Alcohol and food intake

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Purpose of review

Alcohol is commonly consumed around mealtimes, and both the immediate pharmacological actions of ethanol and the energy generated by metabolism of alcohol have the potential to modify food intake. Effects of moderate alcohol consumption on food intake in humans will be reviewed, and potential mechanisms considered.

Recent findings

Unlike other macronutrients, there is minimal evidence for any reduction in food intake to compensate for the potential energy in alcohol. In contrast, moderate alcohol consumption prior to a test meal leads to a short-term increase in food intake. This stimulatory effect of alcohol is not apparent beyond acute administration, but the inability to reduce voluntary energy intake in response to energy from alcohol metabolism is evident over extended periods. Alcohol suppresses fatty acid oxidation, increases short-term thermogenesis and stimulates a number of neurochemical and peripheral systems implicated in appetite control, including inhibitory effects on leptin, glucagon-like peptide-1, and serotonin, and enhancement of γ-aminobutyric acid, endogenous opioids and neuropeptide Y. All of these effects could lead to overeating, and mechanisms underlying appetite stimulation through alcohol require further substantiation.

Summary

Alcohol is a complex component of the diet, and appears to have multiple effects on appetite. Failure to reduce food intake in response to energy from alcohol makes moderate alcohol consumption a risk factor for obesity. Further integration of evidence from nutrition and neuroscience will be crucial to our understanding of effects of alcohol on appetite.

Keywords

alcohol, food intake, compensatory eating, leptin, neuropeptide Y, fatty acid oxidation

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Abbreviations

BMI	body mass index
FAO	fatty acid oxidation
GABA	γ-aminobutyric acid
GLP-1	glucagon-like peptide-1
NPY	neuropeptide Y

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Introduction

Alcohol is a unique component of the human diet. Firstly, alcohol can be considered as a macronutrient providing 29 kJ (7 kcal) per gram, second only to fat as a potential source of energy. Secondly, alcohol acts pharmacologically on the nervous system, altering a number of important neurochemical systems. Thirdly, it has no storage capacity which means priority in oxidation compared with fat and carbohydrates. All actions are relevant to effects on food intake. Energy derived from alcohol should impact on the appetite control system through feedback mechanisms associated with energy balance in general. Paradoxically, the balance of current evidence consistently shows energy from moderate alcohol consumption is additive to energy from other sources, yet the relationship between moderate alcohol intake and obesity remains at best unclear, with no clear relationship between alcohol consumption and risk for weight gain. Therefore this review re-evaluates the current literature on the relationship between alcohol, food intake and energy balance. The short-term pharmacological effects of alcohol could have both direct and indirect effects on food intake, and again recent studies highlight the nature of such effects. Pharmacological actions of alcohol are characterized by short (typically 30–60 min) onset time, and then reduced potency as ethanol is metabolized (Fig. 1). Conversely, the metabolism of ethanol generates energy, and therefore maximum energy from metabolism of alcohol inevitably occurs some time after peak pharmacological actions. Thus, the predicted pharmacological and energetic effects of alcohol on appetite should be dissociated by time: food intake in the period shortly after alcohol consumption would be predicted to result primarily from pharmacological actions, while delayed effects should represent a combination of these early pharmacological actions and adjustments in intake arising from the metabolism of ethanol. Here we separate studies examining immediate or short-term (hours) effects of alcohol on food intake from longer-term (days to years, primarily epidemiological) studies since the outcome of these two types of study should result from different underlying processes.

Short-term stimulation of food intake by alcohol

The standard methodology for examining short-term effects of alcohol on food intake has been to contrast intake and appetite in a laboratory test situation between alcohol and appropriate control conditions [1•,2–10]. In all of these studies, there is no evidence of any

