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Emotional arousal and recognition memory are differentially reflected in pupil diameter responses during emotional memory for negative events in younger and older adults

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ABSTRACT

A better memory for negative emotional events is often attributed to a conjoint impact of increased arousal and noradrenergic modulation (NA). A decline in NA during aging is well documented but its impact on memory function during aging is unclear. Using pupil diameter (PD) as a proxy for NA, we examined age differences in memory for negative events in younger (18–30 years) and older (62–83 years) adults based on a segregation of early arousal to negative events, and later retrieval-related PD responses. In keeping with the hypothesis of reduced age-related NA influences, older adults showed attenuated induced PD responses to negative emotional events. The findings highlight a likely contribution of NA to negative emotional memory, mediated via arousal that may be compromised with aging.

1. Introduction

Better memory for emotionally arousing events is well documented. Emotional stimuli ranging from stories (Heuer and Reisberg, 1990) to words (Phelps et al., 1998), film clips (Cahill et al., 1996), and pictures (Bradley et al., 1992) are all related to improvements in long-term memory recall. This emotional enhancement was suggested to be due to an effect of arousal, as this emotional bias extends to both positively and negatively valenced stimuli (Bradley et al., 2008; Garavan et al., 2001; Mather, 2007). Negative emotional arousal is accompanied by the activation of the locus coeruleus (LC) and the concomitant release of the neurotransmitter noradrenaline (NA) that serves to improve memory for the negative event by mediating long-lasting synaptic plasticity in the medial temporal lobe (Klukowski and Harley, 1994; Sara, 2009). In line with this role of noradrenaline in negative emotional memory, memory enhancement for negative emotional items has been found to be abolished with administration of a beta-adrenergic antagonist, propanolol, during early retrieval or encoding (Kroes et al., 2010; Strange and Dolan, 2004).

By the age of 60, older adults have lost between 20% and 40% of the neurons in the LC (Mann, 1983; Vijayashankar and Brody, 1979). This cell loss might occur as a correlate of healthy aging or might reflect a presymptomatic reduction in LC integrity related to tau pathology (Mather and Harley, 2016). The age-related decline in noradrenergic (NA) modulation is expected to contribute to cognitive decline during healthy aging (Arnsten and Goldman-Rakic, 1985a,b). Although this has been a prevalent hypothesis in the field for several decades, very little progress has been made in addressing this question. In particular, encoding and consolidation of declarative long-term memory is affected in healthy aging (Nyberg et al., 2012). This is the case for more complex episodic memory contents and negative emotional memory events (Jacques et al., 2009; Naveh-Benjamin et al., 2003). A recent study in rats showed that an age-related deficit in negative emotional memory formation is accompanied by reduced levels of extracellular noradrenaline and can be attenuated by administrating noradrenaline or blocking noradrenaline reuptake (Luo et al., 2015). Here, we investigated whether physiological indicators of LC activation

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can inform age differences in emotional memory for negative events.

Given the LC's small size and its location deep within the brainstem, it is difficult to obtain noninvasive recordings of its activity using approaches such as functional neuroimaging. However Samuels and Szabadi (2008) observed that when monkey LC neurons were stimulated, pupil diameter (PD) increased in parallel to its firing rate. Similarly, Joshi et al. (2016) used electrical microstimulation of LC in monkeys to show that phasic LC activation produces robust changes in PD. Therefore, PD can be taken as an indicator of LC activation and serve as a proxy measure for LC firing to salient, arousing (Chen and Sara, 2007), or task-relevant events (Aston-Jones et al., 1994).

In line with the above, larger PDs have been consistently observed in response to emotional events such as the viewing of pleasant and unpleasant stimuli, relative to neutral stimuli (Bradley et al., 2008). This effect is seen across valences (and modalities), and is therefore analogous to the noradrenergically-mediated modulation driven by bottom-up stimulus properties as seen in emotional memory findings (Partala and Surakka, 2003; Sara, 2009).

Studies investigating PD during memory encoding or recognition tasks have furthermore consistently shown larger PD responses to old as opposed to novel stimuli (recognition effect, also known as familiarity effect) (Heaver and Hutton, 2011; Otero et al., 2011; Võ et al., 2008). These larger PD responses to old compared with new stimuli have been attributed to increased effort necessary for memory retrieval (Võ et al., 2008). However, an alternative strength-of-memory trace account (Otero et al., 2011) provides contradictory evidence as the PD to old stimuli was larger for deeply encoded items which would seem at odds with an increased retrieval effort account. Given LC-NA activation in occurrence with goal-oriented target stimuli (such as old stimuli in a recognition test), the old/new effect could, therefore, be a combination of task-goals and also memory strength which reflect the saliency of old stimuli in a recognition task.

