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MODIFICATION OF SEMANTIC MEMORY IN NORMAL SUBJECTS BY APPLICATION ACROSS THE TEMPORAL LOBES OF A WEAK (1 MICROT) MAGNETIC FIELD STRUCTURE THAT PROMOTES LONG-TERM POTENTIATION IN HIPPOCAMPAL SLICES

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ABSTRACT

Normal, right-handed human volunteers listened to a 5-min story and were then exposed to 15 min (3 successive segments of 5 min on/5 min off) of magnetic pulses (1 microT; 10 mG) whose temporal structure has been shown to enhance long-term potentiation (LTP) in hippocampal slices. There were four conditions: no stimulation, bilateral stimulation (across both temporoparietal regions), primary stimulation of the left temporoparietal lobes or primary stimulation of the right temporoparietal lobes. Reconstructions of the story were completed by the same subjects within 30 min (intermediate memory) and about 10 days (long-term memory) later. The strongest effect size (25% of the variance was accommodated) was due to the approximately two fold increase in the numbers of accurate details for the long-term memories for subjects who had received the left hemispheric stimulation. These results suggest that contemporary technology may have the capability to access fundamental algorithms of the neuronal activity associated with declarative memory.

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INTRODUCTION

Complex processes that emerge from massive aggregates of units are susceptible to extremely weak energies if they are presented in sequences that access a fundamental algorithm. The consolidation of declarative (semantic and episodic) memory within the human brain (1,2) is a complex process that depends upon specific electromagnetic and chemical parameters that encourage long-term potentiation (LTP) (3). In this study we investigated the possibility that precise electromagnetic signals that imitate the basic algorithm for the experimental induction of LTP (4) should evoke changes that are measurable at the organismic level.

Primacy and recency are conspicuous effects that accompany serial learning and have been observed in a variety of both mammalian and nonmammalian species (5). Information that is presented at the beginning (primacy) and at the end (recency) of a stimulus sequence is later recalled with greater accuracy than information that is presented within the middle of the sequence. Sommerhoff (6) suggested that the primacy effect is contingent upon a specific microstructural arrangement of neuronal aggregates that encourages both reentry (7) and amplification of earlier signals (sequences) while the recency effect is generated by a different process.

Normal consolidation of semantic memory is strongly dependent upon the integrity and the processes of the hippocampal formation and the functionally related components (e.g., the amygdala) of the temporal stem (8). This structure: (1) contains the microcircuitry that satisfies Sommerhoff's conditions, (2) is electrically labile and sensitive to very weak electric current inductions, and (3) generates a specific and reliable electrical signature (LTP) that is associated with the proficiency of memory. Whereas the left hippocampal formation is more associated with consolidation of linguistic information, the right homologous area is associated primarily with nonlinguistic information (9,10).

If Sommerhoff is correct, then the application along (particularly the left) temporal lobes of an electromagnetic field that encourages LTP should enhance the consolidation and hence the recall of information (declarative memory) that is presented during the middle of the verbal sequence. The weak effects of the electromagnetic induction of LTP should be masked by the earliest and strongest portions of the primacy effect and should not be evident in the recency portion of the curve because it involves a different mechanism. Because individual differences constitute the largest source of variance in behavioral studies, the effect should be evident when each person is employed as his or her own control. On the basis of previous studies (11–13), we anticipated an effect size that is equivalent to a correlation coefficient of about 0.35. This expectation also determined the sample size of our population.

MATERIALS AND METHODS

To test this hypothesis a total of 33 20-30-year-old, male and female, right-handed university students who completed both components of the experiment served as subjects. They were rewarded for participation by a 2% bonus that was added to their final grade in a first-year arts course. The subjects were assigned sequentially in the same repeated serial order to one of four conditions: (1) LTP pulse over the right hemisphere ($n = 9$), (2) LTP over the left hemisphere ($n = 9$), (3) LTP over both hemispheres synchronously ($n = 9$), and (4) sham-field control ($n = 6$). There were four to five men or women per group and no more than two subjects were tested per day.

Each person was tested singly. The subject sat in a comfortable armchair within a commercial acoustic chamber. After goggles were placed over the eyes, a modified motorcycle helmet was placed over the subject's head. Four solenoids were embedded along the temporal plane on each side of the helmet; specific details of the engineering and design have been reported elsewhere (13). Each homologous pair of solenoids was activated for 10 s through a commutator such that a complete sweep of the temporal area (four pairs of solenoids) occurred every 40 s.

