Human Sign-Tracking: an Investigation into its Mechanisms, Measurements and Neuropsychological Correlates

Thesis submitted in accordance with the requirements of the University of Liverpool for the degree of Doctor in Philosophy by Jay Joseph Duckworth.

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Jay Joseph Duckworth

Thesis Abstract

Sign-tracking describes the behaviour of individuals who attribute incentive salience to irrelevant, reward-associated cues, whereas goal-tracking pertains to individuals who use such cues only as predictive tools for upcoming rewards. The importance of the sign-tracker/goal-tracker phenotypes has been noted in the preclinical literature, with researchers suggesting that they are useful for the study of addiction. This thesis provides translational data, examining sign-tracking and goal-tracking in human social drinkers across six separate experiments.

Chapter One reviews the relevant literature on sign-tracking, covering the history of its discovery, its mechanisms, correlates, effects and aetiologies. *Chapter Two* details the general methods used across experiments (computer tasks and questionnaires). *Chapter Three* is the first experimental chapter; it presents the largest study of human sign-tracking to date, assessed via the additional singleton tracking task (ASTT). Results revealed a sign-tracking effect in a sample of social drinkers; however, no association to individual differences (e.g., weekly alcohol consumption, impulsivity etc.) was found. This study suggests that human sign-tracking is real, automatic, and driven by pavlovian conditioning.

Chapter Four contains two alcohol priming experiments, the first testing a 0.3 g/kg dose, the second a 0.6 g/kg dose. The lower dose, but not higher, magnified sign-tracking compared to a control drink. *Chapter Five* used a novel variant of the ASTT which contained three

(rather than the usual two) reward-associated distractor cues. Results revealed that sign-tracking pertained only to the high-value and medium-value cues, with the low-value cue seemingly being ignored. This study provides unique insight into how sign-tracking changes in more complex reward displays. *Chapter Six* attempted to compare three sign-tracking tasks: two variants of the ASTT and a Pavlovian-to-Instrumental Transfer (PIT) task. However, all tasks failed to observe sign-tracking, perhaps due to boredom and/or fatigue effects. *Chapter Seven* recruited participants from previous studies to complete the ASTT while undergoing functional magnetic resonance imaging (fMRI). Results revealed subcortical activations (namely in the striatum and other 'reward-motivation' structures) and correlations with sign-tracking, though sign-tracking was found to be unstable over time.

Chapter Eight assessed the potential influence of covariates and confounds on sign-tracking; participants' gender, whether they believed they would obtain extra rewards for good task performance and cues' physical salience (regardless of value) were all shown to have no significant effect on sign-tracking as measured by the ASTT. *Chapter Nine* showed that sign-tracking is automatic/reflexive (as shown by quicker responses towards distractor cues compared to target cues), that distractor cues of different value attract attention with the same 'force' (as shown by identical reaction times [RTs] to the differently valued cues), and that the two measures of sign-tracking in the ASTT – RTs and omissions – do not consistently correlate. *Chapter Ten* reviews the methods, results, limitations and potential applications of this research. This thesis suggests that humans attribute incentive value to irrelevant, reward-associated cues, that this attribution can be exacerbated by low levels of alcohol consumption, is unstable over time, and is associated with activity in the subcortical 'value-driven attention networks'.

Declaration

No part of this work had previously been submitted in support of another application for a degree or qualification at this or any other university or institution of learning.

Acknowledgments

Chapter One

General Introduction

1.1 Drug and Alcohol Use: Estimates, Problems and Treatments

An estimated 4.9% of the world's adult population (~240 million people) experience an alcohol use disorder, which causes an estimated 257 disability-adjusted life years lost per 100,000. Alcohol, and tobacco, use are the most prevalent addictive behaviours and cause the majority of the harm (Gowing et al., 2015). In England, approximately 9 million adults drink at unsafe levels (defined as the consumption of >14 alcohol units per week on a regular basis, with consumption of >8 units per drinking episode considered a drinking binge) (Department of Health, 2016; National Health Service, 2016). An estimated 1.6 million suffer with an alcohol use disorder, 70% of Accident & Emergency admissions at the weekend (between midnight and 5 a.m.) are thought to be alcohol related, and around 21,000 deaths per annum are directly attributable to alcohol. In England and Wales, approximately 49% of violent crimes involve alcohol. The NHS incurs £3.5 billion annually in alcohol-related costs, with the total annual cost to society estimated at £21 billion (Public Health England, 2014). It is clear that alcohol misuse, abuse and dependence cause considerable individual and societal harm.

