Cognitive and Neurobiological Mechanisms of Alcohol-Related Aggression

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Preface

Alcohol-related violence is a serious and common social problem. Moreover, violent behaviour is much more common in alcohol-dependent individuals. Animal experiments and human studies have provided insights into the acute effect of alcohol on aggressive behaviour and into common factors underlying acute and chronic alcohol intake and aggression. These studies have shown that environmental factors, such as early–life stress, interac with genetic variations in serotonin-related genes that affect serotonergic and GABAergic neurotransmission. This leads to increased amygdala activity and impaired prefrontal function, which together predispose to both increased alcohol intake and impulsive aggression. In addition, acute and chronic alcohol intake can further impair executive control and thereby facilitate aggressive behaviour.

Bullet points:

- Alcohol use is implicated in about 50% of all violent crimes and sexual assaults in industrialized nations
- Both acute and chronic alcohol intake increase the risk for alcohol-associated aggression
- Not all individuals who drink alcohol become aggressive and psychological studies have identified several gender and individual differences that confer risk for alcohol-related aggression
- Twin and adoption studies observed a significant disposition towards violent behaviour only in association with an increased risk to develop alcohol dependence
- Animal experiments and a limited number studies in humans show that alcohol-related aggression is found in a subset of individuals who were exposed to social adversity and carry certain risk genotypes

- Genetic and environmental factors associated with aggressive behaviour findings point to an important role of the serotonin system and its interactions with GABAergic neurotransmission in determining vulnerability to alcohol-associated aggression
- Chronic alcohol intake impairs serotonergic neurotransmission, which (according to studies in healthy controls but not yet in alcohol-dependent patients) modulates limbic processing of aversive stimuli and prefrontal functions associated with behavioural control
- Here we suggest that acute alcohol intake facilitates aggression in vulnerable individuals because it impairs prefrontal executive functions, disinhibits limbic processing of threatening stimuli and elicits expectancies for alcohol-associated aggression

Introduction

Of all psychoactive substances, alcohol is arguably the most potent agent for eliciting aggression and reducing behavioural control in certain individuals[1]. The relationship between acute and chronic alcohol intake, aggression and violence is well documented in the epidemiological literature and is linked with burdensome economic costs. For instance, acute alcohol use is implicated in approximately one-half of violent crimes[2] and sexual assaults[3] and also confers risk for intimate partner violence[4]. Additionally, crime trends indicate that the prevalence of alcohol-related aggression has grown over the past fifty years[5].

Alcohol-related aggression is also associated with chronic alcohol intake and alcohol dependence: the incidence of violent behaviour in various samples of male alcohol-dependent subjects is estimated to be between 20 and 50%[6-9], and individuals with alcohol abuse or dependence are more likely to be involved in violence compared to individuals without a psychiatric disorder[10,11]. A meta-analysis of studies on chronic alcohol use and criminal and domestic violence indicated that compared to individuals with very low or moderate alcohol use, those who get drunk at least once a year are 2 and 1.7 times more likely to engage in criminal and domestic violence, respectively[12]. With regard to intimate partner violence, a study showed that treatment-seeking alcoholic men were four times more likely to exhibit violence towards their female partner than non-alcoholic controls[13]. Interestingly, partner violence decreased one year after treatment and this effect was clinically significant only in patients who did not relapse. Finally, a cross-sectional study in Britain reported that hazardous drinking was associated with injury to the victim and perpetrator, and this risk almost doubled for individuals with alcohol dependence[14].

Experimental data for the acute effects of alcohol on aggression in more chronic and problem drinkers are limited, in part due to ethical limitations. Among individuals in treatment for substance abuse, general patterns of alcohol use, as well as alcohol use on the day of conflict, were related to

severity of partner violence; moreover, alcohol use was higher on days involving interpersonal conflict than on other days[15]. Additionally, compared to nonviolent partner conflicts, alcoholic men consumed more alcohol in the 12 hours prior to violent partner conflict[16]. Finally, among alcohol-dependent individuals in New Zealand, violence was most robustly explained by substance use (including alcohol) before the offence[10].

Numerous studies have sought to determine the mechanisms and processes that underlie alcohol-related aggression, and have indicated that multiple mechanisms play important roles in the relationship between acute and chronic alcohol consumption and aggressive behaviour. This review attempts to integrate findings regarding the social, cognitive and biological mechanisms that drive aggressive behaviour in response to acute alcohol intake and the facilitating role of chronic alcohol consumption. We discuss animal experiments and human studies that address why despite alcohol's well-established and robust effect on behavioural inhibition, some individuals respond aggressively following acute consumption, and that describe genetic and environmental factors that point to an important role for the serotonin system in determining vulnerability to alcohol-induced aggression. In piecing together conclusions from animal experiments and human correlative studies, we aim to develop an integrative model of alcohol-related aggression and to highlight research areas that warrant further, interdisciplinary study.

Acute alcohol effects on aggressive behaviour

Studies in animals

Studies in rodents show that low doses of alcohol facilitate aggression in a subset of animals, while higher doses induce sedation and motor incordination[16-18]. Additionally, rodents with alcohol-heightened aggression display an increased number of aggressive acts during a bout of aggression, e.g. when confronted with intruders in their cages[18,19]. Rhesus monkeys exposed to early social isolation stress show excessive alcohol intake and impulsive aggression. Such monkeys with a lifetime history of severe competitive physical aggression also display higher rates of aggression when intoxicated by alcohol[20]. Again, alcohol appears to increase the number of aggressive behaviours within each aggressive burst[19].

Studies in humans

Numerous studies have employed controlled experimental paradigms to examine the acute effects of alcohol on aggressive behaviour in humans. In these settings, direct physical aggression is typically operationalized as the intensity and duration of shocks or tone blasts administered to a fictitious opponent

under the guise of a competitive reaction time task (Taylor Aggression Paradigm[21]) or to a "student," played by a confederate, for providing incorrect answers (teacher-learner task[22]). Aggression is also measured with the Point Subtraction Aggression Paradigm[23], where participants can take points (which can be exchanged for money) away from an opponent. Collectively, data from these studies indicate that alcohol consumption is causally, though indirectly (see indirect-cause model **Table 1**[24]), related to the expression of aggressive behaviour (e.g.[25]). More specifically, among a subset of consumers, behavioural manifestations of alcohol-induced aggression have been linked to neuropsychological variables. These include, first, alcohol-induced interference with or impairment of executive control mechanisms (e.g., attention-allocation, inhibition, social information processing); second, various situational factors (e.g, provocation, threat, social pressure, self awareness); and third, person-based, individual differences (e.g., subjective expectations for the effects of alcohol, gender, aggressive disposition, sober-state executive functioning) (for review see[25-28]). **Tables 1, 2** and **3** attempt to summarize the most prominent cognitive and social-cognitive mechanisms and theories of alcohol-related aggression that have emerged from decades of research with humans. Although increased collaboration across disciplines is needed to garner empirical support for the advancement of these models, their inclusion is intended to inform more comprehensive research directives to address the serious social problems associated with intoxicated aggression. Studies in animals and, to a lesser extent, in humans have aimed to investigate the mechanisms by which alcohol affects these variables and the brain areas that mediate them.

