



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.

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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, propranolol, 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 administering 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](#); $N_{\text{negative}} = 48$, $N_{\text{neutral}} = 27$) and partly taken from an image set collected from the Internet ($N_{\text{negative}} = 72$, $N_{\text{neutral}} = 93$). 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

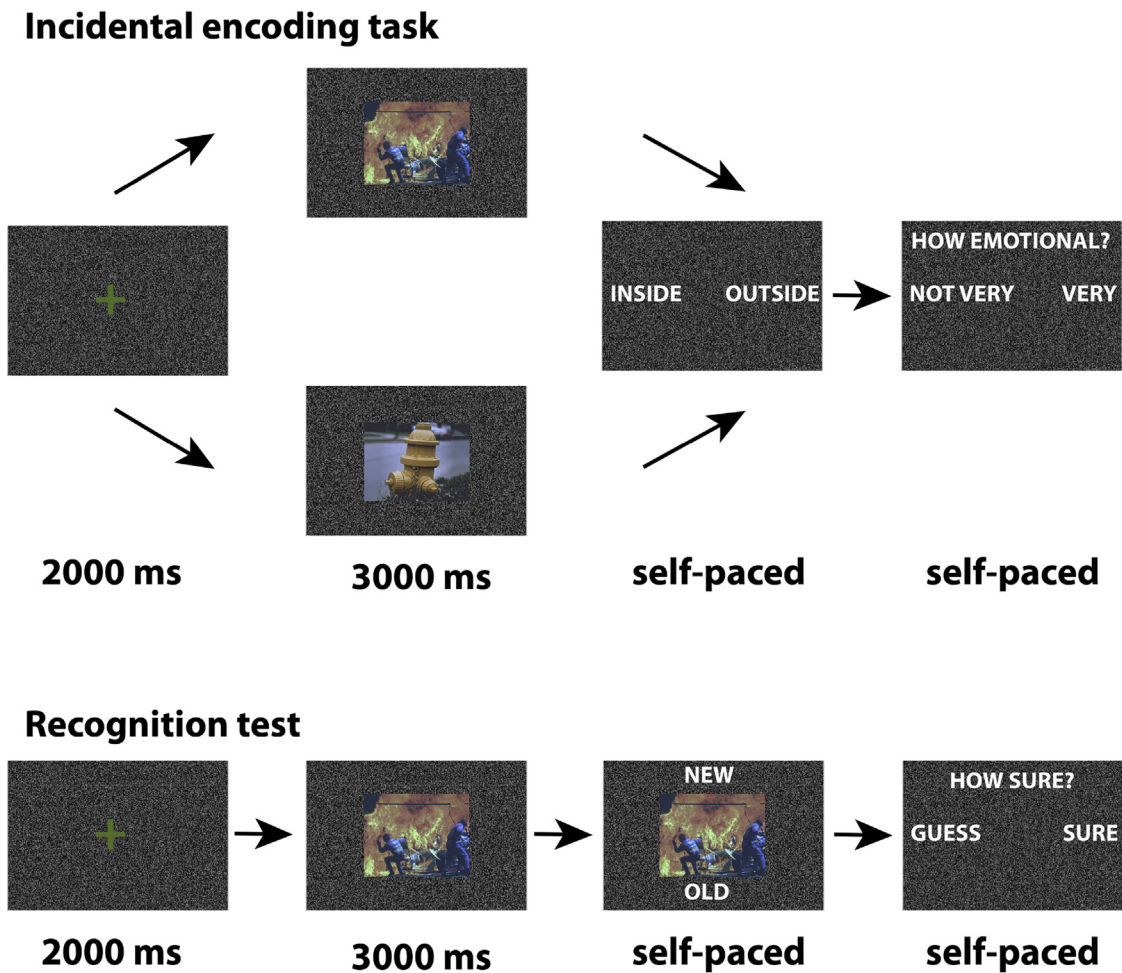


Fig. 1. Incidental emotional memory task. During incidental encoding (upper plot), participants classified neutral and negative emotional stimuli as indoor or outdoor scenes and indicated how emotional the picture made them feel on every trial. During early and delayed recognition tests (lower plot), participants classified pictures as new or old and indicated how certain they were in their memory judgment on a 4-point scale (4 buttons, with certainty increasing from left to right). Responses were withheld during the initial 3 seconds of stimulus presentation. Background, fixation cross, and scene stimuli were adjusted in luminance to avoid changes of pupil diameter due to stimulus luminance.

participant's right eye using a standard 9-point or 6-point calibration and validated using the same calibration setup.

2.3.1. Incidental encoding task

The incidental encoding task consisted of 120 trials, with a short break after 60 trials. As a cover task, participants were asked to classify scenes as indoor or outdoor. Each trial began with a gray fixation cross, followed by a picture showing a neutral or negative inside or outside scene. The amount of inside, outside, negative, and neutral scenes were balanced yielding 30 trials per emotional and stimulus category.

After the picture had disappeared, participants were prompted to classify the picture as indoor or outdoor and then indicate using a 4-point scale (4 buttons) how emotional the picture made them feel ("not very emotional, somewhat emotional, quite emotional or very emotional"). This provided a subjective measure of negative emotionality of the pictures for manipulation evaluation as well as the assessment of interindividual differences in perceived emotionality. Button positions were matched to the display to facilitate responding for the older adults in particular.

Inside/outside responses, and emotional ratings, were self-paced and could only be given after the picture disappeared and the respective question was displayed to avoid confounds of PD responses to stimuli and response execution.

2.3.2. Early and delayed recognition tests

Each test consisted of 120 trials with a short break after 60 trials. Trials for each test were separated into 60 old (from the incidental encoding task) and 60 new pictures balanced for inside and outside as well as negative and neutral scenes. Trial structure and timing were kept similar to the encoding task. However, in this phase, the pictures did not disappear after 3000 ms and stayed on the screen when participants were prompted to classify pictures as old or new as well as how certain they were in the old or new classification on a 4-point scale (4 buttons).