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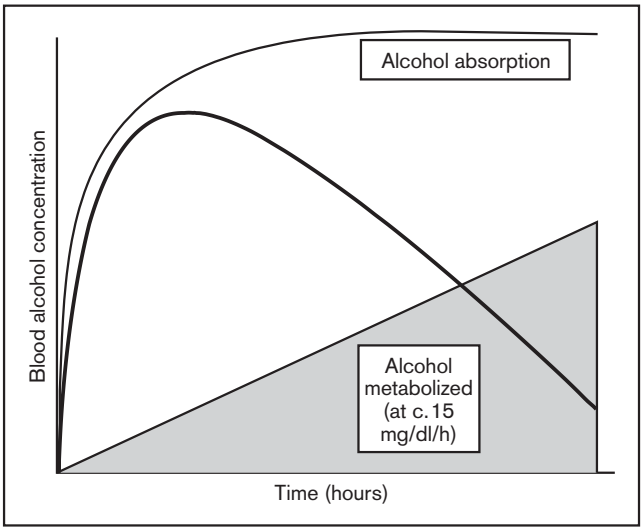
Figure 1. Idealized representation of blood alcohol concentration as a function of absorption and metabolism



compensatory reduction in food intake to accommodate the energy consumed as alcohol. Given that studies either provide alcohol with the test meal [3,4,8,10], or 15–30 min prior to the meal [1•,2,5–7], and it typically takes 1 h to fully metabolize a single unit of alcohol, it is not surprising that alcohol fails to produce immediate compensation in food intake. Provision of extra energy in the form of carbohydrate shortly before a test meal, however, results in decreased intake [11–15] despite evidence that the extra energy would not have been fully metabolized in the time between preload ingestion and intake. Indeed, the most recent study reported compensatory reductions in food intake in response to a carbohydrate preload even with minimal delay between the preloads and test meal [16]. The implication is that the initial metabolism of alcohol does not generate metabolic cues which allow reductions in subsequent energy intake; that is, alcohol is the least satiating of all macronutrients.

Rather than simply reporting no compensatory reduction for the energy in alcohol, most recent studies measuring food intake following a moderate alcohol preload or alcohol with a meal have reported greater food intake following alcohol than after appropriate control preloads [1•,2,3,5,9,10]. This suggests that the pharmacological action of alcohol in the short term increases food intake. This observation is consistent with long-standing notions in medicine, where alcohol prior to a meal was recommended as a treatment for reduced appetite. The most plausible explanation is that this stimulation of appetite results from pharmacological actions of alcohol, and possible mechanisms for that effect are discussed later in this review.

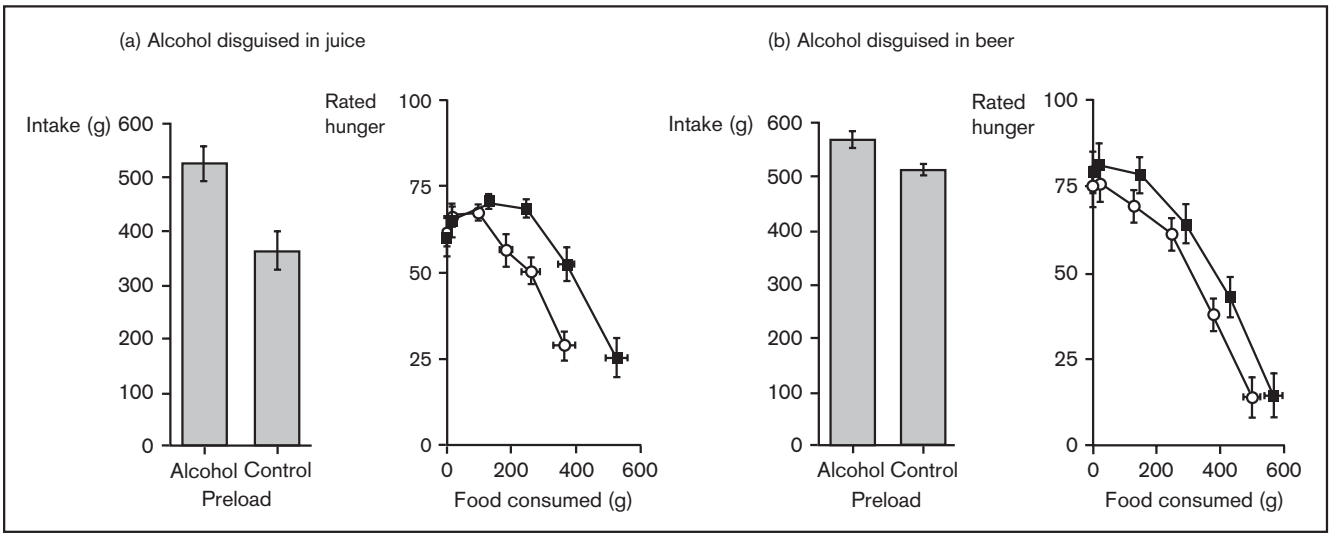
Expectancy and context effects associated with alcohol