Acute alcohol effects on brain function

Alcohol effects on neurotransmission

Animal experiments showed that acute alcohol intake stimulates serotonin and dopamine release, e.g. in the ventral and dorsal striatum[29-31]. It also exerts an inhibitory effect on cortical activation, by inducing GABA release and stimulating $GABA_A$ and $GABA_B$ receptors, and via a blockade of glutamatergic neurotransmission (e.g. via interference with a glycine binding site that modulates NMDA receptor function)[32-35]. Some of the alcohol-induced neurotransmitter alterations resemble effects of social stress: for example, stress induces both striatal and frontocortical dopamine release, while alcohol increases extracellular dopamine mainly in the striatum but stimulates frontal dopamine release only when applying rather low doses [29,30,36,37] In rodents, social defeat stress affects amygdala and prefrontal cortex (PFC) functions and their modulation of dopaminergic neurotransmission, and this seems to underlie increased intake of a drug of abuse (cocaine) in animals exposed to social stress[38]. Socially subordinate monkeys display increased striatal dopamine concentrations (measured indirectly via competition with radioligand binding to dopamine D2 receptors), which correlates with increased intake of dopaminergic drugs of

abuse[39]. Elevated dopamine in the PFC and nucleus accumbens/ventral striatum is associated with the initiation of aggressive attacks and threatening behaviour in rodents, and dopaminergic stimulation of D1 and D2 receptors in the hypothalamus facilitates active defensive behaviour in cats[40]. Animal studies further suggest that both alcohol and conditioned fear stress induces dopamine release in the amygdala[41,42], and in humans, dopamine synthesis capacity in the amygdala correlates with functional activation of the amygdala and anterior cingulate cortex elicited by aversive visual stimuli[43]. Acute alcohol effects on monoaminergic, excitatory and inhibitory neurotransmitter systems thus affect prefrontal and limbic brain areas that are implicated in social conflict and defeat, and alcohol-associated increases in dopamine release may facilitate aggressive and defensive behaviour.

Acute alcohol intake, prefrontal cortex function, and aggression

In humans, most research on alcohol-related aggression focused on acute effects on executive functions associated with the PFC[26]. In individuals in whom PFC function is impaired, marked changes in behaviour have been repeatedly observed, including emotional lability and aggression, apathy, anticipating, planning and sequencing deficits, deficiencies in initiating behaviour, problems in shifting, adapting and stopping behaviour and deficient abstract reasoning[44,45]. Interestingly, several placebo-controlled studies employing neuropsychological measures have shown that alcohol consumption confers similar impairments in PFC functioning, including planning[46], information processing, inhibitory control and response flexibility[47-50], attention[51] and set-shifting[52,53]. Additionally, an electrophysiological study showed that very small quantities of alcohol reduce activity in the medial PFC in response to errors of performance, and that this effect is associated with a reduced ability to adjust behaviour after such errors[54]. Such deficits may lead to careless, inappropriate or exaggerated behaviour that can render one more vulnerable to aggressive or even violent responding when confronted with provocations or emotional challenges of the environment[55].

Importantly, several PFC subregions, notably anterior cingulate cortex and ventromedial PFC, send (inhibitory) projections into limbic areas, i.e., the amygdala[56,57], and are thought to be part of a circuit that helps to regulate emotional behaviour[58]. Dysfunction of the amygdala seems to play a key role in various forms of aggressive behaviour, with instrumental or ‘cold’ aggression being associated with reduced, blunted amygdala responses and reactive or ‘hot’ aggression with increased amygdala reactivity[59-65]. Functional neuroimaging in aggressive individuals suggests that deficient activation of medial prefrontal structures coupled with exaggerated amygdala responses in emotionally challenging situations is a key mechanism in reactive aggression[62-64], and thus supports the notion that PFC plays an important role in the regulation of aggressive behaviour[66] (**Figure 1**).

Taken together, the acute effects of alcohol on the PFC may indirectly promote aggression by impairing prefrontal executive functions, including prefrontal control of emotional behaviour[67].

Unfortunately, no published studies to date have attempted to measure activation in brain regions associated with executive functions (with imaging or electrophysiological techniques) under alcohol while aggressive behaviour is being elicited.

Vulnerability factors

In animals and in humans, only a small number of individuals become aggressive after acute alcohol intake, suggesting that alcohol engenders aggression only for those who meet a certain risk profile. In mice, alcohol-heightened aggression is a selectable trait[68]. In humans, manifestation of aggressive behaviour following acute alcohol intake depends on individual factors such as gender (higher risk in males[69,70]), executive functioning[71], personality (trait anger[72]; sensation seeking[73]; difficult temperament[74]; poor anger control[75]; irritability[76]; dispositional empathy[77]), motives for drinking (e.g., drinking to cope, drinking to enhance experience[78]), approving beliefs about aggression[79] and expectancies for alcohol to elicit aggression[28,80,81]. Situational features such as provocation[82,83], threat[84], social pressure[85], and environmental context (e.g., being in a bar vs. home[86]) can also interact with extant risk factors to promote alcohol-related aggressive behaviour.

A central role for serotonergic dysfunction

One factor that seems to facilitate alcohol-associated aggression in vulnerable humans is the effect of chronic alcohol intake (plus the often comorbid abuse of tobacco) on monoaminergic, specifically serotonergic, neurotransmission. Five lines of evidence point in this direction. First, serotonin depletion is associated with increased aggression in individuals with high levels of aggression or hostility, and additional alcohol intake has an additive effect on aggression[87-89]; second, a subgroup of alcohol-dependent patients with early disease onset and a rather high genetic disposition towards alcohol-dependence (so-called type 2 alcohol-dependent patients) display low serotonin turnover rates (measured via the serotonin metabolite 5-HIAA in the CSF) and increased aggressive behaviour[90,91]; third, chronic alcohol and nicotine consumption induces neuroadaptive and neurotoxic changes in monoaminergic, glutamatergic, and GABAergic neurotransmission — including a reduction in raphe serotonin transporters, which seems to quickly reverse during alcohol detoxification in non-smokers but not smokers[92,93]; fourth, acute and chronic reductions in central and prefrontal serotonin availability increase behavioural rigidity and reduce inhibitory functions[94,95], which may contribute to a narrowing of attention and response patterns towards threatening stimuli that facilitate aggressive acts; and fifth, the pharmacological agent fluoxetine, which blocks serotonin transporters, reduces anger and physical aggression in alcohol-dependent perpetrators of domestic violence[96].