2.4. Acquisition and preprocessing of pupillometric data and statistical analyses

Pupillometric and eye-tracking data were continuously recorded from the right eye using an infrared EyeLink 1000 Desktop Mount (SR Research), with a sampling rate of 1000 Hz and luminance levels of 100%. PD was acquired using the centroid measure to provide more accurate estimates of changes in PD over time. Both eye-tracking and pupil data were analyzed using custom-made scripts in MATLAB 2015b and the software toolbox FieldTrip (Version 2, <http://www.fieldtriptoolbox.org/>), implemented in MATLAB.

PD data were segmented in a time window of 500 ms before and 3000 ms after picture onsets. A custom-made filter was used to

detect eye-blinks in segmented data based on changes in PD. Periods of missing data due to blink-related eye artifacts were cut out in time windows of 200 ms and 30 ms around large and small artifacts, respectively, and replaced by linear interpolation. Trials with excessively noisy or missing data were excluded (on average 15 trials in younger and 24 trials in older adults). Pupil data were then baseline corrected in a time window -200 to 0 ms before picture onset and z-scored per individual to allow comparing task conditions independent of individual differences in PD size (Nassar et al., 2012). RTs ± 3.5 standard deviations from the mean were excluded from RT analyses.

Negative emotionality and recognition effects were first examined in repeated measures ANOVAs with age groups as a between

subjects factor (Fig. 2). For these analyses, PD responses were averaged in a time window of 1–2 seconds after stimulus onset. Earlier studies have shown that an old-new recognition effect on pupil data is independent of correct and incorrect answers (i.e., hits and misses or correct recognitions and false alarms) (Kafkas and Montaldi, 2015), suggesting that it reflects unconscious or implicit components of episodic memory. We therefore included test trials with correct as well as incorrect (recognition) responses in our analyses, but additionally assessed whether results were robust to excluding incorrect trials.

We then used general linear model (GLM) analyses to examine a concurrent effect of negative emotionality and recognition on PD, as well as to test for the time course of these effects while controlling

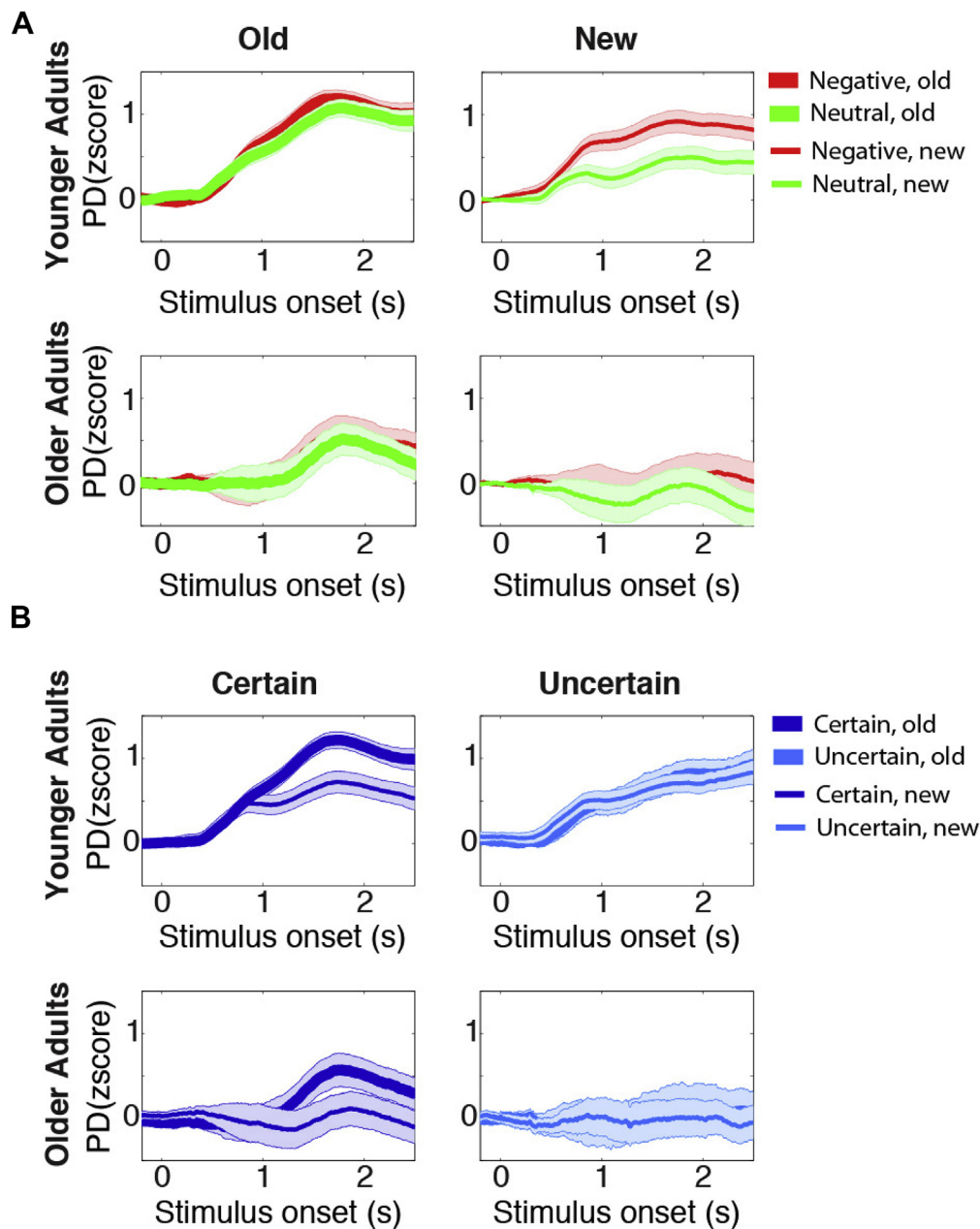


Fig. 2. Mean PD responses related to negative emotionality and recognition of stimuli in recognition tests (collapsed across early and delayed recognition). (A) PD was increased for negative stimuli (red). The effect of negative emotionality on PD was particularly pronounced for new stimuli and in younger adults (thin line, e.g., upper right plot). (B) Pupil diameter was increased for old stimuli (thick line). Memory certainty (dark blue) modulated PD further, but only for old stimuli (thick line, e.g., upper left plot). (A) and (B) Older adults showed an overall reduced responsiveness in PD. Shaded error bars represent standard error (across individuals within age groups). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

