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The effect of a moderate level of white wine consumption on the hypothalamic–pituitary–adrenal axis before and after a meal

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Abstract

The nutritional status of the individual at the time of alcohol consumption may mediate the rate of alcohol absorption and metabolism, thus influencing the systemic effect of alcohol on the body. The aim in the present investigation was to assess the effect of moderate white wine consumption on the hypothalamic–pituitary–adrenal (HPA) axis under variable nutritional conditions. Seven males aged between 19 and 22 years participated in all aspects of the current investigation. The experimental procedure for the fasting trial required participants to ingest either 4 standard units of alcohol (40 g) or the equivalent amount of placebo over a 135-min period before consuming food for 45 min. Alternatively, in the feeding trial, food was consumed for 45 min prior to participants ingesting either 4 standard units of alcohol (40 g) or the equivalent amount of placebo over a 135-min period. Blood alcohol, salivary cortisol, and salivary dehydroepiandrosterone sulfate (DHEAS) levels were assessed at 45-min intervals during the 180-min experimental periods. The results demonstrated a significant alcohol-induced decrease in salivary cortisol irrespective of nutritional status and a significant decrease in salivary DHEAS when alcohol is consumed alone under fasting conditions only. It was concluded that moderate white wine consumption may promote a transient alteration in the functioning of the HPA axis.

Keywords: Alcohol; Hypothalamic–pituitary–adrenal axis; Cortisol; Steroid hormones; Dehydroepiandrosterone sulfate; Sodium; Potassium; Electrolytes; Fasting

1. Introduction

The hypothalamic–pituitary–adrenal (HPA) axis is responsible for the synthesis and release of steroid hormones, the most abundant being dehydroepiandrosterone (DHEA), DHEA sulfate (DHEAS), cortisol and aldosterone (Endoh et al., 1996). The release of either corticotropin-releasing factor (CRH) or arginine vasopressin (AVP) by the hypothalamus stimulates the anterior pituitary to release adrenocorticotropin (ACTH), which in turn promotes the synthesis and release of steroid hormones that have glucocorticoid (i.e., cortisol), mineralocorticoid (i.e., aldosterone), and androgenic (i.e., DHEA, DHEAS) functions (Jacobson and Sapolsky, 1991).

In the central nervous system (CNS), steroid hormones such as cortisol and DHEAS act as modulators of synaptic events. Cortisol may alter the binding of γ-aminobutyric acid (GABA) to inhibitory $GABA_A$ receptors in a biphasic fashion, with potentiation of GABA occurring at nanomolar levels and a reduction occurring at micromolar ones (Majewska et al., 1985). Alternatively, DHEAS may modulate the action of cortisol in the hippocampus (Guazzo et al., 1996) by enhancing the magnitude of hippocampal primed burst (Diamond et al., 1996) and, as a GABA antagonist at the $GABA_A$ receptor (Demirgoren et al., 1991), by potentiating the function of excitatory *N*-methyl-D-aspartate (NMDA) glutamate receptors (Baulieu, 1996).

Chronic alcohol consumption can significantly decrease plasma aldosterone (Guillaume et al., 1996; Wigle et al., 1993), and plasma DHEAS concentration (Andersson et al., 1986). In contrast, the literature with respect to the effect of oral alcohol intake on plasma cortisol release is contradictory. Investigations have shown that blood alcohol concentrations exceeding 1 g/l can elevate plasma cortisol concentration (Guillaume et al., 1994). However, others claim that low to moderate alcohol intake has little (Jenkins

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and Connolly, 1968), if any (Davis and Jeffcoate, 1983; Gianoulakis et al., 1997; Ida et al., 1992; Joffe et al., 1984; Waltman et al., 1993), effect on cortisol release. Furthermore, early work has shown that while alcohol consumption may promote a significant decrease in cortisol initially, this is later followed by a significant elevation in plasma cortisol concentration (Linkola et al., 1979).

In order to explain these differing results researchers have suggested that the discrepancy in findings relating to the effect of alcohol on plasma cortisol concentration is due to differences in stress levels associated with the testing procedure (Cicero, 1981). Cortisol is rapidly released in response to stress (Virgin et al., 1991), and as each individual responds differently to the testing procedure, the differences in stress levels between individuals may be responsible for the discrepancy in findings (Guaza et al., 1983).

