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The association between high levels of cumulative life stress and aberrant resting state EEG dynamics in old age

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ABSTRACT

Cumulative experienced stress produces shortcomings in old adults' cognitive performance. These are reflected in electrophysiological changes tied to task execution. This study explored whether stress-related aberrations in older adults' electroencephalographic (EEG) activity were also apparent in the system at rest. To this effect, the amount of stressful life events experienced by 60 young and 60 elderly participants were assessed in conjunction with resting state power changes in the delta, theta, alpha, and beta frequencies during a resting EEG recording. Findings revealed elevated levels of delta power among elderly individuals reporting high levels of cumulative life stress. These differed significantly from young high and low stress individuals and old adults with low levels of stress. Increases of delta activity have been linked to the emergence of conditions such as Alzheimer's Disease and Mild Cognitive Impairment. Thus, a potential interpretation of our findings associates large amounts of cumulative stress with an increased risk of developing age-related cognitive pathologies in later life.

1. Introduction

Aging research faces a prime challenge: to develop a better understanding of the neurobiological mechanisms that mediate cognitive decline and its associated cognitive pathologies (Albert et al., 2011; Braak & Braak, 1991; Dubois et al., 2007; Nestor, Scheltens, & Hodges, 2004). A widely available, low-cost way to discover neurocognitive markers of age-related decrements is the recording of resting state electroencephalographic (EEG) rhythms (Rossini, Rossi, Babiloni, & Polich, 2007; Babiloni et al., 2015). Abnormalities in the power spectra of different frequency ranges have been linked to altered cerebral blood flow, impaired cognitive functioning as well as reduced structural integrity of associated brain regions (Rodriguez et al., 1999a, 1999b; Sloan, Fenton, Kennedy, & MacLennan, 1995; Babiloni et al., 2012). In recent years, they have gained widespread credibility as an indicator of age-related cognitive change and have been used extensively to study both healthy and pathological aging (Bruce, Bruce, & Vennelaganti, 2009; Knyazeva et al., 2010; Dauwels et al., 2011; Scheltens et al., 2012; Morabito et al., 2012; Babiloni et al., 2016; Cozac et al., 2016; Neto, Biessmann, Aurlien, Nordby, & Eichele, 2016).

1.1. Pathological aging

A consistent finding when comparing old adults suffering from Alzheimer's Disease (AD), Amnesic Mild Cognitive Impairment (MCI) or vascular dementia (VaD) to healthy aging individuals is an increase of resting power in low frequency bands delta (0.5–4 Hz) and theta (4–6 Hz) (Signorino, Pucci, Belardinelli, Nolfe, & Angeleri, 1995; Moretti, Zanetti, Binetti, & Frisoni, 2012; Babiloni et al., 2013; Chen, Hsu, Chiu, Hu, & Lee, 2015) coupled with a reduction of power in higher frequencies such as posterior alpha (8–12 Hz) (Jeong, 2004; Koenig et al., 2005; Babiloni et al., 2015) and beta (12–20 Hz) (Brenner, Reynolds, & Ulrich, 1988; Wu, Chen, & Zhou, 2013). This power shift from high to low frequencies has been found to correlate with the severity of the condition (Kowalski, Gawel, Pfeffer, & Barcikowska, 2001). It has also been documented in longitudinal studies (Rae-Grant et al., 2016; Soininen et al., 1989; Morabito et al., 2015). For example, Coben, Danziger, & Storandt, 1985 observed that over a follow-up period ranging from 2.5 to 5 years, the resting power spectra of elderly AD patients exhibit significantly increased delta and theta power, in conjunction with severely reduced alpha and beta power. Similarly, Luckhaus et al. (2008) reported that compared to healthy controls, individuals suffering from Mild Cognitive Impairment displayed a significant decrease of posterior alpha power over a 1-year follow-up period, which correlated with reduced cognitive performance.

1.2. Healthy aging

Reports on the resting power spectra of healthy aging individuals highlight a reduction of alpha power, particularly over temporal

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regions of the cortex (Busse, Barnes, Friedman, & Kelty, 1956; Cheng, Chan, Baillet, & Lin, 2015). Contrary to findings of elevated theta power among old adults suffering from AD, MCI or VaD, Finnigan and Robertson (2011) reported that resting theta power (4–6.5 Hz) significantly correlated with measures of memory, attention and executive functioning in a sample of 73 healthy older adults. To dissociate their findings from reports on aging decline, the authors suggested the possibility of two forms of theta power: one reflecting 'true' theta network activity which indicates healthy cognitive aging; the other comprised of slowed alpha activity which has dropped into the theta frequency range and indicates cognitive impairment. Further power changes among healthy elderly participants were reported by Babiloni et al. (2006) whose investigation of the resting power spectra of 108 young and 107 elderly individuals highlighted a decrease of occipital delta power with advancing age as well as a global reduction of alpha power which manifested independently of the known slowing of the alpha rhythm.