A personal computer whose software could be programmed to generate specific patterns was the source of the signal. In this experiment we selected a magnetic field structure that was reported to have enhanced LTP by a factor of 2 for at least 30 min within the CA1 region of hippocampal slices (4). It involved a 2-ms pulse (a primer) followed 150 ms later by four successive 2-ms pulses with each pulse separated by 10 ms. Although we employed an applied magnetic field rather than direct electric current to induce the signal, our previous research suggests that the *information content* presented to brain tissue may be the most relevant parameter. Analyses of strip chart signals from an external sensor that was within the range of the induced field indicated a 95% fidelity in signal morphology.

The subject was instructed to listen to a taped story (5 min duration) that was presented through the chamber speaker system. The story was selected because of its affective level and ambiguity (14); in summary, the story is about one evening in the life of a boy who reports an anomalous experience while he is sleeping. Five minutes after the end of the story, the computer was activated and the person was exposed to the LTP pulse once every 4 s for a total of 15 min (successive sequences of 5 min off and 5 min on; total time in chamber 30 min). This duration and pattern of exposure were derived from the empirical latency that has been required to evoke discernible changes in human volunteers as well as for the response characteristics of cell aggregates following activation of applied magnetic fields.

As determined by a magnetic field sensor (Metex 3800 multimeter and probe), the strength of the field at the distance that would have been within the skull along both temporal regions was 10 mG (1 microT) when the field was applied symmetrically. Application of the field along the left hemisphere only involved activating a small switch for the solenoids that were embedded within the left side of the helmet. The left temporoparietal region was then exposed to 10 mG while the residual field on the right homologous side was 1 mG (or 0.1 microT). The opposite measurements were obtained for subjects who received the stimulation on the right side (i.e., 10 mG within the space occupied by the right side of the skull and 1 mG within the homologous left side). The intensity within the helmet for subjects who received the sham field (obtained by deactivating both small switches) was within the background range (<0.1 mG; <0.01 microT) for this frequency.

At the end of the first exposure the subjects were asked to reconstruct (recall) the story by writing a narrative (i.e., intermediate memory), about 20 min after the end of the story. Between 8 and 12 days (average 10 days) later, the subjects were asked, within a group setting, to reconstruct this narrative by writing all of the details of that story. This information was employed to infer the accuracy of long-term memory.

The formal analyses divided the story into 10 successive segments; each item contained either 25 or 26 basic ideas, i.e., actions, phrases, or nouns. The total numbers of ideas that were recalled were scored and recorded by an experienced psychometrist who was not familiar with the hypothesis of the study for each segment from the story. From this information we inferred intermediate memory and long-term memory for each subject. Both direct recall (e.g., verbatim) and minor inferences (e.g., the statement "the boy ate his cereal" to the actual sequence "the boy ate his breakfast") were scored as accurate.

The mean numbers of accurate ideas per segment were obtained for the intermediate and long-term memories. In order to employ each subject as his or her own control, the proportion of the numbers of accurate memories for each segment was determined for each subject by dividing the segment score by the total score for the intermediate memory or for long-term memory narratives, separately. We also reasoned that weak LTP-like fields could also differentially affect the 10 segments of the story as a function of their serial position. Consequently, we calculated the coefficient of variation (the standard deviation for the 10 segments divided by the mean score for the 10 segments, multiplied by 100 for each subject) for the numbers of accurate details that were reconstructed within 30 min and about 10 days later.

One-way analyses of variance for the total accuracy for the narratives as well as their coefficients of variation were completed; post hoc analysis (Tukey's) was set at $p < .05$. To discern the potential interaction between condition (hemisphere of field application) and the serial position (segment) within the story of the reconstructed details, a three-way analyses of variance (MANOVA) was completed with two levels repeated (10 segments; intermediate vs. long-term memories) and one not repeated (conditions). Additional analysis were completed where appropriate. All analyses involved SPSS software on a Vax 4000 computer.

RESULTS

The means and standard deviations for the percentage of correct ideas for the entire Billy Story for the groups that received the different hemispheric stimulations by LTP-simulating magnetic fields are shown in Table 1. One-way analysis of variance demonstrated no significant difference in means [$F\,(3{,}29) = 2.65$, $0.05 < p < 0.10$] between the treatments for intermediate memory. However, there was a statistically significant [$F\,(3{,}29) = 3.54, p < .05$; eta = 0.52] treatment effect for long-term memory. *Post hoc* analysis indicated that the group whose left hemispheres had been exposed to the LTP magnetic field exhibited approximately twice the number of accurate ideas relative to either the sham control or the group who had received bilateral stimulation.

