. B. Sterman PhD [a b] & DeLee Lantz PhD [b]

[a] Departments of Neurobiology and Psychiatry , UCLA School of Medicine

[b] Neuropsychology Research Laboratory, Veterans Administration Medical Center, Sepulveda, California

Published online: 08 Sep 2008.

To cite this article: M. B. Sterman PhD & DeLee Lantz PhD (2001) Changes in Lateralized Memory Performance in Subjects with Epilepsy Following Neurofeedback Training, Journal of Neurotherapy: Investigations in Neuromodulation, Neurofeedback and Applied Neuroscience, 5:1-2, 63-72, DOI: 10.1300/J184v05n01_06

To link to this article: http://dx.doi.org/10.1300/J184v05n01_06

Changes in Lateralized Memory Performance in Subjects with Epilepsy Following Neurofeedback Training

M. B. Sterman, PhD
DeLee Lantz, PhD

ABSTRACT. Both seizure reduction and neuropsychological improvements have been reported following neurofeedback training directed to normalization of the sensorimotor EEG. These findings could be interpreted as nonspecific effects rather than specific changes brought about by EEG training. The present study demonstrated neuropsychological changes of a selective nature that would be difficult to interpret as nonspecific. Epileptic subjects with unilateral temporal lobe lesions were administered memory tests prior to EEG training, after control training, and after sensorimotor EEG normalization training. Successfully trained subjects showed exclusive improvement on memory tasks specific to the hemisphere contralateral to their lesion, and no improvement on memory tasks specific to the hemisphere with the lesion. Such selective changes are difficult to interpret as nonspecific effects of participating in a study, and would seem to require genuine alteration of neural substrates as a result of EEG training.

M. B. Sterman is affiliated with the Departments of Neurobiology and Psychiatry, UCLA School of Medicine. DeLee Lantz has a private clinical practice in San Francisco.

Both M. B. Sterman and DeLee Lantz were affiliated with the Neuropsychology Research Laboratory, Veterans Administration Medical Center, Sepulveda, California at the time these data were collected.

Address correspondence to: M. B. Sterman, Department of Neurobiology, UCLA Medical Center (CHS), 10833 LeConte Avenue, Los Angeles, CA 90085-1763.

USPH Grant # 2 RO1 N4 and the Veterans Administration supported this research.

KEYWORDS. Neurofeedback, epilepsy, complex-partial seizures, lateralized memory, neuropsychological tests

INTRODUCTION

Since 1972 more than a dozen research laboratories from around the world have reported seizure reduction in chronic, drug-refractory subjects with epilepsy following sensorimotor EEG normalization training using operant conditioning principles (Kuhlman, 1978; Lubar et al., 1981; Sterman & Friar, 1972; Sterman, Macdonald, & Stone, 1974; Sterman & Shouse, 1980; Tozzo, Elfner, & May, 1988; Wyler, Robbins, & Dodrill, 1979; see Sterman, 2000 for complete review). Enhanced cognitive and psychological functioning was also reported in subjects participating in an EEG normalization study, provided such participation was successful in reducing seizures and altering EEG patterns (Lantz & Sterman, 1988). Despite the fact that appropriate control procedures were employed, both the seizure reduction and the neuropsychological improvements could be interpreted as nonspecific effects of participating in this study.

The present investigation looks at some very selective changes in cognitive functioning, which would be difficult to interpret as general or nonspecific effects but would seem to require a genuine alteration in neural substrate as a result of EEG training. Specifically, this study examined laterality-related memory changes following sensorimotor EEG normalization training among patients with complex-partial epilepsy. There is abundant evidence for specialization of the two temporal lobes for different kinds of memory, the left for verbal material and the right for visual and other nonverbal material (Delaney, Rosen, Mattson, & Novelly, 1980; Glosser, Deutsch, Cole, Corwin, & Saykin, 1998; Milner, 1967, 1968; Mungas, Ehlers, Walton, & McCutchen, 1985; Novelly, Lifrak, & Spencer, 1985; Scoville & Milner, 2000; Trimble & Thompson, 1983, among others). Memory for both types of material was clearly impaired in the epileptic patients participating in the 1988 Lantz and Sterman study. Differential improvements in these deficits among patients with left vs. right temporal lobe foci following successful and non-invasive neurofeedback training would be significant because such differential memory improvements have been reported after the far more invasive surgical resection of temporal lobe tissue. Preliminary findings have suggested such an outcome (Lantz & Sterman, 1992). The present study provides an expanded re-analysis of this issue.

