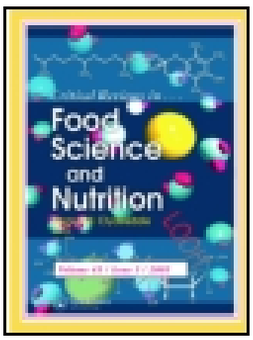

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The Role of Taste in Alcohol Preference, Consumption and Risk Behavior

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1. Abstract:

Alcohol consumption is widespread, and high levels of use are associated with increased risk of developing an alcohol use disorder. Thus, understanding the factors that influence alcohol intake is important for disease prevention and management. Additionally, elucidating the factors that associate with alcohol preference and intake in non-clinical populations allows for product development and optimisation opportunities for the alcoholic beverage industry. The literature on how taste (orosensation) influences alcohol behavior is critically appraised in this review. Ethanol, the compound common to all alcoholic beverages, is generally aversive as it primarily elicits bitterness and irritation when ingested. Individuals who experience orosensations (both taste and chemesthetic) more intensely tend to report lower liking and consumption of alcoholic beverages. Additionally, a preference for sweetness is likely associated with a paternal history of alcohol use disorders. However, conflicting findings in the literature are common and may be partially attributable to differences in the methods used to access orosensory responsiveness and taste phenotypes. We conclude that while taste is a key driver in alcohol preference, intake and

use disorder, no single taste-related factor can adequately predict alcohol behaviour. Areas for further research and suggestions for improved methodological and analytical approaches are highlighted.

Keywords

PROP, thermal taste, sweet-liking, taste phenotypes, sensory properties, ethanol.

2. Introduction

Alcohol consumption is often associated with negative health and personal consequences. For example, college students report missed classes, hangovers, and feelings of regret as a result of alcohol consumption (Park & Grant, 2005). Physical consequences of high risk drinking include liver damage, numbness, ulcers, reduced balance, vitamin deficiency/malnutrition, heart failure, memory loss, and the development of various cancers (Barbor, Higgins-Biddle, Saunders, & Monteiro, 2001). However, it is also positively associated with some measures of well-being, such as increased levels of relaxation, creativity, enjoyment of a meal and greater ability to express oneself (Park & Grant, 2005). It has been argued that research in this area should only concern itself with the negative health consequences of alcohol, however this ignores the equivocal nature of the literature on the healthiness of moderate consumption. Noteworthy, when individuals perceive wine as healthy, they do not consume more than individuals that consider wine unhealthy, and may in fact follow healthier consumption patterns (Saliba & Moran, 2010). A full discussion of the harm and benefit of alcohol is beyond the scope of this review, and the reader is referred to Walzem et al (2008) for more information. Understanding the factors that affect alcohol intake is important for informing disease prevention and management interventions and policy. Conversely, the alcoholic beverage industry is interested in better understanding the drivers of alcohol preference and liking in non-clinical populations, as it can assist with market segmentation, and create opportunities for product development and optimisation.

Alcohol consumption is influenced by a diverse set of factors, including genetics, alcohol reactivity, social expectations and sanctions, gender, coping style, expectancy of alcohol related consequences, depression, self-esteem, sensation seeking, interpersonal relationships, and history of trauma (Nolen-Hoeksema, 2004). Taste also plays a role in mediating alcohol behaviour. For instance, in a study of 517 undergraduate students, alcoholic beverages represented a significant proportion of the food/beverage items to which participants reported taste aversions (the rejection of a substance due to unpleasantness or illness; Logue, Ophir, & Strauss, 1981). More recently, in a study of Japanese wine consumers, taste was rated as the most important factor

influencing wine purchase decisions, behind (in descending order of importance), style, color, price, friend/family recommendation, variety of choice, back label info, wine magazine/critic recommendation, country of origin, sale item, vintage, front label design, brand, closures and alcohol content (Bruwer & Buller, 2012). While numerous, complex and interacting factors influence alcohol consumption and risk behaviour, the focus of this paper is on the role of taste.

2.1. Taste, Chemesthesis, Somesthesis and Orosensation

Formally, taste is the oral sensation produced when food or beverages are consumed, eliciting a response from chemoreceptors within the oral cavity. These sensations – referred to as the prototypical tastes – are sweet, sour, bitter, salty and umami (Bachmanov & Beauchamp, 2007). Two classes of prototypical tastes are recognized: the ion channel tastes (sour and salty) and g protein-coupled receptor (GPCR) tastes (sweet, bitter, and umami) (Bachmanov & Beauchamp, 2007). Sourness and saltiness result from the depolarization of ions channels. Saltiness is elicited when amiloride-sensitive epithelial Na^+ channels (ENaC) are depolarized by Na^+, whereas sourness is elicited when acid-sensing ion channels (ASIC) are depolarized by free protons. Sweet, bitter, or umami are elicited when sapid compounds hydrogen bond to GPCRs on taste buds (Talavera et al., 2005). Taste 1 Receptor (TAS1R) genes encode for sweet and/or umami sensitive proteins, while Taste 2 Receptor (TAS2R) genes encode for proteins involved in bitterness transduction (Bachmanov & Beauchamp, 2007). In addition to the prototypical tastes, chemesthetic and somatosensory sensations are primarily elicited by stimulation of the trigeminal system, typically when transient receptor potential channels (TRP) are activated (Kolindorfer et al., 2015). Often these are also referred to as tactile sensations, and encompass percepts such as astringency, touch, heat, prickling, and burning. Collectively, prototypical taste, chemesthetic and somatosensory sensations are called orosensations.

The other key sensory modality involved in eating and drinking is retro-nasal olfaction, initiated by volatile compounds traveling from the mouth to olfactory receptor cells in the nasal cavity (Jackson, 2009). As orosensations and aroma are experienced simultaneously during eating and drinking, they are often colloquially referred to simply as ‘taste’. However, in this review we will use the term ‘flavour’ to describe the combined experience from orosensory and retro-nasal inputs, and ‘taste’ to indicate general orosensation.

2.2. Differences in Orosensory Perception

The perception of orosensations differs widely across individuals, and varies with several biological and behavioral factors. These include gender (Wardwell et al., 2009), age (Fischer et al., 2013), and smoking status (Pepino & Mennella, 2007; Fischer et al., 2013); factors which may also directly associate with alcohol preference (Bajec, 2010), consumption (Duffy et al., 2004; Pepino & Mennella, 2007; Bajec, 2010) and dependence (Kampov-Polevoy, Eick, Boland, Khalitov, & Crews, 2004; Pepino & Mennella, 2007; Wronski et al., 2007). Orosensation is partially under genetic control, and inter-individual differences can also be understood by grouping people according to their taste genotype and phenotype (e.g., Allen, McGeary, & Hayes, 2014; Bering, Pickering, & Liang, 2013; Garcia-Bailo, Toguri, & El-Sohemy, 2009; Keskitalo et al., 2007; Talavera et al., 2005; Tepper, 2008). Fox (1931) first reported that phenylthiocarbamide was tasteless to some individuals while eliciting a strong bitter sensations for others. This discovery sparked the development of research into taste phenotypes in an attempt to explain the striking differences observed between individuals (Wooding, 2006).

Phenotypes are traits under genetic control such as eye colour or height, which can be observed and used to classify organisms into groups. For example, individuals can be divided by demographic characteristics (age or gender), by similar behaviors (smokers vs nonsmokers) or by similar responsiveness to tastants (taste phenotypes). Three important taste phenotypes from the literature that have been linked to alcohol behaviour are 6-n-propylthiouracil (PROP) taster status (PTS), sweet-liking, and thermal taster status (TTS). However, each phenotype is likely accounted for by different mechanisms. For instance, there is no (Bering et al., 2013; Pickering, Moyes, Bajec, & DeCourville, 2010) or very limited (Yang, Hollowood, & Hort, 2014) association between PTS and TTS, and no association between PTS and sweet-liking has been found (Drewnowski, Henderson, Shore, & Barratt-Fornell, 1997).

Orosensations play a key role in food and beverage preferences and consumption. For example, in a 1998 nationwide study, 2967 American adults rated the importance of nutrition, taste, cost, convenience, and weight control in personal dietary choice (Glanz, Basil, Maibach, Goldberg, & Snyder, 1998). Taste followed by cost were the two most important factors in food choice reported in the study. Genetic variation in orosensory receptors contributes to differences in the

perception of oral sensations across individuals (Figure 1). This in turn, influences the development of food preferences, food intake, and health related outcomes (reviewed in Garcia-Bailo et al., 2009; Hayes, Feeney, & Allen, 2013; Tepper, 2008). One way in which taste phenotypes might link with alcohol behaviour is through increased orosensory responsiveness in some phenotypic groups. For instance, higher perceived bitterness from ethanol might lead to an increase in its unpleasantness, and thus a decrease in total intake of alcoholic beverages (Tepper, 2008).

In this paper, we will critically review the role of orosensation in alcohol consumption, preferences and the risk of an alcohol use disorder/alcoholism. We begin with a description of the sensory characteristics associated with ethanol and their impact on alcohol behaviour. Subsequent sections describe the impact of individual differences in orosensory perception in general, and as operationalized by taste phenotypes. Genotypic differences that influence taste perception are also discussed and, where applicable, gender and age are considered. Next, we examine the influence of orosensory responsiveness and taste phenotypes on alcohol related behaviour. We conclude by arguing for the inclusion of orosensory responsiveness and/or taste phenotype data in future studies to build more comprehensive models of alcohol consumption and risk behaviors.