The present study aimed to examine the age differences in PD responses during emotional memory while disentangling opposing views on the old/new recognition effect in PD responses. An important goal for our study was to separate PD responses associated with retrieval success from PD responses associated with different levels of emotional arousal and to explore age differences in both processes attributed to NA.

Finally, some studies predict that PD at an encoding stage should predict subsequent memory accuracy (Papesh et al., 2012); yet, findings remain inconsistent with others reporting no relationship between PD responses at encoding and subsequent remembering (Võ et al., 2008), or that constriction, as opposed to dilation predicts higher memory recall (Kafkas and Montaldi, 2011). Thus, an additional aim was to investigate subsequent memory in the presence or absence of arousal-based modulation.

2. Methods

2.1. Participants

A total of 44 participants took part in the study comprising 22 healthy younger adults (15 female, aged between 18 and 30, mean 24 years) and 22 healthy older adults (11 female, aged 62–83, mean 71 years). Younger adults were recruited using the Institute of Cognitive Neuroscience subject database and older adults were recruited using advertisements in local newspapers and via flyers. All participants had normal or corrected-to-normal vision and no history of any psychiatric disorders. Informed written consent was gained from each participant and reimbursement was set at £8 per hour. The study was approved by the local ethics committee (UCL Research Ethics Committee reference 5506/001). Three older adults had to be excluded from the analyses. One due to poor performance in the recognition tests, one due to eyesight problems that prevented proper engagement with the task, and one due to unwillingness to complete the task. The final sample, therefore, comprised 41 participants, 22 of which were younger and 19 were older adults. Moreover, 4 participants' (2 younger adults and 2 older adults) performance on the first recognition test was more than 2 standard deviations lower (hit-false alarm on first recognition close to 0%) than that of the rest of the participants due to difficulties in understanding the instruction on the early recognition test. Note that this low performance was not due to general difficulties of understanding the task or overall lower recognition memory, as their performance was in a normal range on the delayed recognition test. We therefore replaced behavioral as well as pupil data on this first test with the group mean of their respective age group for these 4 participants. Replacing the data in these 4 participants did not affect the analyses as control analyses showed that all statistically reliable results were robust to excluding these 4 participants.

2.2. Materials and stimuli

The stimuli consisted of 120 indoor and outdoor pictures containing negative emotional or neutral scenes partly taken from the International Affective Picture System (IAPS) database (Lang and Bradley, 2007; $N_{negative} = 48$, $N_{neutral} = 27$) and partly taken from an image set collected from the Internet ($N_{negative} = 72$, $N_{neutral} = 93$). The Internet-based image set was built as part of a different study and was rated on valence and arousal by a sample of 60 young adults (mean age = 28 ± 2 years, 50% female) Therefore, the Self-Assessment Manikin was used, which is an affective rating system devised by Lang (1980) that also underlies IAPS ratings. For each image to be rated, subjects could select from a 9-point rating scale with 9 representing a high rating on each dimension (i.e., high pleasure, high arousal) and 1 representing a low rating on each dimension (i.e., low pleasure, low arousal). The rating was performed on a total of 387 novel images collected from the Internet as well as 45 IAPS images. Ratings on the IAPS images derived from our sample of young adults did not differ from the established ratings available in the IAPS database ($p > 0.18$), such that both databases could be merged. For the current study, we chose negative emotional pictures with low valence ($M = 2.85$, $SD = 0.45$) and moderately high arousal ($M = 5.87$, $SD = 0.73$), and neutral pictures with neutral valence ($M = 5.26$, $SD = 0.45$) and low arousal ($M = 3.19$, $SD = 0.55$).

Stimuli were displayed on a 22-inch monitor and viewed from a distance of 80 cm. The stimuli, fixation crosses, and the gray-patterned background were adjusted for luminance to control for trivial luminance-related effects on PD responses. Stimuli and fixation crosses were displayed in the center of the screen (cf. Fig. 1). The text was presented in size 50 Arial font and colored white. Participants sat on a comfortable chair, with their head position stabilized with a desktop-mounted chin and headrest. Two 4-choice button boxes were used to record responses during the task.

2.3. Experimental procedure

Participants were invited to attend for a double testing session. Incidental encoding test and early recognition test were performed in the morning and a delayed recognition test was performed 6 hours later on the afternoon of the same day. Participants were familiarized with the use of the button boxes and encouraged to reduce blinking while a picture was displayed on the screen. Before every eye-tracking recording, the eye tracker was calibrated to the