METHODS

Subjects. The original Lantz and Sterman study (1988) included 24 subjects with confirmed complex-partial epilepsy. These were randomly assigned to three equal experimental groups, as described below. By the completion of the experimental design all subjects had received a course of contingent sensorimotor EEG normalization training. In two of the groups this was provided after control conditions. It was found that significant seizure reductions occurred only after contingent EEG training, and not following control conditions ($t = 3.44$, $p < 0.005$). Further, test scores improved for subjects above the group median in seizure reduction (61% reduction) following sensorimotor EEG normalization training, but did not improve for subjects below the median. That is, successful neurofeedback training was required for improved neuropsychological functioning.

Twenty of the 24 subjects were identified as having unilateral temporal lobe lesions (Table 1). The remaining four had generalized or bilateral foci. Because of the smaller number of subjects with unilateral lesions, a less stringent definition of "successfully trained" was employed. Using a criterion of 50% or greater reduction in seizures, changes in memory test scores before and after control and contingent training in ten subjects with left temporal lobe lesions were compared with the same changes in five subjects with right temporal lobe lesions. These findings were separately compared with test score changes in the remaining five subjects with unilateral lesions that were not successfully trained, and the four successfully trained subjects who had generalized or bilateral lesions.

All subjects were right-handed and presumed to be left hemisphere dominant for language. All had confirmed unilateral focal abnormalities that involved the temporal lobe, although not always exclusively. The side and site of the epileptogenic focus were determined by serial clinical all-night sleep EEGs, computerized tomography scans, clinical evaluation, and by depth electrode recordings in four subjects. All had seizure disorders that were poorly controlled with anticonvulsant medications. Drug regimens remained constant throughout the study. Drug compliance was monitored by obtaining anticonvulsant serum levels at the outset and at six-week intervals throughout the study. Informed consent was obtained at the beginning of the study and debriefing was provided at its conclusion.

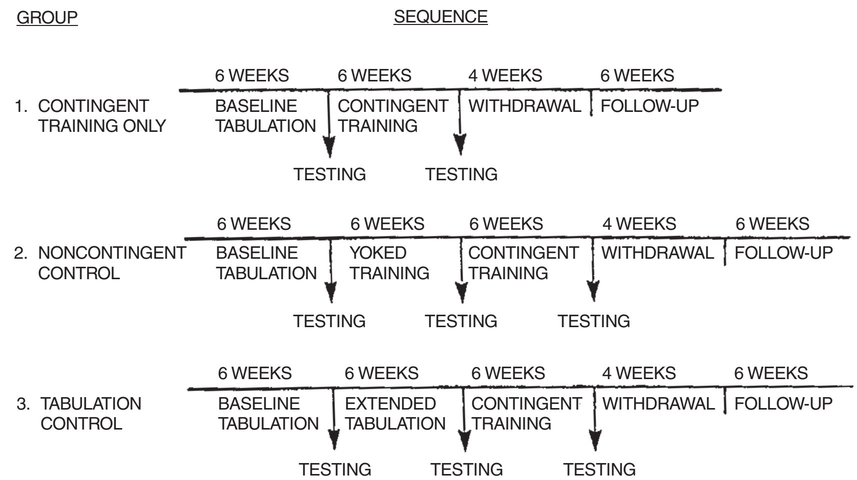
Experimental Design. In the original study, subjects were matched and assigned to one of three groups: a tabulation control group, a

