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CLINICAL NOTE

SUPPRESSION OF SEIZURES IN AN EPILEPTIC FOLLOWING SENSORIMOTOR EEG FEEDBACK TRAINING

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Localized recordings of electrical activity from functionally discrete regions of cerebral cortex in the cat have disclosed specific rhythmic patterns in the waking state which are uniformly associated with certain classes of behavior (Donhoffer and Lissak 1962; Roth *et al.* 1967). The observation of such localized slow wave rhythms related to specific behaviors provides a bio-electric label for these behaviors and the brain processes to which they are related. Of particular interest to us in this regard was a 12–14 c/sec rhythm appearing over sensorimotor cortex during the voluntary suppression of movement (Sterman and Wyrwicka 1967; Wyrwicka and Sterman 1968). Neurophysiological studies in the cat have indicated that this sensorimotor rhythm, or SMR as we have termed it (Roth *et al.* 1967), is generated by neurons within the ventrobasal thalamus, probably through alternate depolarization and recurrent inhibition within a thalamocortico-thalamic network (Andersson and Manson 1971; Howe and Sterman 1972). Extracellular single unit recordings from ventrobasal elements indeed do show recurrent bursting discharge and silence during cortical SMR activity in the cat (Harper and Sterman 1972). These findings have led us to conclude that thalamic and cortical inhibitory elements are activated during the production of this rhythm.

Behavioral studies have shown that the SMR is subject to operant conditioning through the application of biofeedback techniques (Sterman and Wyrwicka 1967; Wyrwicka and Sterman 1968; Sterman *et al.* 1969b). That is, by providing a food reward for the occurrence of this rhythm, cats learn to produce the rhythm in order to obtain food in much the same manner as the bar press is employed in other operant conditioning studies. Prolonged training of the SMR under these circumstances resulted in an enhancement of cortical EEG spindle-burst activity during sleep, accompanied by a reduction in motor activity and prolonged episodes of sustained sleep (Sterman *et al.* 1970). In other studies, such training produced evidence for resistance to drug-induced seizures (Sterman *et al.* 1969a). Convulsive doses of monomethylhydrazine resulted in typical pre-ictal symptoms in trained animals, but actual seizures were significantly delayed or absent in these animals as compared to controls.

These various observations in the cat led us to seek a human analog to the feline SMR. Utilizing techniques modified for studies in man (Sterman and Friar, in preparation), we have established that (1) a localized rhythm resembling the SMR can be recorded from the rolandic area (sensorimotor cortex) with surface electrodes in man, and (2) this rhythm can be brought under operant control through biofeedback techniques as indicated by a significant increase in its rate and amplitude, differentiation from other cortical EEG rhythms and subjective labeling of a distinctive cognitive state.

Because of the evidence for enhancement of thalamic and cortical inhibitory elements, suppression of phasic motor activity and delay of drug-induced seizures in the cat, we were encouraged to examine the effects of SMR training in an epileptic human subject. The positive results of this preliminary investigation appear to warrant communication at this time.

Patient history

The subject studied was a 23-year-old white female with a history of convulsive disorder dating back to 1964. The onset, at age 16, was insidious and consisted of a nocturnal, generalized major motor seizure. There was a history of childhood febrile convulsions but no family history of epilepsy. Neurologic examinations, including angiogram and pneumoencephalogram, have consistently failed to demonstrate a localized lesion. The initial EEG examination was reported abnormal due to "generalized slowing" (intermixed 5–7 c/sec activity), but did not report any paroxysmal discharges. An EEG from 1966 showed generalized spike-wave activity increased by hyperventilation, and others taken in 1968 and 1971 showed some evidence of focal activity in the left fronto-parietal area.

The convulsion is preceded by a non-specific aura, and there have been no localizing features to any precipitating factors in the prodrome or in the post-ictal period. The ictus originally included tonic-clonic movements following loss of consciousness and falling; more recently, however, daytime incidents have consisted of wrinkling of the brow associated with left lateral deviation of the eyes, crossing of the right arm to the left knee, and falling to the left. The majority of incidents are currently nocturnal, occurring in the later portions of a night's sleep.

The frequency of occurrence of the seizures has varied from 2 to 4 per month at the onset to 1 per 3 months one year

later. During the 12 months immediately preceding the present investigation, seizures were experienced irregularly at an average rate of approximately 2 per month. The subject has had variable success with several combinations of Dilantin, Mysoline, Peganone, Diamox and Ritalin. The regimen during the past 12 months includes Dilantin and Mebarol, 200 mg each, daily.

