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Stress-related deficits of older adults' spatial working memory: an EEG investigation of occipital alpha and frontal-midline theta activities

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Abstract

Studies highlight cumulative life stress as a significant predictor of accelerated cognitive aging. This study paired electrophysiological with behavioral measures to explore how cumulative stress affects attentional and maintenance processes underpinning working memory retention. We collected electroencephalographic recordings from 60 individuals (30 older, 30 younger) reporting high or low levels of cumulative stress during the performance of a spatial Sternberg task. We measured mid-occipital alpha (8–12 Hz) and frontal-midline theta (4–6 Hz) as indicators of attentional and maintenance processes. Older, high-stress participants' behavioral performance lay significantly below than that of younger adults and low-stress older individuals. Impaired task performance coincided with reduced event-related synchronization in alpha and theta frequency ranges during memory maintenance. Electrophysiological findings suggest that older adults' reduced performance results from a stress-related impact on their ability to retain a stimulus in working memory and inhibit extraneous information from interfering with maintenance. Our results demonstrate the wide-ranging impact of cumulative stress on cognitive health and provide insight into the functional mechanisms disrupted by its influence.

Keywords

Alpha; Cognitive aging; Cumulative stress; EEG; Theta

1. Introduction

Deficits of cognitive functioning are an established cooccurrence of aging (Colino et al., 2017; Hahn et al., 2011; Salthouse and Babcock, 1991; Vasquez et al., 2014). However, age-related cognitive decline is not uniform as several biological and environmental factors have been shown to influence its trajectory. These range from genetic makeup (Bis et al., 2012;

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Stessman et al., 2005) to certain lifestyle choices such as physical activity and dietary intake (Chang and Etnier, 2009; Tedesco et al., 2000). A further determining factor highlighted by past work is the amount of stressful experiences individuals encounter during their lifetime. The impact of stress on cognitive aging has only recently gained scientific interest. However, since then, several studies have demonstrated that cumulative life stress has a significant impact on cognitive integrity in old age (Dickinson et al., 2011; Munoz et al., 2015; Pesonen et al., 2013). This is not surprising as prolonged exposure to the stress hormone cortisol (glucocorticoids) results in pronounced oxidative damage to areas of the hippocampus and neocortex (Ohl et al., 2000; Shao et al., 2015), brain structures integral for intact executive functioning and memory performance. Stress-induced hippocampal damage has been attributed to glucocorticoids causing a prolonged reduction of glucose reuptake into hippocampal cells (Sapolsky and Meaney, 1986), which results in dendritic atrophy and an inhibition of neurogenesis. Frontal damage is thought to be sustained by an increased number of micro lesions produced by stress-induced hypertonic strain on arteries and veins (Rabbitt, 2005).

Correspondingly, our own work comparing older and younger participant groups with high and low levels of cumulative stress demonstrates stress- and age-related behavioral deficits in the realms of inhibitory control and working memory (WM) (Marshall et al., 2015, 2016a). For WM, we demonstrate that behavioral shortcomings among older high-stress adults coincide with aberrant patterns in the alpha (8–12 Hz) and theta (4–6 Hz) frequency ranges. Specifically, studying WM with a standard version of the Sternberg paradigm (Sternberg, 1966) revealed significantly reduced alpha event-related activity across the parieto-occipital scalp regions of older high-stress adults during periods of memory maintenance (Marshall et al., 2015), highlighting that stress may impact on older adults' ability to successfully inhibit task irrelevant brain regions. Our work thus suggests that, among older adults, cumulative stress has a detrimental impact on oscillatory processes contributing to the successful retention of stimulus material. Findings to this effect highlight the efficacy of pairing behavioral with neurophysiological markers of cognitive functions as the latter provide an insight into the cognitive mechanisms affected by lifetime stress exposure. We extended this work by introducing a spatial component to the WM process by means of an object location memory task (Reagh et al., 2014). This revealed a global change of theta activity during the recall of stimulus material, which was specific to older adults with high amounts of lifetime stress (Marshall et al., 2016b). However, this spatial paradigm did not afford the opportunity to investigate theta activity during WM maintenance. As our past work shows that cumulative stress compromises the maintenance period, this constitutes a necessary extension to investigating the effects of stress on spatial WM. In the present study, we thus explored stress- and age-related changes to the alpha and theta bands during encoding and maintenance periods of a spatial Sternberg paradigm. In addition to extending our work, this also afforded the opportunity to replicate the observed effect of stress on cognitive aging. The impact of stress on cognitive integrity is a recent discovery. Therefore, it does not yet have a large reference body. Given the replication crisis for psychological studies and the crucial impact of these findings for health and well-being, it is imperative to provide sound replications of this effect.

The paradigm used in this study was developed by Lenartowicz et al. (2014) who demonstrated that it successfully captures task-related changes in occipital alpha and frontal-midline theta (FM θ) activities. We measured electroencephalographic (EEG) neural responses to this task in a sample of older and younger individuals who reported varying degrees of stressful life encounters. We analyzed EEG signals using a combination of highly controlled, permutation-based, mass univariate analyses and time-frequency analysis to focus on mid-occipital alpha and FM θ as established correlates of attention/inhibition and memory maintenance, respectively. Based on our foregone work, we predict that members of the older age, high-stress group will show significantly reduced alpha and theta event-related activity relative to both younger and older low-stress group members. We expect this effect to manifest in encoding and maintenance phases of our task. In the encoding phase, we expect reduced event-related desynchronization of the alpha frequency range. In the maintenance phase, we predict reduced event-related synchronization of the alpha and theta frequencies among older adults with high levels of lifetime stress.

2. Materials and method

2.1. Participants

Thirty young adult participants (14 females; mean age = 22.5, standard deviation [SD] = 3.18; range = 18–30 years) were recruited from the University of Essex student population via institutional e-mail advertising. A second group of 30 older participants (18 females; mean age = 68.73, SD = 4.65; range = 61–79 years) were recruited from regional clubs and societies and via advertisements placed in local newsletters. Age ranges (18–30 younger; 60–80 older adults) were specified in the advertisement. They were chosen based on a reference body of work comparing cognitive effects between younger and older adults (Fandakova et al., 2014; Isingrini et al., 2015; Reuter-Lorenz et al., 2000) as well as our own previous studies observing robust electrophysiological differences between age groups from similar ranges (Marshall et al., 2015; Marshall et al., 2016a,b). Exclusion criteria specified during recruitment included major medical conditions (i.e., diabetes, heart disease), major neurological damage (i.e., stroke), and a current diagnosis of a mental or psychiatric disorder (dementia, depression, or anxiety disorder), as well as the use of psychoactive medication or a history of substance abuse. To ensure against undiagnosed cognitive pathologies, all older participants completed the mini-mental state examination for which all scored within the normal range (>24 marks). All participants provided written informed consent. The study was approved by the University of Essex Ethics Committee.