2.3. Methodological Challenges

A significant challenge in reviewing and summarising the pertinent literature is assessing the significance of the methodological differences in data collection approaches and measures used across studies, as best practices change and research foci can vary across groups. For example, alcohol use disorder risk can be assessed using several instruments, with for instance, six different screening tools suggested by the Australian government (Haber, Lintzeris, Proule, & Lopatko, 2009). Not only do these instruments differ in length and scale type, researchers must interpret the scores and choose appropriate cut-off points to define individuals with and without an alcohol use disorder. As a result, differences in the definition or criteria used in classification are common. Similarly, differences in the criteria used for classifying orosensory responsiveness and taste phenotypes are common, as are the measures of alcohol categories and intake. Among other factors, it is important to consider the choice of scales, standards/concentrations used for

prototypical tastes, and co-variables examined in each study in assessing its contribution to the central thesis of this review. Importantly, when similar results are reported in studies that have used different methodological approaches, a degree of confidence can be assigned with respect to the robustness of the findings.

Most studies reviewed here use a relatively small sample size (n = 30-200), as recruitment of participants can be challenging and the time required to administer tests limiting. A common theme in the discussion of null findings or those that only approach significance is that the limited sample size lacks the statistical power to establish significance, particularly when multiple variables are being evaluated simultaneously (e.g. Zhao, Kirkmeyer, & Tepper, 2003). As a result, population based studies such as the Beaver Dam Offspring Study (n = 1500--2400; Cruickshanks et al., 2009; Fischer et al., 2014, 2013) or a recent report on over 1000 US wine consumers (Pickering, Jain, & Bezawada, 2014) are valuable in confirming or refuting trends observed in smaller, more traditional lab-based studies. However, the methods used in population-based studies may be overly simplified to allow for large-scale testing outside the laboratory, and lack precision. For example, filter paper disks impregnated with tastants are commonly used to elicit orosensations rather than aqueous solutions, as they are easily transported and can be prepared well in advance (e.g. Cruickshanks et al., 2009; Hayes and Pickering, 2012). However, the orosensations elicited by paper disks are typically localized to the area where the disk is applied, while aqueous solutions coat the entire mouth with sip and spit protocols. Similarly, some orosensory evaluation protocols involve self-administration of the stimuli by participants (e.g. Pickering, Jain, & Bezawada, 2013), potentially introducing extra variability in the responses. Consequently, methodological differences should be considered when population- and laboratory-based studies report different findings.

The inclusion criteria used to select participants for a study may limit the generalizability of the results. For example, the evidence for a link between sweet-liking and alcoholism has been largely limited to male clinical populations. As a result, it is unclear if these results can be generalized to non-clinical populations or to females. Similarly, most research on thermal taste has been limited to convenience samples of college students, despite the fact that this cohort consume more alcohol and binge drink more frequently that their same-age peers who do not

attend college, and typically reduce their alcohol consumption after graduation (Merrill & Carey, 2016). Thus, the drinking patterns of college student may not reflect lifetime drinking behaviour, and studies using college students may not be generalizable to other age cohorts.

3. Ethanol

3.1. Orosensory Characteristics

Ethanol (ethyl alcohol) is present in all alcoholic beverages and may play a key role in their sensory perception. Ethanol detection thresholds in aqueous solution are reported as between 0.87 to 1.43% v/v (Mattes & DiMeglio, 2001; Nolden, McGeary, & Hayes, 2016), and are higher for males than females (Mattes & DiMeglio, 2001). Importantly, this range of threshold values is lower than the ethanol concentration found in most alcoholic beverages, confirming that ethanol likely contributes to the flavour of these products (Table 1). In aqueous solution it elicits sweetness, bitterness (Allen et al., 2014; Mattes & DiMeglio, 2001; Nolden & Hayes, 2015; Nolden et al., 2016; Scinska et al., 2000), sourness (Mattes & DiMeglio, 2001; Scinska et al., 2000), and saltiness (Mattes & DiMeglio, 2001). At and just above detection threshold in aqueous ethanol solutions, ethanol elicits bitterness more strongly than other basic tastes (Mattes & DiMeglio, 2001). Recently, Nolden & Hayes (2015) have demonstrated that the dominant orosensation elicited by ethanol in aqueous solution changes with concentration. Bitterness dominates at 4% and 16% v/v ethanol, whereas burning/tingling is the dominant sensation at concentrations of 32% and 48% v/v. Mean pleasantness values for 0.3% to 10% (v/v) ethanol concentrations were negative on a line scale from -50 to 50 where 0 is assumed to represent a neutral pleasantness score (Scinska et al., 2000). Furthermore, orosensory intensity increased and pleasantness decreased with increasing ethanol concentration (Scinska et al., 2000), perhaps due to greater stinging, tingling, irritation and burning sensations (Allen et al., 2014; Green, 1987, 1988; Nolden & Hayes, 2015; Nolden et al., 2016). Therefore, in aqueous solution, ethanol is likely aversive regardless of the concentration, a finding with implications for alcoholic beverages discussed later.

Repeated exposure to ethanol can cause desensitization in the short term. Prescott & Swain-Campbell (2000) showed that when participants rate the intensity of ten sequential 47.5% ethanol

solutions spaced at one-minute intervals, responsiveness decreases in latter samples. However, intensity ratings recover to near initial levels when an eleventh sample is tasted after a 10-minute break. If similar experiences occur with alcoholic beverages, this finding might predict that the aversive character of ethanol reduces across a drinking session, at least for some consumption patterns. Additionally, this suggests that the number of drinks consumed during a drinking occasion should be captured in studies examining inter-individual differences in orosensation, in addition to the traditional and simpler metric of total intake. However, the ecological validity and limits of the Prescott & Swain-Campbell (2000) finding remain to be determined. For example, taking several shots of spirits or slowly sipping a wine may not produce equal (or any) desensitization. Indeed, considerably more study is still needed to understand to what extent responses to ethanol aqueous solutions translates into perception of alcoholic beverages. The latter are much more complex, and this can affect orosensory ratings (Zamora, Goldner, & Galmarini, 2006). Responsiveness to ethanol aqueous solutions may not be a useful proxy for predicting responsiveness to more complex matrices; this may be especially true for ethanol consumed in solid or gel matrices, such as alcoholic ice cream, chocolates or gelatin desserts (e.g. Jell-o® shots).

3.2. Ethanol Perception and Alcohol Consumption

Only a limited number of studies have investigated this suggested association between ethanol responsiveness and alcoholic beverage behaviour. Nolden and Hayes (2015) recently reported that individual variation in the intensity of suprathreshold ethanol associates with the number of drinking occasions of beer, wine, straight spirits, and all alcoholic beverages when grouped together. In general, individuals who consume alcohol less frequently perceive greater bitterness and burning/tingling from ethanol, likely increasing its aversive character (Nolden & Hayes, 2015). The association between ethanol detection thresholds and alcohol consumption in some studies further supports this limited evidence that ethanol responsiveness and/or sensitivity mediates the number of drinking occasions. Moderate to heavy drinkers have a higher ethanol detection threshold than individuals who abstain from alcohol or are light drinkers (Mattes, 1994). In contrast, no significant difference in ethanol detection thresholds was found when only beer consumption was examined (Mattes & DiMeglio, 2001). However, as these participants

reported consuming other types of alcohol, beer consumption may not reflect trends in overall drinking.

Single nucleotide polymorphisms (SNPs) in three genes – TRPV1, TAS2R13, and TAS2R38 – have been shown to associate with differences in ethanol perception (Allen et al., 2014). These authors suggest that this variation may be predictive of alcohol consumption, as TRPV1 is a nocioreceptor associated with the perception of burning, and TAS2R13 and TAS2R38 are bitter taste receptors. Recently, Nolden et al. (2016) confirmed the link between the suprathreshold bitterness of ethanol and TAS2R38 genotypes; PAV/PAV individuals rate the bitterness of ethanol as significantly higher than AVI/AVI homozygotes or PAV/AVI heterozygotes. Dotson et al (2012) reported that alcohol consumption varied by TAS2R13 and TAS2R38 genotype in patients with head and neck cancer. However, as head and neck cancer patients are typically undergoing radiation treatment and this is associated with taste abnormalities (Dotson et al., 2012), caution should be applied in generalising these results to healthy individuals. However, higher total alcohol consumption has been noted in healthy individuals with AVI/AVI genotypes compared to individuals with PAV/AVI and PAV/PAV genotypes (Duffy, Davidson, et al., 2004; Hayes et al., 2011). With respect to alcohol use disorders, Wang et al. (2007) found no association between the maximum number of drinks consumed in a 24-hour period and TAS2R38 genotypes for Americans of European ancestry in a large study of families with a history of alcoholism. However, in African American females (n = 105) but not males (n = 114), the PA_ (PAV or PAI) haplotypes associated with a reduced number of drinks consumed in a 24-hour period compared to AA_ (AAV or AAI) or AVI haplotypes, although this finding did not extend to increased alcohol dependence.