Training procedure and methods

Techniques presently in use in our laboratory provide for the recording of rolandic (sensorimotor) and occipital cortex EEG activity, together with electrocardiogram (EKG), electromyogram (EMG) of the submental musculature and respiration, from patients seated comfortably in a reclining chair. EEG patterns were recorded from the scalp with needle electrodes. Placement of electrodes over these brain areas has been standardized by reference to the international 10–20 system. Optimal placement for recording the SMR in this subject was achieved by use of a longitudinal bipolar electrode pair, with the anterior lead intermediate between F_3 and C_3 sites and the posterior lead between C_3 and P_3. Recordings of the alpha rhythm were obtained with a bipolar electrode pair placed at P_z and O_1. EKG and EMG were recorded with paste-filled cup electrodes fixed to the skin with tape, and respiration was monitored by a pneumatic belt connected to a transducer and DC amplifier. These data were recorded on an 8-channel Sanborn Model 7700 polygraph. EEG signals were entered from the amplifiers of this polygraph into a 7-channel filter and logic system which was capable of a limited frequency analysis, automatic detection of specific frequencies and selection of precise signal-to-noise, duration and interval criteria for activation of a feedback device. The feedback device consisted of a rectangular unit suspended from the ceiling several feet above and in front of the patient. This unit contained two rows of ten small lamps, each covered by transparent colored plexiglass. When appropriate EEG signals were detected at criterion amplitude and duration, the lamps in the top row were lighted in a left-to-right sequence, each advance being accompanied by the sounding of a single chime. With the eleventh successful EEG response, these lights were extinguished and the first light of the bottom row of lamps was activated together with a double chime. The next response initiated the lighting sequence in the top row again, and so on. This device provided for sets of 100 reinforcements with single and decade lamps and single and double chimes as the reward.

The patient was isolated in a comfortable, dimly lit room and instructions were delivered via standard tape recordings and an intercom unit from an adjacent room which housed the recording equipment and the experimenters. The patient was instructed to keep eyes open, clear the mind and think of past experiences or of nothing at all in an effort to achieve the desired mental state. When the appropriate EEG pattern was produced, the feedback device was operated. In such a manner, 200–300 rewards were obtained during training periods lasting 30 min to 1 h, depending on the point in training. Five min of pre- and post-training baseline data were collected also during each training session. Such sessions were provided once a week during the month of September 1971, and at least twice a week from that time to the present writing (see Table I).

TABLE I

Chronologic record from subject MF indicating occurrence of nocturnal grand mal seizures from September 1970, to end of current phase of study. During this entire period, subject has taken 200 mg Dilantin and 200 mg Mebarol daily. Seizures are indicated by "S". Sensory motor rhythm feedback training was initiated on 24 August, 1971, and subsequent training sessions are indicated by "t". One seizure has occurred since 31 August, 1971.

Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
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Dec	S	t					t		t					t		t					t		t					t		t	