The nutritional status of the individual at the time of testing could also be a factor that may contribute to the variability in the cortisol data when alcohol is consumed. Steroid hormones protect the body from cellular damage when food is not available (Choi et al., 1996; Dallman et al., 1993, 1995), and the adrenocortical system is markedly altered by food availability (Akanji et al., 1990; Lane et al., 1997; Tegelman et al., 1986; Vance and Thorner, 1989). Furthermore, differences in the prior nutritional status of the individual cannot only alter the rate of alcohol absorption (Fraser et al., 1995), but also the site of alcohol metabolism (Caballeria, 1991; Lieber, 1982), which can influence the effect alcohol has on the body (Manzo et al., 1994).

Plasma free cortisol measurement is the most reliable measure of adrenal glucocorticoid activity as plasma total cortisol values may be affected by the alteration of its carrier protein, corticosteroid-binding globulin (Laudat et al., 1988). However, it is not unusual in psychoneuroendocrinology for the assessment of cortisol to be made in saliva (Kirschbaum and Hellhammer, 1994), as the amount of cortisol in saliva is highly correlated with the level of plasma free cortisol (Akanji et al., 1990; Read et al., 1982; Umenda et al., 1981), and the level of cortisol in cerebrospinal fluid (CSF). Moreover, steroid hormone concentration in saliva is not dependent on saliva flow rate and no dilution effect has been observed (Guazzo et al., 1996). Therefore, as cortisol is released in response to stress (Virgin et al., 1991), salivary measures of cortisol may offer a more accurate noninvasive measure of glucocorticoid activity (Ohl et al., 1991) when alcohol is consumed.

The aim of the present investigation was to assess the effect of white wine consumption (alone) on salivary cortisol and salivary DHEAS when nutritional status is held constant. Additionally, as alcohol is often consumed alone before a meal, a secondary aim was to determine whether consuming alcohol prior to food had any significant effect on salivary measures of cortisol and DHEAS in order to further clarify the effect of alcohol on the HPA axis.

2. Method

2.1. Participants

Due to suggestions that DHEAS concentration level may be affected by age and sex differences (Orentreich et al., 1984; Zumoff et al., 1980), seven males aged between 19 and 22 years participated in the present investigation. Participants were excluded if there was evidence that they had (1) a previous history of psychiatric disorder; (2) any neurological disease; (3) any major physical complaint, including eye problems; (4) a history of drug use; (5) taken any prescribed medication within the last 7 days; or (6) satisfied the DSM-IV diagnostic criteria for alcohol abuse and/or dependence (American Psychiatric Association, 1994). Individuals were all white Caucasians of Australian or European origin, and no participant was obese as the weight of all participants when assessed was within the medically recommended range for age and height. The majority of individuals lived at home and no participant reported a family history of alcoholism. All fitted the profile of "binge" drinkers (Kokavec and Crowe, 1999), consuming an average of 9.1 standard units (S.D. = 8.7 U) alcohol on an average of 6.9 occasions (S.D. = 4.4 occasions) per month. All participants reportedly abstained from consuming alcohol for 48 h before each trial and the same participants were used in all trials.

2.2. Measures

Salivary DHEAS was assessed according to the manufacturers instructions using a competitive binding radioimmunoassay kit (Diagnostic Systems Laboratories, TX). No precision statistics were provided by the manufacturer. Salivary cortisol was measured by radioimmunoassay (Orion Diagnostica, Espoo, Finland). As measures of cortisol are much lower in saliva, according to the manufacturers instructions using the 2000 nmol/l standard the following dilutions were prepared in buffer (Tris–HCl, 0.1 M, pH 7.4, 0.2 BSA): 0, 1.0, 2.5, 50 and 100 nmol/l. The antiserum reagent was diluted one part antiserum to four parts buffer (1 + 4) before the assay was run according to the procedure for serum samples using 100 μl of standards and samples. No precision statistics for salivary cortisol measurement were provided by the manufacturer. Measurements of cortisol and DHEAS were obtained from the same saliva sample at each time point, and samples from each pair of experimental and placebo trials were assayed together. All biochemical assessment was performed by staff at Analytical Reference Laboratories (North Melbourne, Australia), who were blind to the experimental manipulations. Semiquantitative urinalysis was performed using Labstix (Bayer Australia), in order to measure ketones (sensitivity was 0.5–1.0 mmol/l acetoacetic acid), glucose (sensitivity was 4–7 mmol/l glucose), blood (sensitivity was 150–620 μg/l haemoglobin), and protein (sensitivity was 0.15–0.30 g/l albumin). Blood

alcohol readings (BAL) were made using a Lion alcolmeter (Lion Laboratories, Cardiff, UK).

