Differences in subjective response to alcohol in heavy- and light-drinking Chinese men versus Caucasian American men

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ABSTRACT

Aims To compare subjective responses to alcohol among Han Chinese and Caucasian American males. **Design** Double-blinded, placebo-controlled human laboratory design. Participants completed three randomized experimental sessions with high and low alcohol and placebo beverages. **Setting** Chinese participants were examined at Xinjiang Medical University, China. Caucasian participants were examined at the University of Chicago, USA. **Participants** Seventy Han Chinese (35 heavy/35 light drinkers) and 75 Caucasian Americans (43 heavy/32 light drinkers). **Measurements** Breath alcohol concentration (BrAC) and the 'stimulation' and 'sedation' subscales of the Biphasic Alcohol Effects Scale were assessed at pre-drink baseline and four time-points after beverage consumption. The 'like' and 'want' subscales of the Drug Effects Questionnaire were also assessed at the post-drink assessments. **Findings** Comparisons with light drinkers showed that high- and low-dose alcohol produced decreases in stimulation, liking and wanting in Chinese versus Caucasians ($P < 0.05$), and dose-dependent increases in sedation in both groups ($P < 0.001$). Among heavy drinkers, high-dose alcohol produced higher stimulation ($P < 0.001$) but with concomitant higher sedation for both doses ($P < 0.05$) for Chinese versus Caucasians. Alcohol also demonstrated significantly lower liking ($P < 0.001$) in Chinese versus Caucasian heavy drinkers for both doses. Interestingly, both groups showed dose-dependent increases in wanting relative to placebo ($P < 0.05$), but the magnitude of the increase was lower in Chinese drinkers. **Conclusions** Stimulating effects of alcohol are predominant in Chinese male binge drinkers, as has been found in Caucasians, but with less hedonic and motivational reward, potentially explaining some of the lower risk for alcohol disorders in Asian subgroups.

Keywords Alcohol, Caucasian, Chinese, ethnicity, heavy drinker, light drinker, reward, sedation, stimulation, subjective response.

INTRODUCTION

Prominent theories have identified various acute alcohol response phenotypes that may affect risk for alcohol use disorders [1–4]. Recent research has shown that alcohol response factors, including both lower and higher responses, depending on the domain, may play a role in the development of alcohol use disorders (AUDs [4,5]). Work by our group in the United States has shown that greater stimulating, hedonic (liking) and motivational (wanting) responses, as well as lower sedative responses, predicted future drinking problems [5–7]. However, the majority of alcohol challenge research examining acute subjective effects has been conducted using primarily Caucasian participants ([4–11]; see [12,13] for reviews). As drinking levels and associated problems are growing in other racial/ethnic subpopulations, such as those of East Asian origin (e.g. [14,15]), a greater understanding

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of subjective responses to alcohol across several positively and negatively valenced domains is needed to determine whether or not results in Caucasian samples can be extrapolated to other ethnic groups. Examination of the drinking habits of those born and raised in their native country is also important to control for confounding related to the effects of acculturation into American society.

While a commonly held notion in the general population is that Asians are at lower risk for developing AUDs, research has shown that alcohol abuse is a world-wide problem [16,17]. Some Asian subgroups, such as Korean and Japanese men, have demonstrated particularly high rates of alcohol consumption and prevalence of alcohol dependence compared to other Asian subgroups (see [17,18] for reviews). In addition, alcohol consumption in China is rising, with 55% of men and 15% of women reporting regular use [19]. Further, life-time prevalence for alcohol use disorders in China is estimated at 9.0% [20]. While this rate is lower than in primarily Caucasian samples (13–17% [21]), it is indicative of significant hazardous drinking in a subpopulation of Chinese drinkers.

These increases in alcohol use in China are problematic, in that excessive drinking in this country has been shown to be associated with increased crime [22] and domestic violence [23], traffic accidents [24], alcohol-related injuries [14] and mortality [16]. There are some cultural factors underlying excessive alcohol use in China, such as peer pressure to drink alcohol and social acceptance of heavy drinking in men [25]. A greater understanding of the predictors of heavy and problematic alcohol use in China is needed to increase our knowledge on the developmental course of AUDs in those of East Asian origin. In particular, it is unknown whether the subjective responses to alcohol shown to predict future problem drinking in primarily Caucasian samples are evident in native Chinese drinkers.