TABLE 1. Description of Subjects

Variable	Right Temporal Lobe Lesions (n = 7)	Left Temporal Lobe Lesions (n = 13)	Total (n = 20)
Sex			
M	4	8	12
F	3	5	8
Mean age,	33.6	23.2	28.4
Range	17-53	15-46	15-53
Primary seizure type			
Complex partial	5	12	17
Simple partial	2	1	3
Seizure freq./month			
Mean	17.7	25.1	21.4
Range	5-50	3-70	3-70
Focus			
Temporal	6	6	12
Frontotemporal	1	6	7
Temporoparietal	0	1	1
Age at onset (mean yr)	19.4	25.1	21.4
Range	8-50	0.5-50	0.5-50
Duration (mean yr)	14.1	15.7	14.9
Range	3-34	6-38	3-38
No. of anticonvulsants	2.6	2.4	2.5
Range	2-3	1-3	1-3

non-contingent training control group, and a contingent training-only group. Figure 1 shows the design of the study and indicates when neuropsychological tests were administered. Following a six-week baseline period during which all subjects tabulated seizures, the *contingent training-only group* began EEG feedback training. Contingent training consisted of feedback for bipolar EEG frequency components of left sensorimotor cortex, with electrodes placed at C1 and C5. Reward was given for increasing 11-15 Hz sensorimotor rhythm (SMR) activity while suppressing 0-5 Hz, 20-25 Hz, and high voltage transients (50 µV or above). Feedback was in the form of an electronic soccer game, with 11-15 Hz represented by a lighted "ball" moving up the field with increases in criterion activity in this band. EEG activity at 0-5 and 20-25 Hz, as well as high voltage transients, was represented by lighted "goal-

FIGURE 1. Experimental Design for Three Groups of Subjects Participating in the Sensorimotor EEG Normalization Study (Adapted from Lantz and Sterman 1988). Arrows Mark Points When Neuropsychological Test Battery Was Administered.



ies," which were to be kept deactivated. A goal could be achieved only by increasing the amplitude of 11-15 Hz activity to a criterion level (100% above the subject's baseline) and by decreasing amplitude in 0-5 and 20-25 Hz to criterion (50% below the subject's baseline level). If that pattern was maintained for at least 0.5 second, the ball entered the goal box, a tone sounded, and a score was registered on the scoreboard for that quarter. Each quarter was seven minutes, with a one-minute rest between quarters. Subjects received 30-minute training sessions three times a week for six weeks. They were withdrawn from training over the next four weeks through a gradual reduction of training sessions. They then completed six weeks of follow-up seizure tabulation.

The *non-contingent control group* also began EEG feedback "training" sessions following the baseline tabulation period. Each subject in this group was yoked to a contingent subject. They received feedback displays and rewards while playing the soccer game but unknown to them these were generated by recorded EEG data from the yoked contingent partner. Non-contingent subjects also came for 30-minute sessions, three times a week for six weeks. The *tabulation control group* continued tabulating seizures during a second six-week period and did not come to the laboratory. Following the six-week control period both the non-contingent control group and the tabulation control group received six weeks of contingent neurofeedback training, followed by four weeks of withdrawal training and six weeks of follow-up seizure tabulation.

