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Title: Induction of self awareness in dreams through frontal low current stimulation of gamma activity

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Abstract:

Recent findings link fronto-temporal gamma electroencephalographic (EEG) activity to conscious awareness in dreams, but a causal relationship has not yet been established. We found that current stimulation in the lower gamma band during REM sleep influences ongoing brain activity and induces self-reflective awareness in dreams. Other stimulation frequencies were not effective, suggesting that higher order consciousness is indeed related to synchronous oscillations around 25 and 40 Hz.

Full Text:

Rapid eye movement (REM) sleep dreams are primary states of consciousness in that they are concerned with the immediate present, with only uncontrolled access to the past or the anticipated future (1-3). After awakening, humans--and supposedly (1) only humans--enter a secondary mode of consciousness that introduces higher order cognitive functions such as self-reflective awareness, abstract thinking, volition and metacognition (1-4). A state of sleep in which primary and secondary states of consciousness coexist is lucid dreaming, a phenomenon that is most likely unique to humans. In lucid dreams, elements of secondary consciousness coexist with normal REM sleep consciousness, enabling the sleeper to become aware of the fact that he is dreaming while the dream continues. Sometimes the dreamer gains control over the ongoing dream plot and, for example, is able to put a dream aggressor to flight. Scientifically, lucid dreams present the unique opportunity to watch the brain change conscious states, from primary to secondary consciousness (2,4), and to arrive at testable predictions about the determinants of these states. At the neurophysiological level, EEG3 and functional magnetic resonance imaging (fMRI) studies (5) have shown that lucid dreams are accompanied by increased phase synchrony and elevated frequency-specific activity in the lower gamma frequency band centered around 40 Hz, especially in frontal (3,5) and temporal (5) parts of the brain. Fronto-temporal activity in this frequency band is related to executive ego functions and secondary consciousness, which is characteristic of the human wake state and atypical for REM sleep (2,3,6). The increase in gamma activity observed during lucid dreaming raises several theoretical questions.

Does lucid dreaming trigger gamma-band activity or does gamma-band activity trigger lucid dreaming? Perhaps the capacity to generate gamma oscillatory activity sets the stage for lucid dreaming, which may then further enhance gamma activity. Furthermore, is lucid dreaming dependent on the presence of gamma activity (necessary condition) or can higher order consciousness in dreams be elicited via other causal routes, such as through stimulation with other frequencies (causally enabling condition)? We tested these hypotheses via fronto-temporal transcranial alternating current stimulation (tACS) at various frequencies (2, 6, 12, 25, 40, 70 and 100 Hz) and under sham conditions (simulated stimulation, but no current flow; Supplementary Fig. 1). This relatively new method of brain stimulation has no such side effects as acoustic noise and tactile sensations, which are known to accompany transcranial magnetic stimulation and might result in sleep disturbance. tACS has already been shown to modify perceptual and cognitive performance in waking (7) and, in combination with superimposed transcranial direct current stimulation (tDCS), in sleep (8).

Brain activity was monitored by continuous EEG, electrooculography (EOG) and electromyography (EMG) (Supplementary Fig. 2a). tACS was applied following ~2 min of uninterrupted arousal-free REM sleep, after which subjects were awakened and asked to rate dream consciousness based on a factor analytically derived and validated scale (LuCiD scale (9)). Previous laboratory research with the LuCiD scale has shown that, in lucid dreaming, three of eight factors are substantially increased: insight into the fact that one is currently dreaming, control over the dream plot and dissociation akin to taking on a third-person perspective (Supplementary Fig. 3).

The EEG was quantitatively analyzed for all stimulation conditions and sham (Fig. 1a-c). Unchanged REMs (Fig. 1a) and continuous muscle atonia (Fig. 1b) documented the persistence of REM-like sleep preceding (phase I), throughout (phase II) and following stimulation (phase III) until awakening (phase IV) (Supplementary Fig. 4).

When representing EEG power as a function of frequency and time, as depicted in the wavelet transform shown in Figure 1c, we confirmed the findings from EOG and EMG, showing that the EEG power spectrum during stimulation remained very similar until awakening (phase IV). Wakefulness was characterized by a strong increase in the alpha frequency band, typical for waking with eyes closed.