Ethanol is not the only compound important in orosensation elicited by alcoholic beverages (Table 1). Sugars, organic acids, phenolics, ions, and carbon dioxide all contribute to the individual character of different alcoholic beverage categories (Piggott, 2012). The concentration and balance between these compounds are frequently manipulated during production to optimize flavour and define different beverage styles (Blackman, Saliba, & Schmidtke, 2010). For example, red and white wine differ in orosensory characteristics primarily due to the length of time the juice/must is in contact with the grape skins; the extra phenolics extracted from skins in

red wine confer greater astringency and bitterness and help to differentiate the products (Brossaud, Cheynier, & Noble, 2001; Yoo, Saliba, Prenzler, & Ryan, 2012). Similarly, hard spirits consumed in the presence or absence of a mixer will differ in orosensory attributes, as the presence of a mix alters the characteristics of the final drink, including moderating the perception of ethanol (Lachemeir, Kanteres, & Rehm, 2014). Thus, the orosensory properties of specific alcoholic beverages may differ based on both ethanol concentration and other compositional differences.

4. OROSENSORY RESPONSIVENESS

4.1. Quinine Bitterness

Differences in suprathreshold responsiveness to prototypical tastants and irritants may partially predict alcohol consumption and preferences. We begin our discussion by considering the link between these behaviors and perception of quinine, a bitterant that has been used extensively in psychophysical research on taste, both in its sulphate and hyrdochloride salt forms. As bitterness is generally perceived as unpleasant (Bredie, Tan, & Wendin, 2014), it has been hypothesized that increased bitter responsiveness associates with lower alcohol consumption. However, no difference in the responsiveness to quinine and overall alcohol consumption was found by Fischer et al. (2013, 2014) in their large study of over 2,300 participants from the Beaver Dam Offspring Study. However, this result fails to consider differences between alcoholic beverage types. For instance, intake of unmixed spirits might be expected to vary more with quinine responsiveness than other beverage categories, as they most closely resemble pure ethanol (Wisniewska et al., 2015), and increased responsiveness to ethanol has been previously shown to associate with alcohol consumption. Surprisingly, however, consumption of unmixed spirits was not associated with suprathreshold differences in quinine bitterness in the recent report of Thibodeau, Bajec, & Pickering (2016). However, the bitterness of different compounds is typically associated only if they bind to the same TAS2R bitter receptor (Roura et al., 2015). Most previous studies have relied on quinine as a general proxy for bitterness, which elicits a response from 9 TAS2Rs (TAS2R4, TAS2R7, TAS2R10, TAS2R14, TAS2R39, TAS2R40, TAS2R43, TAS2R44, and TAS2R46; Meyerhof et al., 2010), whereas ethanol to date has only

been shown to excite 2 bitter receptors; TAS2R38 and TAS2R13 (Allen et al., 2014). Thus, as ethanol and quinine do not appear to activate the same bitter taste receptors, it is possible that the expected effects on consumption from ethanol bitterness aversion are not fully captured when quinine is used, which may account for the null result for unmixed spirits intake in Thibodeau et al. (2016). These results suggest that when examining the relationship between orosensory responsiveness and alcohol response, preference or consumption, quinine is not an effective proxy for ethanol bitterness. Instead, an individual's response to or liking for ethanol should be measured directly or with a proxy that elicits the same TAS2R.

In contrast to unmixed spirits, quinine bitterness was associated with the monthly consumption of all alcoholic beverages (wine, beer, spirits and other combined) and all spirits combined (a combination of both mixed and unmixed spirits) in Thibodeau et al. (2016), with similar trends observed for beer intake and frequency. The pattern of results was non-linear, with individuals of intermediate quinine responsiveness consuming more alcohol than individuals with high or low responsiveness. It is possible that quinine responsiveness may be serving as a partial proxy for non-ethanol bitterants in alcoholic beverages that are present at optimal levels for the 'average' palate, particularly iso-α-acids (beer) and the phenolics malvidin-3-glucoside and (-) epicatechin (wine), all of which bind to TAS2Rs that overlap with quinine (Intelmann et al., 2009; Soares et al., 2013).

Further evidence that intake may be associated with differences in the perception of compounds in alcoholic beverages other than ethanol comes from the study of Tanimura & Mattes (1993). These authors demonstrated that the detection threshold for iso-alpha-acids is approximately 4 times higher for heavy drinkers (> 8 beers weekly) than for slight consumers (<2 beers weekly), while that of moderate drinkers (3-7 beers weekly) was intermediate to but not statistically differentiated from the other two groups. However, sample sizes were very small (n = 19, 5--8 per group), and thus some caution should be applied. It is possible that higher levels of beer intake lead to a greater tolerance for the bitterness of iso-alpha-acids, which in turn may facilitate a further increase in beer consumption.

There is some, limited, evidence that quinine bitterness may also influence the risk of developing an alcohol use disorder. In-patient individuals undergoing treatment for alcoholism had higher quinine taste thresholds than a control group of non-alcoholics (Smith, 1972). However, there are several shortcomings in the information provided in the paper that make it difficult to fully evaluate the claims; specifically, what type of threshold was tested and what diagnostic criteria were used for alcoholism. A limited examination of individuals who abstain from all alcohol was conducted by Thibodeau et al (2016), and they showed a tendency toward higher responsiveness than alcohol consumers to quinine bitterness, in addition to sweet, sour, and salty stimuli, perhaps suggesting that broadly-tuned orosensory responsiveness may be protective against alcohol use and misuse. Significantly more research is needed to expand on these initial findings and speculations.

4.2. PROP Bitterness

4.2.1. Classification & Orosensory Advantage

PTS (PROP taster status) measures an individual's responsiveness to the bitter compound, 6-n-propylthiouracil (PROP). As such, individuals are typically classified into three phenotypic groups; PROP non-tasters (pNTs) for whom PROP elicits little or no sensation, PROP medium-tasters (pMTs) for whom PROP elicits a mildly bitter sensation, and PROP super-tasters (pSTs) for whom PROP elicits a highly bitter sensation (Bartoshuk et al., 1999; Bartoshuk, Duffy, & Miller, 1994). The majority of studies examine the role of PROP responsiveness in perception and behavior by parsing individuals into one of these three groups, although several treat PROP responsiveness as a continuous variable; an approach that can be especially useful with modeling or correlation analysis (Lanier, Hayes, & Duffy, 2005). The methods used to classify individuals into PTS groups have varied over the years, and may contribute to some of the contrasting results on alcohol. Importantly, the early use of threshold methods to determine PTS has largely been replaced by suprathreshold methods as the later allows for the separation of pMTs and pSTs (Bartoshuk et al, 1994; Hayes and Keast, 2011; Tepper, 2008). A full discussion of the classification systems is beyond the scope of this review, and the reader is referred to Tepper (2008) for an in-depth consideration of the topic.

PROP bitterness is positively correlated with suprathreshold sweetness, bitterness (Bajec &

Pickering, 2008; Bartoshuk et al., 1994; Fischer et al., 2014), saltiness, sourness, (Bajec & Pickering, 2008; Fischer et al., 2014), astringency, and metallic intensity (Bajec & Pickering, 2008) in aqueous solutions. As a result, it has been suggested that PTS may be a useful proxy for general orosensory responsiveness, should the findings in aqueous solutions extend to food and beverages (Bajec & Pickering, 2008). Several studies have established such an association between PROP responsiveness and perception of orosensations elicited by sampled foods and non-alcoholic beverages (Akella, Henderson, & Drewnowski, 1997; Bell & Tepper, 2006; Lanier et al., 2005); below we review the extent to which this extends to ethanol and alcoholic beverages, and summarise the findings in Tables 2A-C.

4.2.2. Genes associated with PROP Bitterness

PROP phenotypes are partially explained by genetic variation in the TAS2R38 gene for which two common haplotypes have been reported (Tepper, 2008). The recessive AVI "nontaster" allele is associated with reduced PROP responsiveness, while the dominant PAV "taster" allele is associated with higher PROP bitterness intensity (Calo et al., 2011; Duffy, Davidson, et al., 2004). As a result, typically three diplotypes are studied; AVI/AVI homozygotes who rate PROP bitterness lowest (putatively pNTs), PAV/PAV homozygotes who rate PROP bitterness highest (putatively pSTs) and PAV/AVI heterozygotes (putatively pMTs) whom rate PROP bitterness higher than AVI/AVI at all concentrations and at high concentrations rate PROP bitterness lower than PAV/PAV (Calo et al., 2011; Duffy, Davidson, et al., 2004; Fischer et al., 2014). The response of heterozygous individuals is variable, as higher within-group variation exists (Lipchock, Mennella, Spielman, & Reed, 2013), possibly due to greater variation in gene expression (Lipchock et al., 2013). Three less common haplotypes also exist – PAI, AAV and AAI – with a prevalence of only 4% within the Caucasian population (Wang et al., 2007), and most studies do not report on them.

Polymorphism in the gustin gene (rs2274333; A/G), a trophic factor in taste bud development, is also associated with differences in PROP responsiveness (Calo et al., 2011). While the A allele may be required for supertasting, the gustin gene does not fully explain the variation in PROP responsiveness or PROP taster groups. However, when both TAS2R38 and gustin genotypes are accounted for, approximately 60% of the variation can be explained (Calo et al., 2011). New

research determining how both genes might interact to modulate alcohol consumption, preferences and use disorder risk would be very appropriate.