for interindividual differences in the intercepts. We included interactions between negative emotionality and recognition as well as recognition and certainty of responses as repeated measures ANOVAs showed a modulation of negative emotionality and recognition effect with old/new stimuli and certainty of response, respectively (see paragraph above as well as [Results](#) below). Thus, the entered trial-wise regressors were the negative emotionality of the stimuli, the old/new status of stimuli, certainty of old/new responses, retention interval (early or delayed), old/new and negative emotionality interaction and old/new and certainty interaction (as 6 concurrent logistic regressors in a GLM per person, predicting PD per trial). GLMs were calculated separately for every sampling point. At the individual level, group-level GLMs were tested for differences between age groups in trial-wise effects and for additional variation of the trial-wise effects with other behavioral variables of interest (e.g., modulation of old/new effect on pupil data by mean memory accuracy per person). Time points of significant differences in PD between conditions as well as between age groups were assessed with permutation analyses (compared against time series of effects resulting from randomly shuffled condition labels across trials for the individual logistic regressors [100 repetitions] or participant IDs for GLMs across individuals [1000 repetitions], respectively). On every permutation, the largest beta in a time window of 0.5–2.5 seconds after stimulus presentation was saved. Effects on unpermuted data were considered significant if the largest beta exceeded the 95% or 90% percentile of the distribution of maximal betas on permuted data. In this manner, we provided significance tests corrected for multiple comparisons against sequences of PD responses which did not differ in the extent of autocorrelation ([Cohen, 2014](#)). Time periods of significant condition or group-level effects are indicated as lines below pupil effects (cf [Fig. 3](#)). To assess whether negative emotionality effects manifested earlier than recognition effects, we extracted peaks of the

respective betas per individual in a time window 0.75–2.0 seconds after stimulus onsets. Differences in the timing of negative emotionality and recognition peak effects were assessed using nonparametric tests, given the non-normality of the data.

In the analyses of tonic PD responses for subsequent memory effects, data were segmented and cleaned as for the phasic data and were then z-scored across all concatenated trials ([Nassar et al., 2012](#)). In this manner, trial differences in the mean (or tonic) pupil response could be analyzed independently of individual differences in overall pupil size. The analysis interval was –0.2 to 2 seconds around stimulus onsets. Five younger adults and 2 older adults had too few not remembered trials and had to be excluded from analyses, resulting in a final sample for the analyses of tonic data of 17 younger adults and 17 older adults.

3. Results

3.1. Behavioral results: performance on incidental encoding task

Both age groups attended to the cover task (in-out classification), with the younger ($M = 96$, $SD = 0.03$) and older adults ($M = 96$, $SD = 0.03$) both showing high accuracy ratings. There was no significant difference between the 2 age groups ($t(39) = 0.67$, $p = 0.42$, indicating that both age groups followed the instructions relevant for incidental encoding. Subjective emotionality ratings (4-point scale) of the stimuli reflected negative and neutral stimulus types. Both age groups rated the negative pictures ($M = 2.45$, $SD = 0.59$) higher than the neutral pictures ($M = 1.22$, $SD = 0.20$; $t[40] = 16.862$, $p < 0.05$, $r = 0.51$) with no age difference in emotionality ratings for either type of stimulus (ratings for negative pictures $t[39] = 0.71$, $p = 0.49$ and neutral pictures $t[39] = 0.29$, $p = 0.77$). Age groups were hence