2.3. Procedure

The alcohol and placebo trials were held on separate occasions with a 1-week interval between trials. Participants assumed that all trials involved the ingestion of alcohol.

2.3.1. Fasting trials

Participation in the two fasting trials was preceded by a 6-h fast, which commenced at 1100 h Eastern Standard Summer Time (ESST), and testing began at 1700 h ESST. Blood alcohol level (BAL) was assessed prior to participation and then participants were asked to provide a 5-ml saliva sample for measurement of DHEAS and cortisol, and a 50-ml urine sample for urinalysis before slowly ingesting either 4 standard units of alcohol (40 g) as Hardy's RR 1997 Medium Dry white wine containing 12% alcohol (315 kJ per unit), or the equivalent amount of placebo in the form of white nonalcoholic grape juice (285 kJ per unit) over a 135-min period. Salivary measures of DHEAS and cortisol were made and BAL was assessed regularly at 45-min intervals between 1700 and 1915 h. Food and a nonalcoholic beverage in the form of pizza and Coca-Cola soft drink was provided at 1915 h, and readings for all parameters were taken once participants had finished eating at 2000 h. All individuals reported moderate feelings of intoxication at the completion of the alcohol study, and no participant experienced gastrointestinal or other distress during either trial.

2.3.2. Feeding trials

Participants consumed some pizza and Coca-Cola soft drink between 1600 and 1700 h ESST. Testing began at 1700 h ESST and BAL was assessed prior to participation in the alcohol and placebo feeding trials. Participants were then asked to provide a 5-ml saliva sample for measurement of DHEAS and cortisol, and a 50-ml urine sample for urinalysis, before slowly ingesting either 4 standard units of alcohol (40 g) as Hardy's RR 1997 Medium Dry white wine containing 12% alcohol (315 kJ per unit), or the equivalent amount of placebo in the form of white non-alcoholic grape juice (285 kJ per unit), over a 135-min period. Salivary measures of DHEAS and cortisol and BAL was assessed regularly at 45-min intervals between 1700 and 1915 h. At the completion of the alcohol trial all participants reported mild feelings of intoxication. No participant experienced gastrointestinal or other distress during either trial.

3. Results

Ketone bodies were detected by urinalysis in all participants prior to their participation in the two fasting trials, which confirmed that participants had complied with the fasting conditions. Alternatively, when urinalysis was performed immediately following food intake in the two feeding trials, ketone bodies were not detected in the urine of any participant confirming that participants were not fasted prior to alcohol being consumed. Urinalysis also failed to detect any abnormality in urinary protein, blood, or glucose excretion in any participant when either a placebo or alcohol was consumed in either trial.

During the alcohol fasting trial BAL increased steadily, reaching a mean peak of 0.06 mg/100 ml (S.E.M. = ± 0.005 mg/100 ml), with little variability after 40 g of alcohol had been consumed over 135 min. After food was consumed in the alcohol fasting trial a mean BAL of 0.046 mg/100 ml (S.E.M. = ± 0.018) was recorded. In contrast, during the alcohol feeding trial BAL reached a mean peak of 0.04 mg/100 ml (S.E.M. = ± 0.017 mg/100 ml) after 40 g of alcohol had been consumed over a 135-min period.

The mean salivary cortisol level during the alcohol and placebo fasting trial conditions is shown in Fig. 1A. Measured salivary cortisol levels prior to participation in the alcohol and placebo fasting trials (0 min) were statistically