In the analyzed EEG samples, subjects maintained typical signs of REM sleep during stimulation, as evidenced by EMG, EOG and EEG (Fig. 1a-c and Supplementary Figs. 4 and 5). Unlike in normal REM sleep, however, activity in the lower gamma frequency band increased during stimulation with 40 Hz (mean increase between 37-43 Hz = 28%, s.e. = 4.82) and, to a lesser degree, during stimulation with 25 Hz (mean increase between 22-28 Hz = 12%, s.e. = 5.82). During sham or stimulation in lower (2, 6, 12 Hz) or higher frequencies (70 or 100 Hz), no such change in any frequency band was observed. This led us to speculate that, although sleep was maintained, REM sleep was altered and that stimulation actually resulted in a state change similar to the state of lucid dreaming (2,3). We confirmed this by comparing the relative changes during and before stimulation, computed as ratios of fast Fourier transform (FFT) grand average power at fronto-temporal electrode sites (Fig. 2).

Regarding subjective ratings of lucidity, lucid dreams were most prominent during stimulation with 25 (58%) and 40 Hz (77%) (Supplementary Table 1). Even in the absence of perceived lucidity, power in the lower gamma band was increased following stimulation in these frequencies. This increase was significantly stronger ($[P.sub.40Hz] = [degrees].00003$, $[P.sub.25Hz] = 0.0098$)

following lucid dreaming (Fig. 2e,f), suggesting a reciprocal effect of induced brain activity and reflective thought. Regarding the focusing of the observed increases in a relatively narrow frequency band, our findings are consistent with both animal (10,11) and simulation (12) studies showing that it is possible to induce synchronized oscillatory activity in, for example, a precisely defined frequency band around 40 Hz and that lower frequencies are not as easily induced.

[FIGURE 1 OMITTED]

[FIGURE 2 OMITTED]

Multivariate analyses of variance (MANOVA; Supplementary Table 2) yielded a significant overall effect on self-reflective awareness (LuCiD scores) for stimulation frequency ($F = 3.29$, $df = 56$, 1039 , $P < 10^{-9}$). Univariate statistics showed an effect for five of eight LuCiD scales (Online Methods): insight into the fact that one is dreaming ($F = 4.97$, $df = 7$, 199 , $P = 0.00003$), control over the dream plot ($F = 4.68$, $df = 7$, 199 , $P = 0.0001$), sense of realism ($F = 3.24$, $df = 7$, 199 , $P = 0.0028$), access to waking memory ($F = 3.12$, $df = 7$, 199 , $P = 0.0038$) and dissociation akin to taking on a third-person perspective ($F = 10.62$, $df = 7$, 199 , $P < [10.sup.-9]$). Systematic frequency-specific effects were identified for insight, control and dissociation (Fig. 3 and Supplementary Table 2), coinciding with those factors previously identified as main determinants of lucid dreams (9). The strongest effect was observed for dissociation, showing that subjects more often took on a third-person perspective following stimulation with 40 Hz than with any other frequency except 25 Hz (all contrasts, $P < 0.0001$ except 25 Hz). Insight into the fact that one is dreaming while the dream continues differed significantly mainly for 40-Hz stimulation ([P.sub.sham] = 0.0009, [P.sub.2Hz] = 0.0159, [P.sub.12Hz] = 0.0466, [P.sub.70Hz] = 0.0099) and for 25 Hz versus sham ([P.sub.sham] = 0.0248). Increased ratings for the factor control were observed for 25 Hz only ([P.sub.2Hz] = 0.0004, [P.sub.6Hz] = 0.0150, [P.sub.12Hz] = 0.0074, [P.sub.40Hz] = 0.0010, [P.sub.70Hz] = 0.0003, [P.sub.100Hz] = 0.0007), suggesting that 25-Hz oscillatory activity may be functionally distinct from 40-Hz activity.

