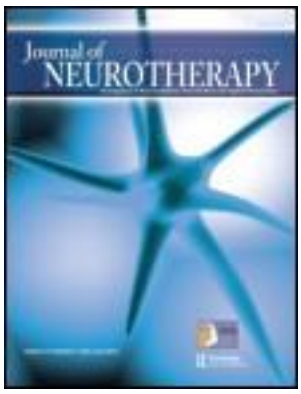

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Why Do Patients with Partial Epilepsy Improve Their IQ After Training to Self-Regulate Slow Cortical Potentials?

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WHY DO PATIENTS WITH PARTIAL EPILEPSY IMPROVE THEIR IQ AFTER TRAINING TO SELF-REGULATE SLOW CORTICAL POTENTIALS?

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In patients with epilepsy, not only seizures but also cognitive, emotional, and social functioning are of increasing interest in research (Kelley, Jacobs, & Lowenstein, 2009). As a decrease in cognitive functions over the course of the illness is usually reported, we wanted to explore changes in Intelligence Scores observed after a neurofeedback treatment in patients with drug-resistant epilepsies. In a controlled study that compared the outcome of three different interventions (training to regulate slow cortical potentials, $N = 34$; training to regulate breath rate and the amount of carbon dioxide in the end tidal volume of the exhaled air, $N = 11$; modification of drug regime, $N = 25$), pre- and postmeasurements of a short version of the Wechsler Intelligence Scale were applied. The interval between the two assessments was more than 12 months, with a mean of 61 weeks. Mean age of the patients was 35, with a range from 17 to 57. The highly significant 7-point increment of IQ only after training of slow cortical potentials was not related to clinical (e.g., seizure reduction) or neuropsychological (e.g., attention and memory) variables. Instead, it was related to psychophysiological measures: IQ change was inversely related to the Latency of the P300 component of event-related brain potentials and directly related to the Latency of the P2 component and the increase of N2 Amplitude during training. We conclude that regulation training of slow cortical potentials improves IQ in patients with refractory partial epilepsy, which might be related to an improved ability for controlled allocation of cognitive resources.

INTRODUCTION

Patients with epilepsy do not suffer only from seizures; impairment of cognitive functions as well as psychological and social distress may accompany the disorder (Bell, Lin, Seidenberg, & Hermann, 2011; Gilliam, Hecimovic, & Sheline, 2003; Johnson, Jones, Seidenberg, & Hermann, 2004; Moore & Baker, 2002). After a detailed neuropsychological assessment of a large sample of patients with temporal lobe epilepsy, Moore and Baker (2002) concluded that patients experience significant difficulties in intelligence tests, verbal memory, and language performance. Improvement in these functions after the treatment with antiepileptic drugs, surgery, or Vagus nerve stimulation is rarely reported (Seidenberg, O'Leary, Berent, & Boll, 1981; Wachi et al., 2001). We investigated why changes in IQ could be observed in patients with epilepsy after neurofeedback training. Neurofeedback is feedback of neuronal activity, mostly oscillatory, or event-related potentials (ERPs) of the brain. By using a brain-computer interface, patients with neurological conditions such as refractory epilepsy, Attention Deficit/Hyperactivity Disorder (ADHD), or learning disabilities learn to self-regulate those components of the electroencephalogram (EEG) that are thought to correlate with their symptoms through operant-instrumental conditioning (e.g., Kotchoubey et al., 2001; Lubar, Swartwood, Swartwood, & O'Donnell, 1995; Monastra, Monastra, & George, 2002;

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Rockstroh et al., 1993; Sterman & Macdonald, 1978).

Linden, Habib, and Radojevic (1996) reported a 7-point increase of full-scale IQ in children with ADHD and learning disabilities after neurofeedback training of theta and beta oscillatory activity. Gains in IQ scores were observed in children with ADHD, but none of these studies controlled the outcome for non-specific effects (Leins et al., 2007; Lubar et al., 1995; Strehl et al., 2006). Only Fernandez and colleagues observed changes in IQ scores using a blind controlled design in children with learning disabilities (Fernandez et al., 2003). These results were obtained in children with superior brain plasticity, whereas in intractable epilepsy, the technique of EEG self-regulation was mostly used in adults with many years of heavy medication load and much less room for improvement. This study seeks to explain why, for the first time in a controlled design, changes in IQ scores were observed in adult patients with refractory epilepsy after having learned to self-regulate cortical excitations thresholds. The improvement might indicate that long-lasting operant (voluntary) regulation of brain function can restore or even block some of the deterioration of brain plasticity in patients with treatment resistant focal epilepsy.