While there are some published reports of alcohol response in people of East Asian origin, they have focused mainly on the genetic deficiency in the aldehyde dehydrogenase (*ALHD2*) allele and physiological reactions to alcohol. The ALDH2 enzyme deficiency, prevalent in 30–50% of Asians but 0% of Caucasians [26,27], has been associated with negative reactions, such as flushing, headache, palpitations, nausea and vomiting ([28–30]; see [26,27,31] for reviews). However, very few studies of people of East Asian origin have focused systematically on subjective effects of alcohol. The majority of studies that address subjective effects of alcohol in Asians or Asian Americans have used retrospective self-reports of alcohol effects (e.g. [32–35]). Others have examined general sedative-like intoxicating effects, such as clumsy or confused, without consideration for concomitant hedonic effects [36–39], or have assessed global effects

such as 'feeling terrible (or great) overall' using instruments that are established as reliable and valid measures of alcohol's effects [36–41]. Thus, a direct comparison of alcohol effects using psychometrically sound instruments to assess positive- and negative-like effects in native Chinese and Caucasian Americans is needed to elucidate more clearly if there are ethnic differences in subjective alcohol response [12].

In the present study, we provide the first direct examination of native Chinese versus Caucasian American heavy- and light-drinking men on a range of validated subjective alcohol responses (i.e. stimulation, sedation, liking and wanting) found previously to be related to risk for future drinking and AUD symptoms in primarily Caucasian samples. The Caucasian comparison sample was extracted from our larger prior study [5]. As the majority of heavy drinking in China occurs in men and is relatively rare among women [19], we focused upon male drinkers in this study. The design of this study included administration of two doses of alcohol and a placebo control beverage, with the measurement of multiple subjective effects of alcohol across time-points corresponding to the rising limb, peak, early and later declining limbs. This allowed for a full assessment of subjective alcohol response, which may vary based on the dose administered, the domain measured and the temporal interval from the acute alcohol absorption, peak blood levels and slow elimination phases. Consistent with the literature on negative effects of alcohol experienced by people of Asian descent, we hypothesized that there would be dose-dependent differences between Chinese and Caucasian heavy drinkers, with the Chinese having lower alcohol stimulation and reward and higher sedation than Caucasians. Given that light drinkers show primarily sedative responses to alcohol [5,7], we expected both Chinese and Caucasians to show dose-dependent sedative effects with few discernable positive effects.

METHOD

Participants

Participants recruited for the study met the following inclusion criteria: age 21–35 years, in good general medical health with no current or past physical or psychiatric disorders and no history of DSM-IV alcohol or substance dependence, including moderate to severe nicotine dependence. The Chinese sample consisted of 70 (35 light/35 heavy drinkers) men of Han Chinese descent living in Xinjiang, China. The Caucasian American group consisted of 75 (32 light/43 heavy drinkers) self-reported Caucasian/white non-Hispanic men extracted from the larger male and female ethnically and racially diverse first wave of the Chicago Social Drinking Project (CSDP)

sample of 86 light and 104 heavy drinkers [5]. For both the Chinese and Caucasian groups, inclusion criteria for heavy social drinkers were: (i) consuming at least 10 but no more than 40 standard alcoholic drinks per week; and (ii) engaging in regular binge drinking, defined as consuming five or more drinks on any one occasion one to five times on average per week [42]. For light social drinkers, inclusion criteria were: (i) consuming at least one but no more than five standard alcoholic drinks per week; and (ii) engaging in no binge drinking.