4.2.3. PROP Bitterness and Responsiveness to Ethanol and Alcoholic beverages

PTS may be associated with suprathreshold responsiveness to ethanol. When a probe with 50% v/v alcohol was placed on the tongue, individuals who rated PROP bitterness lower also rated less burning sensation and greater liking of the stimulus (Duffy, Peterson, & Bartoshuk, 2004). Similarly, PROP tasters rated the intensity of a 47.5% w/v ethanol aqueous solution higher than non-tasters (Prescott & Swain-Campbell, 2000), and pSTs rated the bitterness and irritation of an ethanol solution (concentration not stated) significantly higher than pMTs and pNTs (Bartoshuk et al., 1994). These differences have not been replicated to date with phenylthiocarbamide (PTC) – a PROP analogue used primarily in the earlier literature; no difference was found for suprathreshold ethanol responsiveness across the concentration range examined of 4.3% to 17% v/v between PTC tasters and PTC non-tasters (Mattes & DiMeglio, 2001). However, given that PTC and PROP activate the same TAS2R receptors and typically elicit similar orosensory responsiveness and behavioural correlates (Roura et al., 2015), this null result may be due to the PTC categorisation method used. That is, grouping individuals with intermediate PTC responsiveness with those of high responsiveness (analogous to combining pMTs and pSTs) may not allow for differences in ethanol perception to be fully captured. Given that the intensity and predominance of both bitterness and burning elicited by ethanol change with concentration (Nolden & Hayes, 2015), further research should examine the responsiveness of all PTS and PTC groups across the range of ethanol levels typically found in alcoholic beverages (3-45% v/v).

The perception of alcoholic beverages differs across PTS groups. In a small study of untrained panellists (n = 25), pNTs reported lower bitterness, astringency, and sourness from red wine than pMTs and pSTs (Pickering, Simukova, & DiBattista, 2004). In a subsequent study, a panel of individuals trained in descriptive analysis (n = 16) largely confirmed these results, with sourness, saltiness, heat/irritation, and overall astringency (although not bitterness) rated less intense by pNTs than pSTs across sixteen commercial red wines (Pickering & Robert, 2006). With beer, pSTs rated the bitterness of Urquell pilsner but not Budweiser as significantly higher than pMTs

and pNTs (Intranuovo & Powers, 1998). In contrast, no differences in orosensory responsiveness were found across PTS groups by Pickering, Moyes, et al., (2010). As speculated by Bajec, Pickering, & DeCourville (2012), this may be attributable to the use of pectin as an inter-stimulus rinse in the study; pectin is capable of binding proteins and may have interacted with gustin to reduce its contribution to perceptual differences between the PTS groups. Alternatively, Pickering et al. (2010) used a higher concentration of PROP to classify individuals than the earlier studies (3.2 mM vs 0.32 mM), which may explain the contradictory findings. On balance, the existent literature suggests that PROP responsiveness mediates the perception of orosensations in some alcoholic beverages, with pSTs being more responsive than pNTs.

4.2.4. PROP Bitterness and Alcoholic Beverage Preferences and Consumption

Despite these differences in orosensation, the literature is somewhat equivocal on whether PROP responsiveness predicts or mediates preference and consumption behaviours. Daily consumption of alcoholic beverages was lower for PROP tasters (pMTs and pSTs combined) than for pNTS in a convenience cohort of Australians drinkers (Beckett et al., 2017), while no association was found between PROP bitterness and alcohol consumption in a study of 329 Canadian alcohol consumers (Pickering & Hayes, 2016). Similarly, Fischer et al (2014) reported no significant association between PROP bitterness ratings and alcohol consumption. However, while their population-based study had a large sample size (n = 2359), the questions asked likely did not capture alcohol consumption fully. Alcohol intake was measured by asking two dichotomous questions; whether participants had consumed “any alcohol in the past year” and whether they had “ever drank 4+ drinks/day”, with yes/no response options for both. Thus, their data did not discriminate finer aspects of the consumption patterns of drinkers, and a continuous measure of alcohol intake may be more illuminating. Indeed, when alcohol consumption is more precisely measured (e.g. monthly frequency and total intake), some variation with PROP responsiveness has been reported. For instance, Pickering et al. (2014) found that total wine intake decreased as PROP bitterness increased in a study of over 1000 US wine consumers.

Australians with the TAS2R38 tasting genotype (PAV/PAV and PAV/AVI combined) reported lower daily consumption of alcoholic beverages than participants with the non-tasting genotype (AVI/AVI) (Beckett et al., 2017), while no association was found in a study of Korean adults

(Choi, Lee, Yang, & Kim, 2017). However, Koreans with PAV/AVI or AVI/AVI diplotypes were more likely to have never consumed alcohol than individuals with the PAV/PAV diplotype (Choi et al., 2017).

Liking and preferences may also vary with PTS, and are of particular interest to alcoholic beverage producers and marketers. pSTs report lower liking scores than other PTS groups for dry table wine, fortified wine (Pickering et al., 2014) and sparkling wine (Pickering & Cullen, 2008; Pickering et al., 2014); all wine styles that are potentially more unpleasant due to higher sourness, irritation, and/or bitterness. pSTs preferred sweet wines and wine-based beverages (Pickering et al., 2014), consistent with the higher liking scores for all five sweet wine styles of the most PROP responsive individuals in Pickering & Hayes (2016). However, in contrast with Pickering et. al (2014), the latter study of 320 participants showed that the most PROP responsive individuals also gave higher liking scores for wines that elicit the predominantly aversive orosensations of dryness, carbonation, and heat. The authors speculate that the discrepancy in findings may largely be attributed to differences between the cohorts, as non-drinkers were excluded from their study, and one third of participants were wine professionals, indicating a higher than normal involvement with wine. Bajec (2010) found that pMTs preferred sweet table and desert/ice wines more than pNTs, with pSTs indicating an intermediate liking score. A general trend of higher liking from pMTs was reported across all alcoholic beverage types in the latter study. Finally, Intranuovo & Powers (1998) showed that male pNTs reported higher liking of sampled beer than male pSTs, a finding which may have contributed to pNTs reporting higher beer consumption than pSTs (genders combined) during their first year of drinking.

Some studies have failed to find a relationship (Catanzaro, Chesbro, & Velkey, 2013; Pickering et al., 2010). The liking scores of American college students (n = 139) for beer and red wine did not differ with PTS in the report of Catanzaro et al. (2013), although the scale used (1 = “I hate it” to 5 = “I love it”) was likely more restrictive than those employed by Bajec (2010) (7-point hedonic) and Pickering et al (2014) (gDOL). Further, the latter two studies allowed participants to indicate that they were unfamiliar with an alcohol beverage, ensuring that liking ratings were only obtained from individuals who reported familiarity with each beverage type.

4.2.5. PROP and alcohol behaviour – mediators

It has been suggested that food neophobia – the fear of trying new foods resulting in food avoidance (Pliner & Hobden, 1992) – mediates the effect of PTS on food liking. Ullrich et al. (2004) reported that food adventurous PROP tasters liked more foods than their non-adventurous counterparts, while adventurousness had minimum effect in non-tasters. The possibility that the neophobia trait might also mediate the relationship between PROP responsiveness and alcohol behaviour, however, has not been thoroughly investigated. While preferences/liking of alcoholic beverages have been associated with both food (Logue and Smith, 1986; Ullrich et al., 2004) and alcoholic beverage (Pickering et al., 2014) neophobia, PTS did not mediate this relationship in the study on wine liking of Pickering et al., (2014). In contrast, Ullrich et al. (2004) reported that PROP tasters who were more food adventurous

liked strong alcohol more than tasters who were less food adventurous, providing some preliminary evidence that food/alcoholic beverage adventurousness may mediate the association between PROP responsiveness and alcohol liking. However, this finding should be replicated, and consideration given to incorporating a more discriminating hedonic scale than their dichotomous ‘like’ or ‘dislike’ measure, as well as assessing intake behavior.

Few studies have directly assessed and modeled the role of sensory factors as predictors or mediators of alcohol liking and behavior by examining responses to sampled beverages. The work of Lanier et al (2005) is the noteworthy exception, in which the relationship between the bitterness and sweetness elicited by sampled scotch and beer were investigated in relation to PROP responsiveness, alcohol preference and alcohol intake in college students using linear regression analysis (Figure 2). Lower PROP responsiveness predicted higher sweetness and lower bitterness ratings in scotch, which in turn contributed to higher alcohol consumption. Similarly, lower PROP responsiveness predicted lower bitterness in beer, and both bitterness and sweetness ratings independently predicted higher preference for the beer which in turn contributed to higher total alcohol consumption. Interestingly, while PROP responsiveness associated with the bitterness of both sampled beverages, it did not directly mediate alcohol intake, suggesting the need to collect broader orosensory data when investigating taste/alcohol behaviour relationships. In particular, responsiveness to product components presented at

ecologically-valid concentrations are important, given that the dominant orosensations elicited by ethanol are highly dependent on concentration (Nolden & Hayes, 2015). The use of partial structural equation modelling in the Lanier et al. (2005) study allows for the relative contribution of each measure to be examined in relation to the other variables, which can facilitate deeper insights into the complexities of alcohol behavior. Further research using their general approach would be valuable, and should be extended to include consideration of the full range of orosensations elicited by alcohol and a wider range of alcoholic beverage types.

