Short Communication

Chronic stress and emotion: Differential effects on attentional processing and recognition memory

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ABSTRACT

Previous research indicates that acute stress around the time of learning facilitates attention and memory for emotionally salient information. Despite accumulating evidence for these acute stress effects, less is known about the role of chronic stress. In the present study, we therefore tested emotional and neutral scene processing and later recognition memory in female participants using hair cortisol concentrations as a biological marker for chronic stress. Event-related potentials recorded during picture viewing indicated enhanced late positive potentials (LPPs) for emotional, relative to neutral contents. These brain potentials varied as a function of long-term hair cortisol levels: hair-cortisol levels were positively related to overall LPP amplitudes. Results from recognition memory testing one week after encoding revealed better memory for emotional relative to neutral scenes. Hair-cortisol levels, however, were related to poorer memory accuracy. Taken together, our results indicate that chronic stress enhanced attentional processing during encoding of new stimuli and impaired later recognition memory. Results are discussed with regard to putatively opposite effects of chronic stress on certain brain regions (e.g., amygdala and hippocampus).

1. Introduction

Stress effects on attention and memory vary depending on stress intensity, duration and timing (Schwabe, 2017). For example, it is well-known that emotionally arousing events are preferentially processed and better remembered than neutral ones, and that acute stress even strengthens this effect (Weymar et al., 2012; Wirkner et al., 2017). Following the neuro-modulation hypothesis (McGaugh, 2015), this emotional memory enhancement is due to an interplay of noradrenergic and glucocorticoid (cortisol in humans) action during emotionally arousing experiences, involving the amygdala and the hippocampus (Schwabe, 2017). It has been suggested that acute stress especially triggers the amplifying role of the amygdala as the center of a widespread salience network (including the dorsal anterior cingulate cortex [ACC], the anterior insula [AI] and the locus coeruleus [LC]), thus promoting hypervigilance towards potentially threatening stimuli (Hermans et al., 2014). In line, acute stress induction shortly before encoding, relative to a control procedure, has been found to enhance the late positive potential (LPP) for unpleasant, relative to neutral pictures (Weymar et al., 2012). The LPP is an event-related potential (ERP) marker for motivated attention (Cuthbert et al., 2000) and, among other cortical and subcortical regions, correlated to amygdala activity (Sabatinelli et al., 2013). In addition, memory for emotional scenes is also enhanced following acute stress around the time of encoding (Weymar et al., 2012; Wirkner et al., 2013).

In contrast to acute stress, chronic stress has been linked to amygdala hyper-excitability towards new stimuli, but detrimental effects on memory in rats, paralleled by dendritic atrophy and reduced neurogenesis in the hippocampus as neural substrate for these impairments (Rosenkranz et al., 2010; McEwen, 2016). In humans, however, chronic stress effects on cognition are less well studied (Lupien et al., 2018).

To examine the impact of chronic stress on emotion processing and long-term memory in healthy humans, we used a well-established emotional picture viewing and recognition memory paradigm (Weymar et al., 2009; Wirkner et al., 2017). As a biological marker of chronic stress, we assessed hair cortisol concentrations for the last 6 months (Steudte et al., 2013). Given that animal models suggest opposing effects of chronic stress on amygdala and hippocampus functioning, we expected high hair cortisol levels to be associated with enhanced affective stimulus processing, as indicated by the LPP, but negative...
associations with recognition memory performance (McEwen et al., 2016). Because acute stress primarily affected processing of emotionally arousing stimuli (Weymar et al., 2012; Wirkner et al., 2013), we assume that chronic stress influences should also be more pronounced for emotional, relative to neutral pictures.

2. Material and methods

2.1. Participants

Twenty healthy women (age, mean ± SD: 21.1 ± 2.5 years; hormonal contraceptive use: n = 11; right-handed: n = 18) participated in the study. Exclusion criteria were any current or chronic medical conditions, history of mental illness, and familiarity with the stimulus materials. Participants had normal or corrected-to-normal vision. All participants provided informed written consent for the study protocol approved by the Review Board of the Medical Faculty of the University of Greifswald and received financial compensation or course credit.