Procedures

The study used a double-blind, placebo-controlled alcohol challenge design, with two within-subject factors (dose and time) and two between-subject factors (ethnicity and drinking group). Experimental conditions were identical between sites, with each subject participating in three sessions and consuming a beverage containing a high dose of alcohol (0.8 g/kg; 16% volume alcohol), low dose of alcohol (0.4 g/kg; 8% volume alcohol) or placebo beverage (0.0 g/kg; 1% volume of ethanol as taste mask) in random order, with a minimum 48-hour interval between the two sessions. The volume of the high- and low-dose beverage was identical across sessions, with only the alcohol content differing. Given differences in locally available ethanol and mixers, for Chinese the beverage consisted of 52-proof alcohol mixed with iced tea beverage and for Caucasians the 95-proof alcohol was mixed with water, flavored drink mix and a sucralose-based sugar substitute. To minimize expectancy bias, the participants were told that they would consume a beverage containing a sedative, stimulant, alcohol or placebo (no drug/alcohol).

Participants were asked to abstain from alcohol for 24 hours and cigarette smoking for 3 hours before and for 5 hours during each of the three sessions. Upon arrival, participants underwent a breathalyzer test to confirm compliance with alcohol abstinence instructions [breath alcohol concentration (BrAC) < 0.003]. They also completed baseline measures of subjective measures (i.e. stimulation and sedation). After 30 minutes, the participants consumed the beverage, divided into two equal parts, within 15 minutes in the experimenter's presence. They then completed subjective measures (i.e. stimulation, sedation, liking and wanting) at 30, 60, 120 and 180 minutes after initiation of the beverage to approximate the rising limb, peak BrAC, early and late declining limbs, respectively. The data collections were approved at the respective Institutional Review Boards for each site.

Measures

Study instructions and measures were given in the participants' native language, i.e. Mandarin Chinese and English. For Mandarin Chinese, the measures were translated and back-translated by two independent bilingual staff.

Biphasic Alcohol Effects Scale (BAES [43])

The BAES is a reliable and valid measure of biphasic subjective response to alcohol [44]. The questionnaire consists of seven items that assess stimulant response and seven items that assess sedative response on an 11-point rating scale, ranging from not at all (0) to extremely (10). The alphas for the current Chinese/Caucasian samples for stimulation ranged, respectively, from 0.88 to 0.98/0.93 to 0.97 for heavy drinkers and 0.87 to 0.97/0.88 to 0.96 for light drinkers, and for sedation ranged from 0.77 to 0.85/0.87 to 0.96 for heavy drinkers and 0.77 to 0.87/0.81 to 0.96 for light drinkers.

Drug effects questionnaire (DEQ [45])

The DEQ is a reliable and valid instrument consisting of several adjectival items of drug effects using 100-mm visual analog scales. The two items used in the current study assessed alcohol liking ('Do you LIKE the effects you are feeling right now') and wanting ('Would you like MORE of what you consumed right now'). Liking was rated from 0 = dislike to 100 = like very much, with mid-point indicating neutral. Wanting was rated from 0 = not at all to 100 = very much, with mid-point indicating moderate levels of wanting.

BrAC

BrAC was collected 30 minutes prior to beverage consumption, as well as 30, 60, 120 and 180 minutes after consumption using the CA2000 Digital Alcohol Detector (South Korea) for the Chinese sample and the Alco-Sensor IV, Intoximeter (St Louis, MO, USA) for the Caucasian sample. Approximately 7% of the BrAC values were ≥2.0 standard deviations (SD) above the mean during the rising limb to peak BrAC. This was due to experimenter error, i.e. not having participants rinse with a small amount of water prior to the first reading. As such, these outlier data points were excluded in BrAC analysis.

Data analytical strategy

Subjective alcohol responses were analyzed with generalized estimation equation models (GEE) to account for correlations among repeated measures. GEE analyses were conducted separately for light and heavy drinkers to examine the effects of ethnicity (Chinese and Caucasian), dose (high, low and placebo) and post-beverage time [30 minutes (rising limb of BrAC), 60 minutes (peak BrAC), 120 minutes and 180 minutes (early and later declining

Table 1 Means and standard deviations of light and heavy drinkers of Caucasian American or Chinese ethnicity.