4.2.6. PROP Bitterness and Alcoholism

In two early studies using phenylthiocarbamide, the proportion of PTC tasters and non-tasters did not differ between alcoholics undergoing treatment and a control group (Smith, 1972; Swinson, 1973). However, little detail is provided about the control groups in these reports, including their size, which makes it challenging to evaluate these null results. Subsequent studies have shown conflicting findings. Pelchat & Danowski (1992) reported that children of alcoholics were significantly more likely to be pNTs than children of non-alcoholics, as defined by the Michigan Alcohol Screening test (MAST). Conversely, family history of alcoholism did not differ with PTC (Mattes & DiMeglio, 2001) or PROP (Kranzler, Moore, Pamela, & Hesselbrock, 1996; Kranzler, Skipsey, & Modesto-Lowe, 1998; Robb & Pickering, 2016) responsiveness in subsequent reports, with Robb and Pickering (2016) also failing to show a relationship between PTS and Alcohol Use Disorders Identification Test (AUDIT) classification. One possible explanation for the null results of these latter studies is that relevant co-variables, including depression, were not assessed.

DiCarlo & Powers (1998) reported that college students with a family history of alcoholism (either parent) are more likely to be pNTs if there is no family history of depression, or more likely to be pSTs if there is family history of depression, hinting that PROP responsiveness may be differentially associated with the two different types of alcoholism. Type 1 alcoholism, know as ‘milieu-limited’, is associated with depression, late onset (after age 25), genetic predisposition (family history) and environmental factors (family home with high levels of alcohol consumption) (DiCarlo & Powers, 1998). In contrast, Type 2 alcoholism, ‘male-limited’, is typically experienced by males (onset before age 25) with alcoholic fathers regardless of their

upbringing (DiCarlo & Powers, 1998). The age range of the cohort used in DiCarlo and Powers (1998) study should be expanded in future work beyond college students, as the onset of Type 1 alcoholism typically occurs after the age of 25.

One theory for the association of PTS with alcoholism is that pNTs experience the aversive orosensory qualities of alcohol less strongly, leading them to consume alcohol at a younger age, which may put them at increased risk of developing alcoholism. However, no difference in TAS2R38 genotype was found between age of first intoxication or age of commencing regular drinking in a study of high-risk families (Wang et al., 2007). The balance of the existent literature does not support an association between PROP/PTC responsiveness and alcoholism, although as indicated above, family history of depression amongst other possible mediating factors should be considered in future studies.

4.3. Other Bitter Taste Receptors

Two SNPs in TAS2R16 have been associated with increased alcohol consumption. Homozygous AA (rs846672) individuals reported consuming alcoholic beverages more frequently than AC or CC subjects, and CG and GG individuals trended toward higher total intake and frequency of consumption than CC homozygotes (Hayes et al., 2011). As noted by the authors, a larger sample should be examined (current n = 96) as the two SNPs are not in linkage disequilibrium. It is currently unknown if these SNPs make independent contributions to alcohol consumption patterns. However, the K172N (rs846664) allele is associated with an increased risk of developing alcohol dependence (Hinrichs et al., 2006) and an increased maximum number of drinks consumed in a 24-hour period (Wang et al., 2007), suggesting it may play an important role in alcohol consumption. However, this may not extend to sampled scotch whisky, as TAS2R16 genotypes were not predictive of the intensity of taste sensations (sweet, sour, bitter or salty) or liking elicited by this product (Hayes et al., 2011).

4.4. Sweet-liking

4.4.1. Introduction

Sweet-liking is a measure of an individual's hedonic response (liking or preference) to sweetness, and is typically measured by determining preference for a series of sucrose solutions

of increasing concentration. While no standard method of classification has been established, individuals are often defined as sweet-likers if they most prefer high sucrose concentrations (0.4-0.8M) and sweet-dislikers if they most prefer lower sucrose concentrations (Kampov-Polevoy, Garbutt, & Janowsky, 1997; Kampov-Polevoy et al., 2014; Kampov-Polevoy, Tsoi, Zvartau, Neznanov, & Khalitov, 2001; Kampov-Polevoy, Garbutt, & Khalitov, 2003; Kranzler, Sandstrom, & Van Kirk, 2001; Lange, Kampov-Polevoy, & Garbutt, 2010; Tremblay, Bona, & Kranzler, 2009; Wronski et al., 2007). However, other methods have been employed (e.g. Looy, Callaghan, & Weingarten, 1992; Looy & Weingarten, 1992; Asao et al., 2015), and indeed, contradictory results in the sweet-liking and alcohol use disorder literature are often attributed to differences in the classification of sweet-likers and sweet-dislikers. Results with other sugars suggest that sweet-liking is a robust phenomenon which may be generalizable to complex sweet substances (Looy et al., 1992).

Preference for liking of sweet solutions is partially heritable; approximately 50% of the variation in liking of a 20% w/v sucrose solution was associated with genetic factors in a study of 663 female twin pairs (Keskitalo et al., 2007). As the molecular mechanisms underlying sweet preferences are largely unknown, candidate genes and allele studies are not yet possible to further current understanding of the phenomenon (Hayes et al., 2013). As a result, the studies reviewed below have all measured sweet liking at the phenotypic level.

4.4.2. Sweet-liking and Alcohol

Sweet-likers may consume more alcohol and be at greater risk of developing an alcohol use disorder. As previously discussed, ethanol elicits sweetness and has been shown to activate sweetener responsive neural fibres in gustatory nerves (reviewed in Bachmanov et al., 2011). In addition, ethanol and sweet solutions activate overlapping central mechanisms, namely the opioidergic, serotonergic and dopaminergic systems, potentially making the reward associated with alcohol consumption consistent with that of sugar consumption (Bachmanov et al., 2011; Levine, Kotz, & Gosnell, 2003). In a preliminary imaging study, sucrose solutions were shown to activate the bilateral orbitofrontal cortex and the right ventral striatum, both areas associated with reward (Kareken, Dzemidzic, Oberlin, & Eiler, 2013). Interestingly, the number of drinks consumed on a day when drinking was positively correlated with left orbitofrontal cortex

response when consuming a sucrose solution (Kareken et al., 2013). As a result, it has been theorized that individuals at risk of alcoholism may experience an enhanced reward to alcohol if they also experience greater preference for sweetness (Kampov-Polevoy et al., 2001). In individuals with an abnormally low basal level of endogenous reward, stronger stimulation, such as a sweeter tasting food or more alcohol, may be required to elicit equivalent responses to individuals with high basal levels of endogenous reward (Kareken et al., 2013).

Individuals with the CT genotype for TAS1R3 rs307355 are more likely to be heavy drinkers (>30 g alcohol/day) than light drinkers (<30 g/alcohol/day) compared to individuals with the CC genotype (Choi et al., 2017). These results suggest a genetic mechanism that may impact sweetness perception and further research is warranted to determine if TAS1R3 is associated with sweet-liking.

The link between sweet-liking and alcohol was first reported in a study of male alcoholics with a diagnosis of alcohol dependence based on the DSM-III-R and males who had never received a diagnosis of alcoholism. Significantly more alcoholic men preferred the highest sucrose solution (0.83M, 65% vs 16%) and were classified as sweet-likers compared to the nonalcoholic group (Kampov-Polevoy et al., 1997). This finding was subsequently confirmed when the sample size of the above study was expanded (Kampov-Polevoy, Garbutt, Davis, & Janowsky, 1998) and in a report comparing hospitalized men with and without alcoholism (Kampov-Polevoy et al., 2001). Within alcoholics, greater consumption of alcoholic beverages was associated with a higher detection threshold for sucrose (Silva et al., 2016). Additionally, alcoholics had a higher detection threshold for sucrose than non-alcoholics who were matched for age, gender and income (3.78 vs 1.39 g/L in water; Silva et al., 2016).

In contrast, no differences in sucrose solution preferences or sweet-liking phenotypes was found when abstinent alcoholic men and men without a history of alcohol use disorder were compared (Bogucka-Bonikowska et al., 2001; Wronski et al., 2007). Additionally, Tremblay et al. (2009) found no difference between alcoholics and a control group for liking of a 0.83M sucrose solution, but reported that alcoholics did prefer 0.05M sucrose more than the controls. However, when sex, age, education, smoking status, number of drinking days and number of standard

drinks during the 30 days preceding testing were included, the effect was no longer significant, suggesting that the differences between groups were due to factors other that a diagnosis of alcoholism.

Interestingly, alcohol dependent individuals were more likely to be sweet-likers than control individuals when newly sober (4-30 days), but no difference was found at 6 months (Krahn et al., 2006). Furthermore, sweet-liking alcohol dependent individuals were less likely to maintain their sobriety during the 6 month period (Krahn et al., 2006). In contrast, no difference in sweet-liking was found between alcohol dependent individuals and control groups when tested twice within 30 days of beginning a treatment program (Kampov-Polevoy et al., 2001; Kampov-Polevoy, Ziedonis, et al., 2003). Thus, it remains unclear if alcoholism leads to a preference for sweeter solutions, or if a preference for sweeter solutions predisposes individuals to alcohol use disorders (Kampov-Polevoy et al., 1997).