METHODS

Participants

This study was approved by the ethics committee of Tuebingen University Hospital, and all patients signed informed consent. Patients were selected from three large epilepsy centers (Ravensburg, Ulm, and Kehl) or referred by neurology residents. Criteria for selection were partial seizures, intractable epilepsy (continuous seizures after more than 2 years with adequate anticonvulsive medication), with more than two seizures per month, a full-scale IQ of at least 80, and a minimum age of 15. Patients were allowed to choose between three different treatments (for details see the Procedures section): self-regulation of slow cortical potentials (SCP), feedback of parameters of respiration (RESP), and modification of drug regime (MED). Therewith, positive expectations of patients were maximized. As reported in Kotchoubey et al. (2001), the treatment groups did not differ on terms of patients' expectations, satisfaction, and trust with the therapist.

Procedure

Three different treatment strategies were offered. One group received self-regulation training of SCP. The second group was treated with a self-regulation training of respiration rate and end-tidal carbon dioxide ($ETCO_2$; RESP). Fried (1993) developed this biofeedback technique in which patients can learn to avoid hyperventilation. Hyperventilation is known to be seizure provoking. Breath rate and $ETCO_2$ (the amount of carbon dioxide in the end tidal volume of the exhaled air) were continuously fed back to the patient. The task was to reduce breath rate to 15 cycles per minute and to increase $ETCO_2$ by 5%. In both of these ''feedback groups,'' patients were trained to apply the learned self-regulation skills in everyday life situations. Patients of the third group underwent a modification of their drug regime, which was accompanied by sessions of non-specific interventions, for example, art therapy, occupational therapy, physiotherapy, and individual and group psychotherapy (MED). In each group, patients received 30 to 35 treatment sessions. The SCP and RESP groups attended as outpatients for two phases of training with a 4- to 6-week break between training blocks. The MED group consisted of seven inpatients and 18 outpatients. The change of medication was accomplished after a period of 6 to 8 weeks. One aim of this study was to analyze changes in Seizure Frequency after treatment compared to a 12-week baseline. Follow-up evaluations took place 26 and 52 weeks after the end of therapy. Analysis of patients included several measures of cognitive function, personality, mood, and social adjustment. A significant decrease of Seizure Frequency was observed in the SCP and in the MED groups, whereas there were no changes in the RESP group. Treatment effects are reported in detail elsewhere (Kotchoubey

et al., 1996; Kotchoubey et al., 2001), whereas the present analysis focuses on changes of IQ following treatment. Although the paradigm of SCP training and the details of data acquisition and results have been described in these publications, a short description of the training procedure is given here.

SCP neurofeedback consists of a training of phasic shifts of brain potentials. Negative shifts reflect widespread depolarization of apical dendrites of pyramidal neurons (Birbaumer, Elbert, Canavan, & Rockstroh, 1990). They facilitate paroxysmal activity, and inhibition of these negative shifts corresponds with reduction of epileptic discharge. Training to regulate SCP leads to reduction of Seizure Frequency (Kotchoubey et al., 2001; Rockstroh et al., 1993).

As depicted in Figure 1, training was subdivided into two phases of 20 and 15 sessions each. Each session consisted of 145 trials. The task within each trial was to produce either electrically negative or positive potential shifts and was indicated by a discriminative signal (''A'' for the negative and ''B'' for the positive polarity) on the video screen (see Figure 2). Mean EEG Amplitudes were calculated every 100 ms as an average of the preceding 500 ms. They were corrected online for blinks and vertical eye movements. The position of the feedback signal corresponded to the difference of the Amplitude of every 500 ms to the pretrial baseline of 2 s (for a more detailed description of technical requirements and signal processing in SCP, see Strehl, 2009). In each session the ''feedback'' trials, in which the

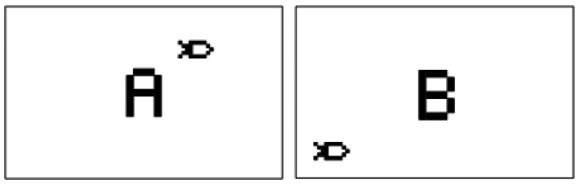

FIGURE 2. Symbols characterizing the tasks during SCP training. *Note.* The letter indicates the task and the rocket shows the change of the SCP. Left panel: A trial with required negativity. The performance in this trial is successful as the rocket is moving to the right edge of the screen. Right panel: The performance in this trial with required positivity is not successful as the rocket sticks at the left edge of the screen.

patient's SCP were continuously visually fed back, were presented in two blocks with 21 trials and one block with 31 trials. Further, in two ''transfer'' blocks with 31 and 41 trials, only the discriminative stimuli were shown (A or B), but no feedback was given. The ratio between negativity tasks and positivity tasks changed from 50:50% during the first training phase to 33:67% during the second phase.