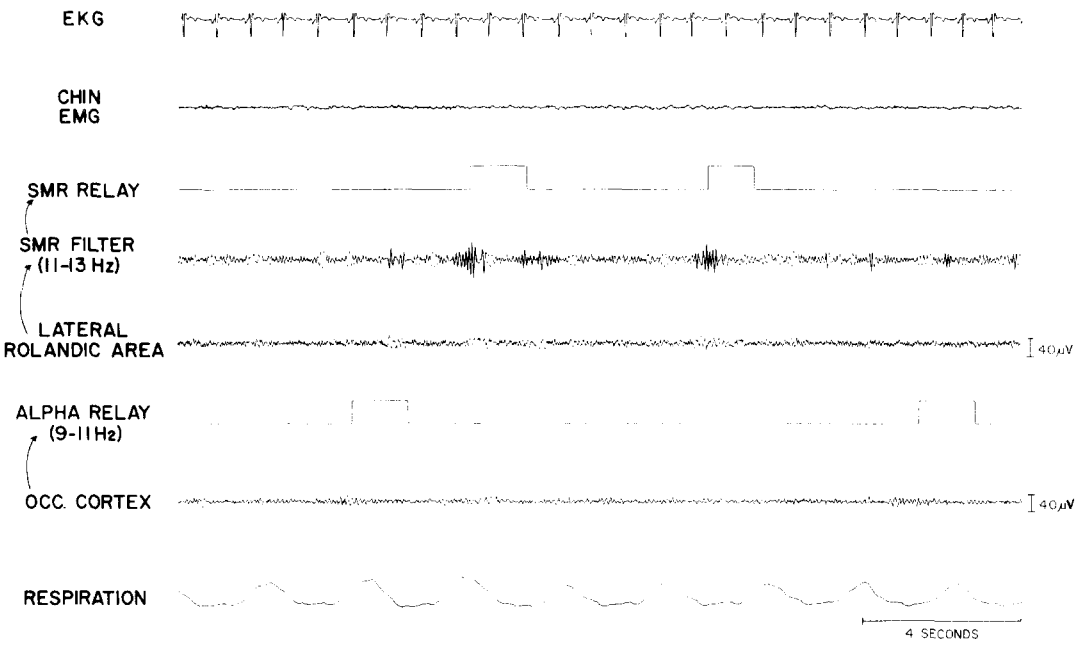

Fig. 1. Sample tracings of rolandic and occipital cortex EEG, showing detection of the sensorimotor and alpha rhythms by a system of tuned frequency filters and logic. Polygraphic EEG sensitivities were attenuated below 1 and above 40 c/sec. The signal-to-noise ratio and duration of the two rhythms required to activate feedback were subject to adjustment by the investigators. Other physiological measures obtained simultaneously included EKG, chin EMG and respiration.

RESULTS

As has been our experience with other subjects, this patient initially demonstrated a moderately low level of SMR activity spontaneously during the initial pre-feedback baseline recording. Because of her generalized EEG slowing mentioned earlier, it was decided to reward large amplitude trains in the 11–13 c/sec frequency range. This represented a slight adjustment from the 12–14 c/sec frequency utilized with other subjects. A typical tracing, showing filter response and relay detection of the SMR in this patient, is presented in Fig. 1, together with the relay detection of occipital alpha rhythm activity (9–11 c/sec) during the same period. Polygraph and logic system sensitivities were comparable for both signals. The peak SMR frequency rewarded was 12 c/sec, with 50% attenuation at 11 and 13 c/sec and a very sharp drop-off beyond these limits.

During the first several sessions of SMR feedback training, no evidence of learning could be detected in measurements of SMR and alpha production over time (Fig. 2). By the fourth session, the production of SMR had increased slightly in the pre-training baseline, and both rhythms showed a gradual increase in occurrence during training. Both post-training baselines were increased over initial levels. This generalized increase in the production of both rhythms was replaced by a selective enhancement of the SMR and depression of alpha during training by the 12th session. Pre-post levels of alpha were high but consistent, and production during feedback training was clearly reduced (Fig. 3). Pre-training levels of SMR were greatly increased over earlier sessions, and the striking enhancement of this rhythm with feedback was sustained in the post-training period.

During the 12 month period between September 1970, and August 1971, the patient had averaged 1.92 grand mal seizures per month (Table I). In the 6 month period immediately preceding training, this rate dropped slightly to a mean of 1.67 per month. These seizures frequently occurred during sleep and were detected by blood stains on the bedwear the next day, and a sore mouth, tongue and jaw. Training was initiated on August 24, 1971, and continued, as described above, to the time of this communication. Six days after the first training session the patient experienced two seizures. Concurrent with evidence for acquisition of the SMR response by the third session, there were no further seizures for a period of 3 months. Additionally, the patient showed some interesting changes in personality during the course of training. Having previously been a quiet and unobtrusive individual, she progressively became more outgoing, showing increased personal confidence and an enhanced interest in her appearance. She also spontaneously reported experiencing a shorter latency to sleep onset, a more restful sleep, as indicated by a reduction of her normal physical re-orientation in bed throughout a night, and a more rapid awakening in the morning. None of the latter changes could be documented objectively, but they were particularly interesting in terms of the similar, quantified findings obtained with SMR in the cat.

