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Specific Patterns of Weak (1 microTesla) Transcerebral Complex Magnetic Fields Differentially Affect Depression, Fatigue, and Confusion in Normal Volunteers

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Normal young adults were exposed for 20 min once per week for a total of 3 sessions to 1 of 7 configurations of weak (1 microTesla) magnetic fields or to a sham field. The fields were spatially rotated and applied through the brain at the level of the temporoparietal lobes. The Profile of Mood States was taken before and after each session. Before, during, and after the treatments, heart rate, plethysmographic activity, and skin conductance were measured by computer. The results indicated that the burst-firing pattern previously demonstrated to be effective for clinical depression, improved mood and vigour compared to the sham-field or other treatments. Subjects who were exposed to a burst-firing pattern, a complex-sequenced pattern, and a pattern whose electrical equivalents stimulate long-term potential in hippocampus slices also exhibited less psychometric fatigue after the sessions compared to subjects who received the sham field or random-sequenced fields. These results replicate previous studies and indicate that rationally designed complex patterns of magnetic fields may simulate pharmacological treatments.

Keywords Moods; Magnetic fields; Sensitive populations; Patterns.

Introduction

The essential principle of modern neuroscience is that all experiences are generated by the dynamic matrix of electromagnetic and chemical patterns that exist within the brain at any given time. Pharmacological agents are effective because they can be sequestered by a variety of different classes or subclasses of receptors within the cerebral volume and consequently modify neuropatterns by influencing the movement of ions through cell membranes or the activation of cytoplasmic proteins that modify these movements. Martin et al. (2004) proposed that the appropriate spatial complexity and temporal structure of weak magnetic fields applied through the brain can both simulate and augment the effects of pharmaceutical agents.

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Weak, complex magnetic fields generated by geomagnetic activity or by active weather systems (Persinger, 1980) have been reported to affect autonomic function and to influence mood (Persinger, 1975, 1987) and their analogs in non human animals (Galic and Persinger, 2004). Ehrmann et al. (1976) reported that nociceptive experiences could be attenuated and affect or pleasantness could be improved during brief exposures to symmetrical pulsed magnetic fields whose frequencies varied randomly between 1 and 20 Hz. As personal computers and their software were developed, the possibility of generating an unlimited number of complex patterns that might simulate the myriads of pharmacological activities was realized.

The application of a weak (1 microTesla) burst-firing magnetic field, whose temporal structure had been extracted from the pattern of amygdaloid neurons from an epileptic's brain, has been inferred to reduce pain in rats (Fleming et al., 1994). Some patients who had experienced chronic pain subsequent to a closed head injury (Baker and Price, 2003) reported a permanent attenuation of this experience following two or three weekly transcerebral exposures to this pattern. Maintained elevations in pain thresholds were also observed in rats with seizure-induced damage following 30 min, weekly exposures to these fields (Martin and Persinger, 2005).

A similar magnetic field pattern improved depression (Baker-Price and Persinger, 1997, 2003) in patients who had sustained closed head injuries. The temporal schedule of the treatment employed by Baker-Price and Persinger (1997) was derived from the clinical tradition of weekly visits rather than empirical results. Recently Tsang et al. (2002) exposed normal volunteers for three sessions either once per week or for three successive days and also found that weekly sessions produced significant decreases in psychometric depression.

The present study was designed to answer specific questions that would be relevant before substantial resources were committed to labor-intensive and costly clinical trials. There were three primary questions. First, are there other rationally designed patterns of magnetic fields that can positively affective mood in "normal" volunteers? Second, are the changes in psychometric indices of depression also associated with appropriate alterations in physiological variables? Third, are there any conspicuous adverse effects associated with applications of fields whose temporal structure approaches the 20 ms interval ostensibly associated with the re-entrant processes (Edelman, 1990; Llinas and Persinger, 1991) producing human consciousness?