	Light drinkers (n = 67)			Heavy drinkers (n = 78)		
	CH	CA	t-test	CH	CA	t-test
Age (years)	23.7 (4.0)	26.0 (3.4)	2.51*	25.6 (4.0)	25.0 (3.0)	−0.76
Education	14.9 (2.6)	17.2 (2.2)	3.71*	15.1 (3.0)	16.0 (1.5)	1.54
Age of first drink	16.1 (2.5)	17.3 (2.9)	1.99	16.1 (2.7)	14.7 (2.8)	−2.39*
AUDIT	3.2 (0.7)	3.3 (1.0)	0.80	9.8 (2.2)	11.9 (3.2)	3.38**
Drink days/month	6.5 (2.0)	7.0 (3.6)	0.61	13.0 (2.9)	14.2 (5.4)	1.18
Drinks/drinking day	2.4 (0.7)	1.8 (0.6)	−4.00**	6.3 (1.4)	5.6 (2.0)	−1.75
Binges/month	–	–	–	6.8 (2.1)	7.9 (2.8)	1.90
Cigarettes per day	5.3 (3.2)	5.3 (5.5)	−0.01	9.4 (4.3)	6.5 (5.2)	−1.97

AUDIT = Alcohol Use Disorders Identification Test; CH = Han Chinese; CA = Caucasian American. Cigarettes per day are for current smokers: CH light drinkers (n = 16), US light drinkers (n = 4), CH heavy drinkers (n = 18), US heavy drinkers (n = 29). *$P < 0.05$; **$P < 0.01$.

limb of BrAC)] and their interactions. For stimulation and sedation, the pre-drink baseline measure was included as a covariate, but not for liking and wanting, as there was no pre-drink baseline measure. For each outcome, the GEE model with the three-way and all the two-way interaction terms and the main effects was examined first. If the three-way interaction was not significant, then the model was repeated after removing this interaction term. Subsequent post-estimation comparisons were limited to a significant ethnicity × dose × time interaction, as well as the ethnicity × dose interaction and main effect of ethnicity. All analyses were conducted in Stata version 12.0.

RESULTS

Background characteristics

A comparison of general demographic and alcohol drinking characteristics between Chinese and Caucasian light and heavy social drinkers are reported in Table 1. The groups were largely similar on most characteristics, with the exception that Chinese versus Caucasian heavy drinkers started drinking at an older age and had slightly lower Alcohol Use Disorder Identification Test (AUDIT) scores. Among light drinkers, Chinese were younger, had fewer years of education and reported 0.6 more drinks on average per drinking occasion. Further, smoking prevalence was higher in Chinese versus Caucasian light drinkers (46 versus 13% current smokers, respectively, $P < 0.01$), but smoking was relatively light, with both groups averaging 5.3 cigarettes per day. The heavy-drinking Chinese and Caucasian groups did not differ on smoking status (51 versus 67%, respectively) or cigarettes per day (9.4 versus 6.5, respectively). Smoking status was not correlated with any subjective effects.

BrAC levels and associations with subjective effects

Post-drink BrAC at low and high doses was compared between ethnic groups, and there was a significant three-
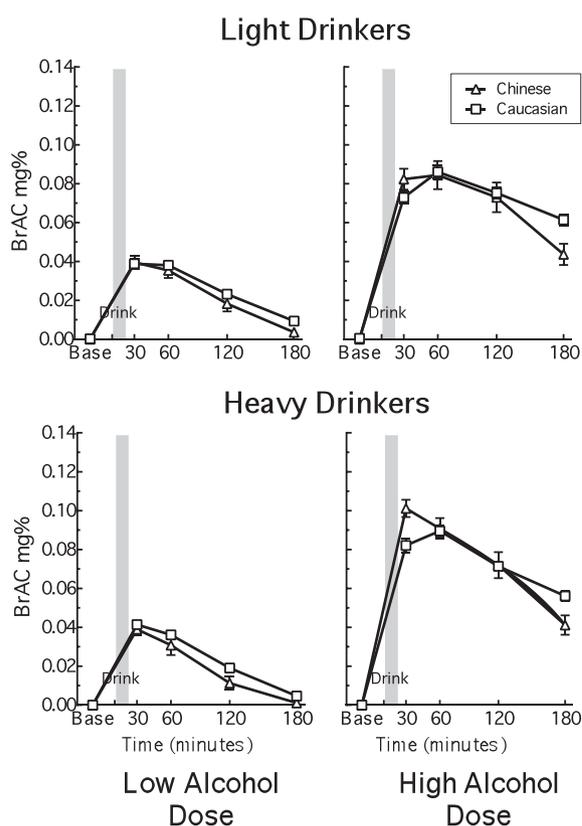

