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Cortisol awakening response and emotion at extreme altitudes on Mount Kangchenjunga

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ABSTRACT

The cortisol awakening response (CAR) was examined over a 45 days stay at extreme altitudes (above of about 5500 m) on Mount Kangchenjunga. The CAR refers to a peak cortisol response during the waking period that is superimposed to the diurnal rhythmicity in cortisol secretion, whose function has been proposed to be the anticipation of demands of the upcoming day (the CAR anticipation hypothesis). According to this hypothesis, we distinguished between resting days on which the expedition team engaged in routine activities in the base camp, and ascent days on which it planned to climb up a very demanding track. We were also interested in examining the association of testosterone with emotional anticipation, given the role of this steroid hormone in reward-related processes in challenge situations. Results showed that the climber group had a bigger CAR on ascent days, relative to the Sherpa group at the same altitude and the non-climber group at sea level. Several methodological issues, however, made it difficult to interpret these group differences in terms of the CAR anticipation hypothesis (e.g. a seemingly influential covariate was awakening time). Although based on tentative results, correlational and regression analyses controlling for awakening time coherently showed that the CAR was associated with anticipation of a hard day and feelings of fear, and testosterone was associated with feelings of energy and positive affect. Whether or not the anticipation of a hard day played a key role in regulation of the CAR, the observation of an intact CAR in the climber group under hypobaric hypoxia conditions would require in-depth reflection from the perspective of human adaptive evolution.

1. Introduction

The Earth's highest mountains are inhospitable places that cause enormous alterations in physiological milieu. These alterations transiently permit adaptation to physical stress caused by reduced pressure of oxygen in the air (hypobaric hypoxia) but inexorably lead to a process of body deterioration with fatal consequences (West, 2006). We studied here the cortisol awakening response (CAR) during an expedition to Mount Kangchenjunga in order to assess potential alterations in a severe hypoxic environment. The CAR is an abrupt rise in cortisol levels within the first hour after awakening from sleep which is observed in the majority of healthy individuals (Pruessner et al., 1997). It can be altered nevertheless by multiple factors such as ambient illumination, awakening time and sleep quality, as well as physical and psychiatric disorders (Fries et al., 2009), but to our knowledge no study has still focused on the CAR over a prolonged stay at extreme altitudes. As shown by Wilhelm et al. (2007), under sleep laboratory conditions, the CAR is a genuine response to awakening superimposed to the diurnal rhythmicity in cortisol secretion, and as such can reflect

psychophysiological processes during the transition from sleep to wake, when the spread of arousal activity from the brainstem to the neocortical networks profusely occurs. That amnesic patients with brain damage in the medial temporal lobe exhibit an absent CAR (Buchanan et al., 2004; Wolf et al., 2005), suggests the involvement of memory-related hippocampal processes in the control of this facet of the hypothalamic-pituitary-adrenal axis (Wilhelm et al., 2007). The CAR has thus been proposed to have a role in the “activation of prospective memory representations at awakening enabling individual's orientation about the self in time and space as well as anticipation of demands of the upcoming day” (Fries et al., 2009, p. 71; Schulz et al., 1998). Prior research has congruently shown bigger CARs on weekdays vs. weekend days (Kunz-Ebrecht et al., 2004; Liberzon et al., 2008; Schlotz et al., 2004; Thorn et al., 2006), on competition days vs. resting days (Filaire et al., 2009; Rohleder et al., 2007), and on days anticipated to be busier and relying more heavily on prospective memory (Elder et al., 2017; Stalder et al., 2010; Wetherell et al., 2015). This proposal has been aptly called the CAR anticipation hypothesis (Powell and Schlotz, 2012), by which the magnitude of the cortisol response can vary

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according to the demands of the day ahead to supply energy in advance (Clow et al., 2010; Fries et al., 2009; Law et al., 2013; Stalder et al., 2016).

The present study examined whether a bigger CAR could be observed on ascent vs. resting days at extreme altitudes in European climbers and Sherpas. A comparison between these two groups was relevant because, like many other tribes of Tibetan descent, the Sherpas have resided at high altitude for hundred of generations, and evidence is accumulating that their extraordinary tolerance to hypobaric hypoxia has metabolic and genetic basis (Gilbert-Kawai et al., 2014; Horscroft et al., 2017). The Sherpas who work in climbing expeditions spend roughly one third of the year at altitudes higher than 4500 m, interspersed with short stays at extreme altitudes (from ~6500 to ~8000 m), what implies a high degree of familiarization with this environment. It seems clear that Sherpas' physiological adaptations contribute to their superior performance at extreme altitudes, possibly making them to perceive less physical exertion and stress. Furthermore we think that the Sherpas, in comparison with many climbers, possibly are less competitive, having no need for fame and glory, and that such emotional and motivational differences could also have an impact on anticipatory stress responses. Additionally, we examined a group of non-climber participants from the Andalusian Coast, since a significant deviation from the CAR observed at sea level could be suggestive of altered endocrine function under hypobaric hypoxia conditions.