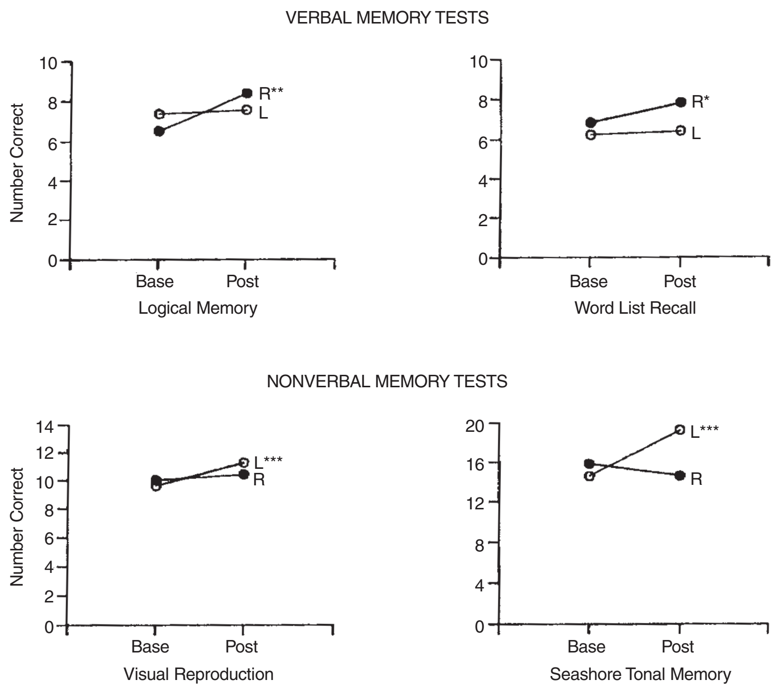
Neuropsychological Tests. The neuropsychological tests used in the Lantz and Sterman study were a subset of Dodrill's Neuropsychological Battery for Epilepsy (Dodrill, 1978), and consisted of 11 cognitive and psychosocial tests. The tests pertinent to the present study were four memory tests that have well documented lateralized temporal lobe involvement. These included the Wechsler Memory Scale: Logical Memory, the Wechsler Memory Scale: Visual Reproduction, the Seashore Tonal Memory Test, and the Buschke Word List Recall Test. These tests were administered to the subjects in each group at the times indicated in Figure 1. They were scored by psychologists who were not associated with the laboratory, and who were blind as to the subject's group assignment and the condition just completed. Alternate forms of the tests were used for repeated administration (except for the Seashore Tonal Memory test for which there is no alternative form), and were given in a counterbalanced order. Statistical analysis consisted of paired-comparison t-tests based on differences between pre- and post-training scores.

RESULTS

Test results at baseline and following EEG training were pooled for successful subjects in the three different training groups (contingent training-only, non-contingent training control preceding contingent training, and tabulation control preceding contingent training) rather than analyzed separately by group. Likewise, test results following control conditions in the two control groups were pooled. This was justified by the fact that the original study had shown no differences among groups at baseline testing or after control conditions. Findings after neurofeedback training in the successful subjects with unilateral lesions were also compared separately with results obtained in the four successfully trained subjects with generalized or bilateral lesions and the five unsuccessfully trained subjects.

Comparisons between baseline and post-training scores shown in Figure 2 revealed that the successfully trained subjects with left hemisphere lesions improved significantly on the Wechsler Memory Scale:

FIGURE 2. Baseline and Post-Training Scores on Memory Tests Specific to Left Hemisphere (Verbal Memory) and Right Hemisphere (Nonverbal Memory). Asterisks Indicate Probability of Significant Differences, with $p < 1.0$*, $p < .05$ **, and $p < .005$***.



Visual Reproduction, and the Seashore Tonal Memory Test (ts = 4.04 and 3.69, respectfully, ps <.005). These tests involve predominantly right hemisphere processing. Scores remained unchanged for the Wechsler Memory Scale: Logical Memory, and the Buschke Word List Recall Test, both involving predominantly left hemisphere processing. The opposite pattern of change was found for the subjects with right hemisphere lesions (ts = 2.18 and 1.82, respectively, ps < .05 and < .10). No significant change from baseline was found following control conditions. Further, no consistent pattern of change was found on any test for the four successful subjects with generalized or bilateral lesions. While the small number of unsuccessfully trained subjects with unilateral lesions (left hemisphere = 3, right hemisphere = 2) precluded a valid statistical analysis, no consistent pattern of change was observed.