Cues which predict the effects of drugs become associated with drug effects, and consequently these cues can affect behaviour in the absence of the drug. In the case of alcohol, these effects could manifest in a variety of ways. Consumption of an alcohol-free drink when alcohol is expected can result in alcohol-like responses [17,18]. The potential complexity of cue–drug interactions is highlighted by detailed evaluation of the short-term effects of alcohol on food intake. Consider two recent studies which reported similar differences in intake of food after alcohol relative to a control drink [1•,2]. In the first, alcohol was served in the absence of alcohol-related cues (the vehicle was a carbonated apple drink), and here the initial response was a reduction in rated appetite both with the alcohol and control drink. Appetite then increased, however, once the subsequent test meal started following alcohol, and food intake was then greater after alcohol than control. Critically, participants were unaware of the presence of alcohol. In the second study, alcohol was served in the context of an alcohol cue (the vehicle was alcohol-free beer). With alcohol cues present, rated appetite was not decreased after either alcohol or control drinks, but instead hunger decreased more rapidly in the absence of alcohol, again resulting in overall greater intake after alcohol than placebo (Fig. 2). Another recent study using alcohol-free beer as the vehicle reported enhancement of food intake after administration of alcohol but again with no dissociation between rated appetite [9]. Together, these data imply a complex interaction between alcohol-related cues and the actual effects of alcohol on the appetite control system, where the pharmacological stimulation of rated appetite may be masked by the effects of drug-related cues. The most recent study [10] further confirms this complexity. Alcohol was served with a meal either as wine or beer, with a carbonated soft drink as the control. When drinks were freely available, overall energy intake was greater in the wine than beer or soft-drink conditions, but when the drinks were served in a fixed portion, there were only marginal enhancements of food intake after the alcoholic drinks. The design of the study was not optimal, since cues (sensory characteristics of beer or wine) and alcohol were confounded. Nevertheless, the study serves to highlight how expectancy, cues and the postingestive effects of alcohol may interact to affect short-term food intake.

Longer-term overconsumption of energy associated with moderate alcohol intake

There is a long-standing debate in the nutrition literature about whether energy derived from alcohol contributes to energy balance [19–22]. Here we re-assess this literature not in terms of overall energy balance, but in terms of whether the short-term stimulatory effects of

Figure 2. Food intake and rated hunger following alcohol and energy-matched control preloads



Presented in an alcohol-free (a, reproduced from [2]) and alcohol (b, reproduced from [1•]) context (solid squares, alcohol; open circles, control).

alcohol on food intake result in longer-term increases in energy intake. The relationship between alcohol intake, diet and obesity in men and women was examined in two large-scale cohort studies, the Nurses Health study and the Health Professionals follow-up study [23]. Overall there was a positive relationship between alcohol consumption and energy intake in both men and women. These epidemiological data are supported by studies using more detailed diary methods to examine the inter-relationship between alcohol and food intake [24]. Again, energy from alcohol was supplemental to energy from other sources, and this pattern appears to be consistent across a wide range of studies, methods and populations. However, whether this excess energy intake leads to body weight gain remains controversial [21,25] and unresolved despite over a hundred years of relevant research. Two recent studies provide further evidence that body mass index (BMI) is positively correlated with alcohol intake [26•,27•], lending further support to the view that alcohol is a risk factor for obesity. Other data suggest that alcohol is more associated with higher waist-to-hip ratio than BMI [28], suggesting that alcohol may promote abdominal obesity in particular. Not all epidemiological studies find evidence of a relationship between alcohol and BMI, and some researchers maintain that energy from alcohol dissipates through inefficient metabolism with no lasting effects on body weight [22].