Figure 1 Breath alcohol concentration (BrAC). These graphs show the BrAC during the rising and declining limbs of the BrAC curve of light and heavy drinkers at low and high doses of alcohol

way interaction for both heavy {β[standard error (SE)] = −0.011 (0.002), $P < 0.001$} and light drinkers [β(SE) = −0.009 (0.003), $P < 0.01$] (see Fig. 1). At the high but not low alcohol dose, the Chinese group, compared with the Caucasian group, had significantly higher BrAC at the rising limb ($P < 0.01$ for light drinkers; $P = 0.001$ for heavy drinkers) with lower BrAC at the later declining limb ($P = 0.001$ for light drinkers; $P < 0.001$ for heavy drinkers). Examination of biphasic

Table 2 Results of GEE analyses for heavy and light drinkers focused on ethnicity.

Subjective response	Light drinkers (n = 67)			Heavy drinkers (n = 78)		
	β	SE	P	β	SE	P
Stimulation						
Ethnicity	−3.233[a]	1.908	0.090	−1.491[a]	1.966	0.448
Ethnicity × dose[a]	−2.241[a]	0.627	0.006	3.028[a]	0.654	<0.001
Ethnicity × dose × time[a]	0.963	0.560	0.085	1.022	0.580	0.077
Sedation						
Ethnicity	3.327[a]	2.480	0.180	−5.983	2.473	0.016
Ethnicity × dose	−1.848[a]	0.807	0.022	6.442	1.494	<0.001
Ethnicity × dose × time	−.465	0.716	0.516	−1.396	0.544	0.010
Like						
Ethnicity	−17.557[a]	4.812	<0.001	−14.225	5.023	0.005
Ethnicity × dose	−5.360[a]	1.731	0.002	−16.661	3.296	<0.001
Ethnicity × dose × time	1.625	1.548	0.294	2.735	1.204	0.023
Want more						
Ethnicity	−9.232[a]	4.677	0.048	−21.750[a]	5.142	0.004
Ethnicity × dose	−1.108[a]	1.550	0.475	−3.234[a]	1.562	0.038
Ethnicity × dose × time	0.117	1.386	0.932	1.849	1.396	0.185

[a]Values are taken from analyses with the non-significant three-way interaction removed. GEE = generalized estimation equation models; SE = standard error.

BrAC levels and subjective responses for both groups and both doses, however, showed no correlations of BrAC level at the rising limb with stimulation, liking or wanting ratings or BrAC level at the declining limb with sedation ratings. Finally, the subjective response to placebo dose was compared between Chinese and Caucasian drinkers and there were no significant differences in either heavy- or light-drinking groups.

Ethnic differences in alcohol effects among light drinkers

None of the three-way interactions of ethnicity, dose and time were significant for light drinkers (Table 2; Fig. 2). The subsequent GEE models revealed significant ethnicity × dose interactions for stimulation, sedation and like (Table 2). More specifically, at both high and low alcohol doses, alcohol produced lower stimulation in the Chinese versus Caucasian group ($P < 0.01$). Alcohol produced dose-dependent increases in sedation for both ethnic groups (high dose > low dose > placebo, $P < 0.001$). Both doses of alcohol reduced liking ratings (versus placebo) for the Chinese ($P < 0.001$), with liking at both doses significantly lower in the Chinese versus the Caucasians ($P < 0.05$ for low dose; $P < 0.01$ for high dose). Finally, there was a significant main effect of wanting, with the Chinese group reporting lower ratings for wanting than Caucasians, but this was not specific to beverage condition.