A paternal history of alcoholism has been associated with greater preference for sweet solutions (sweet-liking) in hospitalized alcoholics when compared to non-alcoholic men (Kampov-Polevoy et al., 2001), in individuals without a lifetime history of alcohol or drug abuse (Kampov-Polevoy, Garbutt, et al., 2003) and in residential patients with a history of alcoholism, drug dependence or psychiatric conditions (Kampov-Polevoy et al., 2004; Kampov-Polevoy, Ziedonis, et al., 2003). Furthermore, greater preference for sweet-solutions was reported in females with a first or second degree familial history of alcoholism (Pepino & Mennella, 2007), and male alcoholics with a first degree maternal or paternal history of alcoholism are more likely to be sweet-likers and rate 0.83 M sucrose higher more intensely than male alcoholics without such familial history (Wronski et al., 2007). Sweet-likers were 2.7 times more likely to have a family history of alcoholism (Lange et al., 2010). However, no difference in the proportion of sweet-likers and sweet-dislikers was found when non-alcoholic men with or without a paternal history of alcoholism were compared (Kranzler et al., 2001), or when sons of male alcoholics and males without a first/second degree family history of alcoholism were compared (Scinska et al., 2001). Further, neither sweet-liking nor responsiveness was associated with familial history of alcoholism in a non-clinical sample of college students (Robb & Pickering, 2016).

Sweet-liking may be more predictive of alcohol related behaviour in males than females. Men but not women with alcohol-related problems (individuals who meet at least one criterion of the DSM-III-R without meeting the requirements for a DSM-III-R diagnosis of an alcohol use disorder) are more likely to be sweet-likers (Lange et al., 2010). Similarly, male sweet-likers have also been shown to consume more alcohol on average per month than male sweet-dislikers (Robb & Pickering, 2016). Therefore, while sweet-liking may be associated with a familial history of alcoholism and alcohol consumption, the nature of the relationship may differ between the sexes.

Personality traits mediate the association between sweet-liking and alcohol behaviour. While sweet-liking is associated with increased risk of alcohol-related problems, that risk is increased in sweet-likers with high novelty seeking traits (Kampov-Polevoy et al., 2014; Lange et al., 2010). Additionally, the finding by Mennella, Pepino, Lehmann-Castor, & Yourshaw (2010) that a family history of alcoholism was associated with an increased preference for sucrose solutions in 5--12 year old children was largely driven by the children who were also classified as depressed, as measured by the 23-item Pictoral Depression scale (Mennella et al., 2010). Individuals with a preference for white wine with added fructose (20 g/L) reported higher levels of impulsiveness and lower levels of openness than individual that preferred the same wine with no fructose addition (Saliba, Wragg, & Richardson, 2009). Thus, it would seem prudent to include measures of openness, depression and novelty seeking (including impulsiveness) as potential co-variables in future studies on sweet-liking and alcohol behaviour.

4.5. Other Orosensations and Alcohol Behaviour

One consistent trend emerges across all orosensations when the association between responsiveness and alcohol consumption is examined; individuals who are the most responsive to orosensations typically consume lower quantities of alcohol (Fischer et al., 2013; Thibodeau et al., 2017). Furthermore, individuals who avoid alcohol are significantly more responsive than alcohol consumers to sourness, with a similar trend reported for bitterness and sweetness (Thibodeau et al., 2017). This may suggest that individuals with increased responsiveness to orosensations experience the aversive sensory characteristics of alcoholic beverages more strongly than individuals with lower responsiveness, leading to lower consumption or avoidance.

In contrast, the highest rates of alcohol consumption have been reported in individuals with low or moderate responsiveness, depending on the specific orosensation under consideration (Fischer et al., 2013; Thibodeau et al., 2017).

In the Beaver Dam Offspring Study (n > 2000), alcohol consumption was not linearly related to suprathreshold responsiveness to saltiness or sourness (Fischer et al., 2013). Moderate alcohol consumers (15-74g ethanol/week) had significantly lower responsiveness to saltiness but not sourness, when compared to non-drinkers or heavy drinkers (>140g/week; Fischer et al., 2013). Furthermore, the consumption of an alcoholic beverage in the past year was associated with significantly lower ratings of suprathreshold sourness and saltiness (Fischer et al., 2013). Sour responsiveness was associated with both beer and wine consumption, and metallic responsiveness with dry wine intake, in the study of Thibodeau et al. (2017). As sour or metallic responsiveness increased, alcohol consumption decreased, suggesting that these sensations may be largely aversive for some consumers when elicited by these alcoholic beverages (Thibodeau et al., 2017).

Astringency responsiveness also appears to associate with wine consumption, but the nature of the relationship varies between red and white wine. Individuals with intermediate astringency responsiveness consumed more red wine than those with high or low responsiveness, whereas white wine intake decreased with increasing astringency responsiveness (Thibodeau et al., 2017). These results suggest that when astringency is expected in wine, as when elicited by the ubiquitous phenolic constituents of red wine, its level is optimized for the average consumer's palate. However, as astringency is not typically expected in white wine, it is perceived as aversive, with a corresponding effect on intake.

Perception of sourness and saltiness may also be linked to risk of developing an alcohol use disorder. Family history of alcoholism is associated with decreased liking of and increased responsiveness to sourness (Sandstrom, Rajan, Feinn, & Kranzler, 2003), and decreased liking of saltiness (Sandstrom et al., 2003; Scinska et al., 2001). However, Sandstrom et al (2003) found no association between sourness or saltiness and alcohol consumption, although their intake measure may have been oversimplified with only two groups (low and high consumption) used

in the analysis. While saltiness and sourness have been reported as sensations elicited by ethanol (Mattes & DiMeglio, 2001; Scinska et al., 2000), bitterness and heat/irritation are the dominant sensations from ethanol at the concentrations found in most alcoholic beverages (Nolden & Hayes, 2015). Consequently, the increased risk of developing an alcohol use disorder noted above in Sandstrom et al. (2003) and Scinska et al. (2001) may simply be reflecting more generalised orosensory responsiveness.

4.6. Thermal Tasting

4.6.1. Introduction

Thermal tasting represents another taste phenotype whereby orosensory responsiveness may associate with alcohol consumption behaviour. Thermal taster status (TTS) is determined when the tip of the tongue is cooled or heated, producing a phantom taste in thermal tasters (TTs) and no taste sensations in thermal non-tasters (TnTs; Green & George, 2004). Individuals who fail to meet these classification criteria (uncategorized; Uncats) are also identified, but typically excluded from studies as part of the initial screening process (Bajec & Pickering, 2008; Yang et al., 2014). TTs tend to rate aqueous solutions of sour, bitter, sweet, salty, umami, metallic and astringent stimuli higher than TnTs (Green & George, 2004; Bajec and Pickering, 2008; Hort et al, 2016; Yang et al., 2014) as well as cold and warm stimuli (Bajec and Pickering, 2008; Yang et al., 2014), and are more discriminating of CO_2 levels (Hort et al, 2016). TTs also have lower detection thresholds for sweetness than TnTs (Yang et al., 2014), and a trend toward lower difference thresholds for sweetness, sourness, and bitterness (Pickering & Kvas, 2016).

These differences in orosensations associate with self-reported liking of a large range of food items (Bajec and Pickering, 2010), particularly significant given that reported liking may be a more accurate proxy for consumption than many traditional dietary intake measures (Duffy, 2007). However, only limited associations were found between TTS and sampled foods and non-alcoholic beverages in the more recent reports of Pickering & Klodnicki (2016) and Pickering et al. (2016), possibly attributable to small samples sizes. It has been speculated that TTS may link with alcohol consumption; specifically, that TTs consume less as they experience the orosensations more intensely than TnTs, and ethanol elicits primarily aversive sensations (Thibodeau et al., 2016).

4.6.2. Thermal Tasting and Alcoholic Beverages

In contrast with most sampled foods, TTs appear more responsive than TnTs to the orosensations elicited by alcoholic beverages. In beer, TTs rated bitterness, sourness, and sweetness, higher than TnTs did (Pickering, Bartolini, & Bajec, 2010), while bitterness, sweetness, sourness, astringency, and overall flavour intensity were rated higher by TTs for white and red wine (Pickering, Moyes, et al., 2010). Noteworthy, these attributes represent the dominant orosensations typically elicited by these products. Further, TTs tend toward lower difference thresholds for sweetness, sourness, and bitterness in neutral white wine; a trend that reached statistical significance for sourness (Pickering & Kvas, 2016). As such, TTs may be able to better discriminate smaller differences in the orosensory properties of alcoholic beverages than TnTs.

These differences in orosensory responsiveness and discrimination may contribute to the increase liking of alcoholic beverages reported by TnTs. TnTs reported significantly higher liking of bourbon, brandy, vodka, mixed tequila, and dry red wine compared to TTs (Bajec, 2010). Furthermore, a trend of higher liking of beer, spirits (overall, mixed and unmixed) and wine (overall, sweet and dry) by TnTs was observed (Bajec, 2010). These results partially support the hypothesis that greater liking is associated with lower responsiveness to the bitterness elicited by alcoholic beverages.