[FIGURE 3 OMITTED]

Consistent with subjective scores, stimulation-induced increases in 40-Hz band activity at fronto-temporal sites (power ratios between phases II/I) correlated significantly with mean scores on the LuCiD scale factors insight ($P = 0.0001$) and dissociation ($P = 3 \times [10.sup.-8]$; Supplementary Table 3). To a lesser degree, albeit statistically significant ($P = 0.0098$), increases in 25-Hz band activity correlated with subjective ratings regarding insight and dissociation ($P = 0.0081$). Overall, this suggests that lower gamma-band activity is indeed related to elevated self-reflective awareness.

Our results provide, to the best of our knowledge, the first causal evidence of frequency-specific cortical oscillations in humans induced by tACS. In addition, our experiment is, to the best of our knowledge, the first to demonstrate altered conscious awareness as a direct consequence of induced gamma-band oscillations during sleep. We assume that lower gamma activity is mediated by activation of fast-spiking interneurons that are known to generate gamma oscillations in cortical networks in animal studies (11,13-15). These cortical networks have been proposed to gate sensory processing (13-15), which might also enable lucid dreaming in a temporally specific manner.

In particular, we found that, below sensory threshold, stimulation with 25 and 40 Hz was able to induce secondary consciousness in dreams. The effect was not observed for lower or higher frequencies, suggesting that the rate and/or periodicity of oscillatory activity in the brain is causally relevant for higher cognitive functioning (13,14) and that lower gamma-band activity may indeed be a necessary condition for the elicitation of secondary consciousness in dreams, perhaps even in waking. However, although a mean increase in lower gamma-band power was significantly stronger in the presence of lucid dreaming, it was also present in its absence. We hypothesize that lower gamma-band stimulation enhances neuronal synchronization in this frequency band, which sets the stage for lucidity in dreams.

Regarding clinical applications, frontotemporal tACS might facilitate reemergence of intrinsic cerebral rhythms and reset thalamocortical oscillators, which may be able to restore dysfunctional network connectivity, such as the dorsolateral prefrontal cortex (DLPFC) in schizophrenia (16,17), activate the PFC in schizophrenia with predominating negative symptoms (18), or synchronize or suppress basal ganglia activity in, for example, obsessive-compulsive disorder (19). Finally, promoting gamma oscillations during REM sleep in post-traumatic stress disorder with reemerging nightmares might trigger lucid dreaming and eventually enable active changes in dream content.

METHODS

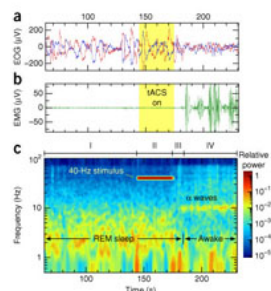
Methods and any associated references are available in the online version of the paper.

Note: Any Supplementary Information and Source Data files are available in the online version of the paper.

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Figure 1 EOG, EMG and EEG data from a single subject before, during and after 40-Hz stimulation. Awakening was marked by a marked change in EOG, EOG and EEG activity. (a) The two-channel horizontal EOG showed a distinct pattern of contralateral eye movements typical for REM sleep (red line: right eye, blue line: left eye). Eye movements were synchronous before (phase I), during (phase II) and after stimulation (phase III), and only changed after awakening (phase IV). This suggests that REM-like sleep continued throughout the stimulation up to the awakening. (b) EMG activity was unchanged until the subject awakened (phase IV), at which time it strongly increased signaling a loss of REM sleep atonia. (c) Continuous wavelet transform of the recorded EEG signal at Fpz using the complex Morlet wavelet (Online Methods). This documents the relatively uniform pattern of standardized power before, during and after stimulation and the change of pattern during waking, characterized by an increase especially in alpha activity and higher frequency bands. Increased alpha activity is typical for relaxed wakefulness with eyes closed. Note that, for illustrative purposes, the 40-Hz tACS signal has not been removed from this particular wavelet transform. It was, however, filtered out for all quantitative analyses displayed in a and b.



AUTHOR CONTRIBUTIONS

U.V., W.P. and M.A.N. designed the study. R.H. developed the filter algorithms and conducted the analyses. J.K.-G. and U.V. collected the data, U.V., R.H., M.A.N., W.P., A.K. and A.H. wrote the manuscript. All of the authors discussed the results and commented on the manuscript.