1.3. Cumulative life stress and cognitive aging

An emerging field in the aging literature concerns the link between cumulative life stress and cognitive decline in old age. Cumulative stress refers to the sum total of stressful life experiences individuals accumulate during their lifespan and has been shown to impair cognition in both its chronic (Juster, McEwen, & Lupien, 2010) and acute form (Dominique, Roozendaal, Nitsch, McGaugh, & Hock, 2000). Long-term exposure to the stress hormone cortisol (glucocorticoids) has been linked to memory impairment and smaller hippocampal volume (Wignall et al., 2004; Gerritsen et al., 2011; Teicher, Anderson,- & Polcari, 2012; Pinheiro et al., 2015). Similarly, memory performance of older adults can be acutely modulated by pharmacological manipulation of glucocorticoids, while in young adults, cognitive performance sustained by the frontal lobes is likewise sensitive to increased levels of glucocorticoids (Lupien et al., 2005; Cao, Cai, Chen, & Zhang, 2010). Acute stress has been found to impact cognition by promoting engagement in repetitive thinking, negative emotions and social isolation, each of which have also been shown to result in decreased memory performance (Scott et al., 2015; Richards & Gross, 2000; Kremen, Lachman, Pruessner, Sliwinski, & Wilson, 2012). In addition, cumulative stress has been shown to produce lifestyle changes such as a poor diet, increased consumption of alcohol/tobacco and reduced physical activity (Steptoe, Wardle, Pollard, Canaan, & Davies, 1996). In turn, these changes can result in chronically reduced perfusion and oxygenation of the brain and may ultimately lead to vascular cognitive impairment or vascular dementia (Román, 2004). Old age has been theorised to coincide with an increased vulnerability to the adverse effects of stress, resulting from decreased cognitive/coping resources (Lupien, McEwen, Gunnar, & Heim, 2009) as well as from neurobiological changes that may enhance the damaging effect of stress on the brain. The aging brain shifts from a homeostatic balance of inflammatory mediators to increased concentrations of active microglia, increased levels of inflammatory cytokines and decreases of anti-inflammatory molecules (Sparkman & Johnson, 2008); a pro-inflammatory state that may constitute increased susceptibility to the adverse effects of stress.

In keeping with this literature, cross-sectional and longitudinal work has demonstrated that large amounts of cumulative stress reduce the performance of elderly participants completing working memory and executive control tasks (Dickinson, Potter, Hybels, McQuoid,- & Steffens, 2011; Peavy et al., 2009; Pesonen et al., 2013). Controlling for age, education and sex, Dickinson et al. (2011) reported that the total number of stressors experienced by old adults acted as a significant predictor of cognitive performance on tasks of working memory, category fluency and verbal learning. Similarly, a longitudinal design by Pesonen et al. (2013) reported that individuals separated from their parents during the Second World War showed accelerated cognitive decline at age 70 when compared to age-matched controls, while no such difference emerged between both groups at age 20. These findings highlight the damaging effect of cumulative lifetime stress, which emerges in later life and accelerates senescence in old adults. Our own work extended these behavioral findings by demonstrating that they coincide with task dependent alterations in the theta, alpha and upper gamma frequencies (Marshall, Cooper, Segrave, & Geeraert, 2015; Marshall, Cooper, & Geeraert, 2016a; Marshall, Cooper,- & Geeraert, 2016b). For example, we recently demonstrated that among old adults, stress-related reductions of memory performance coincided with reduced upper gamma activity (Marshall et al., 2015) while executive impairments correlated with reduced synchronisation of the alpha rhythm (Marshall et al., 2016a). Our findings thus highlight that cumulative stress impacts on cortical neurocognitive processes necessary for intact cognitive performance.

1.4. Overview of experiment

This study aims to investigate whether electrophysiological changes during task execution are associated with altered power differences at rest. To this effect, resting state recordings were obtained from a sample of 120 individuals (60 old, 60 young). These were analysed with regard to power spectrum differences in the delta, theta, alpha and beta frequency ranges. Should the detrimental effects of cumulative stress be associated with changes in the system at rest, significant power spectrum differences were expected to manifest for old adults with high levels of stress compared to young (low and high stress) individuals and low stress old counterparts. Based on reported changes related to healthy aging, reductions of alpha, beta and theta power among high stress old adults were expected. Should stress exposure have resulted in increased vulnerability towards contracting age-related pathologies, an increase in low frequency delta and theta power among high stress older adults was hypothesised.

2. Materials and method

2.1. Participant selection

Sixty young adult participants (41 females; Mean age = 22.3, SD = 1.4; Range = 18–30 years) were recruited from the University of Essex student population via institutional e-mail advertising. Sixty elderly participants (39 females; Mean age = 68.1, SD = 2.3; Range = 60–85 years) were recruited from advertisements to local clubs and societies. Exclusion criteria specified in the advertisement 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 this study focussed on stressful events commonly encountered throughout the lifespan, adverts specified that participation was only possible without the experience of traumatic life events. In addition, participants were asked prior to study commencement whether they had experienced a traumatic stressful incident, such as emotional, physical or sexual abuse at any point in their lives. None of the participants reported the occurrence of past trauma.[1] Potential group differences concerning anxiety levels were further assessed by the State-Trait Anxiety Inventory (Spielberger et al., 1968). However, no stress or age group differences emerged for scores on either the state or trait anxiety subscale (see Table 1). Elderly participants were further screened for the use of psychoactive medication, a history of substance

[1] We must note that we relied on a simple exclusion criterion in this regard. Given that prevalence rates for different forms of abuse and neglect in childhood and later life lie between 12% and 32.1% (Häuser, Kosseva, Üceyler, Klose, & Sommer, 2011; König et al., 2015) we are not able to fully rule out that a more advanced interview technique may have uncovered certain forms of trauma in a subset of our participants. This limitation should be noted when considering present findings.