2.2. Procedure

First, hair samples were collected to determine retrospective cortisol levels (for procedure, see Steudte et al., 2013). After hair sampling, participants viewed 90 pictures (30 unpleasant, 30 pleasant, 30 neutral) on a 20" computer monitor (resolution: 1024 × 768 pixels, viewing distance: 1.5 m) in a dimly lit, sound-attenuated cabin (encoding session). Picture stimuli were taken from the International Affective Picture system (IAPS; Lang et al., 2008) and the Emotional Picture Set (EmoPics; Wessa et al., 2010), including for example, attack and mutilation (unpleasant), nature and objects (neutral) and erotic couples and adventure (pleasant) as semantic categories. Pictures were presented in pseudorandom order (excluding pictures of the same valence category on two consecutive trials) for 3 s with a random inter-stimulus interval of 2.5, 3 or 3.5 s, preceded by a 0.5 s fixation cross. During picture viewing, ERPs were recorded. One week following initial picture viewing, participants performed a surprise recognition memory test: 90 old pictures from the encoding session were presented randomly intermixed with 90 new pictures (30 unpleasant, 30 pleasant, 30 neutral; fixation cross: 0.5 s; picture duration: 3 s), and participants were instructed to indicate via button press whether each picture had been presented previously ("old") or not ("new"). Button location (left vs. right) was counterbalanced between participants (for comprehensive design and stimuli description, please see Wirkner et al., 2017).

2.3. ERP recording

Electroencephalography (EEG) signals were recorded continuously from 257 sensors using an Electrical Geodesic system (EGI, Eugene, OR) and digitized at a rate of 250 Hz, using the vertex sensor (Cz) as recording reference. Scalp impedance for each sensor was kept below 30 kΩ (Cz: 5 kΩ). All channels were band-pass filtered online from 0.1 to 100 Hz. Offline reduction was performed using ElectroMagnetoEncephalographySoftware (Peyk, DeCesarei, and Junghöfer, 2011) and included low-pass filtering at 40 Hz, artifact detection, sensor interpolation, baseline correction, and conversion to the average reference. Artifacts were detected via computerized algorithms (based on absolute maximum, standard deviation and first derivative) from the raw EEG epochs to reject contaminated channels and trials. Following conversion to the average reference, spherical interpolation of all remaining sensors was used to artifact-eliminate contaminated sensors for each trial (Junghöfer et al., 2006; Wirkner et al., 2017). The average number of ERP trials included in the analysis based on artifact detection were mean ± SD: 21.1 ± 4.0 (70.2%) for unpleasant, mean ± SD: 20.6 ± 5.0 (68.2%) for neutral and mean ± SD: 20.9 ± 5.3 (69.8%) for pleasant pictures. No participant had to be excluded due to an insufficient number of ERP trials or outlying ERP values.

2.4. Data analyses

All analyses were performed using SPSS 22.0 (IBM, Armonk, NY, USA). For effects involving repeated measures, the Greenhouse-Geisser procedure was used to correct violations of sphericity. For post-hoc single comparisons Bonferroni-corrected p-values are reported.

2.4.1. ERP analysis: Late positive potential (LPP)

Stimulus-synchronized epochs were extracted from 0.1 s before to 1.2 s after picture onset and baseline-corrected (0.1 s prior to stimulus onset). Averaged ERP signals were computed for each sensor, participant, and each picture category (unpleasant, neutral, pleasant). The LPP was analyzed over centro-parietal recording sites (cluster of EGI sensors 9, 44, 45, 53, 80, 51, 89, 90, 100, 101, 129, 130, 131, 132, 144, 185, 186, 257) in the time interval from 400 to 900 ms, where the LPP amplitude was largest. An ANOVA was conducted on LPP using emotion (unpleasant, neutral, pleasant) as within-subject factor.