However, such correlational data do not clarify whether excessive alcohol use predisposes to aggression or whether there is a common factor that links excessive alcohol use and aggression. Moreover, there is a near complete absence of multimodal imaging studies that explore the interaction between alterations in neurotransmitter systems measured with positron emission tomography (PET) and functional brain activation associated with alcohol-associated aggression. The current state of knowledge is thus mainly based on animal experiments that assess the interaction between genetic and environmental factors and their respective impact on neurotransmitter systems, functional brain activation and alcohol-related aggression. We will discuss these animal models and focus on their relevance for alcohol-associated aggression in humans on the basis of psychological studies that have elucidated neurocognitive factors posited to contribute to aggressive behaviour under the influence of alcohol (see **Box 1**).

Rodent models of vulnerability to alcohol-related aggression

Studies in rodents have assessed the question of why only a subset of animals become aggressive under alcohol. The initiation of aggressive acts has been associated with increased dopamine levels in the prefrontal cortex and ventral striatum[40], and a low availability of striatal dopamine D2 receptors is associated with impulsivity in rodents[97]. However, impulsive behaviour includes a wide spectrum of activities well beyond impulsive aggression, and attempts to causally link individual differences in dopamine release (measured via microdialysis) with levels of aggression (e.g. after exposure to an intruder to the animals' cage) following alcohol intake have failed[98].

Alterations in serotonergic neurotransmission do seem to distinguish between mice with and without alcohol-heightened aggression. For example, serotonin receptor expression is reduced for all receptor subtypes (except for 5-HT3 receptors) in the prefrontal cortex of mice showing alcohol-induced aggression[68]. Stimulation of $GABA_A$ (but not $GABA_B$) receptors in the dorsal raphe area increases alcohol-related aggression, ostensibly via postsynaptic inhibitory effects on serotonergic neurons projecting to the frontal cortex[17]. Together with the observation that cortical serotonin levels decrease during and after an aggressive encounter[99], these findings suggest that a frontal cortical serotonin deficit mediates an increased propensity for violent behaviour, including alcohol-induced aggression.

Newer data emphasize specific roles in conveying vulnerability to aggression for different serotonin receptors and transporters[68]. For example, the effects of agonists of $GABA_B$ receptors and (inhibitory) 5-HT_{1B} receptors on aggressive behaviour seem to depend on the specific localisation of application and the respective effects of these agonists on serotonergic neurotransmission. Application of a $GABA_B$ agonist in the dorsal raphe area increases aggression irrespective of alcohol intake; this effect is dependent on the activation of serotonergic neurons in the raphe area (because it was blocked by a 5-HT1A agonist) and is associated with acute increases in serotonin levels in the medial prefrontal cortex[17,100]. Most interestingly,

application of a 5-HT1B agonist in the medial prefrontal cortex increases aggression in mice with a history of alcohol self-administration, whereas systemic application reduces aggression[101,102]. Additionally, prefrontal serotonin release in these mice is blunted following 5-HT1B receptor stimulation. These data suggest that alcohol intake may interact with the expression patterns of specific serotonin receptors[68], which modulate alcohol's effect on aggressive behaviour[101]. Such differences in the effects on aggression of specific serotonin receptor agonists and antagonists may be explained by their differential effects on GABAergic interneurons, with agonists of 5-HT_{2A}, 5-HT_3 receptors facilitating GABA release in rat frontal cortex and hippocampus and 5-HT_4 receptors regulating the amplitude of GABAergic inhibitory postsynaptic currents, whereas agonists of (inhibitory) 5-HT_{1A} and 5-HT_{1B} agonists in amygdala, hippocampus and ventral tegmental area inhibit GABAergic interneurons, thus facilitating e.g. striatal dopamine release[103,104] (**Figure 1**).

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Primate models of vulnerability to alcohol-related aggression

Studies on brain serotonin metabolism in nonhuman primates have also indicated that individual differences in serotonergic neurotransmission play a role in the biological vulnerability to increased alcohol-related aggressiveness. In rhesus monkeys, environmental factors (e.g. early social isolation stress[105-108]) induce a trait–like reduction in central serotonergic neurotransmission[107-109], and this is associated with increased impulsive aggression and excessive alcohol intake. Specifically, levels of the serotonin metabolite 5-hydroxyindoleacetic acid (5-HIAA) in the cerebrospinal fluid (CSF) were reduced in monkeys separated from their mothers compared with mother-reared monkeys, and this reduction in serotonin turnover rates was trait-like and persisted into adulthood[107,108]. Imaging studies revealed that adult monkeys who experienced early social isolation display a negative correlation between CSF 5-HIAA levels and the availability of brainstem (raphe) serotonin transporters when assessed with a radioligand that is displaced by endogenous serotonin[110].

Importantly, reduced concentration of the serotonin metabolite 5-HIAA in the CSF is not found in all rhesus monkeys separated from their mothers; it occurs only in primates carrying one or two SLC6A4 alleles with a serotonin-transporter-linked polymorphic region (5-HTTLPR) (known as 'short' alleles), which have been associated with decreased transporter function and expression in humans and non-human primates[111,112]. Interestingly, these monkeys showed elevated serotonin transporter (5-HTT) availabilities following social isolation stress[110], which seems to be due to reduced competition between (low) endogenous serotonin and *in vivo* radioligand binding to serotonin transporters rather than to a genetically driven alteration in serotonin transporter density per se[110]. Indeed, *in vivo* serotonin depletion

and restoration studies showed that binding of the 5-HTT radioligand beta-CIT is displaced by restoration of extracellular serotonin concentrations, and that this effect was stronger in monkeys with higher 5-HIAA levels in the CSF[113], suggesting that monkeys with higher CSF 5-HIAA levels also have higher extracellular serotonin concentrations *in vivo*[113]. In accordance with this hypothesis, assessment of 5-HTT density with a radioligand that is not displaced by endogenous serotonin (and thus measures absolute transporter density rather than availability relative to extracellular serotonin concentrations) revealed 5-HTT reductions in the brainstem, thalamus and striatum in monkeys exposed to early social isolation stress[114,115], confirming an overall impairment of serotonergic neurotransmission.