Data Collection

Assessment of IQ. IQ was assessed at baseline (at least 3 months prior to intervention) and 6 months after the end of training. The interval between these two measurements was more than 12 months; the mean was 61 weeks with a range from 56 to 76 weeks.

IQ was measured using a short version of the Wechsler Adult Intelligent Scale (Canavan, Dunn, & McMillan, 1986). This short version allows a valid estimation of full-scale IQ

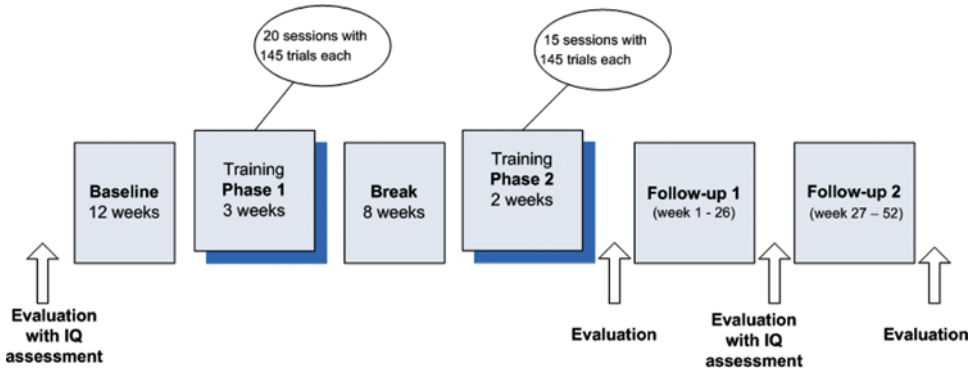

FIGURE 1. Training schedule and IQ assessments. (Color figure available online.)

(WAIS–R; German Version HAWIE–R) and includes the subtests Comprehension, Similarities, Vocabulary, Block Design, and Object Assembly (Tewes, 1984; Wechsler, 1981). The formula to estimate the full-scale IQ is

$$IQ = \Sigma(b) \times 15 + 100$$
$$b = (a - 10)/12$$
$$a = \text{standardized score of a subscale}$$

In addition, a series of neuropsychological tests were administered: subtests Visual Reproduction, Logical Memory, and Digit Span from the Wechsler Memory Test (Wechsler, 1987), Word List (Channon, Daum, & Polkey, 1989), Snodgrass Fragmented Pictures Test (Snodgrass & Vanderwart, 1980), and d2 Test of Attention (Brickenkamp, 1994).

Data Analysis

Correlational Analysis. To explore the nature of IQ change, it was correlated with relevant clinical, psychological, and physiological variables.

Clinical Variables

1. Duration of the disease
2. Seizure frequency
3. Age at the first seizure
4. Number of antiepileptic drugs per day

Physiological Variables (SCP Group)

1. The mean power of the EEG in delta (0.5–3.5 Hz), theta (4.0–7.5 Hz), alpha (8.0–12.5 Hz), and beta (13.0–30.0 Hz) frequency bands, recorded at CZ against linked mastoids.
2. The maximum EEG power in each of those frequency bands.
3. Peak amplitudes and latencies of the components N1, P2, N2, and P3 of visual ERPs to the stimulus signaling the onset of training trials, recorded at CZ against linked mastoids.
4. The amplitude of the self-regulated SCP (mean for the last 2 s in an 8-s trial).
5. The difference between the SCP Amplitudes in trials with required negativity versus required positivity.

These EEG variables were taken from the first 20 training sessions, each session containing four different conditions (for the SCP difference, two conditions). To reduce the number of highly correlated variables, the following values were computed:

a. The mean value over the sessions 1 to 3 (Beginning)
b. The mean value over the sessions 11 to 20 (Plateau)
c. The slope of linear regression over the 20 sessions (Change)
d. The first principal component obtained by means of factorization of the data recorded in all sessions and conditions (Factor Score). This component was responsible for 35% to 60% of the variance of the corresponding variable.