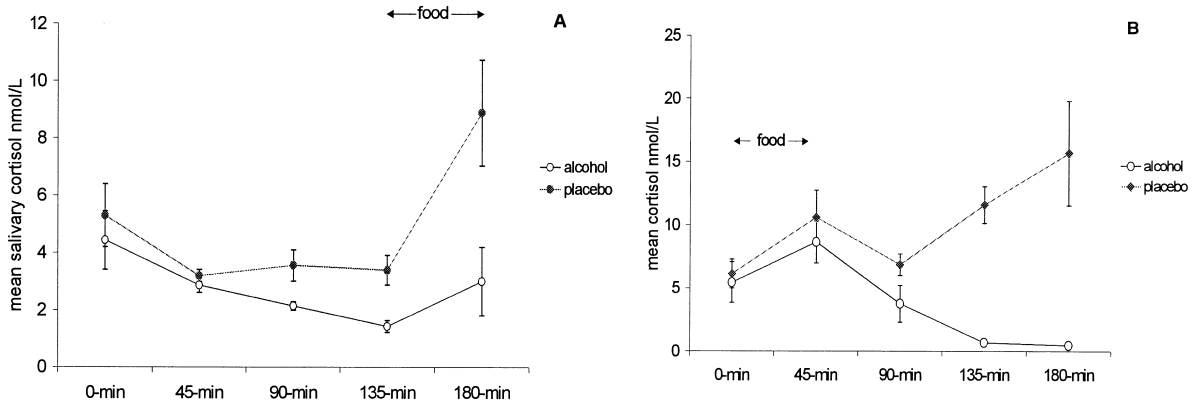

Fig. 1. (A) Salivary cortisol before (0 min) and after ingestion of placebo or 40 g alcohol (45–135 min), and after food consumption (180 min). Data are shown as the mean ± S.E.M. ($N = 7$). (B) Salivary cortisol before (0 min), and after food is consumed (45 min), and during ingestion of placebo or 40 g alcohol (90–180 min). Data are shown as the mean ± S.E.M. ($N = 7$).

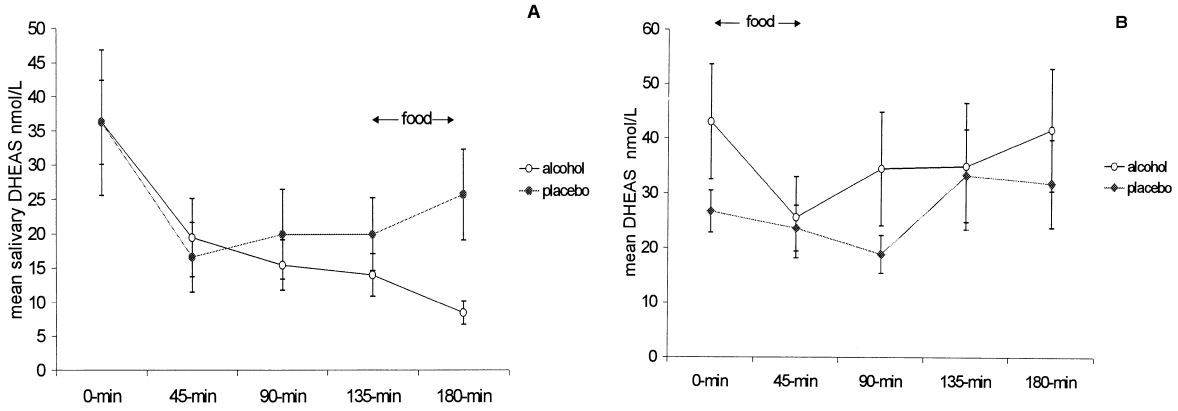

Fig. 2. (A) Salivary dehydroepiandrosterone sulfate (DHEAS) before (0 min) and after ingestion of placebo or 40 g alcohol (45–135 min), and after food consumption (180 min). Data are shown as the mean ± S.E.M. ($N=7$). (B) Salivary DHEAS before (0 min), and after food is consumed (45 min), and during ingestion of placebo or 40 g alcohol (90–180 min). Data are shown as the mean ± S.E.M. ($N=7$).

analyzed by paired t test. No significant baseline differences were observed, $t(6)=-0.45$, $P=.667$.

The two-way ANOVA with Time (4) and Trial (2) as "within-subjects" factors showed a significant main effect for Time, $F(1.43,18)=11.55$, $P=.006$, and significant main effect for Trial, $F(1,6)=12.57$, $P=.012$. No significant Trial × Time interaction was observed, $F(1.11,18)=3.40$, $P=.108$. Any violation of assumptions was corrected for using the Huynh–Feldt epsilon correction.