Attempts at treating alcohol use disorders (AUDs) range from established practices such as 12-step programmes (Donovan & Wells, 2007), talking therapies (Lancaster, Stead, Silagy, & Sowden, 2000), pharmacotherapy (Elkashef & Montoya, in Verster, Brady, Galanter & Conrod, 2012) and, typically, some combination of these (Stead & Lancaster, 2012). More

controversial and/or relatively modern efforts include deep brain stimulation (Yadid, Gispan, & Lax, 2013), cognitive bias modification and cognitive control training (Wiers, Gladwin, Hofmann, Salemink, & Ridderinkhof, 2013). The latter two approaches attempt to treat dependence by focussing on sufferers' automatic and executive cognitive processes (for a review, see Field & Wiers, 2012). In the past few decades research into such cognitive approaches has become ubiquitous, with many sub-components garnering particular consideration (e.g., attentional bias) (Field et al., 2016; Field & Cox, 2008). One of the core mechanisms by which such cognitive changes occur during drug use is conditioning; a fundamental learning process key to the present thesis.

1.2 Conditioning

Alcohol is thought to constrain behaviour by influencing numerous facets of cognition, potentially driving future cravings and alcohol-seeking behaviours (Gould, 2010). One aspect of cognitive function affected by alcohol and which seems central in the development of harmful and dependent drinking is learning; with some referring to addiction as a disease of learning and memory (Hyman, 2005). Broadly, learning allows organisms to draw connections between events (or objects, or agents, or knowledge) and select an appropriate response to a situation, with repeated learning opportunities allowing for faster detection of relevant stimuli and, therefore, faster action. Two distinct – but interrelated – types of fundamental learning are pavlovian (classical) and instrumental (operant) conditioning.

The environment consists of I) stimuli which are inherently rewarding (unconditioned stimuli [US] e.g., food, sex, warmth) and which elicit unconditioned responses (URs) in the organism (e.g., salivation in response to food), and II) stimuli that have no salience to the

individual (neutral stimuli) (discussion of negative stimuli are omitted here). Pavlovian conditioning is the process whereby previously neutral stimuli are repeatedly paired with a US – thus becoming predictive of US availability – and develop salience. Such stimuli are termed conditioned stimuli (CSs) and they can elicit a range of physiological, psychological and behavioural responses (conditioned responses [CRs]) which may be similar or different (e.g., opponent processes; T. E. Robinson & Berridge, 2003) to the UR. In the original demonstration, after repeated pairings of a bell (the CS) and food (the US), dogs produced the same physiological (e.g., saliva production) and behavioural (e.g., excitatory behaviours) responses to the sound of the bell as they did to the sight of the food (Pavlov, 1927).

Instrumental conditioning describes a learning process which operates on a response-outcome basis, whereby positive outcomes reinforce behaviour and negative outcomes (typically) diminish it (Skinner, 1938; Thorndike, 1898). For example, rats will repeatedly press a lever when they have been trained that this response increases the likelihood of rewards (or prevents punishment); conversely, subsequent aversive stimulation (e.g., electric shocks) will typically diminish lever pressing. Although both classical and instrumental learning processes can be studied separately, they can also be observed interacting together in what is called Pavlovian-to-Instrumental Transfer (PIT) (Hogarth, Balleine, Corbit, & Killcross, 2013).