Psychological Variables

1. Attention (d2 Test of Attention; Brickenkamp, 1994)
2. Short-term memory (Digit Span from WAIS–R; Wechsler, 1981)
3. Implicit memory (Snodgrass Test; Snodgrass & Vanderwart, 1980)
4. Verbal memory (Channon Word List; Channon et al., 1989)
5. Visual memory (Visual Reproduction from Wechsler Memory Scale; Wechsler, 1987)

RESULTS

Patient characteristics are shown in Table 1. The distribution of the patients between treatments was not equal because the allocation to groups followed the preferences of patients. Significant differences were found in years of education. The SCP group had significantly more years of education than RESP and MED groups. The pretreatment IQ of the SCP group was significantly higher than in the RESP group. The MED group differed significantly from

TABLE 1. Patient Characteristics

	Treatment groups (*M*/*SD*)					
	SCP	RESP	MED	Test	*F*	*p*
Sex ratio (M/F)	14/20	5/6	13/12	chi-square (0.72)		.70 (*ns*)
Age (year)	34.2 ± 1.26	38.6 ± 3.2	35.73 ± 1.75	ANOVA	1.17	.32 (*ns*)
Education (year)	10.6 ± 0.28	9.1 ± 0.25	9.77 ± 0.27	ANOVA	4.98	.01
				SCP > RESP		.041
				SCP > MED		.036
Duration of illness (year)	22.88 ± 1.5	23.14 ± 3.7	20.36 ± 2.37	ANOVA	0.66	.52 (*ns*)
Focus				chi-square (0.41)		.81 (*ns*)
Left temporal	15	5	9			
Right temporal	9	2	8			
Bilateral/multiple	10	4	8			
No. of AED/day	1.74 ± 0.12	2.00 ± 0.23	1.88 ± 0.13	ANOVA	3.62	.032
				MED > RESP		.022
				SCP vs. RESP		*ns*
				SCP vs. MED		*ns*
WAIS–IQ pretreatment	104.7 ± 1.86	88.8 ± 2.5	100.2 ± 2.66	ANOVA	8.00	.001
				SCP > RESP		.001

Note. SCP = slow cortical potentials; RESP = respiration; MED = drug regime; ANOVA = analysis of variance; AED = antiepileptic drugs; WAIS = Wechsler Adult Intelligence Scale.

the RESP group in regard to the number of antiepileptic drugs per day (see Table 2). Post hoc analyses revealed, however, that these differences did not account for differences in clinical outcome (Strehl, Kotchoubey, Trevorrow, & Birbaumer, 2005).

Differences in IQ were analyzed using a mixed-design analysis of variance with a between-subject factor, group (three levels), and a repeated measures factor, time (two levels). Two significant effects were found, time, $F(1, 67) = 12.41$, $p = .001$, and Time × Group interaction, $F(2, 67) = 4.13$, $p = .02$. Post hoc paired-sample *t* tests, conducted separately for each group, revealed a highly significant change of IQ in the SCP group only ($p < .001$). Table 2 shows mean values, standard deviations, and *p* values for each group.

TABLE 2. Pre and Post IQ (Means and Standard Errors [SE] for Each Treatment Group)

	Pre		Post		
	M	SE	M	SE	*p*
SCP	104.68	1.86	111.1	2.34	<.001
RESP	88.77	2.50	93.0	3.88	.70
MED	100.23	1.58	100.77	1.66	.18

Note. SCP = slow cortical potentials; RESP = respiration; MED = drug regime.

Although the average IQ values in the other two groups also increased, these changes did not approach significance (*p* values of .18 and .7, for MED and RESP, respectively). The distribution of changes within the groups is depicted in Figure 3. It shows that for the SCP group, the mean change characterizes the group as whole and is not an artifact of a large improvement in a few patients. Only about 20% of patients showed no improvement/worsening of IQ, whereas nearly 65% of patients improved IQ up to 1 *SD* and 14% improved between 1 and 2 *SD*. In the MED group, more than half of the patients showed no improvement/worsening, whereas 40% improved 1 *SD* and 4% gained up to 2 *SD*. The results for the 11 patients of the RESP group showed a rather equal distribution between no change or deterioration and positive change.

Pre- and posttreatment IQ scores were highly correlated across the entire sample: $r = .83$, $N = 70$, $p < .001$. Despite the significant increase of the mean value in the SCP group, the pre–post correlation remained very high in this group as well: $r = .78$, $N = 34$, $p < .001$. However, the pretreatment IQ was unrelated to IQ change in any group ($r = .04$ for all patients, $r = -.02$ in the SCP group). Pre- and posttreatment IQ values (but not the change from the