DISCUSSION

At baseline, the right and left hemisphere groups did not differ significantly on these memory tests, all of which assessed immediate recall of material. This is consistent with numerous findings indicating that differences between groups with right and left temporal lobe lesions are not usually found on tests of immediate recall, but are detected on delayed recall (Delaney, Rosen, Mattson, & Novelly, 1980; Ladavas, Umilta & Provinciali, 1979; Milner, 1968,1975; Mungas, Ehlers, Walton & McCutchen, 1985; Russell, 1975; Trimble & Thompson, 1983). However, following EEG training, differential improvements occurred. Subjects with left temporal lobe foci improved on memory tests involving the right temporal lobe. Subjects with right temporal lobe foci improved on memory tests involving the left temporal lobe. That is, improvement was seen in both groups in memory functions specific to the hemisphere contralateral to their lesions. Improvement was not seen in either group on types of memory specific to the impaired hemisphere. Although the number of subjects was relatively small, a clear and consistent pattern of change emerged, which suggested differential lateralized memory improvements, predictable by the side of the lesion.

In a study of patients who had undergone surgical temporal lobectomy, Novelly et al. (1984) found improvement on memory tasks related to the nonresected side in their "good outcome" group. That is, improvement was on the side contralateral to the seizure focus. However, they also found persistent memory *impairment* on memory tasks related to the respected side, as have other post-surgical studies (Blakemore & Falconer, 1967; Milner, 1967, 1968, 1975; Scoville & Milner, 2000). Since, unlike surgery, EEG feedback training does not involve the removal of tissue, it is not surprising that the present study did not find corresponding decrements in ipsilateral memory functions.

We would argue, as did Novelly et al. (1984), that the improvement seen in performance specific to the unimpaired temporal lobe probably occurred as a result of a reduction in disruptive discharge originating from the impaired temporal lobe. Interictal decreases in abnormal electrical activity have been found in both hemispheres following EEG feedback training (Sterman & Shouse, 1980). Also, fewer disruptions in the form of seizures occurred in the more successfully trained subjects displaying this selective improvement. However, the epileptogenic tissue underlying the abnormal activity is still present in the affected hemisphere and apparently continues to impair performance in that hemisphere.

These findings suggest that successful neurofeedback training improved memory functions in a differential manner among individuals with unilateral right vs. left temporal lobe lesions. The specific and selective nature of this improvement, the fact that successful subjects with general or bilateral lesions showed no consistent pattern of improvement, and the lack of improvement following control conditions, strongly mitigate against nonspecific interpretations. They indicate, instead, that both seizure reduction and enhanced cognitive functioning were specific physiological effects of EEG normalization training in this study, and likely in previous studies as well. Alteration of the underlying neural substrate for epileptogenic discharge would seem to provide the best explanation for these results, a conclusion supported by consistent laboratory findings (Sterman 2000).

REFERENCES

Blakemore. C.B., & Falconer, M.A. (1967). Long-term effects of anterior temporal lobectomy on certain cognitive functions. *Journal of Neurology Neurosurgery and Psychiatry*, *30*, 364-367.

Delaney, R., Rosen, A., Mattson, R.C., & Novelly, R. (1980). Memory function in focal epilepsy: A comparison of nonsurgical, unilateral temporal lobe and frontal lobe samples. *Cortex*, *14*, 103-117.

Dodrill, C.B. (1978). A neuropsychological battery for epilepsy. *Epilepsia 19*, 611-623.

Glosser, G., Deutsch, G.K., Cole, L.C., Corwin, J., & Saykin, A.J. (1998). Differential lateralization of memory discrimination and response bias in temporal lobe epilepsy patients. *Journal of the International Neuropsychological Society*, *4* (5), 502-511.

Kuhlman, W.N. (1978). EEG feedback training of epileptic patients: Clinical and electroencephalographic analysis. *Electroencephalography and Clinical Neurophysiology*, *45* (6), 699-710.

Ladavas, E., Umilta, C., & Provinciali, L. (1979). Hemisphere-dependent cognitive performances in epileptic patients. *Epilepsia*, *20*, 493-502.