4.6.3. Thermal Tasting – Other Considerations

To date, all reports on thermal tasting have treated TTs as a homogenous group. However, TTs may experience sweet, salty, sour, bitter (Green & George, 2004; Hort et al., 2016; Pickering & Kvas, 2016; Yang et al., 2014), savoury (Yang et al., 2014), minty (Hort et al., 2016), or metallic (Hort et al., 2016; Pickering & Kvas, 2016; Yang et al., 2014) sensations on lingual thermal stimulation, and up to a third report more than one phantom taste sensation during testing (Green & George, 2004). This heterogeneity of experience amongst TTs led Bajec and Pickering (2008) to speculate that differences in orosensory responsiveness and related behavioural differences between TTs and TnTs may be due to only a subset of TTs. For example, it is possible that the greater bitter responsiveness of TTs overall is only due to higher ratings from those TTs who experience bitterness during the lingual thermal stimulation procedure used to determine TTS. If this is true, the association between alcohol consumption and/or preference and TTS may be

masked by a classification scheme that is too general. For instance, bitter TTs may consume less alcohol than other TTs, as they may experience the aversive bitterness elicited by ethanol more strongly. Conversely, sweet TTs may consume more alcohol than other TTs, as their higher responsiveness to sweetness may help mask ethanol bitterness. Therefore, additional research is required to establish if TT sub-groups based on the orosensation(s) elicited during lingual thermal stimulation represent ecologically valid phenotypes, and how they may vary in their alcohol behaviour.

Up to 40% of individuals in thermal taste studies are not classified as either TTs or TnTs (Uncat). Uncats report experiencing phantom taste sensations during lingual heating and/or cooling, however, these sensations are either rated below the minimum intensity threshold necessary or are not reproducible (Bajec & Pickering, 2008; Yang et al., 2014). Therefore, it is not known if Uncats represent a distinct phenotypical sub-group, or if they are simply TTs or TnTs that have been misclassified. As Uncats have yet to be characterized with respect to orosensory responsiveness and appear to represent a large proportion of the population, further research is warranted, which should also include consideration of TTS and alcoholism/alcohol use disorders.

5. Conclusion

The orosensations elicited by alcoholic beverages are not experienced uniformly across individuals and these differences impact alcohol preferences, consumption and risk of developing an alcohol use disorder. In general, individuals who are more responsive to nominally aversive orosensations (bitterness, irritation, sourness and astringency), report lower preference for and consumption of alcoholic beverages. Furthermore, an increased preference for sweetness may be associated with a familial risk of developing an alcohol use disorder. However, contradictory findings are numerous in the literature, which while in part are attributable to methodological differences, also indicate that the drivers underlying alcohol behaviours are highly complex and cannot be predicted by a single taste-related factor, including genotype, orosensory responsiveness, ethanol responsiveness, PROP taster status, thermal taster status or sweet-liking. Future research would benefit from taking a wider, multi-factorial

approach to studying the key orosensory drivers of alcohol intake, and incorporating statistical techniques such as partial regression modeling that allow for clearer elucidation of the interaction between multiple variables. Finally, as ethanol elicits chemesthetic and prototypical taste sensations, both should be considered when assessing orosensory responsiveness and its association with alcoholic beverage behaviours.

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Table 1: Major alcoholic beverage categories and subtypes with typical ethanol concentrations, dominant tastants[1] and orosensations elicited.

Category and Ethanol Concentration (% v/v)	Major Subtypes	Dominant Tastant	Orosensations Elicited by Tastant	Literature Source
Beer (Typically: 3--7%, up to 16%)	All	Ethanol	Bitterness (Likely dominant), Sweetness, Burning/Tingling, Drying	Hardwick, van Oevelen, Novellie, & Yoshizawa, 1995; Harwick, 1995; Parker, 2012
		Carbon Dioxide	Tingling, Prickling	
		Glycoproteins, Dextrin chains, Polypeptides & Gums	Fullness/Viscosity (By modifying the foam stability)	
		Polyphenols	Astringency, Bitterness	
		Organic Acids	Sourness	
		Sugars	Sweetness	
		Sulphates	Dryness	
		Chlorides	Fullness, Body	
	Hopped Styles	Hop Resins	Bitterness	
Wine (Typically: 11--13%, Full range 7.5%-20%; Fortified wines: 18--21%)	All	Ethanol	Bitterness (Likely dominant at lower concentrations), Burning/Tingling (Likely dominant at higher concentrations), Drying, Sweetness	Jackson, 2009; Jackson, 2012; Tredoux & Silva, 2012; Sowalsky & Noble, 1998.
		Organic Acids	Sourness, Astringency	
		Sugars	Sweetness, Viscosity	
		Glycerol	Sweetness (Minor contribution in dry wine)	

	White	Nonflavonoids (Tannins)	Bitterness, Astringency	
	Red	Flavonoids (Tannins)	Bitterness, Astringency	
	Sparkling	Carbon Dioxide	Tingling/Prickling	
	Desert	Glycerol	Viscosity	
Spirits (Typically: 35%-45%, Full range: 30--86%)	All	Ethanol	Burning/Tingling (Likely dominant), Bitterness, Drying, Sweetness (Minor contribution from ethanol; typically major contribution from mixes/additives to unmixed spirits)	Aumatell, 2012; Bordeu, Agosin, & Casaubon, 2012; Da Porto, 2012; Faria, 2012; Jack, 2012; Louw & Lambrechts, 2012; Lurton, Ferrari, & Snakkers, 2012; Villanueva-Rodriguez & Escalona-Buendia, 2012; Xu & Ji, 2012; Zabetakis, 2012
Other Sake: ~15%	Sake	Organic Acids	Sourness	Furrakawa, 2012; Hardwick et al., 1995
		Amino Acids, Peptides	Umami, Savoury	

[1]Tastant defined here as orosensory stimuli for ease of presentation

Table 2A: Summary of PROP/PTC-related studies on responsiveness to ethanol or sampled alcoholic beverages.

Author (Date)	Stimulus (Concentration)	Method of PROP Operationalization	Participants (n)	Primary Findings
Bartoshuk, Conner, Grubin, et al (1993)	Aqueous Solution (0.001 & 0.0032M)	Threshold & scaling (pNTs vs pMTs vs pSTs)	Not specified	pMTs & pSTs rated the bitterness of 10 – 50% ethanol higher than pNTs.
Prescott & Swain-Campbell (2000)	Paper disk dipped in 0.3g/L PROP	Suprathreshold (pNTs vs pMTs vs pSTs)	College students/staff (61)	PROP tasters rated the intensity of ethanol higher than pNTs.
Mattes & DiMeglio (2001)	Paper disk dipped in saturated PTC solution	Suprathreshold (PTC taster vs PTC non-taster)	Adults (50)	Familial history of alcoholism & responsiveness to 4.3 to 17% ethanol does not differ between PTC tasters & non-tasters.
Duffy, Peterson & Bartoshuk (2004)	Aqueous solutions (0.001 to 3.2 mM)	Threshold & scaling (pNTs vs pMTs vs pSTs)	Adults (83)	Increased PROP bitterness is associated with increased intensity from sampled ethanol & lower alcohol consumption.
Pickering, Simukova & DiBattista (2004)	Aqueous solution (0.32 mM)	Suprathreshold (pNTs vs pMTs vs pSTs)	College students/staff (25)	pNTs rated the bitterness, acidity & astringency of red wines lower than pMTs & pSTs.
Pickering & Robert (2006)	Aqueous solution (Duplicate; 0.32 mM)	Suprathreshold (pNTs vs pSTs)	College students/staff (17)	pNTs rated the acidity, saltiness, heat/irritation, & astringency lower than pSTs in sampled red wines.
Pickering, Moyes, Bajec & DeCourville (2010)	Aqueous solution (Duplicate; 3.2 mM)	Suprathreshold (pNTs vs pMTs vs pSTs)	College students/staff (56)	No difference in orosensory responsiveness between PTS groups in sampled wines.
Carrai, Campa, Vodicka et al (2017)	Taste disks (6 ranging from 0.1 to 10 mM)	Threshold (Staircase … method)	College students/staff or blood donors (528)	PROP sensitivity inversely associated with bitterness of a sampled red wine but no association for astringency or sourness

Table 2B: Summary of PROP/PTC-related studies on alcohol consumption and liking.

Author (Date)	Stimulus (Concentration)	Method of PROP Operationalization	Participants (n)	Primary Findings
Intranuovo Powers (1998)	Paper disk (Concentration not specified)	Suprathreshold (pNTs vs pMTs vs pSTs)	Adults (100)	pNTs consumed the most beer in their first year of drinking. pSTs reported higher bitterness lower liking from sampled beer.
Ullrich, Touger-Decker, O'Sullivan-Maillet Tepper (2004)	Aqueous solution (0.032, 0.32 3.2 mM)	Threshold scaling (PROP tasters vs PROP non-tasters)	Adults (219)	Food adventurousness mediates alcohol liking in PROP tasters but not in pNTs.
Lanier, Hayes Duffy (2005)	Aqueous solution (3.2 mM)	Suprathreshold responsiveness (Continuous)	Adults (49)	PROP bitterness associated with the bitterness sweetness of scotch beer, which mediates alcohol consumption.
Pickering Cullen (2008)	Paper disk dipped in 50mM PROP	Suprathreshold (pNTs vs pMTs vs pSTs)	Alcohol Consumers (406)	pSTs like sparkling wine less than pNTs pMTs.
Bajec (2010)	Aqueous solution (Duplicate; 0.32 mM)	Suprathreshold (pNTs vs pMTs vs pSTs)	College students/staff (132)	pMTs liked alcoholic beverages more than pNTs pSTs. No differences in alcohol consumption across PTS groups.
Catanzaro, Chesbro Velkey (2013)	Paper disk dipped in saturated PROP solution	Suprathreshold (pNTs vs pMTs vs pSTs)	College students (139)	PTS was not associated with difference in beer or red wine preferences.
Fischer, Cruickshanks, Pankow, et al (2014)	Paper disk dipper in 1.0 M PROP	Suprathreshold responsiveness (Continuous)	Beaverdam Offspring Study Adults (2359)	PROP bitterness not associated with having consumed “any alcohol in the past year” or having “ever drank 4+ drinks/day”.

