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EFFECT OF OVARIAN HORMONES ON MEMORY SUPPRESSION OVARYEN HORMONLARIN ANIMSAMADA BASTIRMA ÜZERINDEKİ ETKİSİ

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Abstract

Several studies suggest that memory suppression in humans occur as an active process of executive control, mediated by regions of prefrontal cortex, which is a substrate for ovarian hormones. However the effect of ovarian hormones on this process is not known. In order to address this question, we utilized the quantitative analysis of ovarian hormones in combination with the procedure of a memory control model, the think (T) /no think (NT) paradigm in a within-subject design study. We compared the rate of memory control between the follicular (low estrogen and progesterone) and mid-luteal (high estrogen and progesterone) phases of regularly cycling healthy women. Our data demonstrate that during midluteal phase, 63.6 % of subjects are able to 'suppress' or actively forget (significantly less % recall below the baseline) previously learned word pairs in the 'NT condition; i.e., not to think the target word associated with the cue word'. However during the follicular phase there was no effect of 'NT condition' on the active forgetting of word pairs below the baseline as assessed by the memory test applied after the T/NT procedure. Thus, our results indicate that ovarian hormones are associated with the process of memory control.

Keywords: Memory suppression, Estrogen, Executive control

Özet

Çeşitli çalışmalar, insanlarda bellek kontrolünün (anımsamada bastırma) yürütücü bir işlev olarak prefrontal korteks denetiminde aktif bir mekanizma ile gerçekleştiğini göstermiştir. Prefrontal korteksin ovaryen hormonların müdahalesine oldukça açık olduğu bilinmekle birlikte bu etkinin anımsamada bastırma işlevi sırasında nasıl bir rol oynadığı bilinmemektedir. Burada sunulan çalışma bir bellek kontrolü modeli olan düşün/düşünme paradigmasını (think /no think paradigm) kullanarak ve ovaryen hormonların kantitatif olarak analiz edildiği denek-içi desen düzeneği ile bu soruya cevap aramaktadır. Menstrual siklusun foliküler (düşük estrojen ve progesteron) ve midlüteal (yüksek estrojen ve progesteron) fazlarındaki bellek kontrol oranları kıyaslanmıştır. Veriler göstermektedir ki midlüteal fazda, deneklerin % 63.6 si, önceden öğrenilmiş kelime çiftlerini 'düşünmeme koşulu' yani 'ip ucu kelimesi ile ilişkili hedef kelimesini düşünmeme koşulu' (NT condition)- sırasında aktif unutma (anımsamada bastırma) becerisi göstermiştir (istatiksel olarak anlamlı bir şekilde kendiliğinden unutma oranına göre daha çok unutma ya da daha az hatırlama). Ancak 'düşünmeme koşulunın' bellek kontrolü üzerindeki bu etkisi, düşündüşünme prosedürünü takiben yapılan bellek testleri ile gösterildiği gibi foliküler fazda gözlenmemiştir. Bu sonuçlar bellek kontrolü işleminin ovaryen hormonlar ile ilişkili bir durum olduğunu göstermektedir.

Anahtar Kelimeler: Anımsamada bastırma, östrojen, yürütücü işlevler

1.Introduction

Forgetting can be defined as 'the absence of expression of previously properly acquired memory in a situation that normally would cause such expression' (Hardt et al., TINS, 2013). Although there are various theories of forgetting, there is a consensus favoring interference theory, which is based on the proposition that mental activity involves a competition of various knowledge of encoded memory, interfering with each other and thus causing the loss of some information. This theory has dominated memory research but newly published reports raise questions on it. For example, Anderson and his co-workers (1996, 2003) suggest that the interference theory is insufficient to explain forgetting since forgetting can be caused by inhibitory mechanisms in such a way that people control unwanted memories by recruiting inhibitory mechanisms via executive control.