The patient voluntarily ceased her previous practice of supplementing anticonvulsant medication upon experiencing an aura, without seizure, and reported a reduction in these

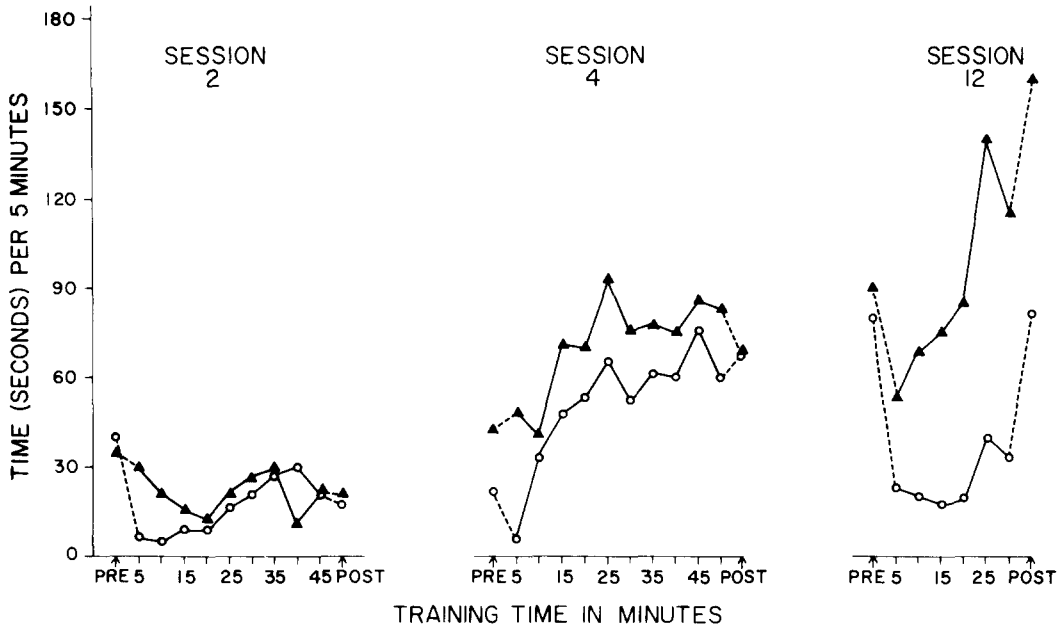

Fig. 2. Plot of SMR (solid triangles) and alpha rhythm (open circles) production during SMR training and pre-post baseline recordings at three points in the training sequence. Output is expressed in terms of the total occurrence of these rhythms, at criterion amplitude and duration, in pre- and post-training 5 min samples and in sequential 5 min epochs during training. Transitions between training and pre-post measures are indicated by broken line.

occurrences. Because of a skin condition, she had been taking 500 mg daily of oral Tetracycline for a period of approximately 6 months. She was taken off this drug on November 19, 1971. On December 1, the patient experienced a mild nocturnal seizure. She reported "knowing it was going to happen that night when I went to bed". It is impossible to determine whether or not any relationship existed between the termination of the antibiotic and the occurrence of this seizure. The patient had been complaining of boredom during training in the preceding weeks and had begun to show signs of drowsiness in concurrent sessions. The day after her first seizure experience in 3 months she requested a small monetary reward for each response and, with our approval, proceeded to perform at the highest rate of SMR production she had ever demonstrated. She has continued in high rate performance since that time and has had no additional seizure experiences.

DISCUSSION

The functional and topographic characteristics of the sensorimotor rhythm in the cat led us previously to compare it with the rolandic *arceau* or "wicket" rhythm described in man by Gastaut *et al.* (1954), and to conclude that both represent, functionally, EEG correlates of voluntary phasic motor suppression (Howe and Sterman 1972). Extension of our studies to man have, indeed, confirmed the presence of a 12–14 c/sec rhythm in the vicinity of the central sulcus and have indicated that it is blocked by phasic motor activity, not disrupted by sensory stimuli in the absence of movement, and related subjectively to a distinct cognitive state (Sterman and Friar, in preparation). This rhythm is subject to operant conditioning also in man and, in the case reported here, continued EEG feedback training of this nature was associated with a suppression of grand mal seizures.

The basis for this effect cannot be specified at this time. Epileptic conditions are subject to a diversity of physiological and psychological influences, and the potential for spontaneous organic change or so-called "secondary gain" should not be overlooked. The patient, nevertheless, demonstrated a rather abrupt change in an active seizure pattern, corresponding to the acquisition, or learning, of this EEG slow wave response. It is possible, therefore, that functional changes associated with the voluntary enhancement of the SMR were related to the observed effect.