In rhesus monkeys exposed to social isolation stress, both low CSF 5-HIAA concentrations and associated brainstem serotonin transporter availability are correlated with self-initiated (impulsive) aggressive acts and other behaviour patterns that are similar to those associated with early-onset alcoholism among humans, i.e., lower social competence and increased anxiety[110]. Importantly, CSF 5-HIAA concentrations are correlated with the level of inhibition of prefrontal glucose utilization by a $GABA_A$ agonist[110,116,117], suggesting that the acute sedative (GABA-mediated) effects of alcohol are reduced in primates with low CSF 5-HIAA levels, e.g. in those exposed to social isolation stress. A low level of sedation following acute alcohol intake is one factor that is known to predispose to excessive alcohol intake, hypothetically because subjects lack a warning sign of harmful use[118,119]. Indeed, monkeys with low CSF 5-HIAA levels and associated alterations in brainstem (raphe) serotonin transporter availability show increased alcohol intake in a free-choice paradigm, and the amount of alcohol intake was positively correlated with the relative availability of brainstem (raphe) serotonin transporters[120]. This behavioural profile is consistent with research in humans which demonstrated that a low response to alcohol (i.e., the effects of alcohol consumption are less acute and less aversive) is a partially heritable trait that is associated with 5-HTT genotype and, in prospective studies, with excessive alcohol intake[118,119].

Thus, findings on the effects of social isolation stress on the serotonin system and behaviour in non-human primates seem to be relevant to humans. Indeed, results from a twin study[121] emphasized the importance of social stress factors in the pathogenesis of both antisocial behaviour and excessive alcohol-intake. In sum, both genetic and environmental factors contribute to the serotonin turnover rate of non-human primates[105,122,123], and this is robustly associated with both alcohol intake and impulsive aggression.

Genetic vulnerability factors for alcohol-related aggression in humans

Studies in humans showed that heritability accounts for about 35% of the variance in CSF 5-HIAA concentrations and that environmental factors, such as early social isolation stress (growing up without a

mother and being separated from peers), have an important role in the regulation of the serotonin turnover rate[117,124]. Furthermore, alcohol-dependent patients with early onset of dependence show reduced serotonin turnover rates (low 5-HIAA in the CSF) and increased levels of anxiety and impulsive aggression[90,125]. Although some studies[117,124] indicate an important role for environmental factors interacting with serotonergic neurotransmission in predisposing to aggressive behaviour, it has often been suggested that aggressive — and particularly violent — behaviour is under strong genetic influence. Moreover, several twin and adoption studies have failed to observe a significant disposition towards violent behaviour that is independent of the increased risk to develop alcohol dependence[121,126,127]. This suggests that a common hereditary factor might predispose individuals to both alcohol dependence and violent behaviour. Again, the serotonin system was implicated in these studies: Cloninger[90] hypothesized that both addictive and aggressive behaviour are manifestations of a failure to learn from mistakes and punishment[90,128], hypothetically due to serotonin dysfunction and resulting impairments in behavioural inhibition[128]. Serotonergic neurotransmission has also been implicated in negative mood states and violent suicide attempts in humans with affective and addictive disorders (i.e., anxiety and depression[117,129]). In addition serotonin dysfunction, as indicated by a low serotonin turnover rate measured via the serotonin metabolite 5-HIAA in the CSF, has been associated with early onset of alcoholism and both anxiety and impulsive aggression in alcohol-dependent patients[90,125,130,131]. Hence, a genetic predisposition towards serotonin dysfunction, possibly exacerbated by adverse environmental experiences, may represent one risk factor for the pathogenesis and maintenance of both excessive alcohol consumption and aggressive behaviour[117].

MAOA and 5-HTTLPR as risk genes

What genes might underlie this genetic predisposition? A risk gene for aggression in humans was identified by the landmark finding that a single mutation in the gene that encodes monoamine oxidase A (*MAOA*, a catabolic enzyme that breaks down biogenic amines including serotonin), was associated with criminal behaviour in a Dutch kindred[132]. Interestingly, a meta-analysis showed that the same *MAOA* genotype is also associated with both increased alcohol intake and negative mood states such as anxiety and depression ([133] but see [134]). To date, *MAOA* is the best known candidate susceptibility gene for human aggression. Although the human functional knockout is rare, common polymorphisms in *MAOA* exist. Most studied among these is a variable-number tandem repeat (VNTR) polymorphism in the upstream region of the gene, known as the *MAOA* u-VNTR. Certain alleles in this region are associated with relatively higher *MAOA* expression (*MAOA*-H alleles), whereas others are associated with relatively lower expression (*MAOA*-L alleles)[135]. The *MAOA*-L variant is associated with increased propensity towards impulsive aggression[136].

Importantly, this *MAOA* gene is located on the X-chromosome, and a sex-by-genotype interaction may contribute to greater occurrence of alcohol-induced aggressive behaviour in males. Functional imaging studies revealed that in both sexes, *MAOA*-L subjects compared to *MAOA*-H subjects display exaggerated limbic (amygdala) and paralimbic (insula) activation during implicit processing of angry and fearful faces, with diminished recruitment of regulatory regions of prefrontal cortex (orbitofrontal and anterior cingulate cortices) (**Figure 2**). Subjects with *MAOA*-L also displayed exaggerated neuronal (cingulate cortex) responses to perceived social rejection[137].Furthermore, a recent study showed that the *MAOA*-L variant, which is associated with increased propensity towards impulsive aggression, predicted increased volume reductions in the limbic system (including cingulate gyrus, amygdala, hippocampus) in MAOA-L subjects relative to *MAOA*-H subjects[138]. However, only male *MAOA*-L subjects showed greater fMRI activation than *MAOA*-H males in two limbic areas, the amygdala and hippocampus, during the recall of negatively valenced visual scenes, and reduced activation in dorsal cingulate during a go/no-go task[138]. Furthermore, connectivity between amygdala and medial prefrontal cortex was modified by genotype in a sex-specific fashion: *MAOA*-L men showed stronger amygdala-ventromedial PFC functional coupling than *MAOA*-H men, whereas no effect of genotype was evident in women[139]. Additionally, Caspi and colleagues observed that the *MAOA* genotype mediates the impact of early-life maltreatment on the development of antisocial — including aggressive — behaviour. More specifically, *MAOA*-L males were more susceptible to the effects of abuse than *MAOA*-H males with respect to the development of antisocial behaviour[140]. This finding now has meta-analytic support[141] and has been extended to variation in the serotonin transporter gene (5-HTTLPR)[142]. More specifically, the common polymorphism of the serotonin transporter gene is associated with increased amygdala activation in response to aversive pictures and with a higher risk of experiencing negative mood states when exposed to traumatic life events[140,143,144]. Indeed, a study in non-human primates observed increased aggressiveness in male rhesus monkeys carrying the 5-HTTLPR s-allele (the genotype correlated with decreased CSF 5-HIAA levels following social isolation stress), and aggressive behaviour was even higher in monkeys carrying this genotype when they were also exposed to early social adversity[145]. It is thus possible that alterations in serotonergic neurotransmission exert their effect during neurodevelopmentally vulnerable periods, which may explain why a recent PET study observed no correspondence between *MAOA*-uVNTR and *MAOA* activity in adults[146].