2.4.2. Recognition memory performance

For each participant and valence category, hit rates (the probability that an old item is correctly classified as old), false alarm rates (FA; the probability that a new item is incorrectly classified as old), and the discrimination index Pr (memory accuracy; Pr = Hit − Fa) were calculated. For hit rates, FA rates and the discrimination index Pr, separate ANOVAs were conducted involving the within-subject factor emotion (unpleasant, neutral, pleasant).

2.4.3. Hair cortisol and correlation analysis

Hair samples were collected from the posterior scalp using scissors, following the standard instructions from Technische Universität Dresden (Dresden LabService GmbH; http://www.labservice-dresden.de) where samples were analyzed (immunoassay). Mean values of 6-months’ hair cortisol storage (1 cm hair length corresponds to approximately 1 month; Steudte et al., 2013) were not normally distributed in the present sample, thus data were log-transformed for further analyses. To investigate the influence of chronic stress on the LPP and recognition memory performance, hair cortisol was introduced as a covariate (HCC) into the ANOVAs described above. Then, Pearson correlations were computed between log-transformed cortisol concentrations and LPPs and between cortisol and memory performance for unpleasant, neutral, and pleasant pictures.

3. Results

3.1. Late positive potential and long-term stress

As expected, the LPP was modulated by emotion (F2,36 = 21.01; p < .001; η2 = .525), showing higher amplitudes for unpleasant (mean ± SD: 4.06 μV ± 1.73; p < .001) and pleasant (mean ± SD: 3.05 μV ± 1.70) relative to neutral pictures (mean ± SD: 1.55 μV ± 1.73; p = .002; Fig. 1).

A mean cortisol level of 24.83 pg/mg (± SD ± 20.2; log transformed mean ± SD: 2.96 ± .70) was found in the 6 cm hair samples. Introducing hair cortisol as a covariate showed a significant influence on ERPs (F1,18 = 7.77, p = .012 η2 = .302). Higher hair cortisol levels were associated with larger LPP amplitudes (r = .549, p = .012). Although the interaction term was statistically non-significant (Emotion × HCC: F2,36 = 1.42, p = .257, η2 = .073), post-hoc analyses (Bonferroni correction 0.05/3 = 0.016) showed that this relationship was particularly driven by unpleasant (r = .563, p = .010) and neutral (r = .545, p = .013) pictures (pleasant: r = .224, p = .343).1

1 As expected, there was a wash-out effect in hair cortisol from the 3 cm-
3.2. Recognition memory performance

A significant main effect of emotion ($F_{2,38} = 15.81; \ p < .001; \ \eta^2 = .454$) indicated better memory discrimination ($Pr$) for unpleasant (mean ± SD: 0.68 ± .17) than for neutral (mean ± SD: 0.50 ± .14; $p < .001$) and pleasant pictures (mean ± SD: 0.54 ± .18; $p = .001$; Fig. 2). This result pattern was also present in hit rates ($F_{2,38} = 23.57, \ p < .001; \ \eta^2 = .554$; unpleasant > neutral, $p < .001$; unpleasant > pleasant, $p = .001$). False alarm rates were not modulated by emotional content ($F_{2,38} = 1.87, \ p = .171; \ \eta^2 = .089$).

High hair cortisol levels were associated with worse memory discrimination ($F_{1,18} = 5.58, \ p = .030; \ \eta^2 = .237$; see Fig. 2). Again, no interaction was found ($F_{1,18} < 1, \ p = .828, \ \eta^2 = .044$). Post-hoc trends (Bonferroni correction 0.05/3 = 0.016), however, adumbrate that this effect was driven by emotional pictures ($r = -.494, \ p = .027$; see Supplement 1 for all bivariate correlations). Further analyses showed that participants who had higher LPP amplitudes during encoding also showed higher false alarm rates ($r = .573, \ p = .008$), resulting in worse memory discrimination ($Pr$ ($r = -.486, \ p = .030$). When controlling for HCC, the negative association between LPP and $Pr$ decreased, but still remained statistically significant (partial $r = -.499, \ p = .030$).