It is known that the interruption or withdrawal of sensory input to neurons and neural systems produces changes in synaptic morphology and alterations in the functional capacities of an entire system. If presynaptic axons to a neuron are severed, a micro-environmental upheaval occurs. Necrotizing presynaptic terminals are engulfed by microglia, and synaptic sites that are affixed to spines are incorporated within the dendrite or by the microglia (Colonnier 1964). The sensitive balance of postsynaptic potentials swings from electrical silence to hypersensitivity (Burns 1958) and, if the input is primary to the neuron, transneuronal degeneration occurs (Hess 1958). Withdrawal of input to a system through sensory deprivation in young animals leads not only to alteration in synaptic morphology but also to clear reductions in sensory cortical volume (Globus 1971).

We are less certain about the influence of enhanced utilization of neurons and neuronal circuits upon their morphology and function, but there are numerous findings which

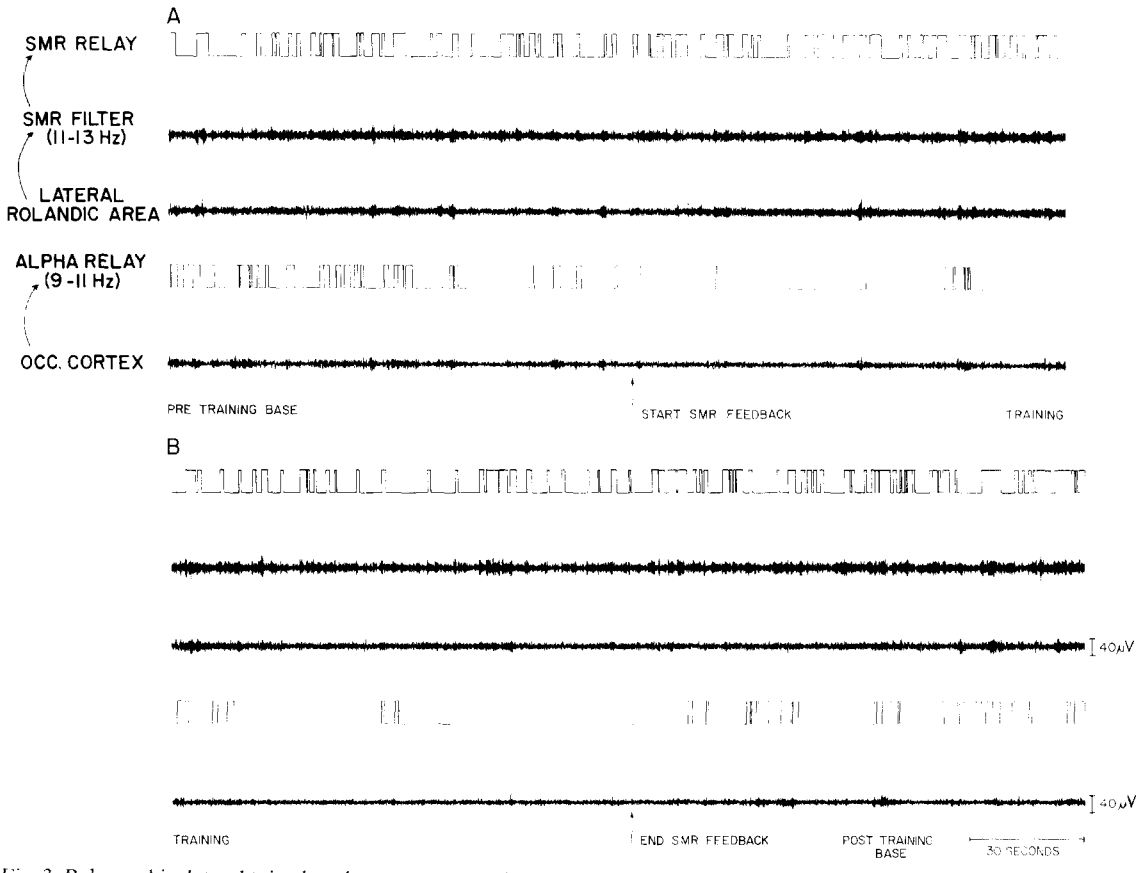

Fig. 3. Polygraphic data obtained at slow paper speed during transitions from pre-training baseline to the initiation of SMR feedback (*A*) and from the end of feedback training to the initiation of post-training measurement (*B*). Note the marked reduction of alpha rhythm activity and general desynchronization of the occipital EEG during SMR feedback occurring in conjunction with a high level of SMR production and a generally synchronized rolandic cortex EEG. SMR production tended to remain elevated or increased even further during post-training baseline measurements.