Together, these findings suggest that these *MAOA*-L subjects whoare have a stronger disposition to display stress-associated aggression, have a higher sensitivity to social rejection, increased amygdala activation when confronted with aversive stimuli, and decreased volume and activation of brain areas associated with behavioural control, such as the cingulate cortex. A recent study implicated further genetic variation in serotonergic neurotransmission in alcohol-associated violence: in mice, knock-out of

the 5-HT2B gene was associated with increased impulsivity and response to novelty. In humans, a stop codon in the 5-HT2B gene blocks receptor expression in the frontal cortex and is associated with high impulsivity in Finnish violent offenders, who mainly aggressed when intoxicated[147].Thus, both animal experiments and human studies support the notion that individual differences in serotonin function contribute to the predisposition to respond aggressively, including after alcohol consumption. Together, the studies reviewed here suggest that genetic effects on serotonin receptor, transporter availability and metabolism, through an interaction with stress exposure, contribute to excessive alcohol intake, aggressive behaviour and negative mood states.

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A role for chronic alcohol consumption

If individual differences in serotonergic neurotransmission and its effect on e.g. the GABAergic system predispose some individuals to react aggressively when consuming alcohol, how could chronic alcohol intake exacerbate the manifestation of violent behaviour following alcohol intoxication? The association between chronic alcohol problems and aggressive behaviour following acute alcohol intake may simply be due to the fact that subjects with chronic alcohol problems consume alcohol more often and thus are more frequently intoxicated. Alternatively, a common factor that results in, for example, low levels of CSF 5-HIAA may underlie both excessive alcohol intake and aggressive behaviour. That is, low CSF 5-HIAA levels and a relatively high availability of brainstem serotonin transporters (arising from genetic factors or early social stress experiences[93,110]) may predispose to both impulsive aggression and a low intoxicating effect of acute alcohol ingestion, which, in adolescents, in turn facilitates excessive alcohol intake[119,148]. Additionally, some studies indicate that in vulnerable individuals, certain neurobiological effects of chronic alcohol intake may interact with exactly those neurotransmitter systems that are already implicated in the disposition to alcohol-associated violence. One example is the effect of chronic alcohol intake on dopaminergic neurotransmission, which seems to increase impulsive behaviour[149].

Impulsivity and neuroadaptation to chronic alcohol

It is posited that alcohol dependence, like other forms of chronic drug abuse, is characterized by dysfunctional reward expectation with an overemphasis on immediate rewards and a discounted value for delayed outcomes (i.e., impulsivity) (for review see[149]). This profile may lead to early onset of alcohol dependence and social problems[117,150]. A number of studies suggested that alcohol-dependent patients are more impulsive than controls[151,152] and that impulse control disorders (including impulsive-violent

behaviour) are more common among alcohol-dependent subjects than in healthy volunteers[125,153]. Impaired reward expectation, putatively associated with alcohol-associated dysfunction of the ventral striatum, may therefore contribute to impulsivity and impulsive aggression. Indeed, rodents with a low striatal dopamine D2 receptor availability display high levels of impulsivity compared to animals with high striatal D2 levels[97]. Although a low dopamine D2 receptor availability in the striatum may be a partially heritable trait, chronic alcohol intake further reduces striatal dopamine D2 receptor availability and sensitivity in animals and humans[154-157]. Such reductions in dopamine D2 receptor availability can interfere with dopaminergic modulation of ventral striatal activation during reward expectation. Indeed, Beck et al. (2009) observed increased impulsivity and reduced ventral striatal activation during reward anticipation (i.e. the processing of reward-indicating cues) in alcohol-dependent patients compared with healthy volunteers. In both healthy controls and alcohol-dependent patients, increased impulsivity was associated with reduced activation of the ventral striatum during reward anticipation[158], suggesting that impulsive subjects may have difficulty maintaining reward expectation, which can contribute to increased delay discounting[159]. Reduced striatal responsiveness to delayed rewards may also provoke increased reward-seeking — such as for alcohol — as a means of compensation, and propel subjects into risky situations that in turn enhance aggressive, violent actions[160]. Such alcohol-related risky behaviour may be further increased when executive functioning is impaired, and a recent study observed that impaired connectivity between the ventral striatum and prefrontal cortex during a reversal learning task correlated with increased craving and a reduced learning rate in alcohol-dependent patients[161]. Given that measures of impulsivity are often associated with aggression[162,163], impulsivity could be a mediating factor for the relationship between alcohol and aggression (**Figure 1**).

Importantly, impulsivity is a multi-faceted construct that can be expressed in several ways, including in the motor (inability to inhibit behavioural responses) and cognitive (impulsive decision-making and inability to maintain intentions and goals) domains[164] and mediated by different neurotransmitter systems. Alcohol acutely increases diverse facets of impulsive behaviour, including response inhibition and rapid decision making[165,166], and it has long been suggested that serotonin dysfunction contributes to impulsive behaviour via impairment of response inhibition[90,167]. Again, effects of chronic alcohol intake on serotonergic neurotransmission may further exacerbate alcohol-associated impulsivity and aggressive behaviour in vulnerable individuals. Animal studies showed that following chronic alcohol intake, both serotonin and dopamine turnover rates increased, suggesting that the low dopamine and serotonin turnover rates that characterize alcohol-preferring animals are counteracted by alcohol-induced stimulation of dopamine and serotonin release (e.g. measured via microdialyses or assessment of the respective metabolites in CSF)[117,168]. However, in mice showing alcohol-induced aggression, there was a blunted serotonin release in the prefrontal cortex following application of a 5-

HT1B agonist[101] (**Figure 1**). This is a key finding, because it suggests that in individuals predisposed to showing alcohol-induced aggression, effects of chronic alcohol intake may interact with serotonergic neurotransmission in the prefrontal cortex, resulting in altered neuronal excitation in this area and thus interfering with behavioural control.