To answer these questions, we measured heart rate, galvanic skin response, and plethysmographic activity before, during, and after each treatment session once a week for three weeks. This protocol was employed rather than daily treatment because both human (Tsang et al., 2002) and rodent research (Martin et al., 2003) showed weekly treatments may be more effective than repeated daily treatments. Before and after each session the subjects were administered the Profile of Mood State (POMS). It contains measures by which psychologists infer confusion, fatigue, vigor, anger, depression, and tension. During each session the subjects were exposed consistently to one of seven different patterns or to a sham-field condition. Our assumption was that if the effects from any of these fields were sufficiently powerful to be of any clinical utility, differences should be evident with only four subjects per group. Such differences at $p < .05$ would be equivalent to effect sizes of about 50%, which is sufficient for any potential clinical utility.

Method

Subjects

A total of 16 men and 16 women, who were enrolled in university courses, volunteered as subjects. Their ages ranged between 20 and 25 years. Reinforcement for participation involved either bonus marks for university courses or a small monetary reward after they completed the experiments.

Procedure

Each subject was tested singly. The subjects signed a consent form that indicated they may or may not be exposed to weak complex magnetic fields and they would be required to return for three sessions. They were then assigned randomly to one of the eight conditions. This condition was applied once per week in the same setting between 12 and 19 h local time during the summer of 2001.

The Profile of Mood States was administered before each session. The subject was then blind folded and fit with earmuffs that reduced the background sound level to less than 30 db. A pair of modified headphones for which the muffs has been removed and replaced with square plastic containers was placed over the temporal regions (just above the ears). Each box contained four sets of solenoids similar to the ones employed by Baker-Price and Persinger (1996). One solenoid on the left and right side of the brain were functionally connected so there were four sets of solenoids. Consequently, the magnetic field was generated through the brain at the level of the temporoparietal lobes.

While the subject sat quietly for 30 min, the following measurements were recorded automatically by computer: heart rate, plethysmographic activity, and galvanic skin response. Without the subject's knowledge for the specific timing, the session was divided into five components: 5 min of baseline (to allow habituation to the sensory deprivation), 20 min of field treatment, and 5 min of post-field baseline. After the goggles and ear piece were removed the Profile of Mood States was readministered.

The magnetic fields were generated by a 286 computer by transforming columns of numbers between 0 and 255 to the equivalent voltages where any value below 127 was negative polarity and any value above 127 was positive polarity. The shape of the pattern was determined by the value between 0 and 255 for each line of code and the numbers of lines. The real-time presentation of the pattern was affected by the point duration defined as the time in ms each point was presented, and the interstimulus duration defined as the time between the presentation of each pattern.

The values were delivered to a custom made d-to-a (digital to analog) converter which transformed the voltage into electric current within each pair of solenoids. They generated the magnetic fields. More detailed descriptions of this equipment have been published elsewhere (Persinger et al., 2000; Richards et al., 1993). The speed of rotation of the delivery of the patterns to each of the four pairs of solenoids was the third parameter. In all but one of the patterns the rotation was 0.5 Hz which means that a given pair of solenoids received the signals from the computer for 0.5 s (2 s for complete cycle).

Seven different patterns of fields and a sham condition were employed for comparison. The parameters of the fields are shown in Table 1. The specific characteristics for the burst firing pattern were selected because of their demonstrated

Table 1
The interstimulus interval (in ms), pixel duration, and frequency of rotation of the fields through the solenoids (Hz) for the different treatments

Pattern	Interstimulus interval	Pixel duration	Spatial frequency
1. Burst-firing	3000	3	0.5
2. Burst-firing (10 min)	3000	3	0.5
Long-Term Potentiation (10 min)	3000	3	0.5
3. Long-Term Potentiation	4000	1	0.5
4. Long-Term Potentiation	20	1	0.5
5. Complex sequence	3000	3	0.05
6. Random	1	3	0.5
7. Random	3000	3	0.5

efficacy for reducing thermal and electric current-induced pain in rodents (Fleming et al., 1994; Martin and Persinger, 2005) and depression in clinical patients (Baker-Price and Persinger, 1997, 2003). To test if a pattern that imitates the effects of long-term potentiation (LTP) when applied directly as electrical currents into hippocampal slices (Rose et al., 1998) could facilitate the effects of burst firing, a tandem sequence of 10 min of burst firing was followed by 10 min of LTP stimulation.