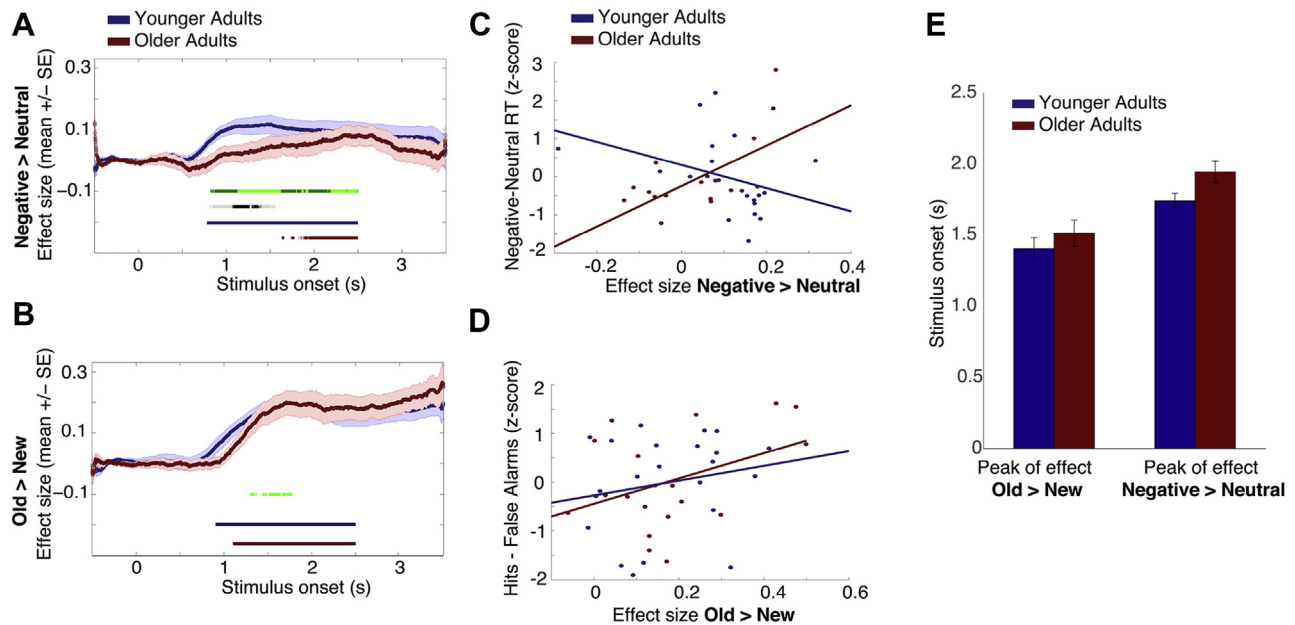


Fig. 3. GLM results. (A) Beta weights (effect sizes) for negative > neutral and (B) old > new stimuli on PD data. Values above 0 indicate a positive effect of the regressor (e.g., PD response to negative stimuli larger than neutral stimuli in 3A). (A) and (B) Lines indicate time points of significant effects based on permutation analyses within age groups (blue: within younger adults, red: within older adults). Lines (light green) indicate time points of significant relationship at $p < 0.10$ of PD to negative-neutral RTs for older adults (A) and to memory accuracy (hit-false alarms) for all participants (B) and significance at $p < 0.05$ (dark green). In (A) Lines (gray) indicate the age group difference of negative > neutral effect at $p < 0.10$ and at $p < 0.05$ (black). (C) Scatterplot shows positive correlation between effect size of the PD response to negative > neutral stimuli and negative-neutral RTs in time window indicated in (A). (D) Scatterplot shows positive correlation between effect size of PD response to old > new stimuli and memory accuracy in time window indicated in (B). (E) Bar chart showing the timing of the maximum value for negative emotionality and recognition effect in the time window 0.75–2 seconds. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Table 1
Descriptive statistics for hits and false alarms (FA) on early and delayed recognition tests for both age groups

Test stimuli	Younger adults			Older adults		
	Hits, mean (SD)	False alarms, mean (SD)	Hits—false alarms, mean (SD)	Hits, mean (SD)	False alarms, mean (SD)	Hits—false alarms, mean (SD)
Early test, negative stimuli	0.96 (0.05)	0.06 (0.05)	0.91 (0.08)	0.95 (0.07)	0.06 (0.05)	0.88 (0.10)
Early test, neutral stimuli	0.91 (0.08)	0.03 (0.04)	0.88 (0.09)	0.91 (0.06)	0.03 (0.06)	0.87 (0.08)
Delayed test, neutral stimuli	0.90 (0.07)	0.05 (0.06)	0.84 (0.09)	0.86 (0.11)	0.14 (0.13)	0.72 (0.16)
Delayed test, neutral stimuli	0.84 (0.13)	0.07 (0.07)	0.77 (0.14)	0.75 (0.18)	0.10 (0.10)	0.65 (0.18)

comparable in terms of elicited emotional responses, as evident in self-reports.

3.2. Behavioral results: early and delayed recognition tests

3.2.1. Overall accuracy hit-false alarm

In line with the hypothesis that negative events improve memory accuracy (assessed as hits-false alarms), we found a main effect of negative emotionality on memory accuracy ($F[1,39] = 13.64, p < 0.05, r_{ICC} = 0.51$), with higher accuracy to negative stimuli ($M = 0.84, SD = 0.09$) than to neutral stimuli ($M = 0.79, SD = 0.11$). Furthermore, a main effect of test interval ($F[1,39] = 71.72, p < 0.05, r_{ICC} = 0.81$) showed an expected reduced memory performance with delayed recognition testing (Table 1).

In line with negative stimuli improving long-term memory accuracy in particular, we found a negative emotionality by test interval (early/delayed) interaction ($F[1,39] = 71.72, p < 0.05, r_{ICC} = 0.80$). We also found evidence for a reduced memory performance in older adults ($F[1,39] = 5.22, p < 0.05, r_{ICC} = 0.34$), as well as a test interval by age interaction ($F[1,39] = 10.28, p < 0.05, r_{ICC} = 0.46$) indicating that older adults' memory was more compromised in a delayed recognition test. This confirms reduced long-term memory performance in older compared with younger adults. We did not observe an age \times negative emotionality interaction. However, when recognition trials with high certainty alone were considered (certainty rating >3), we observed a trend for younger adults to profit more from negative emotional content in their recognition memory (age \times negative emotionality interaction $F[1,38] = 3.02, p = 0.09, r_{ICC} = 0.27$). We did not observe a significant 3-way interaction between negative emotionality, test interval, and age group indicating that both age groups were affected similarly by negative emotional memory content. This might reflect insufficient task difficulty needed to allow for a differential modulation of memory performance by negative stimulus emotionality in the 2 age groups (see Discussion).

Finally, research on time of day effects in testing suggest that in particular older adults' recognition performance can be affected by being tested at suboptimal times (Hasher et al., 2005; May et al., 1993). In our study, this effect might have contributed to the worse recognition performance of older adults on delayed memory tests in the afternoon. To gauge the extent of this effect, we

compared recognition memory as assessed via hits or false alarms. The latter have been shown to be particularly sensitive for time of day effects (May et al., 1993). Indeed, we did observe a somewhat weaker age \times test interval effect for hits ($F(1,39) = 3.84, p = 0.06, r_{ICC} = 0.30$) as compared with false alarms ($F[1,39] = 4.91, p < 0.05, r_{ICC} = 0.33$). However, this difference was not reliable (age \times hit vs. false alarm \times test interval $F[1,39] = 0.34, p = 0.86$).

In summary, these results show expected effects of negative emotion increasing memory (for both age groups, and marginally more so in younger adults) and a reduction in long-term memory performance in older adults, although the latter was not modulated by negative emotion. These effects were observed in the absence of age differences in cover task performance or emotionality ratings (Windmann and Kutas, 2001).