PIT paradigms typically induce a CS-US pairing via pavlovian conditioning, before then presenting an individual with the opportunity to produce a behaviour (e.g., lever pressing) in order to obtain a reward in the absence of the CS. Crucially, the pavlovian and instrumental learning procedures occur separately, before a transfer test is conducted. During this transfer phase, presentation of the CS typically increases the rate of reward-related instrumental responding, indicating increased motivation to obtain the reward (known as conditioned

motivation, see section 1.3.2.2). Such results show the CS exerting influence over behavioural responses, and this occurs despite no direct association between the pavlovian and instrumental contingencies. Such results have also been found in humans, with studies showing that CSs can increase behavioural and neural responding towards drugs of abuse (including alcohol) (Cartoni, Balleine, & Baldassarre, 2016; Corbit & Janak, 2016; Garbusow et al., 2014; Hogarth, Balleine, et al., 2013; Hogarth, Field, & Rose, 2013; Martinovic et al., 2014; Talmi, Seymour, Dayan, & Dolan, 2008).

Conditioning is typically monitored in two ways: attention and behavioural response. Essentially, over time organisms learn to attend to salient stimuli (e.g., CSs) so that they may act accordingly to gain reward or avoid punishment (USs). Therefore attention and behaviour are seen as dual processes in some models of learning, whereby attention becomes 'biased' towards relevant stimuli before an appropriate behavioural response is coordinated (Mackintosh, 1975). However, for several decades researchers have noted unexpected behaviours in animals whereby attention becomes so focused on the CS that some animals will actually forego real rewards (USs, such as food and drugs) in favour of approaching and obtaining CSs (lights and levers). These behaviours were first observed under naturalistic settings, before autoshaping paradigms (section 1.3.2) were employed to experimentally examine such behaviours.

1.3 Sign-Tracking versus Goal-Tracking: Nonhuman Animals

1.3.1 Background

The first descriptions of sign-tracking behaviour were reported as early as 1937 (Zener, 1937) before a later paper recounted how such CS-focussed behaviour was preventing the authors'

training of performance animals (Breland & Breland, 1961). In one example, pigs successfully conditioned to deposit wooden coins in a 'piggy bank' would instead play with and root the coins, very rarely depositing them as taught. Breland and Breland (1961) thought this might just be the "dilly-dallying of an animal on a low drive" (p. 683); however, when the animal's drive was increased – its daily caloric intake was severely reduced – the behaviour not only persisted, it intensified. Additionally, approach behaviours towards the CSs mimicked species-specific consummatory behaviours, suggesting that the CS had itself become rewarding. The researchers reported such observations in numerous species including racoons, chickens, cockatoos, reindeer, porpoises and whales.

Such behaviours were initially referred to as *instinctive drift* (Breland & Breland, 1961) and *autoshaping* (Brown & Jenkins, 1968), before the term *sign-tracking* was finally settled upon (Hearst & Jenkins, 1974). Sign-tracking seems to develop over time in humans and animals (Le Pelley, Pearson, Griffiths, & Beesley, 2015; Morrow, Saunders, Maren, & Robinson, 2014) although not all individuals develop tendencies to sign-track. Individuals who consistently attribute incentive salience to irrelevant, discrete, reward-associated cues are referred to as sign-trackers (STs), while individuals who use such CSs merely to predict the availability of reward are referred to as goal-trackers (GTs). GTs have, however, been shown to imbue incentive value to contextual, rather than discrete, CSs (e.g., to entire environments such as cages) (T. E. Robinson, Yager, Cogan, & Saunders, 2014). Individuals who do not display a particular preference for either type of tracking are typically referred to as member of an intermediate group (IGs) (Lomanowska et al., 2011).

There is a growing literature surrounding tracking behaviours, which became interesting to addiction researchers in the 1990's when similarities between sign-tracking and drug use disorders emerged. One researcher documents seven such similarities (Tomie, 1995, 1996):

- *Excessive responding*: Spatial and/or temporal contiguity of the reward (US) and signal (CS, or response manipulandum e.g., a lever) induces excessive instrumental responding towards the signal/manipulandum.

- *Responses resemble appetitive-consummatory behaviours*: Signal-directed behaviours typically resemble species-specific appetitive-consummatory behaviours, as described by Breland and Breland's (1961) 'instinctive drift'.

- *Responding is refractory to instrumental contingency*: Excessive responding towards reward-independent stimuli persists even though unnecessary to obtaining reward.