This long-term potentiation pattern, which was one pulse followed 170 ms later by four quick pulses, a natural pattern of hippocampal neurons, was the basis for the third and fourth treatments. This "signal," composed of 1 ms point durations for each point (value between 127 and 255) was presented once every 4,000 ms, was selected because of its impact upon the types of memories strongly coupled to hippocampal activity in humans (Richards et al., 1996) and rats (McKay et al., 2000). The interstimulus duration for the fourth treatment was to test if a 20 ms interlude applied transcerebrally across the hemispheres would be as effective as when the onset of a similarly patterned magnetic field was accelerated in 20 ms increments but applied sequentially around the skull (Persinger et al., 2002).

The complex sequenced field was composed of 50 different patterns. These various patterns, all of which have been shown to be physiologically effective, were separated by the LTP pattern. Each of the 50 patterns was presented for 750 ms with point durations of 3 ms such that the total time to complete one sequence was 30 s. This was followed by a period of 3 s with no field. The specific shapes that composed the complex-sequenced pattern have been published previously (Persinger et al., 2001) and were constructed to affect gene expression in the developing rat. In our clinical practice, we found this pattern produced remarkable improvement, after only two sessions, of mood in three patients who had sustained serious head injuries and who had been experiencing chronic depression and inability to work for years. Because of the protracted duration (30 s) of this specific pattern the rotation of the presentation of the signals to each solenoid was slowed to 5 s (one complete rotation every 20 s).

Finally, to discern the importance of specific temporal structures vs random variations, a single random sequence was repeated continuously or once every 3,000 ms. The sequence had been extracted from a random number generator. On the basis of these different combinations we reasoned that we might more effectively discern if length, specific pattern, interstimulus interval, or point duration dominated any particular effects.

For each subject and each session, the mean values for heart rate, skin conductance (galvanic skin response) between the index and third finger of the left hand, and peripheral blood flow through the left thumb (plethysmograph) were obtained for 2 min intervals during the baseline, during the first and last 3 min of the treatment interval, and during the first and last 2 min intervals of the post treatment period.

Skin conductance was measured by two pieces of stainless steel metal (Lafayette standard GSR sensors). Changes in galvanic skin conductance, measured in nano-Siemens, were amplified and filtered through a custom-constructed device. The resulting digital displays clearly discriminated between startle vs relaxation. The plethysmographic device employed the standard sensor (photocell and light source) from Lafayette Instruments. Changes in light intensity due to arterial pulses of the thumb were filtered and amplified before the information was delivered to the Pentium-level computer. The measurements reflected the change in blood volume within the thumb.

A heart rate monitor (LifeGear), often employed for monitoring athlete's performance, measured heart rate. It consisted of a radio transmitter worn around the chest and secured by an elastic strip. The transmitter weighed 4 oz and was powered by a 3 V lithium battery. The radio signals were converted into digital pulses that were accurately validated as beats per min. The software within the 486 computer that collected the data recorded 150 samples from each channel sequentially.

To minimize individual differences, ratios for each of the three measures were completed for the average of the two treatment samples divided by the baseline value and the postbaseline measure divided by the baseline value for each of the three sessions. For the psychometric tests, the means for the scores for each scale of the emotions profile were divided by the pre-test measures for these scales for each session. This allowed the discrimination of any acute effect from the treatment immediately following each session. In addition, the pre-test measures for the second and third sessions were divided by the measure for the first pre-test session in order to discern any potential long-term, cumulative effects that were not acutely associated with the treatments. All analyses involved SPSS software on a VAX 4000 computer.