Assessment of the raw cortisol data following food intake in the fasting trials showed an increase in salivary cortisol in all seven participants after food was presented in the placebo trial with raw scores ranging between 3 and 15 nmol/l. Alternatively, after food was consumed in the alcohol trial cortisol levels either remained the same ($N=2$), decreased ($N=2$), or increased ($N=3$) with concentration levels ranging between 1 and 8 nmol/l.

The average salivary cortisol level under alcohol and placebo feeding conditions is shown in Fig. IB. The two-way ANOVA with Time (4) and Trial (2) as "within-subjects" factors showed a significant main effect for Trial, $F(1,6)=21.68$, $P=.003$, and significant Trial × Time interaction, $F(1.4,8.5)=8.93$, $P=.011$, which indicated that the cortisol level was significantly decreased as more alcohol was consumed. The Time main effect was not significant, $F(3,18)=1.98$, $P=1.52$. Any violation of assumptions was corrected for using the Huynh–Feldt epsilon correction.

The mean salivary DHEAS level under experimental and placebo fasting conditions is graphically depicted in Fig. 2A. Measured salivary DHEAS levels prior to participation in the alcohol and placebo fasting trials (0 min) were statistically analyzed by paired t test. No significant baseline differences were observed, $t(6)=0.00$, $P=.996$.

The two-way ANOVA with Time (4) and Trial (2) as "within-subjects" factors produced a significant Trial × Time interaction, $F(2.4,18)=6.45$, $P=.007$, which showed a significant decrease in the level of DHEAS after food was consumed in the alcohol trial at 135 min and 180 min. No significant Time, $F(3,18)=0.04$, $P=.989$, or Trial, $F(1,6)=1.52$, $P=.264$, main effects were observed. Any violation of assumptions was corrected for using the Huynh–Feldt epsilon correction.

Inspection of the raw DHEAS data following food intake in the alcohol fasting trial showed a decrease in the level of DHEAS in all seven participants. Alternatively, in the placebo fasting trial an increase in DHEAS concentration occurred in all participants when levels were assessed at 180 min.

Fig. 2B shows the mean salivary DHEAS level in the alcohol and placebo feeding trials. The two-way ANOVA with Time (4), and Trial (2) as "within-subjects" factors showed a significant main effect for Time, $F(3,18)=3.44$, $P=.039$, and significant Trial × Time interaction, $F(3,18)=3.62$, $P=.033$, which indicated that a significant increase in the DHEAS level occurred as soon as alcohol was consumed. No significant Trial main effect was observed, $F(1,6)=0.63$, $P=.458$. Any violation of assumptions was corrected for using the Huynh–Feldt epsilon correction.

4. Discussion

The results from the feeding and fasting trials investigating the effect of a moderate dose of white wine on the HPA axis showed that moderate white wine consumption (1) significantly reduces salivary cortisol irrespective of the prior nutritional status of the individual, (2) under fasting conditions significantly reduces salivary DHEAS at 135 min, and (3) when consumed alone after a meal significantly increases salivary DHEAS immediately. Furthermore, when a moderate amount of white wine is consumed prior to food a further decrease in DHEAS was demonstrated.

The data showed an elevation in salivary DHEAS and cortisol under fasting conditions similar to that observed in plasma (Akanji et al., 1990; Lane et al., 1997; Tegelman et al., 1986; Vance and Thorner, 1989). Moreover, the intake of both white wine and grape juice induced an initial

decrease in the level of salivary cortisol and DHEAS similar to that which can occur following food intake (Dallman et al., 1995; Nestler et al., 1995). However, when the two fasting trials were compared, a gradual reduction in cortisol and DHEAS was only observed in the alcohol fasting trial showing that white wine consumption prior to food intake can promote a significant alteration in the functioning of the HPA axis.

