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Decreased salivary alpha-amylase levels are associated with performance deficits during sleep loss

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ABSTRACT

During sleep deprivation, neurobehavioral functions requiring sustained levels of attention and alertness are significantly impaired. Discrepancies between subjective measures of sleepiness and objective performance during sustained operations have led to interest in physiological monitoring of operator performance. Alertness, vigilance, and arousal are modulated by the wake-promoting actions of the central noradrenergic system. Salivary alpha-amylase (sAA) has been proposed as a sensitive peripheral measure of noradrenergic activity, but limited research has investigated the relationship between sAA and performance. In a laboratory-controlled environment, we investigated the relationship between sAA levels, subjective sleepiness, and performance during two days (50 h) of total sleep deprivation. Beginning at 09:00, twelve healthy participants (5 females) aged 22.5 ± 2.5 years (mean ± SD) provided saliva samples, recorded ratings of subjective sleepiness, completed a brief 3-min psychomotor vigilance task (PVT-B) and performed a 40-min simulated driving task, at regular 3 h intervals during wakefulness. Ratings of subjective sleepiness exhibited a constant linear increase ($p < 0.001$) during sleep deprivation. In contrast, sAA levels showed a marked diurnal profile, with levels increasing during the day ($p < 0.001$) and steadily declining in the evening and early-morning ($p < 0.001$). PVT-B (mean reaction time and mean slowest 10% reaction time) and simulated driving performance (speed deviation and lane deviation) also exhibited diurnal profiles across the two days of sleep deprivation. Performance peaked in the afternoon ($p < 0.001$) and then steadily worsened as wakefulness continued into the evening and early-morning ($p < 0.001$). Further analysis revealed that higher sAA levels in the hour preceding each performance assessment were associated with better PVT-B and driving performance ($p < 0.001$). These findings suggest that sAA measures may be suitable indicators of performance deficits during sustained wakefulness and highlight the potential for sAA to be considered for physiological monitoring of performance. In operational environments sAA levels, as part of a panel of physiological measures, may be useful for assessing fitness-for-duty prior to safety being compromised or when performance deficits are unknown.

1. Introduction

Sleep loss has been extensively associated with impaired vigilance, alertness, and attention (Van Dongen et al., 2003). Performance is mediated by the interaction of the homeostatic pressure for sleep, which increases with time awake and dissipates during sleep, and the diurnal rhythm for alertness that declines during the evening (Achermann and Borbely, 1994). During extended wakefulness or work at night, sleepiness increases and performance is impaired as a result of the increased homeostatic pressure for sleep and the reduced diurnal drive for alertness (Dijk et al., 1992; Van Dongen and Dinges, 2003). The detrimental effects of increased sleepiness on operator performance, as a result of extended work shifts or working during the night, have been documented in transportation (Huffmyer et al., 2016), the military (Lieberman et al., 2005), and medical professions (Barger et al.,

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2005). In these settings, continual monitoring of sleepiness and performance is important as impaired performance can lead to serious safety compromises with potentially life-threatening consequences. Currently, self-assessment of sleepiness or performance during extended wakefulness is the most common method of monitoring performance and safety in the workplace (Christodoulou, 2012). However, inter-individual differences in the effects of sleep loss on performance (Van Dongen et al., 2004) and reports of discrepancies between subjective assessment of sleepiness and objective performance (Paech et al., 2016; Zhou et al., 2012), have led to the recent interest in non-invasive, objective, physiological monitoring of operator performance.

Physiological measures such as electroencephalography (EEG) recordings (Horne and Baulk, 2004), electrooculography (EOG) metrics (Jackson et al., 2016), and heart rate variability (Li and Chung, 2013), have been identified as effective objective methods of assessing sleepiness and performance during sleep deprivation. However, instrumentational requirements and confounding factors may limit the implementation of these measures in the field. Thus, it may be that a multimodal method with a panel of physiological markers be a more suitable approach for monitoring performance in the field during extended wakefulness. The non-invasive and simple handling of saliva collection has raised interest in the investigation of salivary components as measures of physiological changes (Chiappin et al., 2007). In the current study, we investigated a salivary marker, alpha-amylase, as a potential measure to be considered for physiological monitoring of performance during sleep deprivation.

Salivary alpha-amylase (sAA) is one of the principal proteins produced by the salivary glands, and has been proposed as a non-invasive peripheral measure of noradrenergic activity (see review by Nater and Rohleder, 2009; van Stegeren et al., 2006). Animal and human studies have revealed that noradrenergic activity is closely linked with alertness and vigilance (Liu et al., 2009; Smith and Nutt, 1996). Additionally, numerous studies have also identified the role of noradrenaline (NA) in mediating sAA secretion and activity (see review by Nater and Rohleder, 2009). For example, isoproterenol (beta-adrenoceptor agonist) treatment of rat parotid acinar cells induced dramatic increases in alpha-amylase secretion (Chen et al., 2014). In humans, propranolol (beta-adrenoceptor antagonist) treatment significantly attenuated increases in sAA levels compared to placebo (van Stegeren et al., 2006), and peripheral infusion of NA resulted in significantly increased sAA levels compared to saline (Kuebler et al., 2014). Further, associations between sAA and plasma levels of NA have also been shown (Thoma et al., 2012).