There were also significant treatment effects for the coefficients of variation within the 10 segments of the stories for both intermediate [$F = 4.02, p < .01$; eta = .54] and long-term [$F = 3.16, p < .05$; eta = .48] memory (Table 1). *Post hoc* analyses indicated that the major source of the difference was due to the greater variability of accuracy of details between segments for the group who were exposed to the bilateral stimulation relative to those who were exposed only to left hemispheric stimulation for both intermediate and long-term memory. Because homogeneity of variance was violated for both types of memory (Bartlett's Box = 14.96, 11.93, $p < .001$, respectively), nonparametric analyses were completed. While the treatment effect was still significant for intermediate memories (chi-squared = 14.17, $p < .01$), it was no longer significant (chi-squared = 7.05, $0.05 < p < .10$) for the long-term memories.

Table 1. Means and Standard Deviations for Percentage of Numbers of Correct Ideas from a Narrative and the Coefficient of Variation from the Different Segments of the Narrative Approximately 30 Min or 10 Days After Exposure to Various Hemispheric Stimulations by the Specific Pulsed Magnetic Fields

	Sham		Both hemis.		Left hemis.		Right hemis.	
Variable	M	SD	M	SD	M	SD	M	SD
% correct memories								
Intermediate	16%	11%	16%	9%	26%	10%	19%	5%
Long-term	8%	2%^{a}	9%	6%	15%	5%^{b}	10%	5%
Coefficient of variation								
Intermediate	79%	25%	112%	66%^{b}	51%	10%^{a}	77%	5%
Long-term	112%	20%	150%	98%^{b}	76%	16%^{a}	82%	20%^{a}

a versus b; *post hoc* $p < .05$.

Table 2. Relative Ratio of Accurate Details for Each of the 10 Segments Recalled Within 30 Min (Intermediate Memory) or 10 Days (Long-Term Memory) After Exposure to the Experimental Conditions

	Sham		Both hemis.		Left hemis.		Right hemis.	
Segment	M	SD	M	SD	M	SD	M	SD
			Intermediate Memory					
1	1.2	0.8	1.2	0.9	1.1	0.5	1.1	0.6
2	0.9	0.6^{a}	2.8	1.6^{b}	1.1	0.4^{a}	1.6	0.9^{a}
3	0.7	0.2	0.8	0.5	1.2	0.4	0.8	0.5
4	0.9	1.1	1.5	1.4	1.1	0.8	0.4	0.5
5	0.8	0.5	0.7	1.0	1.0	0.4	1.2	0.5
6	1.9	1.2^{b}	0.9	0.7^{a}	1.2	0.5	0.8	0.4
7	1.1	0.6	0.5	0.4^{a}	1.0	0.4^{b}	1.0	0.4
8	0.1	0.1^{a}	0.1	0.2^{a}	0.5	0.5^{b}	0.4	0.4
9	1.6	0.7	1.1	0.8	1.4	0.4	1.4	0.7
10	1.4	0.7	0.7	0.7^{a}	1.3	0.6	2.0	1.1^{b}
			Long-Term Memory					
1	1.5	0.6	2.2	2.6	1.2	0.4	1.3	0.9
2	0.6	0.6	0.6	0.5	1.2	1.0	0.8	0.7
3	0.5	0.5	0.7	0.5	0.9	0.7	0.4	0.4
4	0.4	0.9	0.7	1.0	0.9	1.0	0.5	0.8
5	0.3	0.3	1.5	2.1	0.6	0.5	1.1	0.3
6	2.3	1.2	1.3	1.1	1.5	0.6	1.2	0.5
7	1.1	0.9	0.5	0.5	0.7	0.4	0.9	0.3
8	0.0	0.0^{a}	0.0	0.0^{a}	0.5	0.2^{b}	0.4	0.5^{b}
9	1.4	0.9	0.8	0.9	0.8	0.9	1.2	0.8
10	1.3	1.3	0.7	0.6	1.4	0.4	1.7	1.2

a versus b; $p < .05$.

