

# Elevation of Cortisol Levels by Ingesting Liquorice

Simon B. N. Thompson<sup>1,2</sup>, Dilara Savaş<sup>1</sup>

<sup>1</sup>Department of Psychology, Faculty of Science & Technology, Bournemouth University, Poole House (P305), Poole, BH12 5BB, UK, <sup>2</sup>Department of Psychology and Education, International Scientific Council for Research, Université Paris Ouest Nanterre La Défense, 200 avenue République, 92001 Nanterre, France

## ABSTRACT

The effects of liquorice on the hormone cortisol are known but are not well understood. It has been noted anecdotally, but there remains little scientific literature on the link between the effects of liquorice on the body and the fact that cortisol is consistently implicated. This study demonstrates the link between liquorice and cortisol and the role that cortisol plays, together with yawning, in regulating brain temperature which is often compromised in certain neurological disorders such as multiple sclerosis. 13 volunteers aged between 21 and 28-year-old ingested liquorice as well as completing the Hospital Anxiety and Depression Scale, General Health Questionnaire, and demographic and health details. Saliva cortisol samples were collected before and after ingesting liquorice. In all cases, cortisol levels were significantly elevated after ingesting liquorice.

**Key words:** Brain Cooling, Cortisol, HPA-axis, Liquorice, Regulation, Yawning

## INTRODUCTION

The hormone cortisol has been associated with yawning and has been described in the Thompson Cortisol Hypothesis<sup>[1,2]</sup> that suggests links the rise in cortisol triggers which in turn lowers brain temperature. Threshold level rises of cortisol are proposed to be part of a complex mechanism since brain temperature can rise dramatically in people with MS<sup>[3]</sup> possibly due to excessive fatigue and irregular sleep patterns.<sup>[4]</sup> Cortisol is thought to regulate brain temperature within the hypothalamus-pituitary-adrenal (HPA)-axis,<sup>[5]</sup> which is a natural feedback loop to protect our bodies,<sup>[6]</sup> and cortisol may communicate directly with the motor cortex<sup>[7]</sup> as evidenced in mice by Hasan *et al.*<sup>[8]</sup> where sophisticated cortisol-specific receptors were involved during motor learning tasks.

Cortisol is implicated during stressful events and might be modulated by contagious yawning.<sup>[9]</sup> Curiously, the hormone is thought to rise during ingestion of liquorice because of the effects of the main ingredient, glycyrrhizic acid<sup>[10]</sup> on the

kidneys. This may be because of inhibition of the enzyme 11 $\beta$ -hydroxysteroid dehydrogenase type 2 which normally inactivates cortisol in the kidney. Liquorice is likely to inhibit this enzyme and so results in increases in cortisol levels.

Since the first description of side effects of liquorice,<sup>[11]</sup> some researchers have found that girls exposed to high maternal liquorice consumption through mothers during pregnancy had higher body mass index for age and reported more advanced pubertal development as compared with boys.<sup>[12]</sup> Støving *et al.*<sup>[13]</sup> suggested that increased sensitivity to glycyrrhizic acid may also arise in anorexia nervosa which may cause severe hypokalemia when combined with bizarre eating habits. Anecdotally, it would seem that people can overdose on liquorice consumption<sup>[14]</sup> which can cause rhabdomyolysis, the breakdown of skeletal muscle causing the release of myoglobin into the bloodstream.<sup>[15]</sup> Myoglobin is the protein that stores oxygen in muscles; too much myoglobin in the blood can lead to kidney damage.

Ottenbacher and Blehm<sup>[16]</sup> found that liquorice ingestion can lead to increased hypertension and others have shown

### Address for correspondence:

Simon B. N. Thompson, Faculty of Science & Technology, Bournemouth University, Poole House (P305), Poole, BH12 5BB, UK. E-mail: simont@bournemouth.ac.uk

© 2018 The Author(s). This open access article is distributed under a Creative Commons Attribution (CC-BY) 4.0 license.

that there may be many complications arising from liquorice consumption<sup>[17]</sup> including preterm labor,<sup>[18]</sup> and ocular complications.<sup>[19,20]</sup> The link between cortisol and yawning is now established,<sup>[1,7]</sup> and it is interesting to note that liquorice may now also play a role in creating artificially induced levels of the hormone for effects that might be used usefully for diagnosis or treatment monitoring.

## MATERIALS AND METHODS

### Participants

A total of 13 female healthy volunteers were recruited to the study aged between 21 and 28 years (mean of 23.1 years). All were students attending postgraduate courses at Bournemouth University and were approached at the end of teaching sessions. All participants were properly consented according to code of conduct and research guidelines. Exclusion criteria were chronic fatigue, congestive heart disorder, diabetes, fibromyalgia, heart condition, high blood pressure, history of stress, psychiatric disorder, hormone replacement therapy, renal problems, respiratory disorder, stroke, and food allergy including nuts and liquorice. None of the participants were on drugs containing cortisol.