Pickering, Jain Bezawada (2014)	Paper disk dipped in 50mM PROP	Suprathreshold (pNTs vs pMTs vs pSTs)	Wine Consumers (1101)	Increased PROP responsiveness associated with lower alcohol consumption, increased liking of sweet wine higher dislike of dry wine.
Pickering Hayes (2016)	Paper disk dipped in 50mM PROP	Suprathreshold (hypo-tasters vs hyper-tasters)	Alcohol Consumers (329)	PROP hyper-tasters liked sweet, dry fortified wine styles disliked red wine styles more than PROP hypo-tasters.
Beckett, Duesing, Boyd, et al (2017)	Aqueous solutions (6 ranging from 0.000017 to 0.0032 M)	Threshold (PROP tasters vs PROP non-tasters)	Alcohol Consumers undergoing colonoscopy (180)	PROP tasters consumed less alcohol than PROP non-tasters.

Table 2C Summary of PROP/PTC-related studies on alcohol use disorders or family history of alcoholism.

Author (Date)	Stimulus (Concentration)	Method of PROP Operationalization	Participants (n)	Primary Findings
Smith (1972)	Aqueous solution (Duplicate; 0.057 mg/ml)	Suprathreshold (PTC tasters vs PTC non-tasters)	Inpatient alcoholics (27), drug (28) addicts & control group (unspecified)	Alcoholics are as likely as the control group to be PTC tasters or PTC non-tasters.
Swinson (1973)	Aqueous solutions (14 ranging from 0.0009 to 7.64 mM)	Threshold (PTC taster vs PTC non-taster)	Inpatient Alcoholics & Control Group (411)	Alcoholics are as likely as the control group to be PTC tasters or PTC non-tasters.
Pelchat & Danowski (1992)	Aqueous solutions (14 ranging from 0.000732 to 6.00 M)	Thresholds (PROP tasters vs PROP non-tasters)	College students/staff (55)	Children of alcoholics are more likely to be PROP non-tasters than children of non-alcoholics. No difference in the proportion of non-tasters between the children with & without alcoholism.
Kranzler, Moore & Hesselbrock (1996)	Aqueous solutions (14 ranging from 0.000732 to 6.00 M)	Thresholds (PROP tasters vs PROP non-tasters)	Late adolescent & young adults (95)	No association between a paternal history of alcoholism & PTS.
Kranzler, Skipsey & Modesto-Lowe (1998)	Aqueous solutions (14 ranging from 0.000732 to 6.00 M)	Thresholds (PROP tasters vs PROP non-tasters)	Outpatients being treated for AUD (90)	No association between a familial history of alcoholism & PTS (maternal, paternal or both).
DiCarlo & Powers (1998)	Paper disk dipped in saturated PROP solution	Suprathreshold (pNTs vs pMTs vs pSTs)	College aged students (100)	Individuals with a familial history of alcoholism are more like to be pNTs if they are not depressed or pSTs if they have symptoms of depression.

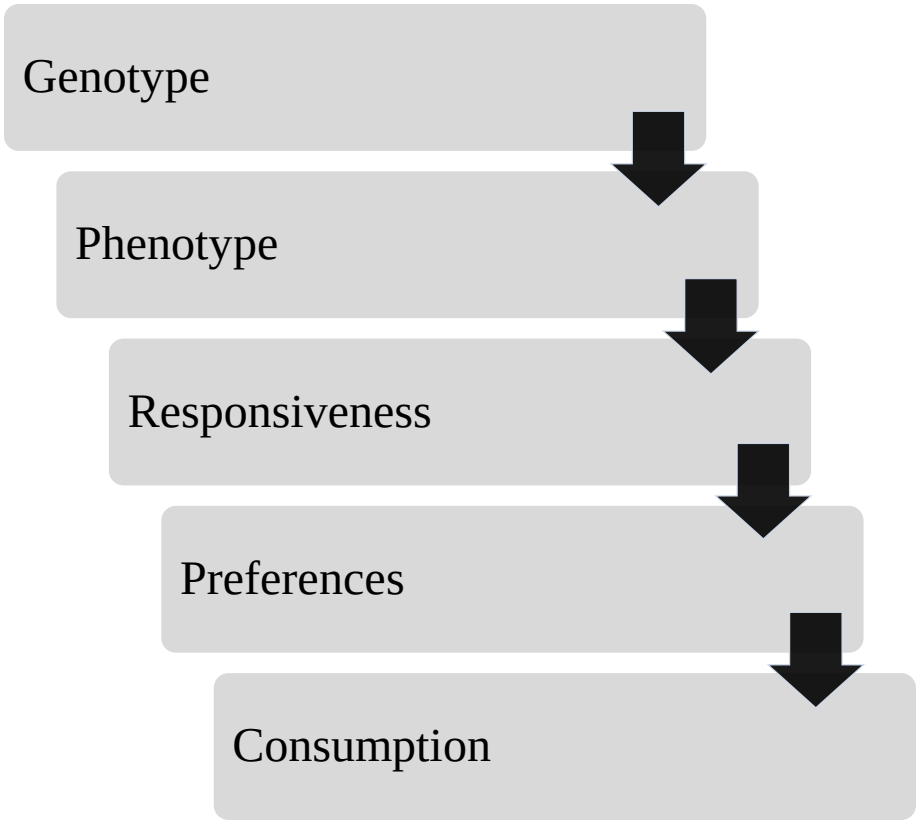

Figure 1: Model for the influence of taste genotype and phenotype on food related behaviour.

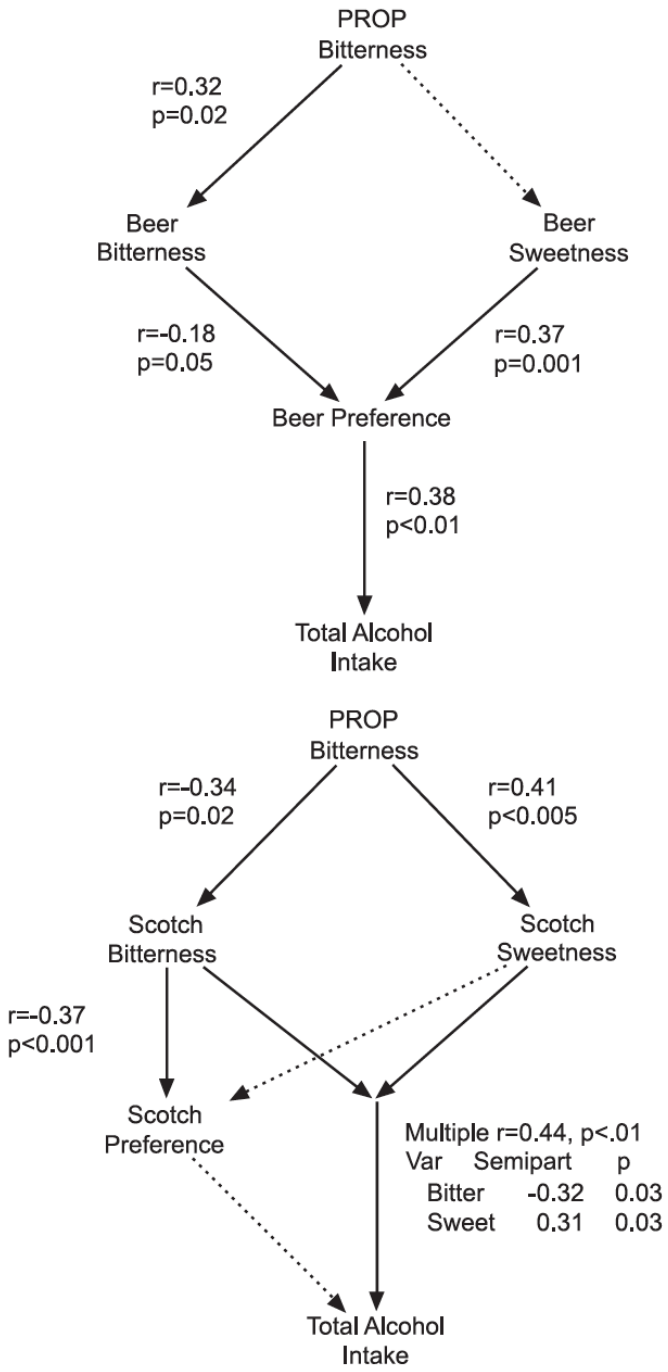

Figure 2: Model of the relationship between PROP bitterness, sweetness, bitterness, preference and alcohol consumption for beer and scotch. Significant relationships are shown with solid lines while dotted lines are not significant. From Lanier et al (2005).