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Improving sleep and cognition by hypnotic suggestion in the elderly☆

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ABSTRACT

Sleep quality markedly declines across the human lifespan. Particularly the amount of slow-wave sleep (SWS) decreases with age and this decrease is paralleled by a loss of cognitive functioning in the elderly. Here we show in healthy elderly females that the amount of SWS can be extended by a hypnotic suggestion "to sleep deeper" before sleep. In a placebo-controlled cross-over design, participants listened to hypnotic suggestions or a control tape before a midday nap while high density electroencephalography was recorded. After the hypnotic suggestion, we observed a 57% increase in SWS in females suggestible to hypnosis as compared to the control condition. Furthermore, left frontal slow-wave activity (SWA), characteristic for SWS, was significantly increased, followed by a significant improvement in prefrontal cognitive functioning after sleep. Our results suggest that hypnotic suggestions might be a successful alternative for widely-used sleep-enhancing medication to extend SWS and improve cognition in the elderly.

1. Introduction

Sleep is vital for our health and well-being, and particularly slow-wave sleep (SWS) has been proven critical for restoration and optimal cognitive brain functioning (Finelli et al., 2001; Van Der Werf et al., 2009). In the elderly, sleep quality is typically strongly reduced and accompanied by an increased rate of clinically relevant sleep disturbances as well as extensive use of sleep-inducing medication (Crowley, 2011; Foley et al., 1995). In particular, SWS continuously decreases across the human life span, possibly reflecting the loss of synaptic density and neural functioning (Mander et al., 2013). SWS is strongly reduced in aging related disorders like mild cognitive dementia and associated with cortical thinning and prefrontal cortical atrophy (Mander et al., 2013; Sanchez–Espinosa et al., 2014). Furthermore, reduced sleep quality and sleep fragmentation in non-demented elderly participants are reliable predictors for later cognitive decline, increased amyloid beta disposition and development of Alzheimer's disease after several years (Keage et al., 2012; Lim et al., 2013; see Pace-schott and Spencer, 2014 for a review). Frequently prescribed sleep-inducing drugs typically hinder the occurrence of SWS, loose their efficacy during long-term treatment, have adverse side effects and often a high risk of addiction (Hajak and Rüther, 2006; Riemann and Perlis, 2009). Therefore, the development of efficient and risk-free approaches to improve sleep and particularly SWS in the elderly is highly needed.

While the sleep-disturbing effects of negative thoughts, stress, and rumination are widely accepted (Saper et al., 2005; Van Reeth, 2000), research on the possibility of positively influencing sleep by psychological interventions is rather scarce. A reason might be the observation that cognitively "wanting" to improve sleep quality typically fails or can even be counterproductive (Ansfield et al., 1996). Thus, subconscious influences might prove more effective in this regard, which could be exerted under the state of hypnosis. Hypnosis was very recently defined as "a state of consciousness involving focused attention and reduced peripheral awareness characterized by an enhanced capacity for response to suggestion" (Elkins et al., 2015, p. 6). Importantly, during the state of hypnosis, suggestible subjects respond more easily to hypnotic suggestions. These are statements given during induction or afterwards, intended to change or influence behavior. They can include e.g., decrease of pain, motor paralysis or posthypnotic amnesia, and recent cognitive neuroscience research has successfully demonstrated effects of these suggestions on underlying brain activation using objective neuroimaging methods (Cojan et al., 2013; see

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Kihlstrom, 2013 for a review). In therapeutic contexts, hypnosis has been proven an effective tool in reducing pain, anxiety and stress related disorders (Flammer and Bongartz, 2003), and several studies provide evidence for a beneficial effect of hypnosis on sleep disturbances and insomnias (Borkovec and Fowles, 1972; Schlarb, 2005; Stanton, 1989). For instance, a randomized controlled trial study demonstrated a substantial improvement in self-rated sleep quality in post-menopausal women after clinical hypnosis intervention. This improvement even continued as indicated by the 12 week follow-up test (Elkins et al., 2013). Very recently, we have shown that listening to a hypnotic suggestion before sleep strongly extends the amount of SWS and slow-wave activity (SWA, 0.5–4.5 Hz) in young healthy females suggestible to hypnosis (Cordi et al., 2014). SWA is regarded as the hallmark oscillatory brain activity characterizing SWS and has been functionally related to processes of brain plasticity and synaptic density (Huber et al., 2004). Control experiments confirmed that the type of hypnotic suggestions was critical for the beneficial effect on SWS and excluded alternative explanation like general relaxation and demand characteristics. Interestingly, less suggestible females did not benefit from the hypnotic suggestions, even when asked to simulate the effects of a hypnotized person (see Cordi et al., 2014). However, it remains an open question whether these results are robust and generalizable to elderly participants. In addition, it remains elusive whether hypnosis-induced increases in SWS and frontal SWA result in an improvement in cognitive functions. We predicted that SWS and SWA will increase after hypnotic suggestions in highly suggestible elderly females. Further, particularly in the elderly, prefrontal SWA has been recently associated with age-related prefrontal brain atrophy and cognitive functions (Mander et al., 2013). Thus, we expected performance in tasks recruiting frontal areas to improve after SWA increases.