2.2. Stress and demographical measures

Demographics included participants' age, level of education, amount of cigarette and alcohol consumption, levels of physical activity, and whether they were currently suffering discomfort from a physical disability that might impact on their task performance. In addition, levels of trait and state anxiety were assessed using the State Trait Anxiety Inventory (Spielberger et al., 1968). We used the State Trait Anxiety Inventory to test for individuals with exceptionally high state or trait levels of anxiety as these may confound the effect of lifetime stress on cognitive performance. Scores on both subscales remained low and an established method to define and detect outliers (Tukey, 1977) did not find any

individuals who greatly deviated from the sample mean. In line with our previous work (Marshall and Cooper, 2017; Marshall et al., 2015, 2016a,b), we assessed the number of participants' stressful experiences using the Social Readjustment Rating Scale (Holmes and Rahe, 1967) for older and the Student Life Events Scale (Clements and Turpin, 1996) for younger adults. Both scales have been validated for respective student and adult population samples and have been shown to provide valid and reliable estimates of cumulative stress (Clements and Turpin, 1996; Gerst et al., 1978; McGrath and Burkhart, 1983). The choice for using different stress inventories for each age group has several reasons. First, older adults were on average 3 times the age of younger participants and thus likely to have experienced more stressful events relative to our young participant sample. Second, these stressful experiences had a high likelihood of being qualitatively different between both age groups. Thus, to assess prolonged stress exposure appropriate to each age group, different instruments had to be used for each age group. Chosen scales were selected based on an identical format to assess life experiences. Each consists of a brief, self-administered scale (43 and 36 items, respectively). Items are weighted according to magnitude so that "death of a spouse/parent" carries a high score of 100 while a mildly stressful incident such as "vacation with family or friends" has a low score of 16 (Student Life Events Scale) or 13 (Social Readjustment Rating Scale). Scores range from 0 to 1466 for the Social Readjustment Rating Scale and from 0 to 1849 for the Student Life Events Scale. Higher scores reflect high amounts of experienced stress for both scales. Both scales are commonly used to assess life events occurring in the past year. To assess the cumulative, lifetime impact of stressful events, we thus modified the instructions. Participants were asked to indicate which events they remembered occurring in their lifetime. We urged participants to be stringent in their assessment and to name only those events they could explicitly remember. Our previous work demonstrates that this modification does not result in ceiling effects for the number of events reported and produces lifetime stress scores that reliably predict variance in cognitive task performance (Marshall and Cooper, 2017; Marshall et al., 2015, 2016a,b). As in previous studies, scores on each scale were used to divide both age groups into high- and low-stress scorers. The divide was based on the median split of scores from the Social Readjustment Rating Scale for older adults (value: 628) and the Social Readjustment Rating Scale for younger adults (value: 574). No significant group differences in mini-mental state performance, age, gender, educational attainment, cigarette/alcohol consumption, or physical activity emerged between stress groups (see Table 1).

2.3. Procedure

To begin, each participant completed an eye-movement calibration session (Croft and Barry, 1998). EEG data gathered from this session were subsequently used to correct for electrical activity reflecting horizontal and radial eye movements and blinks. For the experimental task, we used a spatial version of the Sternberg WM paradigm (Sternberg, 1966) developed by Lenartowicz et al (2014). Participants saw a fixation cross for 0.5 seconds which was followed by an encoding display containing either 1, 3, 5, or 7 yellow circles whose location participants were instructed to remember. Circles were presented for 2 seconds after which a further fixation screen was presented for a 3-second maintenance period. Finally, a single green circle (probe) was presented and participants had to decide whether it was located at a position previously occupied by one of the yellow circles (match) or not (nonmatch). Left

and right arrow keys were allocated to match and nonmatch responses, respectively. The probe was presented for 3 seconds or until a response was registered from a participant. Trials were separated by a 2-second intertrial interval. Participants completed a training block of 8 trials (2 trials for each of the 4 circle displays) until their performance was greater than 50 % accuracy. Subsequently, they completed 8 blocks of 48 experimental trials. Trials were equally balanced between load and match/nonmatch response types. The order of types was randomized within each block.

2.4. Electrophysiological recording and data preparation

EEG was recorded from 64 electrodes placed within a soft cap according to the 10–10 method of electrode positioning. Recordings were referenced to a point midway between Cz and CPz. Impedances were lowered to below 10 k Ω in all electrodes before acquisition. EEG signals were recorded and analyzed using a Neuroscan Synamps2 system in conjunction with SCAN 4.5 software (Compumedics, Melbourne, Australia). Data were recorded at a sampling rate of 1000 Hz with a bandpass filter of 0.05–200 Hz. Acquired data were visually inspected and noisy data blocks, general artifacts, and bad electrodes were rejected. To minimize the impact of eye movements, principal components analysis was performed on the acquired eye-movement data to obtain components reflecting saccades and blinks. To carry out ocular artifact rejection, these components were subtracted from the experimental data trace (Vigário, 1997; Vigário et al., 2000). Data were rereferenced to a common average reference. Using the event-related band power transformation (SCAN 4.5 editing software), data underwent complex demodulation and concurrent filtering (zero phase shift, 24 dB roll off, envelope computed) into the theta (4–6 Hz) and alpha (8–12 Hz) frequency ranges. Event-related activity was calculated as a percentage change between the active period (time spent either maintaining or encoding the items) and the reference period (500 ms period before onset of encoding display) according to the following formula $[(\text{reference} - \text{test}) / \text{reference}] * 100$. According to this method (Pfurtscheller and Aranibar, 1977), positive values represent event-related desynchronization (ERD) of frequency bands while negative values indicate event-related synchronization (ERS). Epochs containing remaining artifacts were removed. This resulted in an average of 190 (SD = 14) epochs for younger adults and 188 (SD = 11) epochs for older adults and led to a minimal amount of 23 epochs per condition.