3.2.2. Certainty ratings

Certainty ratings (on a scale from 1–4) obtained after categorizing old/new stimuli showed that both age groups were more certain in the early ($M = 3.68, SD = 0.32$) compared with the delayed test ($M = 3.43, SD = 0.44, F[1,39] = 36.73, p < 0.05, r_{ICC} = 0.70$), as expected given the lower memory performance on delayed recognition. There was no difference in certainty ratings for negative and neutral stimuli and no difference in certainty ratings between the younger and older age groups for both the early and delayed recognition tests. Certainty ratings and memory performance (hits-false alarms) were overall positively correlated across participants (part 1: younger adults: $r = 0.27, p = 0.23$; older adults: $r = 0.42, p = 0.07$; part 2: younger adults: $r = 0.43, p < 0.05$; older adults: $r = 0.52, p < 0.05$; the correlations between certainty ratings and memory performance did not differ between age groups).

3.2.3. Reaction times for old or new and negative or neutral stimuli

We observed longer RTs for negative stimuli compared with neutral stimuli, independent of the question responded to ($F(1,39) = 52.76, p < 0.05, r_{ICC} = 0.76$ (Table 2). This was seen in the encoding task (indoor–outdoor classification: $F(1,39) = 33.34, p < 0.05, r_{ICC} = 0.68$, emotionality ratings: $F(1,39) = 19.02, p < 0.05, r_{ICC} = 0.57$ as well as early ($F[1,39] = 8.07, p < 0.05, r_{ICC} = 0.41$) and late ($F[1,39] = 8.24, p < 0.05, r_{ICC} = 0.42$) recognition tests). Older adults also showed slower reaction times overall ($F[1,39] = 55.51, p < 0.01, r_{ICC} = 0.77$) and showed more slowing to negative stimuli than

Table 2
Reaction times (in seconds) following negative or neutral stimuli in younger and older adults (mean across individuals, median per individual)

Test stimuli	Younger adults neutral, mean (SD)	Younger adults negative, mean (SD)	Older adults neutral, mean (SD)	Older adults negative, mean (SD)
Task (indoor/outdoor)	0.80 (0.33) ^a	1.03 (0.41) ^a	0.92 (0.23) ^a	1.11 (0.30) ^a
Task (emotionality rating)	0.63 (0.37) ^{a,b}	0.78 (0.52) ^{a,b}	1.40 (0.52) ^{a,b}	2.02 (1.01) ^{a,b}
Early test (old/new classification)	0.51 (0.14) ^b	0.55 (0.19) ^b	1.02 (0.61) ^{a,b}	1.2 (0.87) ^{a,b}
Delayed test (old/new classification)	0.55 (0.23) ^b	0.59 (0.23) ^b	1.02 (0.44) ^{a,b}	1.14 (0.39) ^{a,b}
Early test certainty rating	0.42 (0.14) ^b	0.44 (0.19) ^b	0.88 (0.26) ^b	0.88 (0.26) ^b
Delayed test certainty rating	0.40 (0.19) ^b	0.40 (0.19) ^b	0.94 (0.31) ^b	0.98 (0.35) ^b

Overall, reaction times were longer after negative stimuli.

^a Indicates a significant difference within age groups between reaction times after negative and neutral stimuli.

^b Indicates a significant difference between age groups in reaction times to neutral or negative stimuli.

younger adults $F(1,39) = 8.33, p < 0.05$. This consistent effect of longer reaction times to negative stimuli, independent of whether the negative emotionality of the stimuli is relevant for the response or not, is consistent with the effect of an attentional capture by negative stimuli (Schwartz et al., 2003).

There was also an overall main effect of old/new stimuli on RTs across tasks, $F(1,39) = 7.04, p < 0.05, rICC = 0.39$, with longer RTs for new stimuli ($M = 0.77, SD = 0.26$) than for old ($M = 0.71, SD = 0.26$). A similar effect has been previously reported in a recognition memory task (Kafkas and Montaldi, 2015). Longer RTs to new as compared with old stimuli suggest that participants focused, in particular, on old stimuli when tasked to classify stimuli as old or new (see below for a more detailed discussion of this effect).

3.3. Pupil results

3.3.1. Comparability of PD measures between age groups

Younger and older adults had similar trial numbers for all tasks following artefact correction ($M = 105.89, SD = 10.22, M = 96.07, SD = 19.61$, respectively, $F[2, 78] = 2.56, p = 0.12$), suggesting a comparable quality of pupil measurements in younger and older adults. Similarly, younger and older adults had similar levels of baseline noise, assessed as the mean across trials of the standard deviation in the first 500 ms of pupil data taken on individual trials, $F(1, 39) = 3.06, p = 0.09$. On this basis, we would not expect to see age differences in pupil data solely arising out of age differences in PD measurement noise.

3.3.2. Repeated measures ANOVAs of negative emotionality and recognition effects in pupil data

Cleaned pupillometric data were analyzed with respect to condition and age differences in mean PD responses in a time window of 1–2 seconds after stimulus onsets across the tasks in 2 separate repeated measures ANOVAs. The first analysis examined a 4-way interaction of negative emotionality and recognition effects across the 2 recognition delays as well as age differences therein (Fig. 2A). Younger adults had overall larger PD responses than older adults ($F[1,39] = 9.57, p < 0.05, rICC = 0.44$). As predicted, given higher levels of NA during negative emotional events, there was a main effect of negative emotionality on mean PD ($F[1,39] = 23.49, p < 0.05, rICC = 0.61$), with negative stimuli eliciting a larger mean PD ($M = 0.55, SD = 0.70$) than neutral stimuli ($M = 0.36, SD = 0.64$; Fig. 2A). This was modulated by age group ($F[1,39] = 5.67, p < 0.05, rICC = 0.36$), with younger adults showing a larger reaction to negative stimuli than older adults (Fig. 2A, upper right plot). There was also the expected main effect of old/new stimuli on PD ($F[1,39] = 65.89, p < 0.01, rICC = 0.79$), with larger PD responses observed to old stimuli ($M = 0.64, SD = 0.70$) than to new ($M = 0.27, SD = 0.83$), which was not modulated by age (Fig. 2A, left column). Interestingly, we observed a negative emotionality \times old/new interaction ($F[1,39] = 4.21, p < 0.05, rICC = 0.31$) with negative stimuli eliciting more pronounced PD responses, in particular, for new stimuli during recognition tests (cf. Fig. 2A, right column). There was no main effect of recognition delay (early or delayed tests), but a trend for an interaction of older adults showing less differentiation of negative and neutral stimuli in their PD responses in particular on delayed tests ($F[1,39] = 3.27, p = 0.08, ICC = 0.28$). All effects were robust to excluding error trials, except for the trend of older adults showing less differentiation of negative and neutral stimuli on the delayed test. This suggests that this somewhat weaker effect might be more sensitive to a reduction in trial numbers due to the exclusion of incorrect trials. Finally, negative and neutral stimuli on the encoding task showed an effect of negative emotionality similar to the new stimuli on the recognition tests (Supplementary Material and Supplementary Fig. 1).