### Stimuli and procedure

Saliva samples were collected before and again after ingesting a small piece of “natural liquorice” that also contained molasses syrup, wheat flour, liquorice extract, and natural flavoring (aniseed oil). The salt content was exclusively due to the presence of naturally occurring sodium (0.56 g in 100 g). Fat content was 0.4 g in 100 g, of which 0.0 g was saturated. 67 g in 100 g was carbohydrate, of which 49 g in 100 g was sugars, and 3.7 g in 100g was protein. Product brand was called “Panda” and manufactured by Orkla Confectionery and Snacks, PL 3050, 22111, Maarianhamina, Finland. Each participant ingested 8 g of “natural liquorice” with a “Manufacturing Date” of 08.05.2017 and a “Best Before Date” of 07.08.2018 which was well within the acceptable and recommended period of safe consumption.

Cortisol levels are easily detected in saliva and are a less intrusive collection method than intravenous cortisol collection. The presence of cortisol in saliva is highly correlated with blood assay,<sup>[21-23]</sup> and it is also much cheaper to analyze in the laboratory.

The Hospital Anxiety and Depression Scale (HADS),<sup>[24]</sup> General Health Questionnaire (GHQ28),<sup>[25,26]</sup> and demographic and health details were collected from all participants.

Between- and within-participants comparisons were made using t-tests in the SPSS package version 23. This enabled a comparison to be made between before and after liquorice ingestion.

### Ethics

Bournemouth University Research and Ethics approval granted: FST/17040/15.08.2017. Protective measures were put in place for collection and analysis of saliva samples; for example, disposable gloves were worn during collection and analysis. All data were coded for anonymity, confidentiality, and privacy held in a secure location. The right of participants to withdraw from the study at any time without consequences was upheld, and all saliva cortisol samples were destroyed following analysis.

## RESULTS

There were no significant differences between groups in terms of HADS anxiety and depression scores and GHQ28 scores. Normative data for saliva cortisol during midday period lie within the range: 1.2–3.0 nanograms per milliliter.

The means of the cortisol saliva 2 were higher than those of the first sample taken [Table 1] indicating higher values were reached in the second sample after ingesting liquorice. There was statistically significant difference ( $P < 0.005$ , 2-tailed) between cortisol sample 1 and 2 [Table 2].

## DISCUSSION

This study presents interesting findings in respect of cortisol elevations. The level of cortisol found in the first saliva samples was lower than that found in the second sample after participants had ingested liquorice. Furthermore, a significant difference was found between the levels of cortisol in the first sample compared with the second sample after liquorice ingestion. This concurs with studies that have suggested liquorice ingestion acts on the receptors responsible for cortisol release and causes elevation in blood.<sup>[10]</sup>

Despite reports of possible side effects of liquorice ingestion in terms of its effects on body organs and functionality, it appears that it may be worthwhile investigating further this natural plant for its potential properties in affecting cortisol levels, especially in those who are affected by low cortisol production or an irregular release of the hormone, such as Cushing’s syndrome.<sup>[27]</sup>

**Table 1: Descriptive data of saliva samples**

Paired samples statistics				
Subjects	Mean	<i>n</i>	SD	SEM
Pair 1				
Saliva1	2.8769	13	1.12927	0.31320
Saliva2	3.9538	13	1.14936	0.31877

SD: Standard deviation, SEM: Standard error mean

Table 2: Comparison of Saliva Samples

Subjects	Paired differences			t	df	Sig. (2-tailed)	
	Mean±SD	Std. Error Mean	95% Confidence interval of the Difference				
			Lower				Upper
Pair 1 Saliva1 - Saliva2	-1.07692±1.12706	0.31259	-1.75800	-0.39585	-3.445	12	0.005

SD: Standard deviation

The authors acknowledge that it is a small sample study but also that it supports previous findings that indicate liquorice may be a natural product with potentially far-reaching benefit.

## ACKNOWLEDGMENTS

We are very grateful to all of the volunteers who took part in the study and to Bournemouth University for providing financial support of £1,196 for the laboratory analysis of cortisol samples.