Ethnic differences in alcohol effects among heavy drinkers

The three-way interaction of ethnicity, dose and time was significant for sedation and liking, but not for stimulation and wanting (Table 2; Fig. 3). For sedation, post-estimation analyses for the three-way interaction showed that two effects accounted for the significant interaction: high-dose alcohol increased sedation more in the Chinese compared with the Caucasian groups during the rising limb ($P = 0.05$) and low-dose alcohol increased sedation more in the Chinese compared with the Caucasian groups at peak BrAC ($P = 0.01$) and early declining limb ($P < 0.01$). For liking, post-estimation analyses for the three-way interaction showed that both alcohol doses produced lower liking in the Chinese compared with the Caucasian groups at rising limb and peak BrAC ($P < 0.001$). For stimulation, there was a significant ethnicity × dose interaction (Table 2) such that high-dose alcohol produced significantly greater stimulation in Chinese compared with Caucasian heavy drinkers ($P < 0.001$). For wanting, the significant ethnicity × dose interaction showed that both alcohol doses produced lower wanting in Chinese versus Caucasians ($P < 0.001$), with each group showing dose-dependent increases in wanting relative to placebo (high > low > placebo, $P < 0.05$).

DISCUSSION

The current study investigated subjective responses to alcohol in light- and heavy-drinking Han Chinese and Caucasian American males, and the results supported hypotheses about dose-dependent differences between the two cultural groups. Chinese light drinkers reported lower stimulation, liking and wanting alcohol at both doses than their Caucasian counterparts, but similar
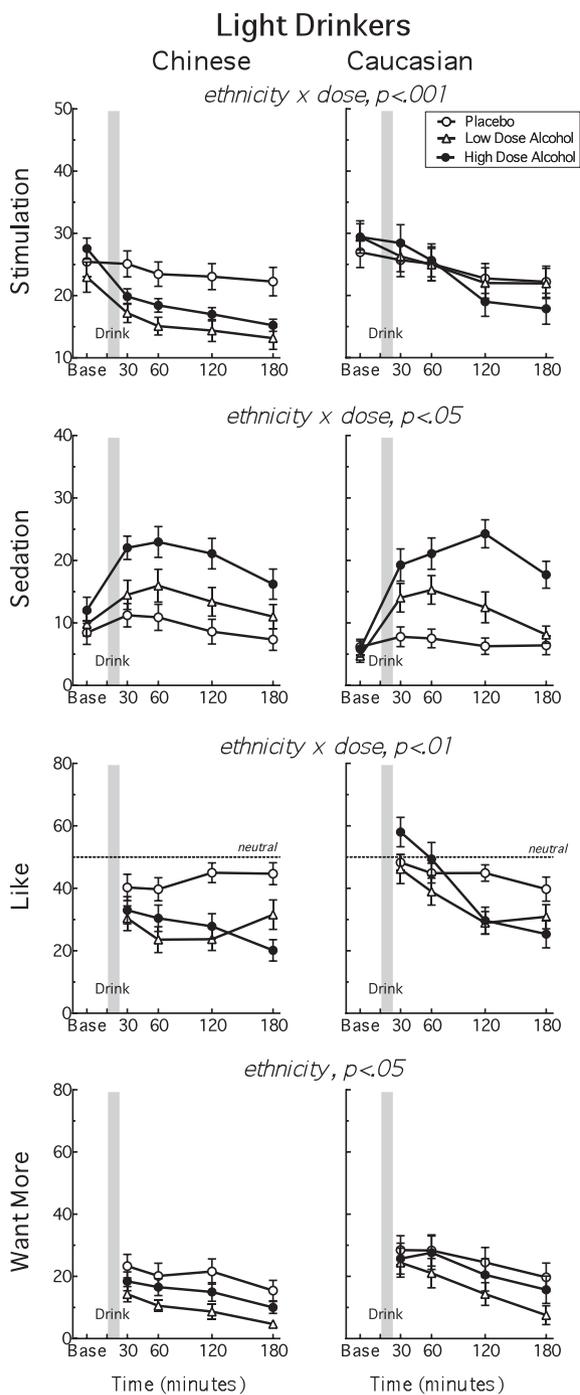
Figure 2 Han Chinese versus Caucasian American light drinkers. These graphs show the acute response to high and low doses of alcohol and placebo in Chinese versus Caucasian American light drinkers across the breath alcohol concentration (BrAC)curve