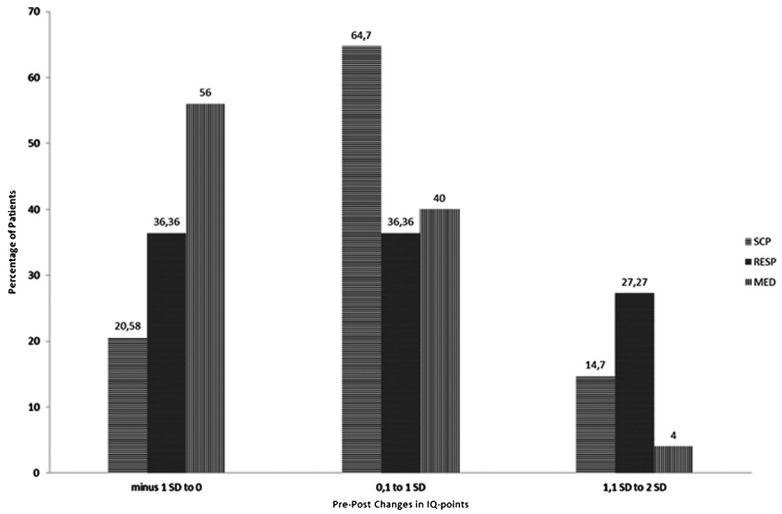

FIGURE 3. Distribution of IQ changes in steps of a standard deviation: comparison of groups. *Note.* SCP = slow cortical potentials; RESP = respiration; MED = drug regime.

former to the latter) significantly correlated with other paper-and-pencil measures of cognitive functions, that is, sustained attention ($r = .40$, $p < .05$, and .45, $p < .01$, for pre- and postvalues, respectively), short-term memory ($r = .51$, $p < .01$, and .32, $p < .10$, for pre- and postvalues, respectively), verbal memory (structured word list: $r = .54$, $p < .001$, and .50, $p < .01$, for pre- and postvalues, respectively), and visual memory ($r = .56$, $p < .001$, and .45, $p < .01$, for pre- and postvalues, respectively). Further, posttreatment IQ was directly related to different measures of theta power of the EEG (correlations between .31, $p < .10$, and .47, $p < .01$). The corresponding positive correlations of pretreatment IQ did not attain significance (*r* values between .21 and .25, *ns*).

The *change* of IQ did not correlate with any clinical variable. Likewise, there was no correlation between EEG spectral data and the baseline measures of cognitive functions (all $r < .2$). However, the improvement of verbal memory after treatment correlated positively with the improvement of the IQ ($r = .37$, $p < .05$, and $r = .39$, $p < .05$, for a nonstructured and semistructured word list, respectively).

Means and standard deviations on the clinical, psychological, and physiological variables are reported in Table 3.

The change of IQ was inversely related to the Latency of the ERP component P3 at plateau ($r = -.39$, $p = .026$), as well as with the factor score for this component ($r = -.36$, $p = .042$). The corresponding correlation with the P3 Latency in the first three training sessions approached significance ($r = -.32$, $p = .074$). In the same direction, the correlation between IQ change and the Latency of the P2 component was positive (factor score: $r = .38$, $p = .031$; plateau: $r = .35$, $p = .052$). In other words, the improvement of IQ was larger in patients with a shorter P3 Latency and a longer P2 Latency.

Furthermore, the Amplitude of the component N2 significantly increased across sessions ($t = 9.06$, $p < .0001$). The rate of this increase was related to the IQ change: $r = .42$, $p = .017$.

DISCUSSION

In this study we analyzed a highly significant 7-point increment of full-scale IQ in a group of epilepsy patients after training to self-regulate the slow potentials of their EEG. Test–retest reliability and stability of WAIS is known to be high. This fact, however, indicates only that individuals retain their relative ranges. It does not necessarily indicate that no changes from multiple testing are to be expected as a

TABLE 3. Means and Standard Deviations on the Clinical, Psychological, and Physiological Variables