COMPETING FINANCIAL INTERESTS

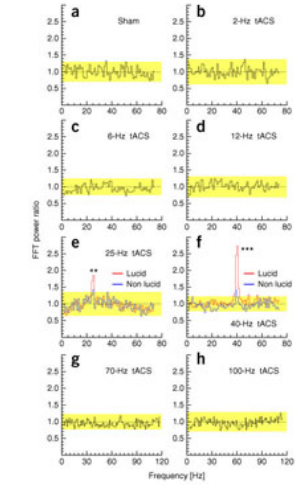


Figure 2 Grand average FFT power ratios of activity during (phase II) versus activity before stimulation (phase I) for the different stimulation conditions: sham ($N = 30$), 2 Hz ($N = 31$), 6 Hz ($N = 19$), 12 Hz ($N = 18$), 25 Hz ($N = 26$), 40 Hz ($N = 44$), 70 Hz ($N = 21$) and 100 Hz ($N = 18$). Yellow shading represents mean values ± 2 s.e. Any excursions outside of this range are considered to be significant at least at the $P < 0.05$ level. Note that, with 40-Hz and 25-Hz stimulation, lucid dreams (red line) were accompanied by a significantly larger increase in the respective frequency band than non-lucid dreams (blue line; independent two-sided t tests between lucid and non-lucid dreams; during stimulation with 40 Hz: $t_{25,44} = 5.01$, $df = 42$, $P = 0.0003$; during stimulation with 25 Hz: $t_{25,24} = 2.80$, $df = 24$, $P = 0.0098$). Independent of lucidity, the 40-Hz band increase was significantly stronger during stimulation with 40 Hz than during stimulation with 25 Hz ($r = 4.55$, $df = 68$, $P = 0.00003$). The increase in 25-Hz band activity was statistically similar during 40-Hz and 25-Hz stimulation ($P = 0.2387$). Furthermore, low pass filters were set at 70 Hz for all recordings except for 70- and 100-Hz stimulations (low pass = 120 Hz). Frequency resolution is 1 Hz. *** $P < 0.001$, ** $P \leq 0.01$.

The authors declare no competing financial interests.

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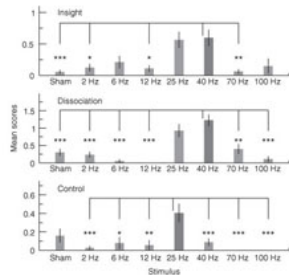


Figure 3 Selected contrasts of mean scores (s.e.) for the LuCID factors insight, dissociation and control ($N = 207$). The contrasts for insight and dissociation were strongest during stimulation with 40 Hz (40-Hz reference condition is shaded, top and middle frame). Control was increased most during stimulation with 25 Hz (25-Hz reference condition is shaded, bottom frame). Contrasts for thought, realism, memory, negative emotion and positive emotion are shown in **Supplementary Figure 6**. *** $P < 0.001$, ** $P < 0.01$, * $P < 0.05$.

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ONLINE METHODS

Approval for experiments with human subjects. The experiment conformed to the principles of the Declaration of Helsinki and was approved by the Institutional Review Board (Ethics Committee) of Gottingen University Medical Center, Germany.

Subjects. Participants were 27 healthy volunteers (15 female, 12 male, ages 18-26). To avoid possible bias (20), we only tested naive subjects who were inexperienced in lucid dreaming. The German version of the SCL90 (ref. 21) (all T scores < 63) and PSQI22 (all scores < 5) was not indicative of psychiatric or sleep disorders in any subject. Participants were free of CNS-acting medication. Informed consent was obtained from all subjects before testing.