Results

The means and standard deviations during the first pre-treatment period for all subjects, regardless of treatment, for the three physiological measures and the six scales from the Profile in Mood States are shown in Table 2. The latter are presented as T-scores with a standardized average = 50 and the standardized standard deviation = 10. Because the repeated measure analysis for sessions revealed main effects between types of fields as the most powerful and statistically significant effects, only the simplified results of the overall effects (mean of the three sessions) are reported. For clarity, these means were analyzed as one-way analyses of variance.

One-way analysis of variance (all dfs = 7,24) indicated statistically significant differences between the eight treatment groups for relative changes in psychometric scores before and after for all three weekly sessions for depression ($F = 2.05$, $.05 < p < .10$; eta-squared = .50), fatigue ($F = 2.56$, $p < .05$; eta-squared = .52), tension ($F = 2.58$, $p < .05$; eta-squared = .53) and confusion ($F = 2.50$, $p < .05$; eta-squared = .48).

Table 2
Means and standard deviations for the physiological measures and scales (T-scores) from the Profile of Mood States for the baseline for all subjects

	M	SD
Measure		
Skin Conductance (nanoSieman)	5646	2579
Plethysmograph	583	97
Heart rate (beats per min)	69	7
Mood profile		
Confusion	39.8	6.8
Fatigue	42.9	6.0
Vigor	50.8	8.2
Anger	42.1	6.4
Depression	42.3	6.4
Tension	39.9	5.6

Table 3
The averages of the means and standard errors of the mean for the relative changes in scores for depression, fatigue, and confusion after the session relative to before the session for three weekly sessions for normal subjects whose brains were exposed to different patterns (Table 1) of weak (1 microT) magnetic fields

	Depression		Fatigue		Confusion	
Field pattern	M	SEM	M	SEM	M	SEM
Sham	1.00[a]	.01	1.08[a]	.05	0.93[a]	.03
Random-continuous	0.97[a]	.03	1.02[a]	.03	0.90[a]	.02
Random-3,000 ms	0.92[b]	.02	0.97	.02	0.90[a]	.03
LTP-20 ms	0.95	.02	1.09[a]	.03	1.15[b]	.06
LTP-4,000 ms	0.97[a]	.02	0.91[b]	.05	0.95[a]	.02
Burst-3,000 ms	0.88[b]	.05	0.89[b]	.02	0.84[a]	.03
Burst/LTP-3,000 ms	0.93	.03	0.96	.03	0.89[a]	.03
Complex sequenced	0.95	.03	0.90	.04	0.86[a]	.02

a vs b in a column, $p < .05$.

There were no statistically significant treatment differences for the other components (vigor, anger, tension) for the POMS.

The averages of the means and standard errors of the mean for the relative changes in scores after the session relative to before the session for the three weekly sessions for depression, fatigue and confusion are shown in Table 3. *Post hoc* analyses (Student-Neumann-Keuls, $p < .10$) indicated that most of the explained variance was due to the reduction in depression scores after the treatment for the group that received the burst-firing and random patterns that were presented once every 3 s compared to the sham-field treated group.

Post hoc analyses indicated that the groups who received the burst firing pattern, the LTP pattern presented once every 4 s, or the complex sequence field reported significantly less fatigue than the groups that had been exposed to the LTP pulse once every 20 ms, the sham-field, or the random pattern presented for 20 min. *Post hoc* analysis showed that the group who had been exposed to the LTP pattern with interstimulus intervals of 20 ms also reported greater confusion following the 20 min of stimulation compared to any of the other treatment groups. There were no statistically significant group differences for changes in either heart rate, galvanic skin response, or plethysmographic readings before and after the treatments.

Discussion

Whereas Transcranial Magnetic Stimulation (TMS) involves very intense (Tesla range) simple, pulsed magnetic fields applied topically over the brain, treatment with transcerebral extremely weak, temporally complex magnetic field involves placing the subject's head between the functional poles of pairs of solenoids that generate intensities within the microTesla range. Baker-Price and Persinger (1996, 2003) reported that weekly applications of weak, complex burst-firing magnetic field once every 3-s across the temporal lobes was associated with a marked reduction in psychometric depression as well as a reduction in clinical presentation of depression in patients that had sustained mild closed head injuries without loss of consciousness. The effect size for or the amount of variance of the psychometric measures explained by the treatment was comparable to those produced by TMS that employs fields strengths a million more intense.