The significant increase in salivary DHEAS observed in the alcohol feeding trial, unlike the significant decrease noted in the alcohol fasting trial, does not lend support to the claim that alcohol consumption reduces DHEAS (Andersson et al., 1986). It was shown that when alcohol ingestion precedes food intake a significant decrease in the level of salivary DHEAS may occur, however the opposite may be true when white wine is consumed on its own after a meal. Additionally, the salivary cortisol data from the feeding and fasting alcohol trials, by showing a significant decrease in cortisol irrespective of nutritional status, do not lend support to the claims that alcohol consumption induces a significant elevation (Guillaume et al., 1994), or promotes little (Jenkins and Connolly, 1968) or no change (Davis and Jeffcoate, 1983; Gianoulakis et al., 1997; Ida et al., 1992; Joffe et al., 1984; Waltman et al., 1993) in cortisol release. In the present investigation, the assessment of cortisol and DHEAS level was performed using the same saliva sample in each trial. Therefore, the data, by showing a significant increase in DHEAS in the alcohol feeding trial, indicate that the significant decrease in salivary steroid hormones observed in the present series of studies is unlikely to be due to a dilution effect (Guazzo et al., 1996).

An elevation in cortisol can occur in response to food intake (Dallman et al., 1993, 1995). The role of cortisol in this instance is to modulate the effects of insulin on glucose utilization when glycogen stores are depleted to ensure that energy stores are replenished (Goldstein et al., 1993). The cortisol data presented here support these claims with food intake in the fasting trials inducing an increase in salivary cortisol concentration. However, the level of cortisol observed in the placebo fasting trial after food was finally consumed at 180 min was measured to be significantly greater than that noted at the same time in the alcohol fasting trial. Thus, the data, by showing a significantly reduced level of salivary cortisol following food intake in the alcohol fasting trial, may support the theory that alcohol administration can reduce brain glycogen content (Marieb, 1998), which could increase the risk of hypoglycemia.

When cortisol is secreted into the circulation, over 95% of the released cortisol binds to cortisol-binding globulin (CBG), a carrier protein that transports cortisol to various areas in the body, including the brain (Marieb, 1998). Research has shown that alcohol may decrease cortisol binding to albumin and CBG, which increases the plasma unbound component (Hiramatsu and Nisula, 1989) and could interfere with cortisol transport into the CNS (Marieb, 1998). Salivary measures of cortisol may be representative of the level of steroid hormones in CSF (Guazzo et al., 1996). Therefore, the results presented here could draw attention to the possibility that while cortisol in plasma may remain unchanged (e.g., Davis and Jeffcoate, 1983; Gianoulakis et al., 1997; Ida et al., 1992; Joffe et al., 1984; Waltman et al., 1993), the level of cortisol in CSF may be significantly reduced when a moderate amount of alcohol is consumed irrespective of nutritional status.

Steroid hormones serve a functional neuromodulatory role in the CNS and any alteration in steroid synthesis may directly affect cognitive functioning (Majewska, 1992). DHEAS and cortisol differentially influence the function of the hippocampus (Diamond et al., 1996; Tombaugh et al., 1992), an area thought to be associated with spatial learning (Morris et al., 1982; Olton et al., 1982) and memory formation (Rickard et al., 1994). Prolonged elimination of glucocorticoids can decrease glucocorticoid receptor activity in the hippocampus and activation of glucocorticoid receptors is necessary for the development of behavioural strategies and storage of spatial information (Morris et al., 1982; Oitzl and de Kloet, 1992; Olton et al., 1982). Impairments in visuospatial (Molina et al., 1994) and problem-solving tasks (Brandt et al., 1983) are well documented in the alcohol literature, and it may be that the deficit in organization, planning and spatial learning often observed in alcoholics is due to an alcohol-induced inactivation of glucocorticoid receptors in the hippocampus (Morris et al., 1982; Olton et al., 1982). The significant decrease in cortisol concentration observed when alcohol is consumed irrespective of nutritional status indicates that even a small to moderate amount of white wine may have some affect on glucocorticoid receptor activity in the hippocampus, which could possibly lead to specific cognitive impairment if alcohol is consumed on a regular basis. The hippocampus regulates glucocorticoid activity at the hypothalamic level via inhibition of AVP (Jacobson and Sapolsky, 1991), and chronic alcohol consumption significantly decreases AVP activity (Guillaume et al., 1994), which lends further support to the claim that glucocorticoid activity may be reduced in the hippocampus.