Procedure. Subjects spent up to four nights at the sleep laboratory of the Department of Clinical Neurophysiology at the University Medical Center Gottingen. Sleep was allowed to continue uninterrupted until 3 a.m. (Supplementary Fig. 1). Starting at 3 a.m., and following at least 2 min and maximally 3 min of uninterrupted, arousal-free REM sleep, transcranial alternating current was applied fronto-temporally (Supplementary Fig. 2a) at a frequency of either 2, 6, 12, 25, 40, 70 or 100 Hz (stabilized at better than [+ or -] 0.01 Hz) or sham for 30 s. The applied stimulation frequencies were counterbalanced across subjects and across nights 1-4 to avoid order effects. During sham stimulations, the push button on the tACS device was operated, but current was not applied. Subjects were awakened by the experimenters shortly after stimulation or sham (5-10 s post stimulation). At this time, participants were asked to provide a full dream report (examples below) and to rate the 28 items of a factor analytically derived and validated scale on sleep consciousness (LuCiD scale (9)). Scale items were read out to subjects by the experimenters. The study was performed double blind. EEG (22 channels; Supplementary Fig. 2a), submental EMG and EOG were recorded throughout all nights. Note that, as subjects had no prior experience with lucid dreaming before the laboratory testing, and as they were not used to recalling their dreams, reports were quite short and often bizarre.

Example of lucid dream report following 40-Hz stimulation. I was dreaming about lemon cake. It looked translucent, but then again, it didn't. It was a bit like in an animated movie, like the Simpsons. And then I started falling and the scenery changed and I was talking to Matthias Schweighofer (a German actor) and 2 foreign exchange students. And I was wondering about the actor and they told me "yes, you met him before," so then I realized "oops, you are dreaming." I mean, while I was dreaming! So strange!

example of a non-lucid dream report (6 Hz). I am driving in my car, for a long time. Then I arrive at this place where I haven't been before. And there are a lot of people there. I think maybe I know some of them but they are all in a bad mood so I go to a separate room, all by myself.

example of a non-lucid dream (12 Hz). It was about shopping. I bought these shoes and then there was such a girl, she went-like-"snap" (snaps her fingers) and cut off her waist, just like that. Interviewer: she cut off her waist? Subject: yeah, just like that.

tACS. Low-intensity sinusoidal alternating current (250 [micro]A peak to peak) was applied through a battery-operated CE-certified stimulator (NeuroConn Stimulator Plus) to induce frequency-specific alterations of the EEG. Specifically, four electrodes (3.5 x 4 [cm.sup.2], connected pair-wise) were attached to the scalp at positions close to F3 and F4 and over the mastoids close to TP9 and TP10 (Supplementary Fig. 2a-c), resulting in a maximum current density of 18 [micro]A [cm.sup.-2] at the scalp. Current flow therefore alternated bilaterally between frontal and temporal positions. Current strength was chosen well below sensory and below phosphene threshold, and smooth ramp-up/ramp-down phases were used to avoid awakening of the subject. The distribution of tACS-induced scalp potentials could be reconstructed from the peak sinusoidal voltages registered at the EEG electrodes during stimulation and visualized using a spherical spline interpolation (Supplementary Fig. 2b). In addition, to investigate the distribution of the electric potential generated by the stimulator on the inner surface of the skull, we calculated dura potentials, which provide an estimated localization of the applied stimulation at the outer layer of the meninges, that is, the dura mater. Dura potentials (Supplementary Fig. 2c) were obtained using a mathematical technique similar to the one applied to the analysis of current source densities, namely the calculation of the surface Laplacian of the recorded scalp potentials (23,24). Supplementary Figure 2b,c documents the respective applied potentials, as deduced from the recorded EEG. Note that, although the distribution of the dura potential is quite similar to the distribution of the scalp potential, dura potentials are increased at the occiput, suggesting that stimulation-induced inner-brain activity is not limited to fronto-temporal sites.

Dura potentials were derived from the measured EEG electrode potentials by first applying a spherical spline interpolation (order of splines = 4, max. degree of Legendre polynomials = 10, $[\lambda] = [10.\text{sup.}-5]$) followed by the calculation of the Laplacian. Note that these potential maps can be taken only as a rough estimate of the actual passages of the stimulating currents through brain matter. A realistic finite-elements modeling (FEM) of the head including electric properties of all involved tissues would be needed for a more quantitative investigation (25,26).