2.5. Statistical analysis

Statistical testing was carried out with analysis of variances and Bonferroni corrected t-tests on behavioral scores and averaged event-related oscillatory values. In addition, we conducted linear regression analysis for all models that produced a significant effect of stress between age groups. For the primary analysis, we treated experienced stress as a categorical variable and formed high- and low-stress groups based on the median split of individual scores. The regression analysis allowed us to treat stress as a continuous variable to ensure this median split approach did not exaggerate the true impact of stress on behavioral and oscillatory performance. For the behavioral analysis, all values were standardized. The formula (Z-scored hits—Z-scored false positives) was used to compute d' —a value representing the proportion of correct responses relative to the participants' false alarm rate. D' and reaction times acted as dependent variables to assess behavioral performance on the task. For the

analyses of our electrophysiological data, we adopted a 2-step approach. We began by identifying the topographical distribution and time course in which to analyze task- and group-related changes in the alpha and theta frequency range. Our previous work (Marshall et al., 2015, 2016a,b) highlights that high levels of cumulative stress exposure exacerbate electrophysiological effects associated with normal aging. We therefore identified neural phenomena that varied with a main effect of age using the following nonparametric approach: (1) F-values associated with the main effect of age were calculated at every electrode site for the topographical distribution and at every time point for the 2 seconds encoding and 3 seconds maintenance phase. (2) Condition-subject assignments were shuffled and statistics computed 1000 times, thereby providing a null distribution associated with each electrode site and time point. (3) The maximal F-value from each time point and electrode comparison was logged for each of the 1000 iterations resulting in a distribution of maximal values under the null hypothesis. (4) Original values were compared to this distribution and those falling into the 95th percentile or above ($\alpha = 0.05$) were deemed significant. Separate permutations were run for alpha desynchronization in the encoding period and for theta and alpha synchronization in the maintenance period. This nonparametric approach is gaining increasing acclaim within the neuroscientific community (Lage-Castellanos et al., 2010; Marshall and Cooper, 2017; Summerfield and Mangels, 2005; Summerfield et al., 2011) and carries a number of advantages specific to dealing with large data sets. The method provides exact statistics corrected for multiple comparisons in a manner equivalent to the “familywise error” gold standard applied in functional neuroimaging (Nichols and Holmes, 2002). Furthermore, a data-driven approach circumvents the issue of imposing a priori restrictions on the data which are often based on an ill-defined reference literature not specific to the exact effect under investigation. In addition, we adopted this approach as it mirrored the bottom-up, source-localization approach Lenartowicz et al (2014) used to define topographical distributions in their original investigation of this paradigm.

3. Results

3.1. Behavioral analyses

We analyzed accuracy (d') and reaction times within a 2 (age: older vs. younger) $\times$ 2 (stress: high vs. low) by 4 (load) mixed measures analysis of variance in which load acted as the within-subjects factor. Analysis of accuracy revealed a main effect of age ($F_{1,56} = 8.7$, $p = 0.004$) and load ($F_{3,168} = 52.7$, $p < 0.001$). The main effect of age indicated higher performance in younger (mean = 0.91) relative to older (mean = 0.86) participants. The main effect of load revealed a linear decrease of performance ($F_{1,56} = 195.77$, $p < 0.001$) that significantly differed between each load level ($p < 0.001$). Analysis further revealed a significant load $\times$ age interaction ($F_{3,168} = 9.16$, $p < 0.001$), which demonstrated that younger participants significantly outperformed older adults at high load levels (5 circles: $p < 0.001$; 7 circles: $p = 0.009$; see Fig.1), but not at low load levels.

Crucially, we also observed a significant age $\times$ stress interaction ($F_{1,56} = 6.58$, $p = 0.013$) that highlighted that older adults in the high-stress group (mean = 0.79) performed significantly worse than older adults in the low-stress group (mean = 0.87, $p < 0.001$) and

younger adults in the high-stress group (mean = 0.92, $p < 0.001$; see Fig. 2). No differences were observed between younger low-stress and younger high-stress participants ($p = 0.98$, see Fig. 2). To test whether we could reproduce the above interaction with stress score as a continuous variable, we ran a 2-step hierarchical regression. In the first step, we regressed age (coded as 1 older and -1 younger), and stress score on the d' score collapsed across load conditions. This produced a significant model ($F_{2,57} = 8.9$, $p = 0.004$), which accounted for 11% of the variance in performance. Including the interaction term age $\times$ stress in the second step accounted for an additional 9% of variance and constituted a significant change to the model ($F_{1,56} = 11.07$, $p < 0.001$). We explored this interaction with a simple slopes analysis (Preacher et al., 2006). This revealed that the addition of a stressful event reduced the performance of older adults to a significant degree ($t_{59} = 7.53$, $p = 0.001$) while causing no impact on performance among younger adults ($p = 0.41$). Results thus correspond to our primary analysis and highlight that our stress effects were not artifacts of our median split approach.

Analysis of reaction times revealed a main effect of age ($F_{1,56} = 7.3$, $p = 0.008$) demonstrating that older adults took significantly longer to respond (mean = 443 ms) than young adults (mean = 397 ms). No further main effects or interactions reached significance (all $p_s > 0.05$).

3.2. Electrophysiological analyses

3.2.1. Alpha during encoding—Within the alpha frequency range, we observed a prominent main effect of age at 300–800 ms of the encoding interval. This effect manifested over mid-occipital scalp regions (POz, PO3, PO2, O1, Oz, O2; Cohen's $\delta > 0.4$). In addition to the main effect of age, analysis of the mean oscillatory activity across this electrode pool revealed a significant load $\times$ age interaction ($F_{3,168} = 3.12$, $p = 0.028$). Bonferroni-corrected follow-up analysis of this interaction revealed that younger adults (mean = 16.3 μV) showed significantly higher levels of alpha ERD at the highest load condition relative to older adults (mean = 5.7 μV ; $p = 0.011$; see Fig. 3). To test for an association between alpha activity during encoding and behavioral scores, we correlated alpha ERD with d' (both averaged across load conditions). We observed no significant correlation ($\rho = 0.13$, $p = 0.43$).