4. Discussion

In the present study, we examined the influence of long-term systemic cortisol levels, as indicator of chronic stress, on emotional and neutral picture processing and later recognition memory. In line with previous research, emotional pictures evoked enhanced LPPs, suggesting increased motivated attention (Schupp et al., 2006; Weymar et al., 2012). High levels of hair cortisol, indicating stronger chronic stress exposure, were associated with larger LPP amplitudes (pronounced for unpleasant and neutral pictures). This parallels previous ERP data showing increased LPP amplitudes under acute stress in healthy participants, especially for unpleasant but also for neutral pictures (Weymar et al., 2012). Larger LPP magnitudes provide an ERP correlate for enhanced activity in the amygdala and the visual cortex, ACC and AI, as revealed by fMRI, indicating preferential stimulus processing (Liu et al., 2012; Sabatinelli et al., 2013). Research on the LPP shows that this ERP component is sensitive for motivational relevance and stimulus arousal, not necessarily depending on stimulus valence, but on stimulus significance (Cuthbert et al., 2000; Schupp et al., 2014). Thus, the present findings seem to suggest that long-term stress enhances sustained processing of significant visual stimuli.

Prior functional imaging findings indicate that acute stress is associated with increased activation of the amygdala and primary visual areas during processing of emotional stimuli, compared with the non-stress condition, suggesting that processing of significant stimuli in the environment is facilitated after acute stress (van Marle, Hermans, Qin, and Fernández, 2009; see also Henckens et al., 2009). Furthermore, increased co-activations between the amygdala and regions of the attentional network (e.g., dorsal ACC and anterior insula) are observed in a resting state without experimental task after continuously watching highly stressful (vs. emotionally neutral) film clips (van Marle, Hermans, Qin, and Fernández, 2010). These results suggest that acute stress sensitizes the organism for prioritized sensory processing of (threat-related) potentially significant information. However, in contrast to acute stress induction, which has been found to especially enhance processing of high arousing, relative to neutral stimuli (Hermans et al., 2014; Weymar et al., 2012), we observed that chronic stress (reflected by higher cortisol levels) enhanced processing for both emotional and neutral pictures, as indicated by an overall increase in

(footnote continued) proximal (mean: 27.02 pg/mg) to the 3 cm-distal (mean: 22.63 pg/mg; $p = .017$) hair segment. However, correlations with hair cortisol concentration were not larger in the proximal compared to the distal scalp segment for LPP ($z = -.45, \ p = .316$, one-tailed) and memory discrimination ($z = -.852, \ p = .197$, one-tailed).
LPP magnitudes. Given that LPP magnitudes are related to activity in the amygdala, the visual cortex and other regions of the attentional network (Sabatinelli et al., 2013), the current findings may indicate that long-term stress produces a hyper-responsiveness of these areas towards new stimuli, irrespective of stimulus arousal.

The second main finding of the present study was a negative relation between hair cortisol levels and memory performance. The present human data support recent animal models pointing to differential effects of chronically elevated glucocorticoid levels on amygdala and hippocampus functioning (Herman, 2013). On the one hand, under chronic stress, dendritic hypertrophy in the amygdala was observed in rodents, leading to the aforementioned hyper-responsiveness towards new stimuli (Herman, 2013; McEwen et al., 2016). On the other hand, chronic stress induced dendritic atrophy and reduced neurogenesis in the hippocampus (McEwen et al., 2016), which was associated with impaired memory performance. In line with these findings and contrary to the emotional memory-enhancement following acute stress during encoding (Weymar et al., 2012; Wirkner et al., 2013), poorer memory discrimination, irrespective of emotion, was observed with increasing hair cortisol levels in the present study. Our results contrast with the findings from Weymar et al. (2012), who observed larger LPP magnitudes during unpleasant picture viewing following acute stress to be positively related to later (free recall) memory performance. This divergence further suggests differential effects of acute and chronic stress on the influence of attention on memory.