Variable	Disease duration	Age at first seizure	Seizure frequency	No. AED
Unit	year	year	per month	per day
M	22.88	11.48	17.62	1.74
SD	8.7	8.6	34.8	0.71
Variable	*M* power delta beginning	*M* power delta plateau	*M* power delta change	*M* power delta factor score
Unit	μV	μV	μV/session	arbitrary
M	0.554	0.570	0.021	0.00
SD	0.075	0.093	0.087	1.00
Variable	*M* power theta beginning	*M* power theta plateau	*M* power theta change	*M* power theta factor score
Unit	μV	μV	μV/session	arbitrary
M	0.415	0.450	0.057	0.00
SD	0.120	0.115	0.098	1.00
Variable	*M* power alpha beginning	*M* power alpha plateau	*M* power alpha change	*M* power alpha factor score
Unit	μV	μV	μV/session	arbitrary
M	0.280	0.288	0.009	0.00
SD	0.097	0.092	0.040	1.00
Variable	*M* power beta beginning	*M* power beta plateau	*M* power beta change	*M* power beta factor score
Unit	μV	μV	μV/session	arbitrary
M	0.140	0.133	–0.003	0.00
SD	0.046	0.040	0.017	1.00
Variable	Max power delta beginning	Max power delta plateau	Max power delta change	Max power delta factor score
Unit	μV	μV	μV/session	arbitrary
M	0.945	0.918	–0.026	0.00
SD	0.109	0.143	0.103	1.00
Variable	Max power theta beginning	Max power theta plateau	Max power theta change	Max power theta factor score
Unit	μV	μV	μV/session	arbitrary
M	0.615	0.675	0.042	0.00
SD	0.223	0.212	0.109	1.00
Variable	Max power alpha beginning	Max power alpha plateau	Max power alpha change	Max power alpha factor score
Unit	μV	μV	μV/session	arbitrary
M	0.492	0.527	0.019	0.00
SD	0.235	0.241	0.068	1.00
Variable	Max power beta beginning	Max power beta plateau	Max power beta change	Max power beta factor score
Unit	μV	μV	μV/session	arbitrary
M	0.229	0.221	0.002	0.00
SD	0.069	0.063	0.040	1.00
Variable	N1 amplitude beginning	N1 amplitude plateau	N1 amplitude change	N1 amplitude factor score
Unit	μV	μV	μV/session	arbitrary
M	.218	–.252	–0.051	0.00
SD	0.976	0.976	0.011	1.00
Variable	P2 amplitude beginning	P2 amplitude plateau	P2 amplitude change	P2 amplitude factor score
Unit	μV	μV	μV/session	arbitrary
M	4.516	1.342	–0.250	0.00
SD	2.87	2.468	0.172	1.00

(*Continued*)

TABLE 3. Continued

Variable	N2 amplitude beginning	N2 amplitude plateau	N2 amplitude change	N2 amplitude factor score
Unit	µV	µV	µV/session	arbitrary
M	3.175	–3.090	–0.457	0.00
SD	4.936	4.535	0.287	1.00
Variable	P3 amplitude beginning	P3 amplitude plateau	P3 amplitude change	P3 amplitude factor score
Unit	µV	µV	µV/session	arbitrary
M	5.077	3.027	–0.143	0.00
SD	4.649	4.650	0.275	1.00
Variable	N1 latency beginning	N1 latency plateau	N1 latency change	N1 latency factor score
Unit	ms	ms	ms/session	arbitrary
M	115.2	113.5	–0.020	0.00
SD	13.4	13.1	1.15	1.00
Variable	P2 latency beginning	P2 latency plateau	P2 latency change	P2 latency factor score
Unit	ms	ms	ms/session	arbitrary
M	256.6	236.5	–1.267	0.00
SD	20.1	23.5	1.26	1.00
Variable	N2 latency beginning	N2 latency plateau	N2 latency change	N2 latency factor score
Unit	ms	ms	ms/session	arbitrary
M	327.2	321.8	–0.411	0.00
SD	16.2	16.2	1.03	1.00
Variable	P3 latency beginning	P3 latency plateau	P3 latency change	P3 latency factor score
Unit	ms	ms	ms/session	arbitrary
M	397.6	417.9	–1.60	0.00
SD	22.8	19.6	1.78	1.00
Variable	SCP *M* amplitude beginning	SCP *M* amplitude plateau	SCP *M* amplitude change	SCP *M* amplitude factor score
Unit	µV	µV	µV/session	arbitrary
M	–1.05	–4.34	–0.60	0.00
SD	9.24	8.84	4.99	1.00
Variable	SCP negativity task beginning	SCP negativity task plateau	SCP negativity task change	SCP negativity task factor score
Unit	µV	µV	µV/session	arbitrary
M	–2.83	–5.69	–0.51	0.00
SD	7.35	9.81	0.80	1.00
Variable	SCP positivity task beginning	SCP positivity task plateau	SCP positivity task change	SCP positivity task factor score
Unit	µV	µV	µV/session	arbitrary
M	1.78	1.35	–0.09	0.00
SD	11.94	12.28	0.69	1.00
Variable	SCP difference beginning	SCP difference plateau	SCP difference change	SCP difference factor score
Unit	µV	µV	µV/session	arbitrary
M	1.70	5.93	0.94	0.00
SD	3.78	12.91	0.91	1.00
Variable	d2	Digit span forward	Digit span backward	Implicit memory[a]
Unit		NRD	NRD	
M	65.83	8.24	7.70	–2.04
SD	30.42	2.12	2.29	0.63