3.2.2. Alpha during maintenance—We observed a strong main effect of age across the same electrode pool reported for the encoding interval (POz, PO3, PO2, O1, Oz, O2; Cohen's $\delta > 0.4$). This effect was most pronounced during 1100–2000 ms of the maintenance period. In addition to the main effect of age, analysis of this electrode pool revealed a main effect of load ($F_{3,168} = 88.89$, $p < 0.001$), which reflected a linear increase of alpha ERS ($F_{1,56} = 33.78$, $p < 0.001$), which was significant at each load transition ($p < 0.001$). Importantly, main effects were qualified by an age $\times$ stress interaction ($F_{1,56} = 4.53$, $p = 0.038$). Corrected follow-up comparisons highlighted that older adults in the high-stress group (mean = -9.92 μV) showed significantly reduced alpha ERS compared to older low-stress adults (mean = -21.62 μV , $p = 0.002$) and younger high-stress adults (mean = -37.55 μV , $p < 0.001$; see Fig. 4). No such differences were found among the younger participant stress groups ($p_s > 0.05$). To explore whether the reported stress $\times$ age interaction remained when treating stress as a continuous variable, we conducted a further regression analysis. In

the first step, we regressed age and stress on alpha ERS collapsed across load conditions. This produced a significant model ($F_{2,57} = 12.31, p < 0.001$) which accounted for 16% of the variance in alpha activity. In the second step, we added the interaction term. This accounted for an additional 7% of variance which constituted a significant extension to the model ($F_{1,56} = 7.54, p = 0.003$). Simple slopes analysis of the interaction revealed that the addition of a stressful life experience reduced alpha ERS significantly among older adults ($t_{59} = 8.77, p < 0.001$) while having no impact on younger adults ($p = 0.21$). Results thus equate the primary analysis in which stress is treated as a categorical variable. To test for an association between alpha activity during encoding and maintenance, we included a further step in the model. In the third step, we therefore added the percentage of alpha ERD during encoding (collapsed across load conditions) as an additional predictor. Inclusion of this variable accounted for a further 4% of variance which constituted a marginally significant change to the model ($F_{1,55} = 3.76, p = 0.053$). Importantly, age ($\beta = 0.29, p < 0.001$) as well as the interaction term age $\times$ stress ($\beta = 0.27, p = 0.002$) remained significant independent predictors despite controlling for previous encoding activity. This indicates that the stress by age effect relates directly to processes concerning the maintenance of items in WM and is not a carry-over effect from weakly encoded items in the previous phase. To explore whether alpha activity during the maintenance phase was associated with behavioral scores, we correlated alpha ERS with d' scores (averaged across load conditions). We observed a negative correlation which indicated that increased alpha synchronization coincided with higher accuracy on the task. However, this association fell outside of conventional significance levels ($\rho = -0.23, p = 0.058$).

3.2.3. Theta during maintenance—Within the theta range, we observed a significant main effect of age across the frontal midline (FP1, FPz, FP2, AF3, AF4, F1, Fz, F2; Cohen's $d > 0.45$). This effect was most pronounced at 900–1800 ms of the maintenance phase. Subsequent analysis revealed an additional main effect of load ($F_{3,168} = 18.03, p < 0.001$), which revealed a linear increase of theta ERS ($F_{1,56} = 27.81, p < 0.001$) at all load transitions ($p < 0.01$). Most importantly, we once more observed an age $\times$ stress interaction ($F_{1,56} = 6.83, p = 0.012$). Corrected follow-up comparisons revealed that high-stress older adults (mean = $-7.96 \mu V$) showed significantly reduced theta ERS compared to both older low-stress adults (mean = $-12.03 \mu V, p < 0.001$) and younger high-stress adults (mean = $-19.87 \mu V, p < 0.001$; see Fig. 5), while no differences were observed between younger high- and low-stress participant groups ($p = 1.73$) and between younger and older low-stress samples ($p = 0.87$). We conducted a further regression analysis to test whether our age $\times$ stress effect was manifest when treating stress as a continuous variable. Regressing age and stress score on theta ERS in the first step produced a significant model ($F_{2,57} = 13.27, p < 0.001$), which accounted for 14% of variance in theta activity. Adding the interaction term age $\times$ stress in the second step accounted for an additional 10% of variance which constituted a significant extension to the model ($F_{1,56} = 8.73, p = 0.001$). Simple slopes analysis revealed that the addition of a stressful event significantly reduced theta ERS among older adults ($t_{59} = 9.83, p < 0.001$) while causing no significant change among younger adults ($p = 0.17$). Exploring the association between theta activity and behavioral scores (d') found a significant correlation ($\rho = -0.38, p = 0.019$). This highlighted that increased theta

synchronization during the maintenance period coincided with increased performance on the memory task.

4. Discussion

We explored the effects of cumulative life stress on oscillatory processes known to contribute to the successful encoding and maintenance of stimuli. This allowed us to extend existing knowledge of the way in which stress impacts cognitive health in older age. Our results show reduced memory performance among older members of the high-stress group. Their performance lies significantly below the scores of older low-stress participants and both groups of young participants. Behavioral impairments of high-stress older participants coincided with reductions of alpha and theta event-related synchronization during the memory maintenance period. Combined, results suggest that the behavioral deficits manifesting after prolonged cumulative stress exposure are the result of a detriment to several subprocesses contributing to the successful retention of encoded items.

4.1. Behavioral performance

Performance scores revealed a significant main effect of age and load. This indicated that young participants obtained higher scores than older adults and that performance was generally higher for lower than for higher load levels. Crucially, older adults reporting high levels of cumulative stress performed significantly below older adults with low levels of stress and younger high-stress adults. Finding a stress-related performance detriment among older adults which does not manifest among younger high-stress participants suggests that the adverse effects of stress are not immediate but manifest over a long period of time. This corresponds to previous reports (Dickinson et al., 2011; Pesonen et al., 2013) as well as our own work (Marshall et al., 2015, 2016a,b) for which we report the same pattern of behavioral findings. For example, studying the behavioral performance of age and stress groups in an object location task revealed that older members of the high-stress group recalled significantly less original object locations than younger and low-stress older counterparts. Combined, this reoccurring data pattern constitutes evidence that the effect of stress exposure acts in a cumulative manner and only manifests during later periods of life.