Figure 3 Han Chinese versus Caucasian American heavy drinkers. These graphs show the acute response to high and low doses of alcohol and placebo in Chinese versus Caucasian American heavy drinkers across the breath alcohol concentration (BrAC)curve

increases in sedation. In addition, Chinese heavy drinkers showed higher sedation and less liking (hedonic reward) during the alcohol absorption phase (i.e. rising limb), and a lower overall magnitude of wanting (motivational reward) alcohol than in Caucasians. However, an unexpected finding showed that Chinese heavy drinkers also showed higher sensitivity to the stimulating effects of the
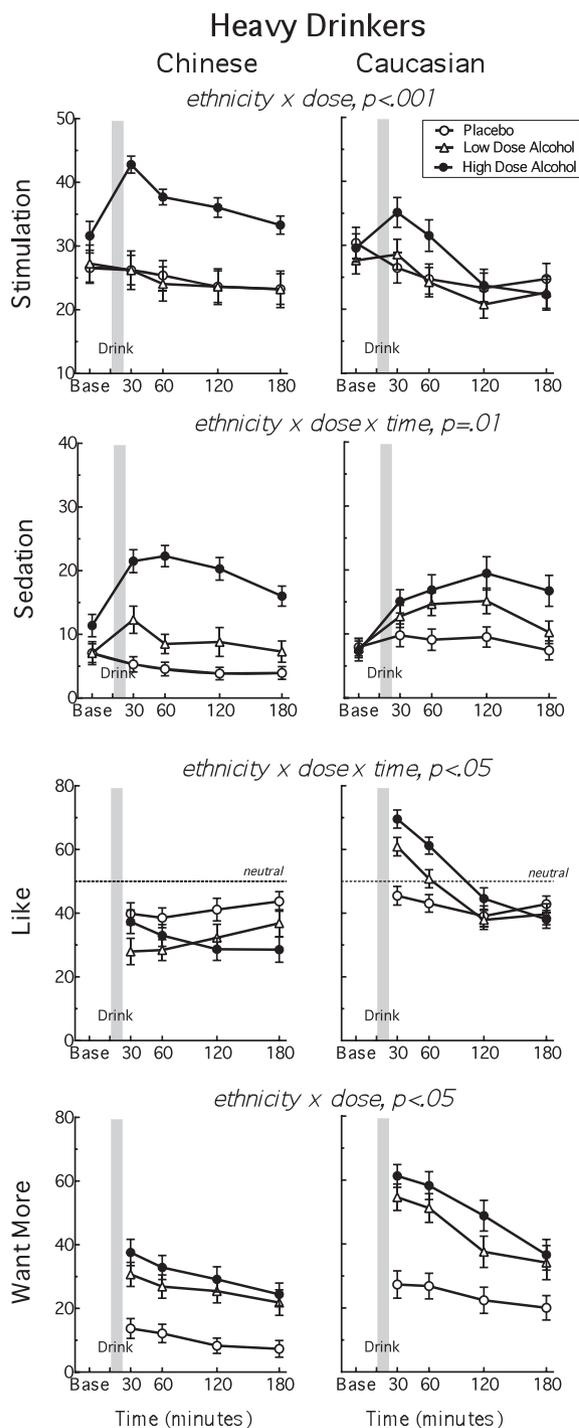
high alcohol dose than their Caucasian counterparts. This is unlikely to be due to metabolism, as while Chinese drinkers had higher BrAC levels during the rising limb compared with Caucasian drinkers, the differences were relatively small and BrAC was not associated with subjective effects.

These results suggest that Chinese social drinkers experience fewer of the hedonic effects of alcohol relative to their Caucasian counterparts, regardless of dose of alcohol or drinking history. Importantly, despite the fact that heavy-drinking Chinese men were more sensitive to alcohol's stimulant effects, this response was not accompanied by hedonic reward (liking). In addition, their relatively high levels of concomitant sedation might have mitigated the observed stimulatory effects, while remaining in motivational salience (i.e. wanting more) in heavy drinkers.