- *Maladaptive*: Excessive responding can actually impair ability to obtain reward. Additionally, such behaviour is known to intensify when the incentives to obtain reward (e.g., to eat for survival) are higher. This and the previous point show that sign-tracking is, to some extent at least, resistant to negative consequences.

- *Uncontrollable*: Given the previous two points, sign-tracking would appear to not be consciously controlled.

- *Compulsive*: Given the above, such behaviour seems necessarily compulsive.

- *Stimulus-bound*: Compulsive, uncontrollable responding occurs only in the presence of the reward-associated signal, never in its absence[1].

[1] Note that more recent work has shown that STs' behaviour can differ from GTs' even in the absence of the CS (Saunders & Robinson, 2011) (see section 1.3.3.2).

These initial observations were made in semi-naturalistic settings (predominantly in zoo and circus animals etc.), but laboratory-based investigations also upheld the Brelands' original interpretation, that these behaviours could not be explained by simple instrumental conditioning procedures. (However, it should be noted that definitive conclusions as to the driving force of sign-tracking are still yet to be drawn, which will be discussed further, below.) Several of these characteristics have clear similarities to diagnostic criteria for AUD, such as "drinking more or for longer than intended… tried to cut down, but couldn't" (*compulsive*), "continued even though it was causing trouble" (*maladaptive*, *uncontrollable*) etc. (DSM-V, 2013). Initially, the evidence linking tracking behaviours with substance misuse came from the preclinical literature. The next section outlines the preclinical work which initially associated tracking behaviour with substance misuse.

1.3.2 Autoshaping procedures

1.3.2.1 Background

One of the first experimental investigations into tracking behaviours, using an autoshaping paradigm, found that Breland and Breland's (1961) original naturalistic observations were generally supported (Boakes, Poli, Lockwood, & Goodall, 1978). For example, they found that in an autoshaping procedure in which rats had to deposit ball-bearings into a hole, some of the rats became slow to relinquish the balls and would chew on them before they were released, despite extensive training (instrumental conditioning) to the contrary. Other observations were only partially supported; for example, the Brelands' claim that food deprivation caused their trained pigs to sign-track more intensely was not supported, but their

experiments did show that deprivation did not diminish sign-tracking behaviours[2] (this was also found in perhaps the first study to investigate the effect of omission contingencies on sign-tracking, Williams & Williams, 1969). However, more recent evidence suggests that both sign-tracking and goal-tracking can be increased by restricting food access, but that the effect is moderated by other factors including age (adolescent versus adult) and social environment (isolation versus no isolation). For example, paired adults sign-tracked more than paired adolescents (no difference between isolated age groups), adolescents who were food deprived and isolated increased sign-tracking, whereas adolescents who were food deprived and paired increased goal-tracking (Anderson, Bush & Spear, 2013). It seems that tracking behaviours may have more complex underpinnings than was initially thought.

1.3.2.2 Differential responding between tracker types

It is important to provide an overview of autoshaping procedures in nonhuman animals as it will allow for a detailed comparison between the animal and human measures presented both in this, and future, chapters. Traditional pavlovian autoshaping paradigms employed for laboratory animals (typically rats, mice and pigeons) briefly run as follows: a US (food or drug reward) is repeatedly paired with a noncontingent[3] discrete CS (light, lever etc.). Via contiguous presentation, and though the administration of the US is independent of any CS response, some animals, some of the time display autoshaping – or sign-tracking – behaviours

[2] Note that some of the outcome measures in Boakes et al's (1978, p. 119) work were influenced by deprivation, such as "'lost ball' times"; however such outcomes do not seem particularly robust measures of sign-tracking and have not stood the test of time in most of the recent literature. Crucially, the outcome measure of how long it took rats to deposit the ball (CS) was not affected by deprivation, and similar measures are still used in virtually every autoshaping procedure today.

[3] 'Reward-noncontingent' or simply 'noncontingent' refers to a cue that does not require any action or attention for the US to be delivered. Conversely, 'contingent' cues require actions for the US to be delivered. CSs in autoshaping procedures are noncontingent and so 'noncontingent' shall be omitted for brevity; however, any situations in which they are contingent shall be stated explicitly.