It is generally accepted that the adaptive function of emotion is to prepare the body for action by means of hormonal and autonomic responses, to deal with threat, challenge and their anticipation (Gray, 1987; Rolls, 2005). This is particularly well illustrated by the hormonal correlates of sports competitions that involve highly rewarding outcomes (Archer, 2006; Casto and Edwards, 2016): namely, the pre-competition anticipatory rise in cortisol and testosterone that is typically observed among athletes, as a reflection (in part) of the likely consequences of their prospective actions. Interestingly, it has been shown, under controlled laboratory conditions, that the anticipation of monetary incentives recruits the ventral striatum (a critical part of the mesolimbic dopamine reward system) after testosterone administration in healthy women (Bos et al., 2012; Hermans et al., 2010); and rodent studies have demonstrated not only that testosterone has rewarding affective properties, but also that the presence of another male, or even a stimulus associated with it, can trigger an anticipatory response of testosterone in mice (Salvador and Costa, 2009). Thereby, we were interested too in studying the association of morning testosterone with emotional anticipation, mainly because this steroid hormone has an important role in reward-related situations that demand vigorous action, by fueling the motivation to act (Bos et al., 2012). Given the fact that testosterone, like cortisol, peaks in the early morning (Brambilla et al., 2009; van Kerkhof et al., 2015), perhaps the strength of hormone-emotion associations obtained over that time period could be higher than those obtained regarding other periods of the day.

The objective of the present study was twofold. First, to assess whether the CAR anticipation hypothesis held true under extreme-altitude conditions, for a bigger CAR occurring solely on ascent days would suggest that it is a primal psychoendocrine response of stress anticipation. And second, to obtain evidence that cortisol is associated with feelings of fear and stress (threat-related affect), and testosterone is associated with feelings of energy and positive affect (reward-related affect; Aguilar et al., 2013; Bos et al., 2012; Gray, 1987; Jiménez et al., 2012; Welker et al., 2015).

2. Methods

2.1. Participants

There were two different groups in the expedition team, the climber and the Sherpa groups, and a third non-climber group at sea level (total sample size, $n = 21$). The climber group (age range: 33–74 years) was

composed of five Spanish men, two Italian men and one Italian woman (she was included in the analyses because, relative to men, her hormonal levels were always ranked in-between), the Sherpa group (age range: 18–41 years) was composed of five Nepalese men, and the non-climber group (age range: 39–63 years) was composed of eight Spanish men (one retired, one musician, two high school teachers, and four university professors) residing in the Andalusian Coast, Province of Málaga. The University of Málaga Institutional Review Board approved the study procedures, and written informed consent was obtained from all participants.

2.2. Procedure

The participants gave the saliva samples (5–10 ml) in plastic tubes 0 min and 30 min after awakening, the CAR being the subtraction of the first cortisol measure from the second one. They were instructed not to eat any food or brush their teeth 30 min prior to the sample time. These instructions were reminded the night before each sampling day. Just after the climber and the Sherpa groups gave their samples, the expedition doctor (C.M.) asked them whether they followed the instructions correctly. The non-climber group immediately froze the samples in home refrigerators, and the climber and the Sherpa groups buried them in the snow. With the exception of few cases, the climber and the non-climber groups woke up by themselves, and the Sherpa group was awoken by the expedition doctor. At the end of the expedition all the samples were conserved in our lab refrigerator until assayed using a commercial enzyme linked immunosorbent assay (ELISA) with a Diametra kit (Milan, Italy) in an automated analyzer (Triturus®, Grifols, Barcelona), following all manufacturer's instructions. The intra-assay and inter-assay coefficients of variation were (respectively) 12.6 and 14.8% for cortisol and 2.5 and 13.3% for testosterone. The lower limits of detection for testosterone and cortisol kits were 3.5 pg/ml and 0.05 ng/ml. After giving the second saliva sample, the climber and the non-climber groups also self-reported their affective states (approximately 35 min after awakening) using Likert scales ranging from 1 ("Not at all") to 9 ("Extremely"), and the Sherpa group did not give these self-reports because they were unfamiliar with paper-and-pencil scales. Participants were given written instructions as follows: "Please, during two minutes think about the activities you have to do today. Also think about to what extent those activities will be easy or difficult to do. When the two minutes have elapsed, then respond to the following scales". Firstly, they responded to the scale aimed to measure the cognitive component of stress anticipation: "Is today going to be a hard or difficult day?"; secondly, they responded to the self-assessment manikin, a set of three pictorial scales assessing three basic affective properties (i.e. affective valence, arousal and dominance; Lang, 1995); and thirdly, they responded to scales of adjectives describing emotions and motivations (e.g. "How energetic would you say you feel?"; see Feldman et al. (2013) for evidence of external validity of the scales in Mount Everest climbers).

In an attempt to rule out altitude effects over days, the analyses focused on data collected in the same base camp, at an altitude above of about 5500 m (i.e. at extreme altitude). To facilitate recovery back to baseline state and minimize the impact of physical stress (strenuous physical exertion and oxygen pressure fluctuations), the measures were taken at least 48 h after an altitude change had occurred. A distinction was made between days on which the expedition team planned to engage in routine activities in the base camp, and days on which it planned for the first time to climb up an exigent track. As some participants did not always conform to the date fixed to give the samples, data collected on other days were included in the statistical analyses if the samples were taken on resting or ascent days according to the above-mentioned criteria; nevertheless, there were missing data for hormonal measures mainly because handwritten codes on some sample tubes were illegible and some sample tubes were engulfed in an avalanche. The resulting design consisted of three resting days and two

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