Psychoneuroendocrinology (2014) 44, 100—111

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/psyneuen

Hair cortisol and cognitive performance in healthy older people

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Received 5 June 2013; received in revised form 4 March 2014; accepted 4 March 2014

KEYWORDS
Stress;
Cognitive performance;
Hair cortisol;
HCC;
Diurnal salivary cortisol;
Hypothalamus—pituitary—adrenal axis;
HPA;
Cortisol;
Aging

Summary Worse cognitive performance in older people has been associated with hypothalamic—pituitary—adrenal axis dysregulation (in particular, higher cortisol levels). Analysis of hair cortisol concentrations (HCC) is a novel method to measure long-term cortisol exposure, and its relationship with cognition in healthy older people has not yet been studied. We investigated whether HCC (measured in hair scalp) and diurnal salivary cortisol levels (awakening, 30 min after awakening, and evening, across two days) were related to cognitive performance (assessed with the Trail-making Test A and B, Digit Span Forward and Backward, word list-RAVLT and Stories subtest of the Rivermead) in 57 healthy older people (mean age = 64.75 years, SD = 4.17). Results showed that lower HCC were consistently related to worse working memory, learning, short-term verbal memory (RAVLT first trial and immediate recall) and long-term verbal memory. In contrast, higher mean levels and higher diurnal area under the curve of diurnal salivary cortisol were related to worse attention and short-term verbal memory (immediate story recall), respectively. Interestingly, a higher ratio of mean levels of diurnal salivary cortisol over HCC were related to worse performance on working memory and short-term verbal memory, suggesting that those individuals with lower long-term cortisol exposure might be more vulnerable to the negative effect of HPA-axis dysregulation on these cognitive processes. Our findings suggest that both low long-term cortisol exposure and a possible dysregulation of the diurnal rhythm of the HPA-axis may account, at least in part, for the inter-individual variability in cognitive performance in healthy older people.

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http://dx.doi.org/10.1016/j.psyneuen.2014.03.002
0306-4530/

1. Introduction

Aging is associated with a decrease in many cognitive functions (Silver et al., 2012). However, the pattern and magnitude of this decline are highly variable and depend on several factors. Stress and cortisol, the end product of the hypothalamic—pituitary—adrenal axis (HPA-axis), have been proposed as potential mediators of this age-related cognitive change. Cortisol can affect cognitive performance acutely through the activation of receptors located in the prefrontal cortex, hippocampus and amygdala (for review see: Lupien et al., 2007). But more interestingly, HPA-axis activity has been linked to cognitive performance in older people, since a marked increase in basal cortisol levels with age has been associated with cognitive decline and a reduction in hippocampal volume (Lupien et al., 1998; Li et al., 2006). In addition, previous studies have shown that patients with Alzheimer's disease and Mild Cognitive Impairment have heightened basal cortisol levels (Arsenault-Lapierre et al., 2010; Venero et al., 2013).

Similarly, most of the studies that have investigated the cross-sectional relationship between basal HPA-axis activity and cognitive performance in healthy older people have shown that HPA-axis dysregulation (particularly, higher cortisol release) is related to worse cognitive performance (e.g. Hodgson et al., 2004; Karlamangla et al., 2005; MacLullich et al., 2005; Li et al., 2006; Kuningas et al., 2007; Lee et al., 2007, 2008; Beluche et al., 2010; Comijs et al., 2010; Evans et al., 2011; Franz et al., 2011; Gerritsen et al., 2011; Johansson et al., 2011), although other studies have not found any relationship between cortisol and cognition (Peavy et al., 2009; Köhler et al., 2010; Schrijvers et al., 2011). In all of these studies, salivary, blood or urinary samples have been used to measure HPA-axis activity. These biological samples are useful to obtain information about HPA-axis dynamics, as repeated samples allow researchers to measure variations in cortisol levels across a given period by comparing different points, and they can also be used to determine day-to-day variations in cortisol levels.

These biological samples reflect point measures (plasma or saliva) or integral cortisol levels over a few hours (urine). Therefore, a large number of samples would be required to measure cortisol exposure over an interval of months. Additionally, cortisol levels measured in saliva, blood or urine may be highly variable, as they are likely to be affected by several factors that may occur shortly before sampling (Stalder and Kirschbaum, 2012). Thus, although these measures have contributed greatly to understanding the short-term relationship between HPA-axis activity and cognitive performance, much more research is needed to explore the relationship between long-term endogenous cortisol exposure (months) and cognitive performance.

The measurement of cortisol levels in hair, a recently developed and more stable way to measure basal cortisol exposure over months than salivary, blood or urine samples, appears to be a good candidate for use in this context. Hair cortisol concentrations (HCC) have been considered an integrated measure of cortisol exposure over a period of up to several months (for more details, see: Russell et al., 2011; Stalder and Kirschbaum, 2012). Previous studies have shown that HCC might be unaffected by circadian rhythmicity and situational context and have a high degree of intra-individual stability (Skoluda et al., 2012; Stalder et al., 2012b; but see also Sharpley et al., 2012). However, as it is a relatively new technique, some questions still remain unanswered, such as the physiological mechanisms through which cortisol gets into hair (Meyer and Novak, 2012). At the moment, several studies support the idea that HCC may be a useful technique in investigating long-term exposure to cortisol in young and older people. These studies have shown, for example, higher HCC in individuals with diseases or conditions that typically show higher cortisol levels, such as Cushing's syndrome (Thomson et al., 2010), coronary artery disease (Pereg et al., 2011), chronic pain (Van Uum et al., 2008), diabetes mellitus in older people (Feller et al., 2014) and hydrocortisone replacement therapy in young and older people (Gow et al., 2011). Moreover, higher HCC have been found in endurance athletes (Skoluda et al., 2012) and long-term unemployed individuals (Dettenborn et al., 2010).

The aim of the present study was to investigate the relationship between cognitive performance in healthy older people and cortisol exposure in the previous months determined by measuring cortisol in hair. We carried out a neuropsychological assessment (learning, short- and long-term memory, attention and executive function) of healthy older people, and we took samples of their hair to measure total cortisol exposure in the previous three months. Additionally, diurnal cortisol levels were measured using salivary samples, in order to compare the results with the findings in hair samples. Based on previous studies with salivary, blood and urine cortisol samples, we expected higher HCC to be associated with worse cognitive performance.

2. Method

2.1. Participants

As a part of a larger study designed to investigate the effects of stress and cortisol on cognitive performance in older people (Mneme Project), we recruited a healthy subgroup of older people to participate in this study. Participants belonged to a study program at the University of Valencia for people older than 55 years of age. We recruited subjects to participate in the present study in the classes of this study program. Two hundred twenty-two individuals volunteered to participate, and these volunteers were interviewed telephonically to determine whether they met the study prerequisites. In order to avoid a large number of potentially confounding factors that could interfere with the study, we selected a homogeneous healthy sample. The exclusion criteria and the number of volunteers excluded for these reasons were the following: smoking more than 10 cigarettes a day ($n = 2$), alcohol abuse (we asked the participants how many glasses and what kind of alcoholic beverages they drank per week; following the UK National Health Service definitions, only lower-risk drinkers were allowed to participate; www.nhs.uk/livewell/alcohol) or other drug abuse ($n = 1$), visual or hearing problems (except wearing glasses) ($n = 2$), presence of an endocrine ($n = 9$), neurological ($n = 6$) or psychiatric ($n = 6$) disease, using any medication directly related to emotional or cognitive function or medication that was able to influence hormonal levels, such as