Tsang et al. (2002) showed that improvement of psychometric depression was greatest when treatments were given once per week for three weeks relative to once per day for three days. In the present studies, healthy young volunteers were also recruited as subjects. The psychometric dimension associated with depression was significantly more reduced than the other types of moods for subjects who were exposed to the same pattern (burst-firing presented once every 3 s) that had been effective for depressed patients. However, we also found that a random pattern presented once every 3 s also produced an acute reduction in psychometric depression in these normal volunteers.

These results suggest that a class of patterns generated once every 3 sec may be effective. Martin et al. (2003) found that the analgesic effects (for rats) of a burst-firing field presented once every 4 s (Fleming et al., 1994) could be simulated by a "chaotic" magnetic field pattern derived from the May algorithm whose structure was different with each presentation. However, a frequency-modulated field presented once every 4 s was not effective. We hypothesize that, like molecular analogs, only specific patterns presented with discrete interstimulus intervals produced specific effects. In the present study the LTP pattern presented once every 4 s was not associated with any significant changes in psychometric depression.

Subjects who were exposed to either the burst-firing pattern presented once every 3 s, the LTP pulse once every 3 s or the complex sequence pattern showed less fatigue from sitting in the experimental setting compared to subjects exposed to the other treatments. These patterns represented the simplest (LTP) to the most complex configurations and indicate that something specific to the information associated with them rather than simple artifacts of intensity might have been responsible for the effects. It may be relevant that the complex sequenced magnetic field was composed of both the LTP and burst-firing patterns.

The increased scores for a scale by which "confusion" is inferred for subjects who were exposed to the LTP pattern with interstimulus durations of 20 ms may have theoretical value for the study of consciousness. "We had selected this value for the duration between the points' (the numbers between 0 and 255) conversions into a magnetic field…." because we hypothesized a resonance interference with the averaged re-entry process described by Edelman (1989) and observed empirically by Persinger et al. (2003) and replicated by Booth et al. (2005). We reasoned the "interference" would be analogous to "confusion" that occurs when information presented to each ear is slightly delayed. Confusion or "tension" would be a factor congruent with a mild disruption in this process.

Although the effect sizes for the field treatments were within the mild to moderate range and were not as large as the effect sizes Baker-Price and Persinger (1996) observed for patients with clinical depression, the importance of these observations should not be underestimated. First, the standard deviations for the POMs scores for the groups of normal subjects in this study were less than 10 and suggested a restricted range in variability. Groups who display more normal ranges in variability, typical of the general population, or elevated scores, typical of individuals with mood disorders not sufficient to seek psychiatric treatment, may have been more psychometrically responsive to the these treatments.

Secondly, Transcranial Magnetic Stimulation also produced very weak effects upon subjective mood rating scales in normal volunteers (Wasserman and Lisanby, 2001). These pulsed fields are much more intense and appear to depend upon the process of electric current induction sufficient to induce perceptible contraction of scalp muscles. The primary direction of the mood changes following TMS have been mildly positive or anxiolytic. Like the antipyretic agent acetyl salicylic acid that lowers body temperature in people with fevers but does not lower temperature in euthermic people, the potency of both TMS and our procedure may require the application to the appropriate population of patients with depression or chronic pain.

Contributions of secondary reinforcement or conditioning might also occur. Stevens (2001) reported that the presentation of 50 microTesla 20 Hz magnetic fields, about 50 times the strength employed in this study, increased the value of the affective rating of concurrently viewed images compared to images viewed during sham-field presentations. If this effect is generalizable to our field configurations than the setting, context, or personnel present during the pleasantness associated with the field might become secondary reinforcers. Repeated presentation of the subject or patient to these settings, even without the field, might be associated with positive experiences. They are considered important contributions for the patient's compliance with treatment.

Declaration of Interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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