(*Continued*)

TABLE 3. Continued

Variable	Verbal memory structured	Verbal memory semistructured	Verbal memory unstructured	Visual memory immediate	Visual memory delayed
Unit	NRW	NRW	NRW	No. details[b]	No. details[b]
M	9.79	8.06	6.50	68.32	60.50
SD	2.87	2.29	2.30	29.27	37.31

Note. No. AED = mean number of different antiepileptic drugs taken per day; factor score = the score of the first factor yielded by the factorization of the corresponding EEG variable over sessions, in arbitrary units with $M = 0$ and $SD = 1$; d2 = total number of marked signs minus false answers as percentage range; NRD = number of digits remembered immediately after the presentation, forward or backward; NRW = number of words remembered immediately after the presentation of a list of 16 words.

[a]Score for Skill and Perceptual learning (subtracting perception threshold of new items from old items).

[b]Number of visual details reproduced immediately or after a delay of 30 min; N1 was measured as the most negative peak between 80 and 140 ms after the visual stimulus (i.e., the letter A or B indicating the patients task) appeared on the screen; P2 was measured as the most positive peak between 180 and 280 ms poststimulus; N2 was measured as the most negative peak between 250 and 350 ms; and P3 was measured as the most positive peak between 280 and 450 ms.

result of interventions. Although Matarazzo and colleagues (Matarazzo, Carmody, & Jacobs, 1980) argue that after a certain interval practice effects may still occur, McCaffrey and Westervelt (1995) showed that such claims are not substantiated. The same criticism holds for the study from Dodrill and Troupin (1975). They examined patients with epilepsy at four time points with retest intervals of 35 weeks, each to study the effect of antiepileptic medication on cognitive functions. Full-scale IQ at the consecutive measurement points was 101, 96, 98, and 102. Medication was given between the first and second examination. According to the authors, even these changes can be attributed to changes in medications and not to practice effects.

To date, there is no systematic research that controls for the influence of the length of test–retest intervals, number of repetitions, and age of the subject in clinical and normal samples. For individual subjects or patients, reliable change indices and regression-based norms may help to evaluate the influence of practice (Chelune, Naugle, Lüders, Sedlak, & Awad, 1993; Hermann et al., 1996; Martin et al., 2002). In those studies, corrections of full-scale IQ for practice effects in a sample of epilepsy patients were, for example, 1 point (test–retest interval 7 months), 2 points (test–retest interval ~9 months), or 6 points in a normal sample (3- and 6-month intervals). It is assumed that in clinical samples, practice effects are smaller than in normal populations (Basso, Carona, Lowery, & Axelrod, 2002). As these results were used for the interpretation of individual changes in IQ, they cannot be directly applied to group studies.

Therefore, comparisons with control groups appear to be the most appropriate way to partial out practice effects (McCaffrey & Westerwelt, 1995). Thus in the present study the increment of 7 points full-scale IQ may probably be attributed specifically to the SCP intervention, because it was not observed after successful change in drug medication regime. Because this change was as successful as SCP training in terms of seizure reduction, the difference in the IQ dynamics between these groups indicates that clinical improvement does not explain the increase of IQ. Although studies that report changes in IQ after medication or surgical treatment conclude that improvement in cognitive functioning is influenced by the reduction in the frequency of seizures, in our study the change of IQ is not linked to seizure reduction (Seidenberg et al., 1981; Sterman & Macdonald, 1978).

The average IQ also did not significantly change after training to self-regulate respiration (breath rate and exhaled carbon dioxide). However, there was a nonsignificant trend to IQ improvement, although the mean frequency rate did not change (i.e., there was no clinical effect). For the reasons described in the Methods section, this group was smaller than the other two, and therefore one cannot completely rule out the possibility that the improvement of full scale IQ would attain

significance after respiration training if the sample size is sufficiently large. A future study specifically devoted to the effect of respiration training should clarify this issue.

A possible way to explore the main result is to compare it with changes of other physiological and psychological variables. The large number of correlation coefficients implies that some of these correlations can be significant simply by chance. However, such randomly ''significant'' findings would be dispersed randomly across the correlation matrix. In the present data, however, all significant correlations were found in two distinct domains: short-term memory and the P2-N2-P3 complex in visual ERPs. The former is almost trivial because short-term memory is a component facility of the formal intelligence as measured with IQ tests. The changes in ERPs need to be discussed in more detail.