The lower alcohol liking and relative lesser magnitude of wanting for Chinese heavy drinkers compared to their Caucasian counterparts suggests that factors beyond subjective effects of alcohol may promote alcohol consumption and/or the development of risky drinking habits in Asian men. While not assessed in this laboratory-based study, there may be differential external cultural and social influences to drink alcohol or engage in binge drinking, such as the social acceptance of heavy drinking in Chinese men [41]. These results suggest that clinical interventions for alcohol use in Chinese men should consider inclusion of the cultural/social influences and motives to drink alcohol and not focus solely on the role of pleasurable and hedonic effects, which have been found in a pilot study by our group in the United States to improve outcomes when added to standard brief intervention [46].

Strengths of this study include the use of a mixed-subject design, direct measures of subjective alcohol response and examination of two doses of alcohol as well as placebo across multiple time-points for a full examination of alcohol response throughout the BrAC. This is important, because there is no ubiquitous response to alcohol, and clarifying differential responses based on the dose, the domain measured and effects throughout alcohol absorption, peak breath levels and the slow elimination phases are essential. Another strength was the use of similar methodologies in China and the United States to facilitate direct ethnic comparisons, and provision of the subjective scales in the native language.

There are also some limitations in this study that suggest future directions for research. First, genetic data were not obtained and therefore effects of the *ALDH* and other genetic polymorphisms were not ascertained. Anecdotal observational reports of the participants in the current Chinese sample indicated that more than half showed some degree of facial flushing, consistent with the effects associated with the ALDH2 deficiency reported in population-based estimates [26]; however, inclusion of genetic data could have added important information about possible genetic underpinnings of the reported subject responses. Interestingly, studies with East Asian samples have demonstrated that ALDH2 deficiency does not offer complete protection against alcoholism [33,47], as suggested by reports of positive response (e.g. 'great' feelings) to alcohol shown in those with ALDH2 deficiency [36,40,41]. Thus, more studies that include assessment of genetic polymorphisms of alcohol metabolizing alleles are needed to elucidate the ways in which this biological factor is related, independently or interactively, to pleasurable and rewarding effects of alcohol as well as sedating and noxious effects. However, caution has been advised in undertaking studies focused on candidate genes without sufficient sample size [48], and alcohol response is probably a multi-factorial and polygenic phenomenon. Thus, future studies that include genetic data should do so with enough power to offer robust findings on genotype–phenotype interactions.

Secondly, only men were examined in this study, so it is unclear whether the same responses would be found in women. Binge drinking in Chinese women remains rare [19], thus recruiting them would have been challenging. Thirdly, the study did not include contextual factors involved in alcohol use, and it is possible that Chinese heavy-drinking men may have different motives for engaging in frequent binge drinking than their Caucasian American counterparts. Finally, the current study focused on light to moderate smokers, and thus factors related to smoking–drinking co-use were not ascertained. Given the high percentage of Chinese who smoke cigarettes, future consideration of the role that smoking may have on subjective effects of alcohol would add to our understanding of heavy and risky alcohol use patterns in Chinese drinkers [49].

In summary, this is the first study of its kind to offer native Chinese versus Caucasian American cross-ethnic comparisons on alcohol use and subjective response to alcohol in people with heavy- and light-drinking phenotypes. The results of this study suggest that Chinese male heavy drinkers show a differential pattern of response to alcohol than their Caucasian American counterparts. While both groups demonstrate stronger stimulant effects than in their light-drinker controls, for Chinese men overall alcohol was experienced as more sedating and less pleasurable than in Caucasians. In spite of this, the heavy-drinking Chinese men engaged in binge drinking at levels similar to their Caucasian counterparts. Importantly, assumptions about subjective effects as risk factors based on Caucasian samples that have guided previous research may not apply to other cultures and racial/ethnic groups, especially those of East Asian origin. Future research is warranted to discern factors involved in acute alcohol response differences in people of East Asian origin from Caucasians and other ethnic subgroups.

Declaration of interests

None.

Acknowledgements

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