The second 4-way, repeated measures ANOVA examined the interaction between the old/new effect and the certainty of the old/new response as indicated on a rating scale (separated into high and low certainty trials, cf. Fig. 2B) across the 2 recognition tests and age groups. Again, there was a main effect of recognition ($F[1,39] = 16.92, p < 0.05, rICC = 0.55$), with old stimuli eliciting larger PD responses (Fig. 2B, thick lines). We also observed higher PD responses if participants were more certain in their old/new responses ($F[1,39] = 4.42, p < 0.05, rICC = 0.32$). Interestingly, there was also an old/new \times certainty interaction ($F[1,39] = 6.87, p < 0.05, rICC = 0.39$), with a higher PD response for old stimuli detected with high certainty (Fig. 2B, left column). This suggests that PD was modulated by the certainty with which stimuli could be classified as old and might therefore reflect a combination of task focus and the strength of the memory trace. There were no age interactions or influence of early/delayed recognition tests. Note, however, that certainty ratings were overall higher on the first test, a difference in PD between early and delayed tests might thus have been captured in the main effect of higher PD with higher certainty. Again, all effects were robust to excluding error trials.

3.3.3. GLM analyses of negative emotionality and recognition effects in pupil data

To examine differences in the time course of negative emotionality and recognition effects, we used GLM analyses which allowed to test for the time course of the effects while controlling for interindividual and age differences in the intercepts of PD responses. As outlined in the Methods section, analyses focused on the old/new and negative/neutral effects, while controlling for interaction effects as evident in repeated measures analyses detailed above. Furthermore, group-level GLMs tested for differences between age groups in these trial-wise GLM effects. Also, interindividual differences of the trial-wise old/new or negative/neutral effects were predicted by interindividual differences in behavioral variables of interest to further validate the cognitive correlates of effects observed in PD (e.g., is there a larger PD recognition effect in individuals with better memory performance?).

3.3.3.1. *Effect of negative emotionality on PD.* As can be seen in Fig. 3A, there is a clear positive effect of negative emotionality for both age groups, indicating that PD responses were larger for emotional than neutral stimuli, with the peak dilation occurring at around 1.46 seconds (cf. Fig. 3E). As expected from the repeated MANOVA results, this effect was slightly larger in younger adults. Furthermore, when emotional RTs were added as a behavioral variable at the individual level, we observed a modulation of the increase in PD with emotional capture as evident in prolonged reaction times to negative stimuli (Fig. 3C). Specifically, those older adults who showed a stronger modulation of PD with negative emotional stimuli show a greater slowing of RTs to negative stimuli (younger adults: $r = -0.36, p = 0.11$, older adults: $r = 0.63, p < 0.05$, age difference in correlation coefficients, $z = -3.09, p < 0.05$). Interindividual differences in neuromodulation can be expressed in larger interindividual differences in cognitive performance in a population which expresses reduced levels of neuromodulation (Hämmerer et al., 2013; Nagel et al., 2008). This has been attributed to a nonlinear, u-shaped association between levels of neuromodulation and cognitive functions which would result in increasingly large effects on cognition as neuromodulation recedes from higher to medium levels (Lindenberger, 2008). Given the weaker PD response to emotional stimuli observed in older adults, one might speculate whether the stronger relationship between negative emotionality and RTs in older adults is indicative of an

increased relevance of altered emotional reactivity to negative events in older adults.

3.3.3.2. Effect of recognition on PD. There is also a clear reliable effect of old stimuli eliciting larger PD in both age groups as evident in Fig. 3B, with the peak dilation occurring at around 1.84 seconds (cf. Fig. 3E). When memory accuracy was added as an individual-level variable, we observed that the recognition PD effect was largest in individuals with higher memory accuracy (Fig. 3D). This indicates that individuals with larger PD response to old stimuli are also more likely to correctly classify those stimuli as old (yas: $r = 0.19, p = 0.39$, oas: $r = 0.41, p = 0.08$, no reliable age difference in correlation coefficients, correlation collapsed across younger and older adults' z-scored data $r = 0.31, p = 0.05$). Finally, as can be seen in Fig. 3E, the maximal peak of the negative emotionality effect was reliably earlier than the maximal peak of the recognition effect ($Z = -2.58, p < 0.05$), suggesting separable processes contributing to PD. All effects were robust to including memory errors as a separate logistic regressor (Kafkas and Montaldi, 2015).

3.3.4. Subsequent memory effects

We found no evidence for a difference in phasic PD during the encoding task for later remembered versus later forgotten stimuli ($F[1,32] = 0.91, p = 0.35$, cf. Supplementary Fig. 2). It has been argued that subsequent memory effects during incidental encoding tasks should be evident in changes in tonic PD that precede stimulus presentation and last throughout the trial as compared with phasic PD responses to stimulus properties. This is because memory is held to be guided by local fluctuations in PD rather than phasic PD responses to stimulus properties for incidental encoding. An examination of tonic PD at encoding showed greater tonic PD for later forgotten stimuli (Supplementary Fig. 3, $F[1,32] = 5.80, p < 0.05, rICC = 0.39$), an effect that was greater for neutral stimuli (interaction negative emotionality \times subsequent memory $F[1,32] = 5.62, p < 0.05, rICC = 0.39$). Note this effect was robust to lowering trial numbers in the remembered condition to a level present for non-remembered stimuli and hence cannot be attributed to a higher likelihood for more extreme values in the later forgotten category.