Central and peripheral levels of NA and adrenaline appear to exhibit diurnal profiles similar to waking performance (Bellesi et al., 2016; Candito et al., 1992). Interestingly, it has been reported that sAA measures also exhibit a similar diurnal profile, with levels peaking in the afternoon and declining towards the evening (Nater et al., 2004; Nater et al., 2007). Additionally, increased sAA activity has also been reported following acute sleep restriction (O'Leary et al., 2015) and total sleep deprivation (Seugnet et al., 2006), suggesting sAA may be a measure of increased sleep pressure. Based on these findings, it is conceivable that changes in sAA may reflect deviations in performance during extended wakefulness. However, few studies have attempted to investigate the association between sAA and performance, particularly during sleep deprivation when sleepiness and performance deficits are increased (Van Dongen et al., 2003).

Under normal sleep-wake conditions, elevated sAA levels have been associated with driver stress (Yamaguchi et al., 2006; Yamaguchi and Sakakima, 2007) and slower reaction times (Muehlhan et al., 2013). Of the few studies that have explored sAA and performance during sleep deprivation, similarities between sAA secretion and performance have been observed, but not directly investigated (Bachmann et al., 2012; Figueiro and Rea, 2011). Although, Bachmann et al. (2012) observed significantly greater sAA levels in individuals with a genetic mutation associated with increased sleep pressure and impaired vigilance during sleep deprivation.

In the current study, we investigated the potential of sAA as a non-invasive physiological measure of performance during two days of total sleep deprivation. We hypothesized that (1) the diurnal profile of sAA levels would reflect the temporal profile of performance during sustained wakefulness, and (2) sAA levels on Day 2 of sleep deprivation would be increase compared to Day 1, which would be associated with greater performance deficits on Day 2. We addressed these hypotheses by investigating the diurnal profile of sAA levels during two days (50 h) of total sleep deprivation, and exploring the relationship between changes in sAA levels and performance on a psychomotor vigilance task (PVT) and simulated driving task. The simulated driving task was used as a measure of operator performance as the operation of a motor vehicle during continuous wakefulness of 36–50 h is common in a range of applied domains including the military (Lieberman et al., 2005) and medical professions (Barger et al., 2005). The PVT was included as it is a validated measure of sustained attention, and sensitive to the effects of both the diurnal rhythm for arousal and the homeostatic pressure for sleep (Lim and Dinges, 2008).

2. Materials and methods

2.1. Participants

Twelve healthy, non-smoking adults (5 females, 7 males) between the ages of 19 and 28 years (mean ± SD: 22.5 ± 2.5 years) were selected to participate in the study after undergoing a telephone interview and two physical in-lab screening sessions. All participants were physically and psychologically healthy, as assessed by toxicology screening and questionnaires, and free from any medication (oral contraceptive use permitted ($n = 2$)) and illicit drug use. Participants were low-moderate consumers of alcohol (<7 standard drinks/week) and caffeine (<300 mg/day), and abstained from both in the week prior to the study. Trans-meridian travel or shift work during the three months prior to taking part in the study was exclusionary. All participants exhibited regular sleep patterns with an average bedtime before 00:00 h (23:48 h ± 00:44 h), wake-up time before 09:00 h (08:13 h ± 00:37 h), and 7–8 h of total sleep time (7.4 ± 0.87 h) per night. Two weeks prior to taking part in the study, daily sleep and wake times were documented in self-reported sleep logs and verified with activity monitors (Actiwatch 2, Philips Respironics, Oregon, USA). One female participant was excluded from analysis after completion of study due to missing saliva samples. Participant demographics ($n = 11$) are presented in Table 1.

This study was approved by the University of South Australia Human Ethics Research Committee and carried out in accordance with the guidelines for human research established by the National

Table 1
Participant demographic information ($n = 11$).

	Mean ± SD	Range
Age (years)	22.3 ± 2.5	19–28
Gender (% male)	63.6%	4 Female; 7 Male
Body Mass Index (BMI) (kg/m^2)	22.4 ± 2.1	19.4–26.9
Habitual Wake-Time (hh:mm)	08:13 ± 0.37 min	07:38–09:26
Habitual Bed-Time (hh:mm)	23:48 ± 0.44 min	22:31–00:34
Total Sleep Time (h)	7.4 ± 0.9	6.5–8.8
Habitual caffeine (cups/day)	1.5 ± 1.5	0.0–5.0
Habitual alcohol (standard drinks/week)	2.0 ± 1.7	0.0–4.0