4.2. Alpha during encoding

Compared to older, younger adults showed significantly higher levels of alpha desynchronization during periods of stimulus encoding. This difference was most pronounced for the highest stimulus load. Our statistical approach discovered alpha activity to be highest across mid-occipital regions. Desynchronization of the mid-occipital alpha rhythm in response to the visual encoding of stimuli is a well-documented occurrence (Vanni et al., 1997). As such, it has been suggested to reflect a visual gating mechanism in which attended information is passed to downstream areas while unattended information is blocked. Zumer et al (2014) reported that decreased occipital alpha power contralateral to an attended object predicted the functional magnetic resonance imaging blood oxygen level dependent response representing the attended object in ventral regions for object selection. Conversely, increased alpha power ipsilateral to attended objects predicted a decrease in the corresponding BOLD signal. The authors thereby highlight the role of alpha in enhancing

attended information while simultaneously suppressing distracting stimulus material during the encoding process. Results thus suggest that young participants are superior at selectively encoding relevant stimulus material. Furthermore, higher, more demanding load conditions elicit greater expenditure of this mechanism.

4.3. Alpha during maintenance

Oscillatory alpha patterns during stimulus maintenance revealed increased event-related synchronization in younger compared to older participants and for high-load compared to lowload conditions. Crucially, we also observed significantly reduced alpha ERS among high-stress older participants relative to older adults with low levels of cumulative stress and younger adults with high stress levels. Despite falling outside of conventional significance levels, a correlational analysis indicated that increased alpha synchronization coincided with enhanced memory performance. Akin to its role during encoding, alpha activity during stimulus maintenance has been implicated in attentional regulation and inhibitory mechanisms that facilitate successful memory retention (Klimesch, 2012). As such, higher levels of alpha synchronization during Sternberg maintenance periods have been attributed to the successful inhibition of brain regions unnecessary for ongoing stimulus maintenance (Klimesch, 2012), thereby reducing the intake of potentially distracting information (Sauseng et al., 2009). In line with this account, past work has linked increases of alpha power with successful Sternberg task performance (Jensen and Tesche, 2002). The reduced alpha synchronization displayed by older high-stress adults may therefore signify reduced capability to inhibit mid-occipital brain regions during the maintenance process. These regions are involved in the visual uptake and encoding of new information. Therefore, impaired capacity to regulate them may result in conflicting information detracting from ongoing memory retention. Our alpha findings could also be interpreted in terms of the active processing hypothesis. This theory suggests that age-related cognitive deficits arise from an inability of cortical neuronal assemblies to maintain an active state (Dringenberg, 2000). It is often used to account for the general slowing of the EEG, a phenomenon we have also observed among older adults with high levels of cumulative stress (Marshall and Cooper, 2017). Dringenberg suggested that a breakdown of active cortical circuits may arise from a cholinergic deficit coupled with lowered serotonergic and noradrenergic activities. Previous work has reported that a cholinergic agonist enhances cortical alpha activity and elevates performance on a visuospatial task (Bauer et al., 2012). Thus, our findings in the alpha range may also signal an impact of stress on cholinergic neurons in the basal forebrain, which are responsible for innervating cortical and subcortical brain regions integral for successful cognitive operations.

Importantly, we observed an effect of alpha ERS in the maintenance period after controlling for alpha ERD during encoding. Stimulus encoding and maintenance are highly related processes. As aging exerts an established effect on encoding speed (Jost et al., 2011), it was necessary to control for a potential influence on alpha ERS during the maintenance period. Including alpha ERD during encoding significantly enhanced the model, corresponding to previous reports emphasizing the relation between both processes (Woodward et al., 2006). However, our stress by age effect during encoding remained a significant predictor which highlights that our reported stress effect concerns cognitive processes relating to the

maintenance of items in spatial WM. This pattern of results mirrors an effect we discovered when comparing age and stress group performance on a standard Sternberg paradigm in which participants memorized strings of letters (Marshall et al., 2015). Here, we likewise reported reduced alpha ERS among members of the highstress older age group during maintenance. The replication of this effect in a memory task for object locations highlights that cumulative life stress affects spatial WM and general forms of WM. Thus, the damaging effects of cumulative stress extend to multiple domains of WM.

4.4. Theta during maintenance

FM θ activity during the maintenance interval revealed a similar pattern as the alpha frequency range. High-stress older adults showed significantly reduced levels of theta ERS compared to younger high-stress and older low-stress counterparts. Crucially, this difference did not manifest when comparing older and younger low-stress groups. In addition, higher levels of theta ERS significantly correlated with enhanced memory performance providing a direct implication of this oscillatory process for the successful upkeep of item locations in WM. Increases of FM θ during the performance of WM tasks have been reported extensively (Hsieh et al., 2011; Meltzer et al., 2007; Raghavachari et al., 2001; Scheeringa et al., 2009). For example, Jensen and Tesche (2002) observed increases of FM θ during the maintenance period of a digit Sternberg task that increased with the number of digits participants were required to retain. A parametric modulation of FM θ by memory load has been reported by a series of studies (Hsieh et al., 2011; Meltzer et al., 2007; Roberts et al., 2013; Scheeringa et al., 2009) and has led to the suggestion that FM θ may reflect medial pre-frontal WM networks operating in conjunction with the anterior cingulate cortex and hippocampus (Burgess and Gruzelier, 2000; Kubota et al., 2001). However, despite its apparent link to WM, the functional significance of FM θ is still unclear. An idea in line with the way FM θ manifests in the Sternberg task claims that FM θ is recruited to maintain temporal order information. Past work suggests that for highly demanding memory tasks, such as the Sternberg, participants may automatically maintain the temporal order of items to aid retention (Hsieh and Ranganath, 2014; Hsieh et al., 2011; Mangels, 1997). According to this account, cumulative stress may impact on older adults' recruitment of this strategy, thereby impacting on the effectiveness of their maintenance process. However, alternate accounts postulate that FM θ reflects the activation of neuronal assemblies corresponding to individual WM items (Lisman and Idiart, 1995; Lisman and Jensen, 2013). Interpreting reduced FM θ in line with this idea would speak to a reduced, possibly more diffuse, representation of encoded items among high-stress older adults, which may be harder to maintain. A final account implicates FM θ in the co-ordination of reactivating visual stimulus information represented in WM (Lee et al., 2005). We explored this possibility by correlating FM θ during the maintenance period with alpha ERD during encoding. Our results show no relationship between activity representing the visual intake and encoding of stimuli and their subsequent maintenance reflected in FM θ activity and thus speak against this interpretation.