4. Discussion

We present the first study, to our knowledge, investigating age-related differences in PD in an emotional memory task with negative events. Our aim was to assess age-related differences in processes attributed to NA, namely arousal to negative stimuli, recognition memory, and encoding (subsequent memory).

We found a reliable increase in PD to negative compared with neutral stimuli in both age groups, with the older adults showing a smaller PD response to negative stimuli (Figs. 2A and 3A). An increased PD response to negative stimuli is a consistent effect in the literature (Bradley and Lang, 2015; Bradley et al., 2008; Partala and Surakka, 2003; van Stegeren, 2008) and thought to reflect phasic bottom-up influences on the LC-NA system elicited by salient stimulus properties (Sara and Bouret, 2012). Furthermore, we add to this literature by showing that an increase in PD to negative stimuli is especially pronounced in older adults who are more susceptible to emotional stimulation, as evident in longer RTs to negative stimuli. The slowing in response to the negative stimuli in our task is in line with the idea of an “emotional capture” effect, whereby the task-irrelevant emotional event diverts attention away from the relevant task (Hodsoll et al., 2011) of in-out classification. Finally, in further support that the emotional PD effect observed was driven by the negative emotional impact of the presented pictures, we observed an increased effect of stimulus emotionality on PD for novel pictures in particular (Bradley and Lang, 2015).

It should be noted that the observed reduced PD in older adults to negative emotional stimuli cannot be necessarily assumed to generalize to positive stimuli. In contrast to their reduced reactions to negative events, previous studies demonstrated that older adults show generally slightly increased memory for positive events or increased startle responses to positive pictures, as compared with younger adults (Feng et al., 2011; Leigland et al., 2004; Mather, 2016). This “positivity effect” in older adults has been suggested to reflect an adaptive emotion regulation strategy in old age which emphasizes positive events and dampens the impact of negative events (Mather and Carstensen, 2005). One might thus rather expect to see a slight increase in PD to positive stimuli in older adults.

Similarly, the current state of research does not allow to judge to what extent a reduction in PD to negative events is due to age differences in NA or age differences in emotional regulation. Studies in humans, rats, as well as primates suggest that a reduction of NA during aging can be relevant for altered cognitive functions (Arnsten and Goldman-Rakic, 1985a; Clewett et al., 2016; Mann, 1983), including memory for negative emotional events (Luo et al., 2015). On the other hand, imaging studies which show increased prefrontal and decreased amygdala activation during negative events in older adults suggest that older adults actively down-regulate their arousal response to negative events (see Mather (2016) for a review). Of course, these 2 views do not have to be mutually exclusive. It is well conceivable that a tendency toward dampening negative experiences is met or even facilitated by a reduced initial arousal response to negative stimuli. However, answering this question conclusively requires measures of LC integrity and function during a concurrent assessment of control areas and ideally also a pharmacologic manipulation of noradrenergic levels in younger and older adults when examining age differences in memory. Finally, valenced information which is not arousing can also lead to improved memory formation (Kensinger, 2004), suggesting multiple cognitive as well as physiological pathways via which valenced material can affect memory.

We observed larger PD responses to old stimuli compared with new during recognition tests (Heaver and Hutton, 2011; Otero et al., 2011; Vö et al., 2008), in both younger and older adults. Moreover, PD during recognition was larger in individuals with higher memory accuracy (Fig. 3D). This profile is supportive evidence for the idea that increased PD to old stimuli is an index of memory strength (Papesh et al., 2012). Our observation that higher certainty ratings modulated this PD effect, such that PD responses to old stimuli were enhanced the more certain the stimulus was classified as old (Fig. 2B), is further evidence in support of the memory strength account.

Our results therefore speak against the idea that an old-new PD effect is related to increased effort in memory retrieval (Beatty and Kahneman, 1966). We can only speculate how an old-new PD response may relate to the physiology of LC neurons. One parsimonious account is that the phasic PD response to old, but not to new stimuli is akin to consistently observed increased phasic responses of LC neurons to target stimuli in oddball tasks (Aston-Jones et al., 1994). This aspect of NA has been shown to be independent of stimulus properties and stimulus frequency and driven by a combination of task set focus and stimulus type (Aston-Jones and Cohen, 2005). Unlike noradrenergic responses to arousing events, these phasic LC responses are considered to reflect attentional top-down modulation of salient events, as determined by a given task set (Sara and Bouret, 2012). In a recognition test, as in ours, the task set might require looking for old stimuli, which would then become the focus of evaluation. Old stimuli on a recognition test could therefore be understood to function similarly to targets in oddball tasks. The fact that we see faster response times to old

compared with new stimuli, when classifying stimuli as old or new, might be seen as in line with a “targetness” interpretation. If PD responses are driven by task focus and response certainty, one would expect faster reactions to stimuli in line with the current task focus.

In a second set of analyses, we used GLM analyses to disentangle the time course of PD effects related to emotional arousal and recognition independent of individual and age differences in baseline PD. Here, emotional effects on PD emerged earlier than a PD recognition effect, a temporal dissociation that supports a bottom-up/top-down distinction in these 2 effects. Specifically, emotional arousal to negative events would seem to be a faster and more stimulus-driven process compared with a slower more top-down–driven old/new recognition effect. Moreover, we also observed specific, but inversely expressed, reaction time effects on these 2 different aspects of PD modulation. In the case of emotional arousal, we observed an ensuing slowing in reaction times indicative of increased emotional capture by stimulus properties. Instead, stronger recognition PD effects were followed by faster reaction times for old responses, suggesting an effect of task focus on old/new classifications. These 2 aspects of PD responses most likely reflect different processes attributed to NA, namely bottom-up emotional arousal and top-down “target detection” (of old stimuli) based on memory traces.