The idea of ability to memory suppression by inhibitory

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mechanisms of executive control is not new. Over a century ago Freud proposed a highly controversial process called repression by which unwanted memories can be pushed into the unconsciousness and become forgotten. Supporting this view, there are certain findings which indicate that humans use executive control processes for memory (Dagenbach & Carr, 1994; Smith & Jonides, 1999: Hasher & Zacks 1988: Anderson & Spellman, 1995: Bjork, 1989), for perceptual distraction (Chao, & Knight, 1995; Dagenbach & Carr, 1994) and for the elimination of habitual responses (Logan & Cowan, 1984; Posner, & Peterson, 1990). Inspired by these findings, Anderson and Green adapted the go/ no-go paradigm, which is used to study executive control over motor responses in primates (Sakagami & Niki 1994) and humans (Casey et al., 1997; de Zubicaray, et al., 2000) for use in a memory retrieval task. So called Think /No Think paradigm (Anderson and Green, 2001), this approach is based on the rate of active forgetting process of previously learned word pairs and has led to the several lines of evidences that memory suppression in humans occur as an active process of executive control, mediated by regions of prefrontal cortex (Anderson and Green, 2001, Anderson et. al., 2004; Depue et al., 2007). According to this neurobiological model, the process of memory control was associated with increased dorsolateral prefrontal activation causing a reduced hippocampal activation (Anderson et. al., 2004; Depue et al., 2007). Thus, prefrontal cortical regions, a substrate of ovarian hormones (Keenan P.A. et al, 2001), actively control the hippocampal activity for a reduced retention of encoded memory. However the effect of ovarian hormones on this process is not known. In order to address this question we utilized the quantitative analysis of ovarian hormones in combination with think (T) /no think (NT) paradigm in a within-subject design study. We compared the rate of memory control between the follicular (low estrogen and progesterone) and mid-luteal (high estrogen and progesterone) phases of regularly cycling healthy women.

2.Materials and Methods

2.1. Participants

Participants were recruited via the posting board at Fatih University. The experimental procedure was conducted in accordance with the Declaration of Helsinki. Prior to experimentation, participants were informed about the experimental procedure in general terms. They gave written informed consent and filled in self-report questionnaires (Aydemir Ö. ve Köroğlu E., 2000) on mood and current affect. Exclusion criteria for participation were irregular menstrual cycle, current and previous psychiatric, neurological, or somatic diseases, alcohol and drug abuse, as well as medication for any of these and for birth control. Participants were 7 healthy, young females, regularly cycling (selected by period calendar data for three months provided by participants) and aged between 18-25 years. For at least three months, all participants were followed by menstrual calendars to establish cycle regularity. Only regularly cycling women were included in the study. Each participant was tested once (see the section of Experimental procedure) in each of the following phases of her menstrual cycle: follicular (days 8–10 from the first day of menstrual bleeding) and luteal (days 6–8 from ovulation). Each time at the end of the experimental procedure, blood sample was collected to verify levels of ovarian hormones.

2.2. Stimulus material

Stimulus material included word pairs presented on a computer screen with a font size of 12, colored as black, red, green according to the phase of the experiment. A word pair is composed of a cue word and a response word which are weakly related. The degree of relatedness of word pairs were determined by the ratings of a separate group of participants (n=100), assigned to rate the relatedness of words from weak (rated as 1) to strong (rated as 5) in a given questionnaire. Word pairs were used as either suppress, response or filler. The suppress word pair corresponds to the word pair with a cue word to be presented with red color which signs the participant to 'suppress', or not to think (No Think) the response word, whereas the response word pair's cue is to be presented by green which signs participant to 'think' the response word, during the Think/No Think Phase of the experimental procedure (see below). The filler word pairs were used as training material to let the participants practice the instructions of experiment. The whole experiment is required to be applied to each participant two times, with one experiment during follicular phase (FP; low estrogen and progesterone) and the second experiment during the midluteal phase (MLP; high estrogen and progesterone) of the menstrual cycle. Thus, two sets of stimulus material, each containing 48 word pairs, i.e., 36 critical (suppress word pairs and response word pairs), 12 filler word pairs, with a total of 384 words, with no significant difference in word length, word frequency and concreteness were selected in accordance with the Turkish word norms (Tekcan & Göz, 2005)

2.3. Experimental procedure

The experimental procedure was adapted from Anderson and Green (2001). Accordingly, the experimental procedure included three phase: Learning Phase, Think (T)/No Think (NT) phase and Recall Phase (Table 1). At the end of the procedure, a blood sample was received from the participants for hormonal analysis. During the learning phase, participants were trained on 36 critical and 12 filler pairs according to procedures reported previously (Anderson and Green, 2001). Subjects were trained until they learned at least the 50% of word pairs. Subjects who were not able to learn at least the 50 % of word pairs at the end of the three times of training session, were excluded from the study. Learning phase is followed by the T/NT phase during which the participants were read the think/no-think instructions, and were then given practice on filler words. Subjects were then given 384 critical

| Think / No Think Paradigm | | | |
|---------------------------|----------------|----------------------|------------|
| | LearningPhase | Think/No Think Phase | Test Phase |
| Suppress | Erozyon-Temiz | Erozyon | Erozyon |
| Respond | İskelet-Balkon | İskelet | İskelet |
| Baseline | Yüzük-Formül | | Yüzük |

Table 1 Adaptation of Think / No Think Paradigm

trials (192 suppress, 192 respond) in which respond and suppression stimuli were intermixed. Suppression and Respond trials were conducted on different pairs, with 12 pairs (repeated 16 times) participating in each. Four blocks of 96 critical trials were presented, separated by 45-second breaks. On each trial, a cue from one of the pairs appeared for 4000ms in red (Suppress) or green (Respond), followed by a 500ms blank inter-trial interval. At the end of the experimental procedure, blood sample was collected to verify levels of ovarian hormones.

