

Yawning and Cortisol as a Potential Biomarker for Early Detection of Multiple Sclerosis

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Abstract—Cortisol is essential to the regulation of the immune system and yawning is a pathological symptom of multiple sclerosis (MS). Electromyography activity (EMG) in the jaw muscles typically rises when the muscles are moved and with yawning is highly correlated with cortisol levels in healthy people. Saliva samples from 59 participants were collected at the start and after yawning, or at the end of the presentation of yawning-provoking stimuli, in the absence of a yawn, together with EMG data and questionnaire data: Hospital Anxiety and Depression Scale, Yawning Susceptibility Scale, General Health Questionnaire, demographic, health details. Exclusion criteria: chronic fatigue, diabetes, fibromyalgia, heart condition, high blood pressure, hormone replacement therapy, multiple sclerosis, stroke. Significant differences were found between the saliva cortisol samples for the yawners, $t(23) = -4.263$, $p = 0.000$, as compared with the non-yawners between rest and post-stimuli, which was non-significant. Significant evidence was found to support the Thompson Cortisol Hypothesis suggesting that rises in cortisol levels are associated with yawning. Further research is exploring the use of cortisol as an early diagnostic tool for MS. Ethics approval granted and professional code of conduct, confidentiality, and safety issues are approved therein.

Keywords—Cortisol, Multiple Sclerosis, Yawning, Thompson's Cortisol Hypothesis.

I. INTRODUCTION

YAWNING is a scientific conundrum. For centuries, there has been a lack of consensus over the mechanisms involved in the production of the yawning reflex despite the fact that most of us yawn, and for some of us, frequently.

René Descartes (Fig. 1), often regarded as the “father” of modern philosophy, believed that the pineal gland, part of the epithalamus which regulates body rhythms, is the seat of the soul. Early Hindus believed that the soul escapes from the mouth when yawning and so was a religious “offense”. Since animals were observed to yawn, it was thought that they cannot possess souls.

Hippocrates in 400 BC included yawning in his list of useful “natures”. Whilst common beliefs of today include: increasing oxygen into the yawning by stretching the intercostal muscles that surround the lungs, and increasing wakefulness; compression of the lungs stimulates the carotid artery, receiving shunted blood, and raises the blood pressure to cause hormones to be released.

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Fig. 1 René Descartes (1596– 1650)

The most convincing explanations have included Hippocrates' original postulation that brain temperature lowers following yawning [1]. This has been evidenced in budgerigars and other animals [2] and has also been observed in people with the debilitating disease, multiple sclerosis (MS) [3], [4] who tend to excessive yawn following fatigue. Patients with major depression also experience excessive yawning which has led researchers to identify specific brain receptor sites as influencing depression, together with brain structures such as the insula and caudate regions, implicated in serotonin regulation and failures following stroke to these regions [5].

Contagious yawning has been observed in humans as well as in animals. It is possible that it has an evolutionary purpose connected with the “fight or flight” syndrome. Mental Attribution Theory [6] explains how people see other humans or animals yawn and wish to subconsciously empathize or identify and belong to the same social grouping. Some of us are more susceptible than others and it is suggested that an underlying susceptibility, possibly similar to that involved in hypnosis, may be involved [7]. Some researchers advocate that people who do not contagiously yawn have an inability to empathize with others though there is no evidence to support this notion.

Preterm and near term infants yawn (Fig. 2) with differing frequency dependent upon age [8]; and it is thought that this is because of the development of the brain structures, namely, the hypothalamus and the medulla oblongata which regulate wakefulness and circadian rhythm [9].



Fig. 2 Pynq Thompson, 28 days old

At the first international conference on yawning, coordinated by La Société Française de Neurologie and La Société des Neurosciences, l'Hôpital de la Pitié-Salpêtrière, Paris, France [10], neuroscientists presented cases on brain-stem ischaemic stroke patients exhibiting parakinesia brachialis oscitans, whereby the paralyzed arm rises uncontrollably upon yawning [11]. This phenomenon has been reported on several occasions since the report of Walshein 1923 [12].

Yawning and cortisol is implicated in fatigue and stress and serves an important role within the Hypothalamus-Pituitary-Adrenal (HPA) axis, the body's natural stress response system [13]. Identifying abnormal rises in cortisol might be the answer to identifying early detection of untoward and underlying neurological symptoms such as those found in early onset of dementia and MS.

Neuroscientists at Bournemouth University, United Kingdom, led by the Author, together with collaborating researchers at the French institutes of Université Paris X Ouest Nanterre La Défense, Hôpital Universitaire Amiens, and Jules Verne Université de Picardie, are beginning work using fMRI (Functional Magnetic Resonance Imaging) to identify cortisol fluctuations during fatigue in MS patients.

II. METHOD

A. Procedure

59 volunteers (37 females and 22 males) aged between 18-69 years were recruited from students at Bournemouth

University using the computerized recruitment system (SONA), and via Facebook.

All participants were properly consented according to code of conduct and research guidelines, and exposed, under randomized controlled trials guidelines, to three conditions intended to provoke a yawning response – photos of people yawning; boring text about yawning; short video of person yawning. Comparisons were made with people exposed to the same conditions but who did not yawn.