(Meneses, 2003)[4]. However, there are variations in setup between studies which have been found to alter the likelihood and/or strength of sign-tracking (as well as general perception, attention and behaviour) (Pessoa, 2014a), some of which are reviewed below.

In terms of typical responding during autoshaping procedures, STs and GTs differ in a number of ways. When exposed to the CS, STs show greater approach frequency towards the CS (or US response manipulandum), with shorter latencies in their approach, while GTs show the same pattern in frequency and latency, but towards the US (Flagel, Akil, & Robinson, 2009; Flagel, Watson, Robinson, & Akil, 2007). Additionally, STs are willing to work – via consistent instrumental responding on a response manipulandum – to obtain exposure to a reward-paired CS, while GTs are not (Lomanowska et al., 2011; Saunders & Robinson, 2010). Crucially, all of these differences in responding have been shown in autoshaping procedures employing both food and various substances such as cocaine, amphetamines, opioids and ethanol (Robinson et al., 2014; Tomie, Grimes, & Pohorecky, 2008).

1.3.2.3 Influence of experimental setup on outcome

The above overview of the differences in the sign-tracking and goal-tracking conditioned responses (CRs) refer to responding under typical autoshaping procedures; however, there are a wide range of experimental manipulations which can alter CRs. Some of these are detailed below.

[4] It should be noted that 'autoshaping' is actually a misnomer as sign-tracking responses are not 'shaped', they often arise *in spite* of training to the contrary, termed 'negative automaintenance' (Hearst & Jenkins, 1974). However, given the popularity of the term, autoshaping will be used synonymously when referring to the paradigmatic setup.

Stimulus presentation order: Brown and Jenkins (1968) showed that when presented in a 'forward-pairing' – CS before US – fashion, all pigeons sign-tracked toward the CS (a key-light) to some extent. However, of 12 pigeons exposed to 'reverse-paired' stimuli – US before CS – only 2 sign-tracked, and to a much lesser degree than those in the forward-pairing group. Additionally, if the key-light was constantly on (CS always present) and food (the US) was administered intermittently, sign-tracking took longer to emerge, developed to a lesser extent, and in only a minority of animals. This highlights the importance of the CS's predictive utility (see below).

CS-US spatial proximity: When three pigeons were exposed to an autoshaping procedure using a short (22 cm) CS-US distance, all showed consistent sign-tracking behaviours (e.g., close proximity to and behavioural action towards the CS), but when exposed to a longer CS-US distance (60 cm), only goal-tracking was observed (e.g., close proximity to and behavioural action towards the area of US administration) (Silva, Silva, & Pear, 1992). Distances in between (e.g., 42 cm) produced intermediate responses. However, it has been shown that sign-tracking behaviours are still observed even when the CS is located in the opposite direction to the US (Brown & Jenkins, 1968), indicating that sign-tracking can still emerge when the CS and US are in relatively distinct locations. It has also been shown that vertical location is important – CSs located atop a cage are more likely to be sign-tracked than CSs below it (Holland, 1977).

CS-US temporal proximity: Temporally distal serial CS elements – in this case, the first of many levers successively inserted into a cage to predict the onset of a food US (in a countdown-like fashion) – were more likely to be sign-tracked than temporally proximate CS elements (Silva, Timberlake, & Gont, 1998). Conversely, temporally proximate CS elements – the last lever inserted into the cage immediately before US administration – were more

likely to induce goal-tracking responses towards the food tray. These results show how important stimulus timings can be when conditioning a CS-US contingency. Crucially, Silva et al. (1998) show that both spatial and temporal features are important and can interact, meaning that *spatiotemporal* characteristics of CS-US parings must be considered in autoshaping paradigms.