In support of evidence for a reduction in NA with aging, we found a reduced PD in older adults. Moreover, we observed a reduced emotional arousal PD effect in older adults to negative events while a recognition memory PD effect appeared comparable with that in younger adults. Subjective ratings of emotional involvement or memory certainty did not differ between age groups and thus did not account for observed age differences in these effects. We can only speculate as to why we find different age effects for negative emotionality and recognition-related PD effects. Under an assumed differentiation of bottom-up–driven arousal PD effects and top-down–driven recognition PD effects, it is conceivable that older adults compensate more easily for a lower baseline level of LC responses for the top-down–driven effects than stimulus-driven arousal effect. We note here that a stronger emphasis of task set in easier task conditions is a well-known finding in older adults (Hämmerer et al., 2014).

We observed an expected decrease in memory performance in older adults on a delayed compared with immediate recognition test, confirming a well-established long-term memory deficit in older adults (Nyberg et al., 2012). Although we observed an altogether reduced PD modulation related to emotional arousal in older adults, and a trend for better memory for negative stimuli in younger adults on high certainty recognition trials, we did not observe a decrease in long-term memory in older adults for negative stimuli or a link between PD to negative stimuli and emotional memory. This might have been due to the fact that we used a comparatively easy memory paradigm, which could have prevented a stronger modulatory effect on memory performance. Indeed, age differences in memory for negative emotional events were larger in a task that put more emphasis on more difficult memory retrieval by asking participants to recall rather than recognize stimuli (Charles et al., 2003). However, given we were interested in assessing PD recordings during the memory tests, which required the use of a chinrest, a recall test could not be included easily in our task.

The present study did not explicitly address to what extent age differences in memory performance may also be related to time of day effects in cognitive capacities as well as changes in circadian patterns in NA. Both, encoding in the morning and delayed recognition in the afternoon should provide more conservative estimates of performance as both older as well as younger adults are not

tested on their peak time of day (Hasher et al., 2005; May et al., 1993). However, older adults can be comparatively more affected by having to perform during nonoptimal test times. It is thus possible that age differences, in particular, in memory performance on the delayed test might be in part due to effects of test time. Time of day effects in older adults have been shown to manifest particularly in increased false alarms during nonoptimal test times (May et al., 1993). We did not observe a stronger age effect on false alarms for the delayed test. However, our study sample might have been too small to capture the effect reliably. Future studies should include short benchmark tests at the respective test time points to assess the time of day effects in cases where test times cannot be optimally adjusted for age comparative testing. In this way, performance differences due to test times can be assessed as covariates. Circadian patterns in NA in humans as well as age differences therein are still relatively unexplored. Diurnal peaks in NA levels have been observed in the afternoon as well as late morning, in CSF NA levels and plasma NA levels, respectively (Prinz et al., 1979; Wood et al., 1976). There is some evidence for elevated plasma NA levels in older adults (Prinz et al., 1979; Ziegler et al., 1976). However, it currently remains unclear how these changes may relate to recognition memory, although more generally, elevated NA in CSF, independent of age, has been shown to negatively correlate with cognition (Wang et al., 2013).

Finally, we did not observe a subsequent memory effect on phasic PD at encoding. The existing literature on subsequent memory effects on PD is sparse and provides a mixed picture (see Goldinger and Papesh (2012) for a review) where one view is that phasic PD effects are present on memory tasks with explicit instructions for encoding whereas incidental memory, as in our task, is better reflected in tonic PD differences during encoding (Kafkas and Montaldi, 2011; Papesh et al., 2012). Accordingly, phasic increases are thought to reflect the strength of an attentional focus or encoding effort in instructed conditions (Papesh et al., 2012). Whereas in the case of incidental memory, subsequent memory is assumed to be influenced by fluctuations in tonic PD preceding or concurrent to stimulus presentation. However, to complicate matters further, theories on the influence of tonic NA on cognitive performance offer contradicting predictions for incidental memory effects related to tonic PD levels. Some accounts associate increased tonic levels of noradrenaline with greater distractibility (Aston-Jones and Cohen, 2005), predicting poorer subsequent memory with high tonic PD levels during encoding. Accounts that associate increased levels of noradrenaline with increased neuronal gain, would predict poorer subsequent memory with lower tonic PD levels at encoding (Eldar et al., 2013). We observed higher tonic PD levels for later forgotten stimuli which support an assumption of greater participant distractibility during encoding of later forgotten stimuli. The effect was considerably weaker for negative stimuli, suggesting that on trials with greater stimulus capture, subsequent memory is less driven by temporal fluctuations in attentional states. A recent theory suggests that the effects of NA on incidental memory should be examined in a context of an interaction of attentional focus on the one hand and temporal modulations of tonic levels on the other hand (Mather et al., 2015; Sakaki et al., 2014). Future studies should address this assumption in more detail by introducing an additional modulation in attentional focus during stimulus encoding combined with PD measurements in the emotional memory task (Sakaki et al., 2014).

5. Conclusion

In summary, we found overall reduced PD responses in older adults as well as a reduced PD response reflecting emotional arousal to negative events. An intriguing possibility is that these reduced

PD responses in older adults indicate age-related LC-NA system degeneration. Further research should investigate if this PD effect is consistent across cognitive paradigms and can be altered by pharmacologic manipulation. Furthermore, we segregated emotional and cognitive processes reflected in PD and provide evidence for a link to dissociable bottom-up and top-down modulation of LC function, respectively. However, despite the existence of causal evidence for a link between PD and LC activity (Joshi et al., 2016), PD measures only provide very indirect physiologic window into NA during emotional memory for negative events. For instance, it is unclear whether the observed general decrease in PD and PD reactivity to altered luminance levels with age might be due to an altered muscular or neurochemical reactivity (Winn et al., 1994). Pharmacologic studies (Kroes et al., 2010; Strange and Dolan, 2004) are needed to firmly establish causal neuromodulatory influences on PD and to explore whether these effects are exclusively due to the LC-NA system or whether there are other neurotransmitters involved.

Disclosure statement

All authors report no actual or potential conflicts of interest.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.neurobiolaging.2017.06.021>.

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