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Review

The relationship between cortisol, stress and psychiatric illness: New insights using hair analysis

A. Herane Vives [a, b, *], V. De Angel [b], A. Papadopoulos [a, c], R. Strawbridge [a], T. Wise [a], A.H. Young [a], D. Arnone [a], A.J. Cleare [a, c]

[a] King's College London, Institute of Psychiatry, Psychology & Neuroscience, Department of Psychological Medicine, UK
[b] Unidad de Trastornos del Ánimo, Clínica Psiquiátrica Universitaria, Universidad de Chile, Chile
[c] Affective Disorders Unit and Laboratory, South London and Maudsley NHS Foundation Trust, London, UK

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ABSTRACT

Background: Stress is an established important contributor to the development of mental illness and stress related disorders. The biology implicated in the homeostasis of pathological stress mechanisms is not fully established. One of the difficulties with current techniques is the limitation in capturing chronic levels of cortisol as an expression of stress levels in humans. Hair samples can be used to evaluate cortisol levels averaged over relatively long periods of time, therefore providing a more valid measure of chronic levels of this hormone. A highly replicable technique to measure long-term cortisol could prove pivotal in improving our understanding of the role of stress in psychiatric disorders.
Methods: This review synthesises all the published studies relating hair cortisol concentration (HCC) to stress and to psychiatric disorders. It describes and summarises their findings with the aim of providing a summary picture of the current state of this line of research.
Results: The strongest finding to date is the replicable increases in hair cortisol associated with stressful life events. Findings in psychiatric disorders are more sparse and inconsistent. There is some support for the presence of raised HCC in major depressive disorders, and for lowered HCC in posttraumatic stress disorder, suggesting chronic hypercortisolaemia and hypocortisolaemia respectively.
Conclusions: HCC is a promising methodology to study chronic cortisol levels with the potential to help characterise psychiatric and stress related disorders. The combination of chronic and acute cortisol measurements has the potential for more accurately determining different aspects of the stress response, and ultimately for the development of a biological marker to aid diagnosis and response to treatment.

Contents

* Corresponding author. Affective Disorders Research Group, Centre for Affective Disorders, Department of Psychological Medicine, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London SE5 8AZ, UK.
E-mail address: andres.herane@kcl.ac.uk (A. Herane Vives).

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1. Background

The reaction of the brain to stress includes activation of the hypothalamic-pituitary-adrenal (HPA) axis. This axis consists of a chain of stimulatory hormones and feedback loops under the control of higher cerebral centres determining its overall activity (Papadopoulos and Cleare, 2012). Cortisol, the steroidal hormone of this axis, is at the centre of a pathophysiological stress response. This response can be either normal (adaptive) or abnormal (maladaptive) (Selye, 1946). A maladaptive response is often associated with extreme stress conditions both in terms of duration of exposure and force of the stressor (Gozhenko et al., 2009). When the ability of the individual to sustain stress is overcome a maladaptive stress response can lead to exhaustion and this can be measured.

Historically the most commonly used methodologies to measure cortisol levels have included samples of serum, saliva, and urine. These sampling methods are particularly effective in measuring acute levels of cortisol. Chronic levels are more difficult to measure and have required collecting multiple samples at many different time points (Pruessner and Kirschbaum, 2003). This approach has resulted in significant variability in the findings mostly due inherently high variability across samples potentially obscuring longer term alterations (Kudielka, 2003; Miller et al., 2007; Warnock et al., 2010). To bypass this limitation a recent method for measuring chronic concentration has included sampling cortisol in hair. The validity of this method, which consists of collecting one sample of hair to cover a longer period of cortisol synthesis, has been investigated in animal models and healthy individuals. Research studies have investigated the correlation between hair cortisol concentration (HCC) in a single sample of hair with a variable number of specimens collected using an alternative sample type. Davenport et al. (2006) found that HCC correlated with 8 saliva samples over a 2 week period in Rhesus monkeys. In healthy humans, Xie et al. (2011) measured 3 saliva samples over a 1 week period and found them to correlate with HCC. D'Anna-Hernandez et al. (2011) found this association in pregnant women, and van Holland et al. (2012) in construction workers. Other similar research utilising other specimens have yielded similar results. Sauvé et al. (2007), for example found that 24-h urinary cortisol correlated significantly with HCC differently from single point saliva or serum assessments. Overall these and other results suggest that HCC reflects long-term cortisol secretion, with the strength of this association increasing with the number of correlating samples (Stalder and Kirschbaum, 2012).

A number of specimens including saliva, urine or blood have been utilised to measure chronic levels of cortisol in a number of psychiatric conditions to understand how HPA axis activity differs in comparison with healthy controls (Russell, 2012). Results have been predictably variable so that more recently HCC has increasingly been used to more effectively measure chronic cortisol levels. Obtaining a long-term cortisol secretion pattern at different points of a psychiatric disorder, such as its development, maintenance and resolution, is an important step in increasing the diagnostic specificity and the categorisation of symptom cluster subtypes. Furthermore, such patterns of cortisol response may have clinical utility when trying to corroborate evidence of response to therapeutic interventions (Fisher and Stoolmiller, 2007). A recently published review (Staufenbiel et al., 2012) was instrumental in highlighting the importance of hair cortisol analysis in psychiatry. Here we present the most up to date and inclusive systematic review published since Staufenbiel et al.'s work by including twice as many reports available in the literature evaluating hair cortisol levels in stress-related conditions and psychiatric disorders. We also offer a view on the significance of this type of research in the development of biological markers in psychiatry, a currently topical research focus in the field.

2. Methods

A comprehensive systematic search was conducted from January 1978 to March 2015 to identify all relevant studies and included the following databases: Pubmed, Embase, Ovid MEDLINE(R), PsycINFO, PsycARTICLES. The first research report identified that met the inclusion criteria was published in 2007 (Yamada et al., 2007). Search terms were: “Long term cortisol” OR “hair cortisol” AND “Psychiatric OR depress* OR “affective disorder” OR psychosis OR bipolar* OR “personality disorder” OR “eating disorder” OR “mental health”. Inclusion criteria were: a) research was conducted in humans; b) the study used scalp hair from the posterior vertex (this measure has in fact been associated with the least variance between different strands, e.g. Sauvé et al., 2007); c) provided sufficient information regarding sampling and cortisol extraction methods; d) stress and/or diagnosis were systematically evaluated; and e) studies were case–control comparisons. Data repetition was avoided by including only the largest sample published to date. Identified reports were cross-referenced for inclusiveness. Fig. 1 shows that a total of 199 research papers were identified; 149 were original articles. Of these, 26 studies met inclusion criteria (see Fig. 1 for the breakdown of the selection process), and are summarised in Tables 1 and 2 and discussed below in detail.

3. Results

3.1. Relationship between hair cortisol and stress-related conditions

Fourteen papers were found investigating cortisol in non-pathological stress-related conditions. The details are shown in