Lantz, D., & Sterman, M.B. (1988). Neuropsychological assessment of subjects with uncontrolled epilepsy: Effects of EEG training. *Epilepsia*, *29*, 163-171.

Lantz, D., & Sterman, M.B. (1992). Neuropsychological prediction and outcome measures in relation to EEG feedback training for the treatment of epilepsy. In T.L. Bennett (Ed.), *The neuropsychology of epilepsy* (pp. 213-231). New York: Plenum Press.

Lubar, J.F., Shabsin, J., Natelson, S.E., Holder, G.S., Whitsett, S.F., Pamplin, W.E., & Krulikowski, D. (1981). EEG operant conditioning in intractable epilepsy. *Archives of Neurology*, *38*, 700-704.

Milner, B. (1967). Brain mechanisms suggested by studies of temporal lobes. In F.L. Darley (Ed.), *Brain mechanisms underlying speech and language* (pp. 122-132). New York: Grune and Stratton.

Milner, B. (1968). Visual recognition and recall after right temporal excision in man. *Neuropsvchologia 6*, 191-210.
Milner, B. (1975). Psychological aspects of focal epilepsy and its neurosurgical management. In D.P. Purpura, J.K. Penry, & R.D. Walter (Eds.), *Advances in neurology* (pp. 299-322). New York: Raven Press.
Mungas, D., Ehlers, C., Walton, N., & McCutchen, C. (1985). Verbal learning differences in epileptic patients with left and right temporal lobe foci. *Epilepsia*, *26*, 340-345.
Novelly, R.A., Augustine, E.A., Mattson, R.H., Glaser, G.H., Williamson. P.D., Spencer, D.D., & Spencer, S.S. (1984). Selective memory improvement and impairment in temporal lobectomy for epilepsy. *Annals of Neurology*, *15*, 64-67.
Novelly, R.A., Lifrak, M.D., & Spencer, D. (1985). Side and site of focal lesion associated with intracarotid amytal memory impairment. AES Proceedings, *Epilepsia*, *26*, 547.
Russell, E. (1975). A multiple scoring method for the assessment of complex memory functions. *Journal of Consulting and Clinical Psychology*. *43*, 800-809.
Scoville, W.B., & Milner, B. (2000). Loss of recent memory after bilateral hippocampal lesions. *Journal of Neuropsychiatry & Clinical Neuroscience*, *12* (1), 103-113.
Sterman, M.B. (2000). Basic concepts and clinical findings in the treatment of seizure disorders with EEG operant conditioning. *Clinical Electroencephalography*, *31* (1), 45-55.
Sterman, M.B., & Friar, L. (1972). Suppression of seizures in an epileptic following sensorimotor EEG feedback training. *Electroencephalography and Clinical Neurophysiology*, *33*, 89-95.
Sterman, M.B., Macdonald, L.R., & Stone, R.K. (1974). Biofeedback training of the sensorimotor EEG rhythm in man: Effects on epilepsy. *Epilepsia*, *15*, 395-416.
Sterman, M.B., & Shouse, M.N. (1980). Quantitative analysis of training, sleep EEG and clinical response to EEG operant conditioning in epileptics. *Electroencephalography and Clinical Neurophysiology*, *49*, 558-576.
Tozzo, C.A., Elfner, L.F., & May Jr., J.G. (1988). EEG Biofeedback and relaxation training in the control of epileptic seizures. *International Journal of Psychophysiology*, *6*, 185-194.
Trimble, M.P., & Thompson, P.J. (1983). Anticonvulsant drugs, cognitive function and behavior, *Epilepsia*, 24 (Suppl.), S55-S63.
Wyler, A.R., Robbins, C.A., & Dodrill, C.B. (1979). EEG operant conditioning for control of epilepsy. *Epilepsia*, 20, 279-286.

RECEIVED: 04/25/01
REVISED: 05/11/01
ACCEPTED: 05/15/01