## REFERENCES

- Thompson SB. Yawning, fatigue and cortisol: Expanding the Thompson cortisol hypothesis. *Med Hyp* 2014;83:494-6.
- Thompson SB, Richer S. How yawning and cortisol regulates the attentional network. *J Neurosci Rehab* 2015;2:1-9.
- Gallup AC, Gallup GG Jr., Feo C. Yawning, sleep, and symptom relief in patients with multiple sclerosis. *Sleep Med* 2010;11:329-30.
- Erkoyun HU, Beckmann Y, Bülbül NG, İncesu TK, Kanat NG, Ertekin C, *et al.* Spontaneous yawning in patients with multiple sclerosis: A polygraphic study. *Mult Scler Relat Disord* 2017;17:179-83.
- Thompson SB, Rose K, Richer S. Yawning with cortisol: examining the neuroscience behind the Thompson cortisol hypothesis for supporting rehabilitation of neurologically impaired individuals. *J Neurosci Rehab* 2014;1:1-11.
- Bellingham K. Chronic stress: A major driver of 'dis-ease'. *J Aust Trad Med Soc* 2016;22(3):177-8.
- Thompson SB. Hypothesis to explain yawning, cortisol rise, brain cooling and motor cortex involvement of involuntary arm movement in neurologically impaired patients. *J Neurol Neurosci* 2017;8:1-5.
- Hasan MT, Hernández-González S, Dogbevia G, Treviño M, Bertocchi I, Gruart A, *et al.* Role of motor cortex NMDA receptors in learning-dependent synaptic plasticity of behaving mice. *Nat Comm* 2013;4:1-9.
- Eldakar OT, Tartar JL, Garcia D, Ramirez V, Dauzonne M, Armani Y, *et al.* Acute physical stress modulates the temporal expression of self-reported contagious yawning in humans. *Adap Hum Beh Physiol* 2017. DOI: 10.1007/s40750-017-0060-5.
- Farese S, Kruse A, Pasch A, Dick B, Frey BM, Uehlinger DE, *et al.* Glycyrrhetic acid food supplementation lowers serum potassium concentration in chronic hemodialysis patients. *Kidney Int* 2009;76:877-84.
- Revers F. Behandelung van ulcus ventriculi en ulcus, duodeni mer succus liquiritiae. [Treatment of gastric and gastric ulcers, duodenal succus with liquiritiae.] *Nederel. Tijdschr Geneesk* 1948;92:2968-72.
- Räikkönen K, Martikainen S, Pesonen AK, Lahti J, Heinonen K, Pyhälä R, *et al.* Maternal licorice consumption during pregnancy and pubertal, cognitive, and psychiatric outcomes in children. *Am J Epidemiol* 2017;185:317-28.
- Støving RK, Lingqvist LE, Bonde RK, Andries A, Hansen MH, Andersen M, *et al.* Is glycyrrhizin sensitivity increased in anorexia nervosa and should licorice be avoided? Case report and review of the literature. *Nutrition* 2011;27:855-8.
- Ainsworth S. Liquorice: It takes all sorts. *Nurse Pres* 2013;11:482.
- Shah M, Williams C, Aggarwal A, Choudhry WM. Licorice-related rhabdomyolysis: A big price for a sweet tooth. *Clin Nephrol* 2012;77:491-5.
- Ottenbacher R, Blehm J. An unusual case of licorice-induced hypertensive crisis. *S D Med* 2015;68:346-7, 349.
- Omar HR, Komarova I, El-Ghonemi M, Fathy A, Rashad R, Abdelmalak HD, *et al.* Licorice abuse: Time to send a warning message. *Ther Adv Endocrinol Metab* 2012;3:125-38.
- Strandberg T, Järvenpää A, Vanhanen H, McKeigue P. Birth outcome in relation to licorice consumption during pregnancy. *Am. J. Epidemiol* 2001;153:1085-1088.
- Hall RC, Clemett RS. Central retinal vein occlusion associated with liquorice ingestion. *Clin Exp Ophthalmol* 2004;32:341.
- Fraunfelder FW. Ocular side effects from herbal medicines and nutritional supplements. *Am J Ophthalmol* 2004;138:639-47.
- Vining RF, McGinley RA, Maksvytis JJ, Ho KY. Salivary cortisol: A better measure of adrenal cortical function than serum cortisol. *Ann Clin Biochem* 1983;20 (Pt 6):329-35.
- Aardal E, Holm AC. Cortisol in saliva—reference ranges and relation to cortisol in serum. *Eur J Clin Chem Clin Biochem* 1995;33:927-32.
- Aardal-Eriksson E, Karlberg BE, Holm AC. Salivary cortisol—an alternative to serum cortisol determinations in dynamic function tests. *Clin Chem Lab Med* 1998;36:215-22.
- Snaith RP, Zigmond AS. Hospital anxiety and depression scale. *Acta Psy Scand* 1994;67:361-70.
- Goldberg D. Use of the general health questionnaire in clinical work. *Br Med J* 1986;293:1188-9.

26. Bridges KW, Goldberg DP. The validation of the GHQ-28 and the use of the MMSE in neurological in-patients. *Br J Psychiatry* 1986;148:548-53.
27. AAES-American Association of Endocrine Surgeons. Cushing's Syndrome (Cortisol-Producing Adrenal Tumor). American Association of Endocrine Surgeons Patient Education Site; 2013. Available from: [http://www.endocrinediseases.org/adrenal/cushings\\_symptoms.shtml](http://www.endocrinediseases.org/adrenal/cushings_symptoms.shtml).

[Last accessed on 2015 Sep 29].

**How to cite this article:** Thompson SBN, Savaş D. Elevation of Cortisol Levels by Ingesting Liquorice. *Clin Res Neurol* 2018;1(1):1-4.