3.Results

3.1. Quantitative verification of hormonal levels

Menstrual cycle is widely used as a model to study the effect of ovarian hormones on various cognitive functions. In parallel with this, our hormonal analysis assessed by the blood sample collected from the participants during FP and MLP show that there is a significant difference between the levels of estrogen and progesterone during these phases (p<0.001) and these hormones, as expected, are significantly higher in our participants during the MLP (data not shown).

3.2. Adaptation of Think/No Think Paradigm for experimental conditions

Two sets of stimulus material, one to be used in the FP and the other to be used MLP, each containing 48 word pairs, i.e., 36 critical (suppress word pairs and response word pairs), 12 filler word pairs, with a total of 384 words, with no significant difference in word length, word frequency and concreteness were selected in accordance with the Turkish word norms (Tekcan, A. İ. , & Göz, İ. (2005). The degree of relatedness of word pairs were determined by the ratings of a separate group of participants (n=100), assigned to rate the relatedness of words from weak (rated as 1) to strong (rated as 5) in a given questionnaire. Word pairs were used as either suppress, response or filler. The model of the stimulus material is shown on the Table 1.

3.3. During MLP participants perform a successful suppression

Our data demonstrate that during MLP, 63.6 % of subjects are able to 'suppress' or actively forget (significantly less % recall below the baseline) previously learned word pairs in the 'NT condition; i.e., not to think the target word associated with the cue word'. As shown by the green squares in the Figure 1, 5 participants are above the baseline, 2 participants are in the level of baseline for the T condition. For the NT condition, 5 participants are clearly below the baseline meaning they showed a significant performance on active forgetting (Figure 1, red squares). However, during the follicular phase, as shown in the Figure 2, there was no a significant effect of 'NT condition' on the active forgetting of word pairs below the baseline as assessed by the memory test applied after the T/NT procedure. Only 3 red square (meaning only 3 people were able to actively forget the previously learned word pairs).



Figure 1 Percentage of recall during midluteal phase (MLP)



Figure 2 Percentage of recall during follicular phase (FP)



Figure 3 Percentage of recall (%) for recall (Think) and suppress (No Think) conditions with respect to baseline during the follicular phase (FP) and midluteal phase (MLP) of participants

T/NT paradigm is based on the determination of active forgetting rate of previously learned word pairs. As explained in the methods section in detail, certain word pairs were excluded from the T/NT phase of the experiment in order to determine the spontaneous forgetting which is called the baseline. The baseline is determined by a memory test applied for all learned word pairs (word pairs used for T condition, for NT condition and those excluded from the T/NT phase for the baseline) at the end of the experiment. Since the baseline corresponds to spontaneous forgetting, the forgetting rate (or % recall) should be below the baseline for NT condition and above the baseline for T condition if there is an active process of memory control. Thus, ideally, for each of the participants (N=7) the distribution of green (T) and red (NT) squares would be separated from each other by being above and below the baseline respectively. This pattern is more likely the case during the MLP (Figure 1) compared to FP (Figure 2). In fact a comparison of percentage of recall during these two phases show this pattern clearly in the Figure 3: Unlike FP, participants are able to show the performance of memory control during MLP as shown by the significantly reduced percentage of recall (patterned bar) compared to baseline (grey bar). During the FP, there is no a significant difference between these bars. Here, it is important to mention that, in order to eliminate any confound that would arise from the learning of paradigm, 4 of the participants were first tested during MLP, then FP and for the remaining 3 participants the test order was reversed, i.e., they were tested first during the FP then MLP.

4. Discussion and Conclusion

Although we have used a very limited number of participants in this study, our preliminary results show that memory suppression is observed during MLP of the regularly cycling women as reflected by the better performance on the T/NT test. The same effect was poorly observed during FP, when these hormones are low. Thus ovarian hormones may likely play a role in the process of active forgetting, most probably by modulating the PFC as this region is known to be involved in the process of active forgetting and highly accessible to ovarian hormones (Keenan P.A. et al., (2001). A replication of this study with higher numbers of participants will clarify our, so far very limited, knowledge of memory suppression and its modulation.

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