Animal experiments and human studies indeed support the hypothesis that serotonin dysfunction interferes with prefrontal cortical functions such as executive controlled behaviour adaptation, particularly in the face of demands for flexible behaviour adaptation and response inhibition, e.g.? for example. in personal confrontations or hostile situations[94,95]. It is well documented that alcohol-dependent patients demonstrate deficits across a range of executive functioning abilities (e.g.,[169-172]). Additionally, a comprehensive review of the PET, fMRI and neuropsychological data concluded that alcoholism is characterized by frontal lobe dysfunction[173]. Correspondingly, in human subjects who demonstrate impulsive-aggression, prefrontal cortex activation following a serotonergic challenge with fenfluramine is blunted, indicating impaired serotonergic modulation of, specifically, orbitofrontal, ventral medial frontal and cingulate cortex[174]. Additionally, relative to controls, impulsive murderers show less prefrontal cortical excitation as indexed by lower bilateral prefrontal glucose metabolism[175]. Given the evidence that the relationship between alcohol and aggression is stronger for individuals with lower levels of executive functioning[71], alcohol-dependent individuals may be more prone to respond aggressively under alcohol due to the chronic effects of alcohol on executive functions. To date, this hypothesis has not been directly tested in patients with chronic alcohol problems and alcohol-associated aggression. Given the social relevance of alcohol-related aggression, such studies in individuals with excessive alcohol intake are highly warranted.

Perception of threat and limbic dysregulation

Beyond the impairment of frontocortical behavioural control, human studies indicate that previous experiences and expectation of alcohol-related violence facilitate the manifestation of aggressive behaviour in intoxicated individuals (see Box 1). Under alcohol, individuals who possess such strong expectancies may be more inclined to perceive relatively harmless social encounters as threatening, and react with violent behaviour. As discussed above, serotonergic neurotransmission in interaction with other transmitter systems has been implicated in the perception of aversive, threat-related and anxiety-provoking environmental stimuli[117,176]. In a study by Knutson et al. (1998), administration of a selective serotonin reuptake inhibitor known to increase synaptic serotonin concentrations in animals[177] was correlated with decreased anxiety and decreased insecurity in human volunteers[178]. These volunteers showed reductions in aggressive behaviour in a competitive game, which may be seen as evidence for a direct link between serotonin and aggression. However, the effect of the serotonergic medication was

even stronger on negative affect, and the observed reduction in aggressiveness was statistically explained by the decrease in negative emotions[178]. This suggests that increased serotonin neurotransmission primarily reduces negative emotions, which then lowers aggressive behaviour, possibly because of decreased perceptions of insecurity or threat. This interpretation is supported by animal experiments showing that increased serotonin turnover is induced by social success and in turn improves social competence in competitive games[179,180]. In contrast, serotonin depletion induced insecure and anxious behaviour patterns[181].

Human studies have suggested a prominent role of limbic brain areas such as the amygdala and its prefrontal regulation in threat perception and anxiety. Additionally, these areas are known to be modulated by serotonin transporter genotype, such that 5-HTTLPR carriers show stronger activation of the amygdala in response to negative affective visual stimuli[143,144]. Such genetic effects on serotonin transporter expression may be exacerbated in alcohol-dependent patients, who display a reduction in brainstem (raphe) serotonin transporter availability, depending their on serotonin transporter genotype[93,176]. Individuals with trait-like alterations in serotonin function (for example carrying the vulnerable *MAOA* or 5-HTT genotype and/or having suffered early social isolation stress)[110,140] (**Figure 1**) may thus display a disposition towards increased limbic activation when confronted with threatening situations (mediated via amygdala activation). However, the experience of threat associated with amygdala activation should not be equated with anxiety – in situations of imminent danger, individuals can react with fight or flight. Human studies confirmed that in social drinkers, alcohol consumption can be associated with either aggression or anxiety[182]. Neurobiologically, whether the balance is tipped towards aggression or anxious withdrawal may depend on individual differences in specific aspects of serotonergic neurotransmission: passive avoidance, e.g. in the rodent paradigm of learned helplessness, has been associated with acutely increased serotonin release[183], whereas alcohol-associated aggression mediated via 5-HT1B receptors (which are inhibitory) was associated with a decrease in prefrontal serotonin release[101]. As prefrontal serotonin depletion and potential impairments in prefrontal functioning impair flexible control of behaviour[94] (which is associated with prefrontal cortex dysfunction), subjects may respond with aggressive behaviour if they have previously experienced that aggressive or violent behaviour is a normal or even appropriate response in such threatening situations. We suggest that when these individuals consume alcohol, aggressive expectancies for alcohol, combined with an attentional bias towards threatening stimuli, plus impairment of executive functions associated with both chronic and acute alcohol intake, may increase the likelihood of engaging in violent behaviour[27].

Summary and outlook

Alcohol-related aggression is characterized by a nexus of interacting factors including, but not limited to, alcohol-associated (pharmacological) alterations of key neurotransmitter systems and their respective effects on frontal and limbic brain areas, cognitive deficits associated with acute and chronic alcohol intake, social learning and contextual influences, and associative connections between alcohol and aggression in memory. Here we suggest that alcohol-associated aggression may result from acute alcohol effects that impair PFC executive functions and disinhibit limbic processing of threatening stimuli, and elicit alcohol-associated experiences of aggression. Individual differences in alcohol-associated aggression seem to be partly mediated by differences in functioning of the serotonin system and its interaction with raphe (brainstem) and prefrontal GABAergic neurotransmission, which affect both limbic processing of aversive, threatening environmental stimuli and flexible behavioural control by the prefrontal and cingulate cortex. The resulting tendency for impulsive aggression may further be augmented by increased discounting of delayed reward due to alterations in the neural correlates of reward anticipation following chronic alcohol intake. It should be noted that this model of alcohol- and stress-associated impulsive aggression, which assumes limbic dysregulation and impaired prefrontal control, does not preclude the possibility that other types of aggression and antisocial behaviour are based on limbic hyporeactivity and lack of empathy[59,184].