As described elsewhere, the presentation of a visual stimulus on the screen, indicating the beginning of each self-regulation trial, elicited a vertex ERP initially consisting of a large N1 with a Latency of about 140 ms and a positive complex P2/P3 (Kotchoubey, Schleichert, Lutzenberger, & Birbaumer, 1997). In the course of training, a negative peak N2 with a Latency of about 250 ms emerged between the P2 and P3 waves and consistently increased from session to session. This process was independent of the task (i.e., to produce positive or negative SCP shifts) and the condition (i.e., self-regulating with or without a feedback signal). It appears plausible that the increasing N2 may reflect the allocation of attentional resources, which increased with practice. This interpretation is further strengthened by the patients' unanimous reports that they did not completely automatize their self-regulation skill. Even at the end of training, patients still required controlled attentional resources to perform the task.

Improved memory after training to self-regulate the cortical sensorimotor rhythm was observed in patients with epilepsy (Lantz & Sterman, 1988). A series of neurofeedback studies with healthy volunteers demonstrated less commission and omission errors in attention tasks as well as improvement in reaction time after training of oscillatory EEG components (Egner & Gruzelier, 2004; Vernon et al., 2003). For SCP training it was shown that response speed is reduced after training (Rockstroh, Elbert, Lutzenberger, & Birbaumer, 1982). Our findings are in line with these improvements of neuropsychological functions after neurofeedback. The aforementioned studies support our assumption that the training of self-regulation of brain activity is causal for the improvement of IQ.

The putative improvement of the resource allocation function in the SCP group of the present study was not manifested in such paper-and-pencil tests as d2 and digit span test. From our point of view, this fact is not paradoxical because both psychological tests reflect only particular aspects of the cognitive resource control, namely, sustained attention (d2) and short-term memory (digit span). The previously described changes of ERP are related to different aspects of this global function, that is, rather to the ability to fast mobilization according to the actual task (see Kotchoubey, Schneider, Uhlmann, Schleichert, & Birbaumer, 1997). Therefore, a strong correlation between the ERP parameters and the psychological measures of attention and memory should not be expected.

One might speculate whether this effect is specific to the neurophysiological change or dependent upon the particular experimental situation. Patients were trained to react to visual stimuli in about 4,900 trials over 35 sessions. As the respiration group had an identical experimental setup (instead of brainwaves respiration parameters were fed back) and no significant IQ changes were observed in this group, we conclude that the training of SCP and not the training situation per se led to the observed changes.

Although there are plenty of data on the relationships between cognitive performance (including IQ), EEG spectral rhythmic activity, and ERPs, the relevance of these data for the present finding is unclear (Klimesch, 1999; Thatcher, North, & Biver, 2005). P300 Latency and Amplitude are reported to correlate with

intelligence in healthy volunteers (Jausovec & Jausovec, 2000; Pelosi et al., 1992; Walhovd & Fjell, 2002). Tandon and Duhan (2000) found a decline in cognitive functions in epilepsy patients with longer N2 and P3 Latencies as well as with lower P3 Amplitude. Prolonged Latencies of P3 and correlations with subtests of WAIS, but not with full-scale IQ, were observed in patients with epilepsy (Wu, Sun, & Rou, 1997). Despite these correlations between IQ and late ERP components, we found no data about a possible relationship between these components and a change of IQ. This may be due to the fact that we looked at full-scale IQ and not at subtests. Features related (even causally related) to *individual differences* in IQ performance are not necessarily linked with the *improvement* of this performance during training. We can even expect that individual differences and performance improvement are completely different. Thus the correlation between the pretreatment IQ and its change was zero, arguing against an effect of preexisting individual differences. The correlation between pre- and posttreatment measures was very high despite the large increase of the mean, which is in line with the well-known fact of the high test–retest reliability of intelligence tests.

Nevertheless, a possibility remains that correlations with other EEG parameters might be possible if a high-density recording, rather than the single CZ channel, is used. For future neurofeedback studies, whole brain pre–post-EEG evaluation is desirable.

We conclude that neurofeedback of SCP in adults improves IQ in patients with epilepsy. The fact that a substantial improvement of intellectual functions was obtained in middle-aged, diseased adults underscores its clinical and theoretical significance. This improvement was not related to clinical outcome. It can be hypothesized that the operant conditioning paradigm, reinforcing patients for every correct brain response, led to an improved ability for controlled allocation of cognitive resources, which subsequently resulted in the improvement of general cognitive performance manifested in full-scale IQ. This positive ''side effect'' of SCP-Feedback confirms results of neurofeedback in children with ADHD and learning disabilities reported in the introduction. Therefore, it would be interesting to investigate neurofeedback as a viable tool for neuroenhancement in patients as well as in healthy persons.

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