Enhanced emotional memory crucially depends on the initial interplay of rapid noradrenaline and (non-genomic) glucocorticoid actions during encoding (McGaugh, 2015; Schwabe, 2017). Then, via delayed (genomic) glucocorticoid-receptor (GR)-dependent effects, further synaptic plasticity in hippocampal neurons is suppressed, preventing consolidation of the stress-related information from interfering new input (Schwabe, 2017). Changes in this fine-tuned hormonal interplay following chronic stress, which, for example, causes decreased hippocampal GR expression (Herman, 2013), and neuro-degeneration might lead to impaired hippocampus-dependent memory consolidation. This parallels findings from clinical populations, showing that long-term elevated systemic cortisol seems to impair (emotional) memory consolidation (McEwen, 2016; Wirkner et al., 2017).

In the animal model, structural and functional changes in response to chronic stress have been observed in the prefrontal cortex (PFC), and related to impaired memory and executive functioning (McEwen et al., 2016). Likewise, in humans, chronic stress seems to alter PFC functioning, resulting in impaired inhibitory control over the amygdala, and structural PFC changes as well as amygdala hyper-reactivity have been described in depressed and anxious individuals (McEwen et al., 2016). Perhaps, amygdala hyper-reactivity, which might be indicated by larger LPP amplitudes (Liu et al., 2012; Sabatinelli et al., 2013), and PFC alterations, together with altered hippocampus functioning as a result of long-term stress exposure might have contributed to worse memory accuracy. Also, larger LPP amplitudes were associated with higher false positive rates, even after controlling for hair cortisol levels, suggesting a more complex contributing of brain mechanisms to the present findings.

It should to be noted that the present results need to be interpreted with caution, as the sample was rather small, and included only females, therefore additional research in this field overcoming these limitations is warranted. Moreover, to further understand the interplay between amygdala, PFC and hippocampus during emotional and neural picture processing and memory testing under the influence long-term stress, functional measures with a higher spatial resolution (fMRI), including a larger sample size and a wider spectrum of chronic stress exposure (e.g., involving clinical samples) are required.

To date, because of a high heterogeneity between study sample characteristics and varying analysis methods of hair cortisol concentration, the classification of hair cortisol levels is limited. However, hair cortisol levels in the present sample (24.83 pg/mg) seem to reflect moderate stress (e.g. 16.32–32.98 pg/mg in a comparable student sample with and without major life events, mean age = 22.1 years; Karlén et al., 2011). But, as values up to 83.1 pg/mg have been reported in middle-aged pain patients, and because of the lack of data for young healthy student samples, normative interpretation of the present hair cortisol levels has to be made with caution (Staufenbiel et al., 2013; Stalder et al., 2017). The present results suggest that future neuroimaging research should include hair cortisol as an easy-to-use measure in order to gain a broader understanding of the complex influences of chronic stress exposure on emotion processing and memory.

5. Conclusions

Overall, the present data support the assumption that chronic stress exposure in healthy individuals is related to enhanced picture processing, possibly due to amygdala hyper-responsiveness, and impaired memory accuracy, which may be related to hippocampal and prefrontal dysfunction as possible underlying neural mechanisms. This pattern associated with elevated systemic cortisol levels parallels findings from clinical populations and thus might provide a risk factor for the development of stress-related mental disorders (e.g., mood and anxiety disorders).

Declarations of interest

None.

CRediT authorship contribution statement

Janine Wirkner: Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Writing - original draft, Visualization.
Carlos Ventura-Bort: Writing - review & editing, Visualization.
Lars Schwabe: Writing - review & editing, Supervision. Alfons O. Hamm: Conceptualization, Resources, Writing-review & editing, Supervision.
Mathias Weymar: Conceptualization, Methodology, Writing-original draft, Supervision.

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Appendix A. Supplementary data

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References