Alcohol administration, by selectively impairing functioning of excitatory NMDA glutamate receptors (Lustig et al., 1992) in hippocampal neurons (Lovinger et al., 1989), potentiates the function of inhibitory $GABA_A$ receptors (Givens and Breese, 1990; Mehta and Ticku, 1988). However, while glucocorticoids inhibit GABA at higher concentrations, they may also potentiate GABA at lower concentrations (Majewska et al., 1985). The present findings, by showing that alcohol decreases cortisol under differing nutritional conditions, thus may support previous work claiming that alcohol may impair NMDA receptor function via potentiation of GABA (Givens and Breese, 1990; Mehta and Ticku, 1988). Additionally, the significant decrease in DHEAS, a known GABA antagonist

(Demirgoren et al., 1991) observed only under fasting conditions, suggests that potentiation of inhibitory $GABA_A$ receptors may be promoted in the absence of adequate nutrition leading to the subsequent inactivation of NMDA receptors in the hippocampus, which could result in memory impairment (Flood et al., 1988; Roberts et al., 1987). However, the significant increase in DHEAS observed immediately after alcohol is consumed in the alcohol feeding trial may suggest that nutritional status could offer some protection against the inactivation of NMDA receptors located within the hippocampus, as DHEAS may modulate the increase in GABA induced by the decrease in glucocorticoids by inhibiting GABA uptake at the $GABA_A$ receptor.

The prior nutritional status of the individual when alcohol is consumed will not only alter the rate of alcohol absorption (Fraser et al., 1995), but also the site of alcohol metabolism (Caballeria, 1991; Lieber, 1982), which can influence the effect alcohol has on the body (Manzo et al., 1994). A moderate amount of alcohol (i.e., <40 g/day) does not directly enter the circulation but instead may undergo first-pass metabolism in the stomach (Di Padova et al., 1987), and gastric metabolism may act as a barrier to alcohol-induced tissue toxicity (Julkunen et al., 1985). However, the effectiveness of this barrier is significantly decreased when alcohol is consumed by fasted individuals (Caballeria, 1991).

During fasting, alcohol within minutes of being consumed is taken up by the systemic circulation (Lieber, 1982), and brain and BALs reach equilibrium rapidly (Marieb, 1998). Alcohol is a highly lipid-soluble substance that has the ability to freely diffuse into cells (Stryer, 1995). The diffusion of alcohol into cells increases the concentration of solute and a hypernatremic dehydration condition may develop as cells gradually become saturated with alcohol. The presence of alcohol within cells promotes K^+ efflux from intracellular stores (Streeton and Solomon, 1954), and this is compensated by a Na^+ gain that more than doubles the glucose consumption by cells at higher alcohol concentrations (Nelson, 1944; Ponder, 1946), in order to minimize the intoxicating effects of alcohol in the CNS (Israel et al., 1965). The alcohol-induced increase in K^+ efflux could increase glial depolarization (Hosli et al., 1981), and glucose demand by neurons and astrocytes, as glucose is required by astrocytes in order to take up the excess K^+ and store it (Kandel et al., 1991). Additionally, an increase in K^+ efflux could stimulate GABA release (Szerb et al., 1981) in order to protect against brain impairment caused by an increase in neuronal depolarization (Hamberger et al., 1976). It has been shown that alcohol's potentiation of GABA is specifically linked to the $GABA_A$ receptor-gated chloride channel (Mehta and Ticku, 1988), and Cl^- is required by astrocytes in order to maintain electrical neutrality (Kandel et al., 1991). However, an increase in K^+ efflux could eventually develop into an extracellular acidosis (Velisek, 1998), and an alteration in the activity of the HPA axis can occur under conditions of chronic osmotic stimulation (Jessop et al., 1990).

A decrease in HPA axis activity under these conditions would be beneficial to the organism as both cortisol and DHEAS decrease GABA activity at higher concentrations (Majewska et al., 1985; Randall et al., 1995), which could increase the risk of brain impairment caused by an increase in neuronal depolarization (Hamberger et al., 1976). Additionally, cortisol (similar to alcohol) increases the loss of body potassium due to the release of K^+ from intracellular stores in mammalian tissues (Streeton and Solomon, 1954), and reduces glucose utilization and transport in neurons and glia (Kadekaro et al., 1988; Horner et al., 1990; Virgin et al., 1991), which could increase the risk of hypoglycemia and hypoxia (Tombaugh et al., 1992). Therefore, the significant decrease in steroid hormones observed in the present study when white wine is consumed prior to food intake may be due to a transient alteration in the activity of the HPA axis caused by the entry of alcohol into cells located in the CNS as suggested by the Salt and Water hypothesis (Kokavec and Crowe, in press).

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