Saliva samples were collected at the start and again after the yawning response, together with electromyography (EMG) data of the jaw muscles (using non-invasive surface-placed electrodes) to determine rest and yawning phases of neural activity (Fig. 3).



Fig. 3 EMG recording of the yawn reflex

If there was no yawning response, then a second saliva sample was taken at the end of the experimental paradigm. Yawning susceptibility scale, designed in a previous study, Hospital Anxiety and Depression Scale [14], General Health Questionnaire GHQ28 [15], [16] and demographic and health details were collected from each participant.

Exclusion criteria: chronic fatigue, diabetes, fibromyalgia, heart condition, high blood pressure, hormone replacement therapy, multiples sclerosis, and stroke. Between-and within-subjects comparisons were made using t-tests and correlations using the SPSS package [version 22]. This enabled a comparison to be made between yawner and non-yawner participants as well as between rest status and yawning.

B. Ethics

Bournemouth University Research & Ethics approval granted: JC28/1/13-KA6/9/13. Professional code of conduct, confidentiality, and safety issues were approved in the Ethics

submission and data collected was made anonymous, coded, securely stored and then destroyed after completion of the study analysis. Protective measures were put in place for collection and analysis of saliva samples and the right of participants to withdraw from the study was made clear to all participants.

C. Funding

This research received funding of £4 000 from the host institution, Bournemouth University, United Kingdom, to support the purchase of essential equipment and materials.

D. Competing Interests

None.

III. RESULTS

There were no significant differences between groups in terms of age, and screening measures. Normative data for saliva cortisol lies within the ranges: (i) Morning 3.7×10^{-9} – 9.5×10^{-9} per ml; (ii) Noon 1.2×10^{-9} – 3.0×10^{-9} per ml; (iii) Evening 0.6×10^{-9} – 1.9×10^{-9} per ml, of saliva.

In saliva cortisol sample 1, the means for non-yawners was 1.9886 (SD = 1.33147) as compared with that of the yawners which was 2.3667 (SD = 1.65310). In sample 2, the means were 2.4914 (SD = 2.15002) for non-yawners, and 3.0208 (SD = 2.00975) for the yawners. Therefore, the yawners had higher levels of resting and post-experiment saliva cortisol levels than the non-yawners.

For the electromyography data, there was a significant correlation between cortisol change between the first and second samples and the EMG score: $\rho(59) = .276, p = .017$ (Table I).

There was a difference between the yawners and non-yawners in EMG, using t-test: $t(57) = -3.986, p = .000$. Using analysis of variance (ANOVA), there was a difference between EMG measures at rest ($p = .000$) and after yawn (or after presentation) ($p < .000$).

TABLE I
 CORTISOL CHANGE AND EMG CORRELATIONS

		Change	EMG Hi
Spearman's rho	Spearman's rho	1.000	0.276*
Change	EMG Hi	-	0.017
Correlation	Correlation	59.000	59.000
Coefficient	Coefficient	0.276*	1.000
Sig. (1-tailed)	Sig. (1-tailed)	0.017	-
N	N	59.000	59.000

* Correlation is significant at the 0.05 level (1-tailed).

IV. DISCUSSION

Significant differences were found in saliva cortisol levels between the first and second samples for those who yawned, which supports the Thompson Cortisol Hypothesis [17]. EMG activity increased with elevated cortisol levels and when yawning.

The yawn reflex may give rise to an increase in cortisol levels in order to afford relief in symptoms of stress, or elevated cortisol levels may be produced by the yawn reflex to

provide symptom relief. Cortisol is involved in the HPA-axis and is likely to play an important role with yawning in the regulation of body (and brain) temperature especially during physical fatigue.

V. CONCLUSIONS

Yawning has been observed in the foetus (Fig. 4), and has been depicted for centuries in Japanese sculpture (Fig. 5); and even the famous Chiricahua Apache Chief of South East Arizona, United States, and Medical Man, Geronimo (1829 – 1909), was named “One Who Yawns” (Fig. 6).



Fig. 4 Yawning in the foetus [18]

The attentional system [19], [20] seems to be reliant upon cortisol for keeping the body awake and alert, and it is perhaps no surprise that yawning may play a significant role in this activity.



Fig. 5 Japanese sculpture depicting yawning

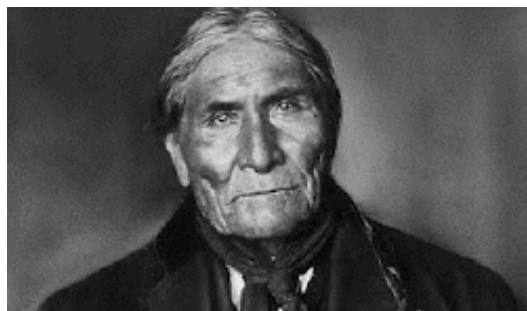


Fig. 6 Geronimo

It is hoped that further research into brain temperature, cortisol and yawning, particularly with MS patients, may provide us with a far better understanding of our natural physical coping strategies, the origin of the yawning mechanism, and about how we cope with stress and fatigue.

Furthermore, developing an early diagnostic tool for detecting neurological disease would be the greatest impact on our knowledge and would benefit our health the future quality of life of numerous patients.

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