2. Methods

2.1. Participants

Forty-two healthy, German-speaking elderly females with a mean age (± standard deviation *[SD]*) of 67.10 ± 4.26 years (age range 60–82) took part in the experiment. Only females were recruited to avoid known gender effects on sleep architecture and suggestibility (Carrier et al., 2001; Fukuda et al., 1999; Page and Green, 2007). One subject was excluded due to lacking sleep, two others did not keep caffeine restriction in one of the two experimental sessions. A prior power calculation based on our previously published study in young females (Cordi et al., 2014) revealed an optimal sample size of $n=38$ participants to detect an effect size of $f=0.33$ ($eta_p^2 \approx 0.1$) with a probability of > 95% (assumed correlation among repeated measures $\rho=0.4$, power calculation performed by G*Power3 (Erdfelder et al., 1996)). For the final sample of 39 subjects included in the analysis, suggestibility to hypnosis was scaled according to the Harvard Group Scale of Hypnotic Susceptibility (HGSHS) prior to the experiment (cut-off score for high suggestibility: HGSHS ≥ 7) (Bongartz, 1985). In this sample, nineteen women were highly suggestible (HS) (mean age 66.42 ± 4.10 years; HGSHS: 7.95 ± .20 *SEM*) and 20 women were low suggestible (LS) (mean age 67.70 ± 4.66 years; HGSHS: 4.03 ± .44). The two experimental groups did not differ in age ($p > .30$). Due to technical problems, memory performance data (paired-associates learning task) are missing for three subjects (2 HS, 1 LS). On average, participants reported normal sleep (Pittsburgh Sleep Quality Index, PSQI mean ± *SD*: 5.33 ± 2.60 (Buysse et al., 1989)). To assure general health of the subjects, a history of neurological or psychiatric disorders, intake of pharmacological sleep medication more than twice a month and acute physical disorders were defined as exclusion criteria. Participants were asked to refrain from caffeine and alcohol during the test day and to get up before 8 a.m.. Participants gave their written consent to take part in the study and were paid 140 Swiss francs for participation. The Ethics Committee of the University of Zurich approved the study.

2.2. Materials

Audio files. Participants either listened to a tape including hypnotic suggestions to sleep deeply or a control tape, both taken from Cordi et al. (2014). While hypnotic suggestions were given with a calming, soft voice and slow rate of speaking, the control text was as neutral as possible with neither activating nor calming words and an everyday intonation. Both texts are publicly available (http://www.psychologie.uzh.ch/fachrichtungen/allgpsy/biopsy/links.html). Participants were allowed to fall asleep during or after the tape, and were, in all conditions, constantly awakened after 90 min in bed (see Fig. 1, for the procedure).

2.2.1. Memory measures

Memory functions were tested before and after the nap. In the semantic verbal fluency test (SVT), subjects were asked to generate as many words of a given category as possible within 2 min. The number of acceptable, listed words was taken as measure of retrieval performance of long term memory storage (Lezak, 1995). This test has proven to be age-sensitive (Haugrud et al., 2010) and dependent on frontal functioning as shown in several lesion studies (Miceli et al., 1970). For analyses, percentage of postsleep performance was computed relative to presleep performance. Parallel versions were used in a randomized order (four categories (animals, hobbies, fruits, professions) for pre-and postsleep measures in both sessions were used). As percentage of improvement across the nap strongly correlated with SVT performance before sleep ($r(45)=-.71$, $p < .001$ for hypnosis, $r(45)=-.52$, $p < .001$ for control), presleep performance was regressed out and the analyses were run on the adjusted values. Second, an episodic word pair learning task (Rasch et al., 2006) was conducted. Hippocampus-dependent declarative memory consolidation of word-pairs is known to depend on early, SWS rich sleep (Plihal and Born, 1997; Rasch and Born, 2013). Subjects had to learn a list of 30 semantically related word pairs adopted from Rasch et al. (2006) and also used in Cordi et al. (2014), although presented more slowly (see Table S4). After a fixation cross, the first word appeared for 2 s, followed by a 500 ms blank interval and the second word, which was presented for 2 s. A blank interval of 500 ms preceded the next fixation cross. The words were presented in black font on white screen via E-Prime (Psychology Software Distribution, High Sittenham, UK). Each word pair was presented only once. Cued recall was tested immediately after learning and again after the nap. After the first word was displayed, participants were asked to come up with the corresponding second word aloud. Response time was not restricted. The order of the word pairs during recall differed from learning phase. Performance was measured as percentage of words recalled at postsleep retrieval relative to the number of word pairs remembered immediately after learning. Also in the declarative memory test, parallel versions were used (parallel word lists, see Table S4).

2.2.2. Psychomotor vigilance test

After sleep, the psychomotor vigilance test (PVT) was conducted to overcome sleep inertia and measure the effects of sleepiness on vigilance (Dinges and Powell, 1985). A millisecond counter appeared on the screen at random intervals and subjects were asked to press the space key as soon as they recognized the counter counting upwards. The reaction time was displayed in ms for 1 s after the keypress.