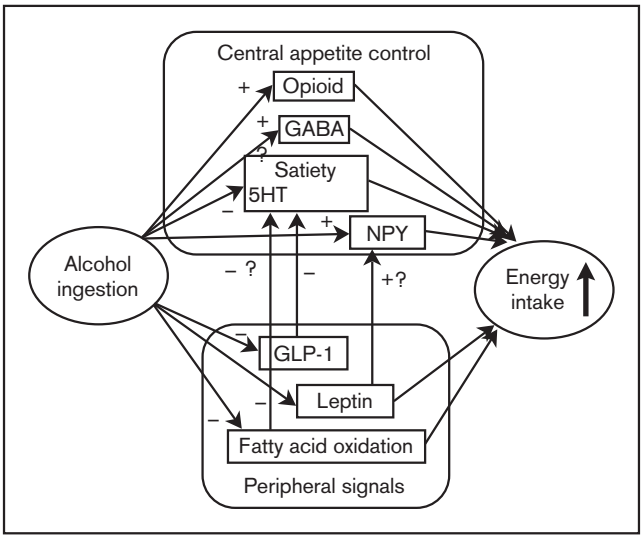
Despite the consistency of the acute stimulatory effects of alcohol on food intake discussed earlier, these effects do not correspond with an increase in food intake measured over days [24], or tested beyond 5 h after alcohol ingestion [29••]. This implies either that the acute stimulatory effects of alcohol are not sustained, and may be compensated for by subsequent adjustments to food intake, or that since the acute increases in appetite are relatively small, it is possible that longer-term studies lack the necessary sensitivity to detect small increases in long-term food intake. Either way, the vast majority of studies clearly show that moderate alcohol intake is associated with an overall increase in energy intake.

In contrast to moderate alcohol intake, excessive alcohol consumption is associated with lower intake of energy from fat and carbohydrates [30]. This could be interpreted as evidence of satiety associated with alcohol energy at higher doses. Interpretation of data from individuals with high alcohol intake has to be viewed with caution, however, since alcoholism causes major physiological disturbances, most notably to the liver, and so reduced food energy intake in alcoholism may be a consequence of the disease process rather than a reflection of the effects of alcohol on appetite.

Mechanisms underlying effects of moderate alcohol intake on food intake

Although the evidence for short-term increase in food intake associated with alcohol in humans is compelling, the mechanisms underlying this effect remain unclear and, given that alcohol will enter every cell in the body, may involve multiple mechanisms. A number of possible mechanisms are reviewed, all of which have the potential to result in short-term stimulation of appetite (Fig. 3).

Figure 3. Putative mechanisms underlying short-term stimulation of appetite by alcohol



5HT, serotonin; GABA, γ-aminobutyric acid; GLP-1, glucagon-like peptide-1; NPY, neuropeptide Y.

The metabolism of alcohol has been subject to a comprehensive and recent review [31]. Several investigations have demonstrated the capacity of alcohol to suppress fatty acid oxidation (FAO) [32–35] especially in the liver, where fatty acids are directed towards triacylglyceride synthesis as opposed to oxidation [36]. The oxidation of alcohol changes the redox state of the liver thus reducing hepatic FAO [37]. More importantly, suppression of hepatic FAO increases food intake in both rats [38,39] and humans [40]. It is likely that signals encoding FAO contribute to the development of a satiety signal and so if these signals are delayed an increase in food intake is likely to occur. Thus recent data indicative of delayed satiety in short-term intake tests [1•,5,9] could be interpreted as a consequence of alcohol-induced reductions in FAO.