4.5. Further directions, limitations, and conclusion

Our data highlight the wide-ranging impact cumulative stress exerts on older adults' cognitive health. It complements a body of work indicating that lifetime stress exposure produces performance deficits in the domains of memory, inhibition, executive control, and

pattern separation by demonstrating that performance decrements among older adults also manifest in spatial WM. Importantly, analyses of oscillatory patterns provides insight on the functional mechanisms disrupted by prolonged exposure to stressful encounters. Thus, findings in the alpha and theta frequency highlight that stress impacts on older adults' attentional/inhibitory capacity and specific maintenance processes relating either to the retention strategy or the representational strength of maintained items. Promising follow-ups to our study include exploring the effects of cumulative stress in a paradigm that contrasts the 2 accounts of FM θ . Exploring the impact of stress across conditions in which either item information or their temporal order needs to be maintained would shed light on the functional significance of FM θ and provide insight on the way stress affects WM maintenance. A further extension lies in applying this work to less able-bodied and active older populations. For this study, we recruited older participants from regional clubs and societies which resulted in a sample of socially and cognitively active individuals. To increase the findings' generalizability and external validity, an important further step would therefore lie in exploring the impact of stress on less active and socially engaged older individuals who for example live in residential housing and or care homes.

We would also like to note that we used a modified version of the stress item scales. Rather than indicating events of the past year, we requested that participants highlight stressful experiences across a much longer (life-) time period. We asked participants to be stringent concerning their recollections. However, it is plausible that despite the item list to trigger their memory, certain events may have been forgotten or misremembered. Furthermore, our measure of stress differed between age groups. To assess the severity of stress relative to longer and shorter life spans, we adopted scales tailored to younger and older adults. However, this means we are unable to fully rule out that the effects of stress between age groups are not in part driven by a difference in commensurability. Thus, direct comparisons between older and younger adults for the different levels of stress should be interpreted with caution. However, we also find a difference in performance and oscillatory activity between older adults with high and low levels of stress. This difference manifests between groups assessed with the same scale and indicates that stress has a tangible impact on older adults' cognitive performance which cannot be captured to the same extent among younger individuals.

Present findings demonstrate that higher numbers of stressful life events coincide with reduced spatial WM and alter oscillatory activity in frequencies tied to successful memory operations. Furthermore, we established a direct link between performance and theta activity in the maintenance phase of the task. This suggests that stress-incurred reduction of theta oscillations may act as one of the underlying cortical mechanisms by which stress hampers spatial memory. Findings extend a newly developing field, which suggests that the accrual of stressful experiences across the life span exerts an adverse effect on the cognitive operations of older adults. This highlights the importance of recognizing and minimizing exposure to stressful situations and environments from an early age onward to facilitate cognitive health in old age.

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References

- Bauer M, Kluge C, Bach D, Bradbury D, Heinze HJ, Dolan RJ, Driver J, 2012 Cholinergic enhancement of visual attention and neural oscillations in the human brain. *Curr. Biol* 22, 397–402. [PubMed: 22305751]
- Bis J, DeCarli C, Smith A, van der Lijn F, Crivello F, Fornage M, Debette S, 2012 Common variants at 12q14 and 12q24 are associated with hippocampal volume. *Nat. Genet* 44, 545–551. [PubMed: 22504421]
- Burgess AP, Gruzelier JH, 2000 Short duration power changes in the EEG during recognition memory for words and faces. *Psychophysiology* 37, 596–606. [PubMed: 11037036]
- Chang Y, Etnier J, 2009 Effects of an acute bout of localized resistance exercise on cognitive performance in middle-aged adults: a randomized controlled trial study. *Psychol. Sport Exerc* 10, 19–24.
- Clements K, Turpin G, 1996 The life events scale for students: validation for use with British samples. *Pers. Individ. Dif* 20, 747–751.
- Colino FL, Howse H, Norton A, Trska R, Pluta A, Luehr SJC, Handy TC, Krigolson OE, 2017 Older adults display diminished error processing and response in a continuous tracking task. *Psychophysiology* 54, 1706–1713. [PubMed: 28621460]
- Croft RJ, Barry RJ, 1998 EOG correction: a new aligned-artifact average solution. *Electroencephalogr. Clin. Neurophysiol* 107, 395–401. [PubMed: 9922084]
- Dickinson W, Potter G, Hybels C, McQuoid D, Steffens D, 2011 Change in stress and social support as predictors of cognitive decline in older adults with and without depression. *Int. J. Geriatr. Psychiatry* 26, 1267–1274. [PubMed: 21370277]
- Dringenberg HC, 2000 Alzheimer's disease: more than a 'cholinergic disorder'—evidence that cholinergic-monoaminergic interactions contribute to EEG slowing and dementia. *Behav. Brain Res* 115, 235–249. [PubMed: 11000423]
- Fandakova Y, Sander MC, Werkle-Bergner M, Shing YL, 2014 Age differences in short-term memory binding are related to working memory performance across the lifespan. *Psychol. Aging* 29, 140–149. [PubMed: 24660802]
- Gerst MS, Grant I, Yager J, Sweetwood H, 1978 The reliability of the social readjustment rating scale: moderate and long-term stability. *J. Psychosomatic Res* 22, 519–523.
- Hahn M, Wild-Wall N, Falkenstein M, 2011 Age-related differences in performance and stimulus processing in dual task situation. *Brain Res* 1414, 66–76. [PubMed: 21871612]
- Holmes TH, Rahe RH, 1967 The social readjustment rating scale. *J. Psychosomatic Res* 11, 213–218.
- Hsieh LT, Ranganath C, 2014 Frontal midline theta oscillations during working memory maintenance and episodic encoding and retrieval. *Neuroimage* 85, 721–729. [PubMed: 23933041]
- Hsieh LT, Ekstrom AD, Ranganath C, 2011 Neural oscillations associated with item and temporal order maintenance in working memory. *J. Neurosci* 31, 10803–10810. [PubMed: 21795532]
- Isingrini M, Angel L, Fay S, Taconnat L, Lemaire P, Bouazzaoui B, 2015 Age-related differences in the reliance on executive control in working memory: role of task demand. *PLoS One* 10, e0145361. [PubMed: 26700019]
- Jensen O, Tesche CD, 2002 Frontal theta activity in humans increases with memory load in a working memory task. *Eur. J. Neurosci* 15, 1395–1399. [PubMed: 11994134]
- Jost K, Bryck RL, Vogel EK, Mayr U, 2011 Are old adults just like low working memory young adults? Filtering efficiency and age differences in visual working memory. *Cereb. Cortex* 21, 1147–1154. [PubMed: 20884722]