EEG data analysis. During application of a tACS current, the cortical EEG signals are completely masked by the very much larger induced potentials, as exemplified in Supplementary Figure 4. To also quantify cortical activity during stimulation it is therefore mandatory to suppress this strong background signal. In our data analysis, we have achieved this via a two-step procedure. First, we applied a noise cancellation concept (27), in which we subtracted from each EEG channel a properly scaled and phase-shifted fraction of the sum of the TP9 and TP10 channels. Second, we applied a digital notch filter ($Q = 40$) at the respective stimulation frequency, that is, 2, 6, 12, 25, 40, 70 or 100 Hz, as well as at the first two harmonics of the latter, furthermore a high-pass filter (fifth-order Bessel) at 0.7 Hz and a low-pass filter (eighth-order Butterworth) at 70 Hz (120 Hz for 70- and 100-Hz tACS). The first step suppressed most of the tACS-induced background in the EEG, and possible small remnants of the stimulation signal were removed by the notch filters in the second step. Note that efficient notch filtering requires a sinusoidal stimulation of low harmonic distortion and good frequency stability. The subtraction of a conformal tACS reference, in our case $(TP9+TP10)/2$, does not have these limitations, however. We verified with data taken in the sleep laboratory on a dummy, that is, void of intrinsic cortical EEG activity, that the combined application of both techniques resulted in an overall suppression of the tACS background of [greater than or equal to] 100 dB. EMG channels were likewise notch filtered ($Q = 40$) at the tACS stimulation frequency as well as at its first and second harmonics, high-pass filtered at 0.7 Hz (fifth-order Bessel) and low-pass filtered at 70 Hz (eighth-order Butterworth). EOG channels were low-pass filtered at 20 Hz. All signals were in addition notch-filtered at 50 Hz ($Q = 40$) to suppress power line noise. The cleaned EEG signals were furthermore corrected for ocular artifacts, using the standard procedure (28), and then subjected to a frequency analysis using Fast Fourier Transform (FFT) and continuous wavelet transform techniques (29). Grand averages of FFT power as function of EEG frequency (Supplementary Fig. 5) were obtained by averaging over frontal and temporal electrode sites, stimulations (sham or tACS at a given frequency), and subjects. From these results, the power ratios shown in Figure 2 were computed.

Assumption of lucidity. Lucidity was assumed when subjects reported elevated ratings ($>\text{mean} + 2 \text{ s.e.}$) on either or both of the LuCiD scale factors insight and dissociation. Both factors were significantly correlated ($r = 0.32$, $P = 0.000002$), suggesting a high degree of shared variance.

Statistical analyses. Analyses are based on 207 EEG tracings coupled with valid dream reports following electrical stimulation (30 x sham, 31 x 2 Hz, 19 x 6 Hz, 18 x 12 Hz, 26 x 25 Hz, 44 x 40 Hz, 21 x 70 Hz, 18 x 100 Hz). In total, we stimulated 324 times; however, in 89 cases, subjects did not provide a dream report. In 28 cases, subjects awoke spontaneously from REM sleep (Supplementary Table 1). Sleep variables were analyzed using ANOVAs (Supplementary Table 4), LuCiD ratings were compared through MANOVA (Supplementary Table 2), Bonferroni-corrected tests for post hoc comparisons. Questionnaire data and EEG power ratios were correlated using two-sided Spearman correlation coefficients (Supplementary Table 3). Lucid versus non-lucid dream reports were analyzed using two-sided unpaired t tests. The data meet the assumptions of the chosen statistical tests (for example, normality). t tests were performed based on a Levene test for similarity of variance. s.e. was used as variance estimates in Figures 2 and 3 and Supplementary Figure 6.

A priori subject exclusion criteria were the use of CNS acting medication, a history of epilepsy, a history of a sleep (assessed through interview and PSQI) or psychiatric disorder (interview and SCL90). Laboratory data (LuCiD scores and the respective EEG data) were excluded when subjects awoke spontaneously during or following stimulation (frequencies listed in Supplementary Table 1). The rate of awakenings per subject was variable, but no subject had to be excluded entirely.

As there were no a priori effect size estimates available, we based our sample size on the assumption of a medium effect size and, as this was a repeated measures design, also on justifiable strain on our subjects.

A Supplementary Methods Checklist is available. 20

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