Whether or not alcohol is used as efficiently as other macronutrients is also unclear, and inefficient metabolism may contribute to the failure to find acute reductions in subsequent food intake which are evident with other macronutrients. Several investigations have suggested that energy expenditure is raised following alcohol ingestion [29••,41,42] whilst others report no difference [32,33,41,43,44]. Alcohol is a competitive substrate and displaces the utilization of other nutrients, shifting the partitioning of carbohydrate and fat towards carbohydrate. Resultant degradation of glycogen selectively spares fat stores, which may contribute to increased adiposity if alcohol is consumed in excess of energy requirements in the long term. It is unclear, however, how these metabolic effects could lead to short-term appetite stimulation, although they offer a plausible explanation of why short-term enhancement of food intake does not necessarily lead to weight gain.

Alcohol administration affects many neurotransmitter, hormonal and other afferent signals, including leptin, neuropeptide Y (NPY), serotonin (5HT), γ-aminobutyric acid (GABA), opioids and glucagon-like peptide-1 (GLP-1). Changes to any one or all of these may underlie the lack of compensatory reduction in food intake following alcohol ingestion, or the short-term stimulation of appetite by alcohol. Serotonergic dysfunction has been well documented in alcoholics [45,46]. Central 5HT levels may be reduced following alcohol intake, leading to reduced satiety and consequent increased meal size. There is also limited evidence that leptin production and 5-HT are related [47]. The link between alcohol ingestion, changes in 5HT and leptin, however, remains to be investigated. NPY is known to have hyperphagic effects, which are attenuated by the presence of leptin [48]. Moreover, it is not yet clearly understood whether or not leptin has an inhibitory effect on NPY in normal weight humans. It has been demonstrated in animals that alcohol ingestion leads to an increase in central NPY levels [49]. Recent investigations [29••,50] examined the effect of alcohol ingestion on secretion of leptin in normal weight volunteers. It was found that moderate amounts of alcohol produced an inhibitory effect on leptin secretion. Raben *et al.* [29••] also reported a reduction in GLP-1, an endogenous peptide signal involved in meal termination, following moderate doses of alcohol (20–25 g, equivalent to 3 units of alcohol). Thermogenic response was raised following alcohol, however there was no significant increase in energy intake following alcohol, in contrast to other studies reported here. However, the test meal was presented 5 h after the alcohol preload, well beyond the period when the short-term stimulatory effects of alcohol have been reported in other studies. Moreover, the dose of alcohol used and the timing of the alcohol administration (09:45) may also have affected the outcome of this study. Despite these shortcomings, if the reduction in GLP-1 reported in this recent study is found to be a robust finding, a combination of enhanced stimulation of appetite through NPY release coupled with reduced satiety signals (5HT and GLP-1) could all contribute to short-term overeating associated with alcohol.

Many of the physiological and pharmacological actions of alcohol have been attributed to its effects on the GABA system [51•]. GABA also has a role in normal control of feeding, since drugs which enhance GABAnergic activity such as baclofen [52,53] and the benzodiazepines [54] reliably increase food intake in animals. Benzodiazepines also consistently increase food intake in humans [55], and the short-term effects of alcohol discussed in this

review appear to resemble the stimulation of appetite reported with benzodiazepines, implying a potential GABAnergic role in short-term stimulation of appetite. There have been no specific tests of this model, however, and further research is needed in this area. Alcohol also releases endogenous opioids [56], and opioid release has been implicated in mediating the reinforcing effects of alcohol, an idea reinforced by recent data showing opioid involvement in hedonic responses to alcohol in animal studies [57]. Opioids are also implicated in orosensory reward components of eating [58•]. Whether alcohol-induced opioid release modifies subsequent food-induced opioid release is also untested, but is another potential neural component of the stimulation of appetite by alcohol.

Conclusion

Overall, acute doses of alcohol within the normal consumption range apparently fail to generate reliable satiety signals, and there is no evidence of compensatory reductions in food intake in response to the energy in alcohol. Moreover, recent studies clearly indicate a short-term stimulatory effect of alcohol on appetite in humans, resulting in greater food intake when alcohol is administered. Potential mechanisms underlying the failure to reduce food intake in response to the energy in alcohol are emerging, with a combination of altered FAO and enhanced thermogenesis both likely to be important. There are a number of potential mechanisms for short-term stimulation of appetite by alcohol, however, none of which can be discounted at present, and future research should be directed at a comprehensive elucidation.

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