Our model is thus compatible with an imbalance between “hot” and “cold” systems of emotion regulation and aims to integrate social, cognitive and neurobiological findings. Specifically, human and primate studies point to the relevance of maltreatment and social isolation or exclusion stress in the development of aggressive behaviour, and highlight findings that suggest gene-environment interactions may be involved in this[110,117,138,140]. Although to date animal experiments provide a rather coherent picture of the neurobiological correlates of alcohol-related aggression, more research in humans is warranted, especially considering the societal impact of alcohol-induced aggression. Such studies in humans need to take into account that beyond the effects of acute and chronic alcohol intake suggested by animal experiments, cognitive variables such as implicit and explicit expectations regarding the effects of alcohol and previous experiences of violent encounters can modify alcohol-associated aggression.

Box 1. Individual differences in human cognition and their relation to alcohol-associated aggression

Executive function

It has been suggested that acute alcohol intake increases aggressive behaviour because it impairs executive behavioural control and disinhibits impulsive responding, including violent behaviour.

Executive functioning comprises several cognitive abilities that contribute to the planning, initiation and regulation of goal-directed behaviour[185]. Burgeoning evidence from clinical populations suggests that individual differences in executive functioning may have a distal and indirect influence on alcohol use and drinking outcomes more generally (see[186] and [27]). According to an integrative executive functioning framework of alcohol-related aggression[27], alcohol promotes impulsive aggression indirectly by disrupting executive functioning, and this relationship is strongest in individuals with lower sober-state executive functioning (**Table 3**). Empirical studies have primarily examined the effect of alcohol on isolated executive functions, and compelling evidence suggests that individuals with low executive functioning are more prone to aggressive behaviour (e.g., [187]) and one study demonstrated that males with low executive functioning (compared to high executive functioning) reacted more aggressively under alcohol[71]. Future research should include neuropsychological testing batteries to better account for the contribution of executive functioning to individual differences in proclivity towards intoxicated aggression and impulsive behaviour.

Alcohol Outcome Expectancies (AOEs)

It has also been suggested that some individuals react aggressively under the influence of alcohol because of their expectation that alcohol makes them act more aggressively. Traditional accounts of expectancy theory[188] (**Table 2**) propose that this purely psychological effect is the driving force behind intoxicated behaviour. Within this framework it is thought that the act of drinking activates AOEs stored within an individual's schematic representation of alcohol in memory[189], that in turn influence behaviour (for review see[189]) (**Table 2**). Importantly, AOEs have powerful predictive validity concerning a wide range of drinking outcomes, including alcohol effects on aggressive behaviour[190,191]. AOEs have been documented in young children who have never consumed alcohol[192], and the development of AOEs is therefore perhaps best explained under Bandura's Social Learning Theory[193].

Although AOEs are initially shaped by social learning, their potency is thought to increase with increasing experience with alcohol such that the outcomes of using alcohol reinforce expectations and in turn, expectancies influence outcomes[194,195]. Hence, connections between expectancies and outcomes in memory become solidified and can be accessed with greater efficiency[195]. Consequently, explicit awareness of AOEs declines and upon activation, they may influence behaviour in a seemingly automatic fashion (see[196]). Indeed, AOEs are theorized to function as a memory "template" and activation of alcohol concepts in memory can bias the generation and selection of behavioural options as well as how events are interpreted[189,195]. For instance, one study found that even in the absence of drink consumption, exposure to alcohol-related primes elicited faster response-times to aggressive words, and perceptions of ambiguous behaviour were judged as more hostile by participants exposed to alcohol-related advertisements, especially in participants with stronger AOEs for aggression[197]. Thus, ambiguously

hostile encounters in the presence of alcohol cues (e.g., a bar) or under the influence of alcohol would be more likely to provoke aggressive responses in individuals with stronger memory associations between alcohol and aggression.

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Figure 1: A neurobiological model for alcohol-associated aggression.

Above: Brain areas strongly implicated in alcohol-associated aggression. Acute alcohol impairs executive functions associated with the prefrontal cortex (PFC) and stimulates dopamine release in the ventral striatum (which can facilitate initiation of aggressive attacks[40]). Chronic alcohol intake may facilitate alcohol-associated aggression by impairing serotonergic neurotransmission in the amygdala and PFC, which can disinhibit limbic processing of threatening stimuli and impair flexible control of behaviour[94,143,144]. Furthermore, dopamine D2 receptor down-regulation in the ventral striatum following chronic alcohol intake can increase impulsive and risk-taking behaviour[156,158].
Below: Neurotransmitter system alterations implicated in alcohol-associated aggression are shown in blue. Systems influenced by genetic variation and environmental events are indicated in purple. Genetic variation in serotonin reuptake (serotonin transporter genotype, 5-HTTLPR) and monoamine metabolism (MAO*A*) modulates amygdala functioning and connectivity. In individuals exposed to averse life events this predisposes to increased aggression[137-144]. Animal studies further suggest that alcohol intake plus experimental $GABA_A$-mediated inhibition of raphe serotonin neurons[17] as well as a blunted serotonin release in the prefrontal cortex following local $5HT_{1B}$ stimulation[101] is associated with alcohol-heightened aggression in rodents with a history of alcohol-related aggressive behaviour. Reduced dopamine D2 receptors as a heritable trait and/or following chronic alcohol intake contribute to increased impulsivity[97,155-158]. Dotted arrows indicate inhibitory (mainly GABAergic) neurotransmission; black arrow indicate excitatory (mainly glutamatergic) neurotransmission.

Figure 2. Functional and structural neural correlates of aggressive behaviour and genetic risk towards violence.

(A) Functional magnetic resonance imaging (fMRI) reveals reduced activation of dorsal anterior cingulate cortex during the viewing of negative compared to neutral affective pictures in adolescents with heightened levels of aggression (drawn from data from Sterzer et al. 2005[64]). Anterior cingulate cortex plays a key role in the inhibitory regulation of activity in limbic brain areas. Reduced activation of this brain region in aggressive individuals is consistent with the notion of impaired cognitive control of negative affects as a basis of aggressive behaviour.

(B) Structural (left) and functional (right) MRI summary statistics data comparing healthy individuals carrying or not carrying the MAOA-L aggression risk variant (based on data from Buckholtz and Meyer-Lindenberg, 2008[198]), which is associated with an increased likelihood of engaging in stress-related aggression and violence. Left: reduced volume in amygdala and cingulate cortex (blue) for both sexes in MAOA-L carriers, and a sex by genotype interaction with increased volume in orbitofrontal cortex (red) in male MAOA-L carriers only. Right: reduced activation of anterior cingulate (top and middle areas) and increased activation of amygdala (bottom area) in carriers of the risk allele in both sexes.