To discern the potential impact of the treatments on the serial position effect (i.e., more information is recalled from the beginning and ending of a string of stimuli), MANOVA with two levels repeated (intermediate vs. long-term memory relative score and blocks within the story) and one not repeated (conditions) was completed. The means and standard deviations for the ratios of correct items per segment for the intermediate and long-term memories are shown in Table 2.

Although there was obviously no main effect for condition (since the ratio for each segment was based on each individual's total score), there were statistically significant interactions between the type of memory (intermediate vs. long-term) and the position of the segment [$F(9,216) = 7.16, p < .001$; eta-squared estimate = 19%] and between condition, type of memory, and the position of the segment [$F(27,261) = 3.36$, $p < .001$; partial eta-squared estimate = 26%]. *Post hoc* analysis indicated that the major source of the three-way interaction between the type of memory and the segment of the story and the treatment was due to the greater number of statistically significant differences between the treatments for segments within the middle of the story for the intermediate memory relative to the long-term memories.

DISCUSSION

The consolidation of memory can be disrupted when either chemical or electromagnetic stimulation is presented during the subsequent 30 min following acquisition. As predicted, the presentation of a pulsed electromagnetic field along the left hemisphere during this classical consolidation period for declarative memory facilitated the accuracy for a 5-min narrative when it was reconstructed about 10 days later. We had selected this particular pattern for the applied magnetic field because the same temporal parameters, presented as direct electrical stimuli to hippocampal slices, had doubled the magnitude of LTP.

Subjects who had been exposed to the LTP pulse for 15 min during the 30-min period after they heard the story remembered about twice the number of accurate details relative to the subjects who had been exposed to either the sham field or the bilateral hemispheric stimulation. The effect size, which indicates that the experimental treatments accommodated 25% of the variance in the numbers of long-term memories, is sufficient to have potential practical application. The fact that a pulse pattern that evoked a twofold increase in LTP for 30 min in hippocampal slices was associated with a comparable magnitude of improvement in actual memories must be considered interesting but probationary until replicated. An isomorphic transformation would appear unlikely.

The failure of bilateral stimulation to enhance the memory recall and the similarity of its effects to the sham field condition suggest that symmetrical induction, at least with this configuration, could promote functional cancellation. A requirement for neuroelectrical asymmetry within the hemispheres is also commensurate with the emerging conceptions that minute contrasts or extractions in simultaneous, homologous hemispheric functions are the core processes from which the most complex neurocognitive functions and phenomenology emerge (7,15).

The intermediate scores for subjects who received the right hemispheric stimulation would be commensurate with the hypotheses that: (1) there are linguistic operations within the right hemisphere (16), and (2) stimulation of one hemisphere can induce activity in the homologous region of the other hemisphere in order to maintain homeostasis (analogous to the "mirror" focus that is sometimes seen in complex partial epileptic patients).

Scores that reflect the total accuracy or numbers of details per story or per serial frame of a story are often dominated by the subjects who had the greatest numbers of memories. Consequently, the relative numbers of accurate details per serial frame for subjects are more optimal to discern any weak effects upon the serial order effect. The results of this study suggested that bilateral presentation of the LTP fields facilitated details for the early portion of the story but interfered with the middle and final segments of the 10 segments of the Billy Story (relative to the other treatments). This differential effect on the "primacy" and "recency" portions of the serial position curve would be consistent with, but not exclusively supportive of, Sommerhoff's (6) hypothesis of two separate microneural processes.

The only significant residual effect, approximately 10 days later, was the small but significantly more accurate reconstruction of details for segment 8 for those subjects who had been exposed to either the right or the left hemispheric stimulation relative to those who received the sham field or bilateral stimulation. The etiology of this difference could be spurious, but it may be relevant that this segment contains words with significantly more emotional meanings within both the hedonistic and activity dimensions (17) than any of the other segments. It is also the segment that contains the most emotional (crying, nausea, blackness) and ambiguous metaphors regarding the trauma to the main character of the story.

The results of this study indicate that the complexity of the signature or the "information" within an external magnetic field may be more important than the intensity and that the effects are measurable and discriminable when ecologically valid stimuli (such as the recollection of emotional narratives with multiple implications rather than lists of words or nonsense syllables) are reconstructed. There is also one theoretical implication of this theme of research that deserves attention. Simulation of the neuronal algorithms that mediate the fundamental processes of memory and consciousness by external, weak but complex magnetic fields that exhibit the appropriate temporal structure could be employed to modify a person's memory (and consequently) the sense of self by circumventing traditional sensory modalities or normal awareness.

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