favor the conclusion that alterations do occur which lead to a functional enhancement of the mechanisms in which these elements participate. The prolonged post-tetanic potentiation recorded after high frequency stimulation of spinal cord synapses led Eccles and McIntyre (1953) to propose the intriguing possibility that such stimulation results in a swelling of afferent terminals, a process which might also occur at higher levels of organization in relation to learning. More recently, Bliss *et al.* (1968) found that constant stimulation of short-latency neuronal pathways in an isolated slab of cat cortex resulted in persistent alterations of synaptic conductivities in these pathways. Directly related to the present considerations are the findings of Rutledge *et al.* (1967). They reported that daily stimulation of undercut segments of marginal cortex in the cat prevented the development of neuronal supersensitivity in these areas, as indicated by the absence of electrically induced after-discharges characteristically observed in unstimulated animals. Repeated activation of the thalamocortical network found to mediate the SMR in cats (Howe and Sterman 1972), associated as it is with the synchronous discharge of inhibitory neuronal pools (Andersen and Andersson 1968; Harper and Sterman 1972), could provide a basis for such functional alterations. In turn, alterations of this nature would not be incompatible with the suppression of seizure activity reported here.

Numerous attempts have been made in the past to utilize operant conditioning in the treatment of epilepsy (Efron 1957; Stevens 1960; Guerrero-Figueroa *et al.* 1963; Stevens *et al.* 1967). These efforts relied upon behavioral concepts, associating distractive or aversive stimuli with the patient's aura or epileptic paroxysms, with limited success. In contrast, the present attempt developed from a neurophysiological framework, and based its predictions upon the possibility of achieving an altered neuronal integration through repeated activation of specific neural circuits with EEG feedback training.

SUMMARY

Previous studies of a 12–14 c/sec slow wave rhythm localized to sensorimotor cortex in the cat indicated its functional relationship to thalamo-cortical inhibitory discharge, sup-

pression of phasic motor behavior and suppression of drug-induced convulsions. Investigations in man showed the presence of a similar rhythm in rolandic cortex. Biofeedback techniques for the operant conditioning of this rhythm developed in studies of the cat provided a basis for similar EEG feedback training in man. The functional characteristics mentioned above suggested that this training could be of some benefit in the treatment of epilepsy. This communication reports preliminary findings from such a study in a 23-year-old female subject with moderately controlled major motor seizures of frontoparietal origin. Biofeedback training of this sensorimotor rhythm resulted in a striking enhancement of the rhythm's occurrence, differentiation from simultaneously recorded alpha rhythm activity, and a marked suppression of seizures. Changes in sleep patterns and personality were noted also.

RESUME

SUPPRESSION DES CRISES CHEZ UN EPILEPTIQUE APRES APPRENTISSAGE FEEDBACK EEG SENSORI-MOTEUR

Des études antérieures d'un rythme lent de 12 à 14 c/sec localisé au cortex sensori-moteur du chat, ont indiqué sa relation fonctionnelle à la décharge inhibitrice thalamo-corticale, la suppression du comportement moteur phasique et la suppression des convulsions chimiquement induites. Des investigations chez l'homme ont montré la présence d'un rythme similaire au niveau du cortex rolandique. Les techniques de bio-feedback pour conditionnement opérant de ce rythme, mises au point dans les études sur le chat, ont fourni une base pour un entraînement feedback EEG similaire chez l'homme. Les caractéristiques fonctionnelles mentionnées ci-dessus ont suggéré que cet apprentissage pouvait entraîner un certain bénéfice dans le traîtement de l'épilepsie. Cette communication rapporte les résultats préliminaires d'une telle étude chez une femme âgée de 23 ans, présentant des crises motrices majeures, généralisées, relativement contrôlées. L'apprentissage bio-feedback de ce rythme sensori-moteur provoque une augmentation frappante de sa survenue, une différenciation de l'activité alpha enregistrée simultanément, et une suppression nette des crises. Des modifications des patterns de sommeil et de la personnalité ont été également notées.

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