- Klimesch W, 2012 Alpha-band oscillations, attention, and controlled access to stored information. *Trends. Cogn. Sci* 16, 606–617. [PubMed: 23141428]
- Kubota Y, Sato W, Toichi M, Murai T, Okada T, Hayashi A, Sengoku A, 2001 Frontal midline theta rhythm is correlated with cardiac autonomic activities during the performance of an attention demanding meditation procedure. *Cogn. Brain Res* 11, 281–287.
- Lage-Castellanos A, Martínez-Montes E, Hernández-Cabrera JA, Galán L, 2010 False discovery rate and permutation test: an evaluation in ERP data analysis. *Stat. Med* 29, 63–74. [PubMed: 19941298]
- Lee H, Simpson GV, Logothetis NK, Rainer G, 2005 Phase locking of single neuron activity to theta oscillations during working memory in monkey extrastriate visual cortex. *Neuron* 45, 147–156. [PubMed: 15629709]
- Lenartowicz A, Delorme A, Walshaw PD, Cho AL, Bilder RM, McGough JJ, Loo SK, 2014 Electroencephalography correlates of spatial working memory deficits in attention-deficit/hyperactivity disorder: vigilance, encoding, and maintenance. *J. Neurosci* 34, 1171–1182. [PubMed: 24453310]
- Lisman JE, Jensen O, 2013 The theta-gamma neural code. *Neuron* 77, 1002–1016. [PubMed: 23522038]
- Lisman JE, Idiart MA, 1995 Storage of 7 plus/minus 2 short-term memories in oscillatory subcycles. *Science* 267, 1512–1515. [PubMed: 7878473]
- Mangels JA, 1997 Strategic processing and memory for temporal order in patients with frontal lobe lesions. *Neuropsychology* 11, 207–221. [PubMed: 9110328]
- Marshall AC, Cooper NR, 2017 The association between high levels of cumulative life stress and aberrant resting state EEG dynamics in old age. *Biol. Psychol* 127, 64–73. [PubMed: 28501607]
- Marshall AC, Cooper NR, Geeraert N, 2016a Experienced stress produces inhibitory deficits in old adults' Flanker task performance: first evidence for lifetime stress effects beyond memory. *Biol. Psychol* 113, 1–11. [PubMed: 26542527]
- Marshall AC, Cooper NR, Geeraert N, 2016b The impact of experienced stress on aged spatial discrimination: cortical overreliance as a result of hippocampal impairment. *Hippocampus* 26, 329–340. [PubMed: 26332910]
- Marshall AC, Cooper NR, Segrave R, Geeraert N, 2015 The effects of long-term stress exposure on aging cognition: a behavioral and EEG investigation. *Neurobiol. Aging* 36, 2136–2144. [PubMed: 25834937]
- McGrath RE, Burkhart BR, 1983 Measuring life stress: a comparison of the predictive validity of different scoring systems for the social readjustment rating scale. *J. Clin. Psychol* 39, 573–581. [PubMed: 6874998]
- Meltzer JA, Negishi M, Mayes LC, Constable RT, 2007 Individual differences in EEG theta and alpha dynamics during working memory correlate with fMRI responses across subjects. *Clin. Neurophysiol* 118, 2419–2436. [PubMed: 17900976]
- Munoz E, Sliwinski MJ, Scott SB, Hofer S, 2015 Global perceived stress predicts cognitive change among older adults. *Psychol. Aging* 30, 487–499. [PubMed: 26121285]
- Nichols TE, Holmes AP, 2002 Nonparametric permutation tests for functional neuroimaging: a primer with examples. *Hum. Brain Mapp* 15, 1–25. [PubMed: 11747097]
- Ohl F, Michaelis T, Vollmann-Honsdorf GK, Kirschbaum C, Fuchs E, 2000 Effect of chronic psychosocial stress and long-term cortisol treatment on hippocampus-mediated memory and hippocampal volume: a pilot-study in tree shrews. *Psychoneuroendocrinology* 25, 357–363. [PubMed: 10725612]
- Pesonen A, Eriksson J, Heinonen K, Kajantie E, Tuovinen S, Alastalo H, Henriksson M, Leskinen J, Osmond C, Barker DJ, Räikkönen K, 2013 Cognitive ability and decline after early life stress exposure. *Neurobiol. Aging* 34, 1674–1679. [PubMed: 23337341]
- Pfurtscheller G, Aranibar A, 1977 Event-related cortical desynchronization detected by power measurements of scalp EEG. *Electroencephalogr. Clin. Neurophysiol* 42, 817–826. [PubMed: 67933]
- Preacher KJ, Curran PJ, Bauer DJ, 2006 Computational tools for probing interactions in multiple linear regression, multilevel modeling, and latent curve analysis. *J. Educ. Behav. Stat* 31, 437–448.