Table 1
Theories inciting cognitive disruption in intoxicated aggression

Theory/Terms	**Basic Tenets**	**Citation**
Indirect cause model	* Alcohol does not directly cause aggression rather it compromises important processes in multiple domains and thereby increases the probability of aggressive behaviour	Graham (1980)[24]
Disinhibition Hypothesis	* Pharmacological properties of alcohol disrupt brain centres implicated in maintaining inhibitory control over behaviour	Best articulated by Graham (1980)[24]
Alcohol Myopia	* General term employed by several theories which describes an alcohol-induced narrowing of attentional resources that limits the perceptual field *Analogy: disinhibition is looking at a scene through a distorted or blurry camera lens; myopia is using the zoom function so that only a small part of the scene can be viewed with clarity.	Steele & Josephs (1990)[199]
Attention-Allocation Hypothesis	* Alcohol limits amount of attention available to process information; as such proximal, instigatory cues in the immediate context (e.g., being bumped into in a bar) are awarded far more salience and attention than external, inhibitory cues (e.g., considering that it was accidental). * Inhibition conflict (competition for attention between inhibitory and instigatory cues) must be present for alcohol to elicit aggressive behaviour. * Under the influence of alcohol and in the presence of cognitively-taxing inhibition conflict, decisions are more influenced by instigatory cues and less so by conflict-mitigating information.	Steele & Josephs (1990)[199]; Steele & Southwick (1985)[200]; Giancola & Corman (2007)[201]
Hostile Attribution Bias	* Alcohol disrupts processing of threat-related information – so that under the influence of alcohol, ambiguous interpersonal cues may be misinterpreted as hostile intentions. *Alcohol is more likely to impact aggression under conditions of low provocation because the effect of high provocation on aggression is already so robust that alcohol has little additional impact.	Nasby et al., (1980)[202]; Giancola et al., (2002)[82]
Self-Awareness Hypothesis; Social-Cognitive Information Processing	* Alcohol engenders aggressive behaviour to the extent that it disrupts higher order encoding of self-relevant information necessary to sustain self-awareness. Increasing self-focused attention (looking into a mirror) can bridge the alcohol-induced gap between internal states and external standards of comportment[28] * Intoxicated individuals are more likely to respond aggressively to interpersonal provocation because alcohol disrupts critical aspects of social information processing	Hull (1981)[203]; Sayette (1993)[204]
Impaired Fear Response	Alcohol elicits aggression because it disrupts	Ito, Miller & Pollack

	ability to accurately detect and evaluate cues that signal danger and threat (detect less threat; failure to consider physical size of opponent).	(1996)[28]; Pihl, Peterson & Lau (1993)[205].
Increased Arousal	Alcohol increases general arousal but dampens the physiological stress-response (e.g., response to threat or provocation) which in turn promotes increased aggression.	Hoaken, Campbell, Stewart, & Phil, (2003)[206]

Table 2:
Theories inciting social learning, memory structures and functional relationships with alcohol expectancies.

Theory/Terms	**Basic Tenets**	**Citation**
Expectancy Theory	Conservative accounts posit that expectations for alcohol engender aggressive behaviour – not the pharmacological properties of alcohol	MacAndrew & Edgerton (1969)[188]
Alcohol Outcome Expectancies/Schematic Memory Structures	Under the influence of alcohol, individuals with strong associations in memory between alcohol and aggression and those who expect alcohol to make them more aggressive are more likely to demonstrate aggressive behaviour upon encountering stimuli perceived as threatening.	e.g, Goldman et al., (1999)[190]

Table 3: Multidimensional social-cognitive conceptualizations of intoxicated aggression

Theory/Terms	**Basic Tenets**	**Citation**
Two Channel Theory	Links alcohol expectancy and cognitive disruption theories and is based on the supposition that alcohol interferes with individuals' ability to accurately evaluate the ambiguous behaviours of others. Once memory structures representing alcohol expectancies are activated (primed), it becomes difficult for individuals to objectively evaluate the behaviour of others – especially when intoxicated – because increased cognitive effort is required to think outside of the primed schema. In these circumstances we tend to rely on our expectancies and use only the most salient information to reach a conclusion (e.g., he bumped into me, he did it on purpose).	Lange (2002)[207]
Impairment of Executive Functioning	4 key abilities associated with executive function are used to inhibit impulsive acts of aggression are impaired by alcohol (i.e., attending to and appraising situational information, taking the perspective of others, considering consequences of one's actions, defusing a hostile situation). Impulsive aggression, in response to provocation, is only engendered by alcohol to the extent that it disrupts EF. Alcohol is more likely to promote aggressive behaviour among individuals with lower executive functioning.	Giancola (2000)[27]
Dual-Process Model	2 types of processes dictate addictive behaviours. 1) Impulsive process: fast, associative, automatic appraisal of stimuli based on affective and motivational significance 2) Reflective process: slow, rule based, deliberate, goal-regulated, heavily dependent on executive control (EC) functions. As alcohol begins to cause EC to wane, reflective processes diminish and impulsive processes dominate. Individuals who hold aggressive associations with alcohol will be more prone towards aggression under alcohol.	Wiers et al., 2009[208] Deutsch & Strack, 2006[209]

Glossary Terms:

Alcohol Outcome Expectancy: predictions or beliefs about the social, cognitive, and affective consequences of alcohol consumption that are shaped by social learning and personal experience with alcohol.

Alcohol Schema: the theoretical structure in which information (e.g., experience, beliefs) about alcohol is organized and stored in memory.

Bandura's Social Learning Theory: posits that learning takes place in a social context whereby we can learn from observing others and this learning can occur without a change in behaviour.

Delay Discounting: Delay Discounting is the reduced ability to choose larger but delayed rewards compared to smaller but earlier rewards (seen as an index of impulsive tendencies).

Fenfluramine: a pharmacological drug that releases serotonin; it reverses reuptake by serotonin transporters and disrupts vesicular storage of serotonin

Go/No-Go task: Task that requires participants to press a key in response to one type of stimulus and to not press a key when another stimulus type occurs. Go/No-Go tasks are typically used to assess cognitive inhibitory control of behaviour.

Hot and Cold System of Emotional Processing: neural systems implicated in emotion regulation; the cold system refers to the rational and logical reasoning usually conducted under low emotion and arousal whereas the hot system in indicated in decision making under high levels of emotion and arousal that occurs in the immediate situation.

Reward Expectation: Reward expectation describes an anticipatory processing in the face of upcoming positive reinforcement (reward)