- Rabbitt P, 2005 Frontal brain changes and cognitive performance in old age. *Cortex* 41, 238–240. [PubMed: 15714914]
- Raghavachari S, Kahana MJ, Rizzuto DS, Caplan JB, Kirschen MP, Bourgeois B, Lisman JE, 2001 Gating of human theta oscillations by a working memory task. *J. Neurosci* 21, 3175–3183. [PubMed: 11312302]
- Reagh ZM, Roberts JM, Ly M, DiProspero N, Murray E, Yassa MA, 2014 Spatial discrimination deficits as a function of mnemonic interference in aged adults with and without memory impairment. *Hippocampus* 24, 303–314. [PubMed: 24167060]
- Reuter-Lorenz PA, Jonides J, Smith EE, Hartley A, Miller A, Marshuetz C, Koeppe RA, 2000 Age differences in the frontal lateralization of verbal and spatial working memory revealed by PET. *J. Cogn. Neurosci* 12, 174–187. [PubMed: 10769314]
- Roberts BM, Hsieh LT, Ranganath C, 2013 Oscillatory activity during maintenance of spatial and temporal information in working memory. *Neuropsychologia* 51, 349–357. [PubMed: 23084981]
- Salthouse T, Babcock R, 1991 Decomposing adult age differences in working memory. *Dev. Psychol* 27, 763–776.
- Sapolsky RM, Meaney MJ, 1986 Maturation of the adrenocortical stress response: neuroendocrine control mechanisms and the stress hyporesponsive period. *Brain Res. Rev* 11, 65–76.
- Sauseng P, Klimesch W, Heise KF, Gruber WR, Holz E, Karim AA, Hummel FC, 2009 Brain oscillatory substrates of visual short-term memory capacity. *Curr. Biol* 19, 1846–1852. [PubMed: 19913428]
- Scheeringa R, Petersson KM, Oostenveld R, Norris DG, Hagoort P, Bastiaansen MC, 2009 Trial-by-trial coupling between EEG and BOLD identifies networks related to alpha and theta EEG power increases during working memory maintenance. *Neuroimage* 44, 1224–1238. [PubMed: 18840533]
- Shao Y, Yan G, Xuan Y, Peng H, Huang QJ, Wu R, Xu H, 2015 Chronic social isolation decreases glutamate and glutamine levels and induces oxidative stress in the rat hippocampus. *Behav. Brain Res* 282, 201–208. [PubMed: 25591473]
- Spielberger CD, Gorsuch RL, Lushene RE, 1968 State-trait anxiety inventory (STAI): test manual for form X Consulting Psychologists Press.
- Sternberg S, 1966 High-speed scanning in human memory. *Science* 153, 652–654. [PubMed: 5939936]
- Stessman J, Maaravi Y, Hammerman-Rozenberg R, Cohen A, Nemanov L, Gritsenko I, Gruberman N, Ebstein RP, 2005 Candidate genes associated with aging and life expectancy in the Jerusalem longitudinal study. *Mech. Aging Dev* 126, 333–339. [PubMed: 15621215]
- Summerfield C, Wyart V, Mareike Johnen V, De Gardelle V, 2011 Human scalp electroencephalography reveals that repetition suppression varies with expectation. *Front. Hum. Neurosci* 5, 67. [PubMed: 21847378]
- Summerfield C, Mangels JA, 2005 Coherent theta-band EEG activity predicts item-context binding during encoding. *Neuroimage* 24, 692–703. [PubMed: 15652304]
- Tedesco I, Russo M, Russo P, Iacomino G, Russo G, Carraturo A, Faruolo C, Moio L, Palumbo R, 2000 Antioxidant effect of red wine polyphenols on red blood cells. *J. Nutr. Biochem* 11, 114–119. [PubMed: 10715597]
- Tukey JW, 1977 Exploratory data analysis. Addison-Wesley series in behavioral science: quantitative methods Addison-Wesley, Reading, MA.
- Vanni S, Revonsuo A, Hari R, 1997 Modulation of the parieto-occipital alpha rhythm during object detection. *J. Neurosci* 17, 7141–7147. [PubMed: 9278548]
- Vasquez B, Binns M, Anderson N, 2014 Staying on task: age-related changes in the relationship between executive functioning and response time consistency. *J. Gerontol. B. Psychol. Sci. Soc. Sci* 71, 189–200. [PubMed: 25395345]
- Vigário R, Sarela J, Jousmiki V, Hamalainen M, Oja E, 2000 Independent component approach to the analysis of EEG and MEG recordings. *IEEE Trans. Biomed. Eng* 47, 589–593. [PubMed: 10851802]
- Vigário RN, 1997 Extraction of ocular artefacts from EEG using independent component analysis. *Electroencephalogr. Clin. Neurophysiol* 103, 395–404.

- Woodward TS, Cairo TA, Ruff CC, Takane Y, Hunter MA, Ngan ET, 2006 Functional connectivity reveals load dependent neural systems underlying encoding and maintenance in verbal working memory. *Neuroscience* 139, 317–325. [PubMed: 16324799]
- Zumer JM, Scheeringa R, Schoffelen JM, Norris DG, Jensen O, 2014 Occipital alpha activity during stimulus processing gates the information flow to objectselective cortex. *PLoS Biol* 12, e1001965. [PubMed: 25333286]

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Fig. 1.

Box plots displaying the performance of old and young participant groups across all 4 load conditions (whiskers represent standard deviations). Young adults outperformed old adults for the high memory load conditions. $*p < 0.05$.

Fig. 2.

Box plots of accuracy scores displayed across age and stress groups (whiskers represent standard deviations). Old adults reporting high levels of cumulative stress performed significantly below old low-stress and young high-stress group members. $*p < 0.05$.

Fig. 3.

Grand average wave forms displaying the percentage change of event-related alpha desynchronization during stimulus encoding. While no age difference manifested for low (load 1) demands on WM, young participants showed higher levels of alpha ERD than old adults for high (load 4) demands on working memory. Abbreviations: ERD, event-related desynchronization; WM, working memory.

Fig. 4. Grand average wave forms of the percentage change in alpha event-related synchronization during stimulus maintenance. Old adults with high levels of stress displayed significantly reduced mid-occipital alpha activity compared to young high-stress and old low-stress counterparts. Abbreviation: ERS, event-related synchronization.

Fig. 5. Grand average wave forms of the percentage change in theta event-related synchronization during stimulus maintenance. Old adults with high levels of cumulative stress displayed significantly reduced levels of frontal-midline theta synchronization compared to young high-stress and old low-stress individuals. Abbreviation: ERS, event-related synchronization.

Table 1

Demographics of old and young participants split by experienced stress group

Demographic	Older adults		Younger adults	
	High stress	Low stress	High stress	Low stress
Group size	15	15	15	15
Age	68.9 (3.8)	68.6 (5.4)	24.0 (3.7)	23.8 (1.8)
Gender	10 females	8 females	6 females	8 females
Education	4.07 (1.1)	3.98 (1.1)	4.69 (0.5)	4.71 (0.9)
Cigarette consumption	0	0	0.54 (0.8)	0.29 (0.9)
Alcohol consumption	1.5 (1.2)	2.69 (1.9)	1.46 (1.1)	1.65 (1.2)
Presence of physical disability	3	4	0	2
Exercise	2.36 (1.1)	2.06 (0.9)	1.62 (0.7)	2.06 (0.9)
Mini-mental state score	28.4 (2.1)	29.3 (1.4)	n/a	n/a
Trait anxiety score	32.76	33.04	35.94	34.22
State anxiety score	36.88	35.38	34.87	33.93
Experienced stress score	899.1 [*] (103.4)	473.6 [*] (97.7)	730.4 [*] (93.7)	351.7 [*] (89.2)

^{*} $p < 0.05$ when comparing high vs. low stress individuals within each age group.