CS-US predictive strength: CSs are not always reliably predictive of USs, a fact used to investigate how reward uncertainty relates to sign-tracking. When CSs predict US onset only 50% of the time, sign-tracking increases (and at the expense of goal-tracking) relative to CSs that are 100% predictive (Robinson, Anselme, Fischer, & Berridge, 2014; Robinson, Anselme, Suchomel, & Berridge, 2015). This suggests that the incentive value of a CS during autoshaping procedures may become dissociated from its predictive value (as the CS is still incentivised even when lacking predictive validity), which is supported by neurological evidence revealing that prediction and incentive salience are controlled by separate neural circuits (Smith, Berridge, & Aldridge, 2011).

US/CS modality: Stimulus type is broader than the previous paradigm features; covering whether the US is food or drugs, whether the CS can be classified as discrete, contextual or interoceptive, and whether the CS is a visual or auditory cue. The influence of US specificity will be discussed in sections 1.3.3.3 and 1.3.3.4, here I shall focus on general and specific cue types.

The sensory features (i.e., physical or perceptual properties) of a cue have been found to affect responses in autoshaping procedures (Singer, Bryan, et al., 2016). For example, Cleland and Davey (1983) found that rats exposed to a visual CS (a white light) would, after repeated CS-US pairings, consistently sign-track towards the CS. Conversely, when the CS was a localizable auditory tone, virtually all sign-tracking disappeared. Crucially, rats *did* approach

the area of the auditory CS when this resulted in instrumental reinforcement (i.e., when they were directly rewarded for doing so), indicating that they could locate and approach the cue. More recent work shows that localizable auditory cues reinstate cocaine-seeking equally well in STs and GTs, indicating that cue modality can determine whether and which individuals may be influenced by that cue (Pitchers, Wood, Skrzynski, Robinson, & Sarter, 2017). Finally, general cue modality has been recognised as one of the most important and influential aspects of autoshaping procedures there is – the three types examined here are *discrete*, *contextual* and *interoceptive*.

Discrete: As mentioned, discrete, localizable cues reliably induce incentivised approach behaviour to CSs in some subset of animals. Recent research has shown that animals who sign-track towards discrete, food-paired CSs (STs) also sign-track towards discrete drug (cocaine and opioid) CSs, while GTs do not (Flagel, Akil, et al., 2009; Meyer, Ma, & Robinson, 2012; Saunders & Robinson, 2010; Saunders, Yager, & Robinson, 2013; Yager, Pitchers, Flagel, & Robinson, 2015; Yager & Robinson, 2013).

Contextual: In opposition to discrete cues, contextual cues (e.g., a particular cage) induce greater renewed extinguished cocaine seeking and psychomotor sensitisation (see section 1.3.2.2) in GTs compared to STs (Saunders, Aurbach, & Robinson, 2012; Saunders, O'Donnell, Aurbach, & Robinson, 2014), indicating that GTs *do* imbue cues with incentive salience, but only contextual ones.

Interoceptive: Research has shown that interoceptive cues – the pharmacological and/or psychological effects of substances – evoke greater instrumental responding in STs compared to GTs during US (drug) extinction. In these particular setups, instrumental responding is an indication of drug seeking. For example, a priming dose of cocaine induces increased cocaine

seeking, even when the cocaine is not available, in STs compared to GTs (Saunders & Robinson, 2011).

1.3.2.4 Autoshaping Outcome Measures

There are three key measures when assessing a CS's ability to elicit sign-tracking: *conditioned approach*, *conditioned reinforcement* and *conditioned motivation* (Robinson, Yager, Cogan, & Saunders, 2014):

- *Conditioned approach*: A noncontingent CS's ability to elicit approach behaviour towards it in much the same way as the US typically does.

- *Conditioned reinforcement*: A reward-paired CS's (e.g., light) ability to prompt instrumental responses (e.g., lever pressing) to obtain its presentation in the absence of the US, but after repeated pairings with the US. For example, Anderson and Spear (2011) showed that (some) rats will repeatedly nose poke in order to gain access to an illuminated lever (noncontingent CS).

- *Conditioned motivation*: Typically studied via PIT paradigms in which a US is contingent on an instrumental response (e.g., lever pressing) in one session, while in another session a noncontingent CS is paired with the US. Conditioned motivation is observed if the CS, presented alongside the lever for the first time, increases instrumental responding towards the lever (response manipulandum) in order to obtain the US, even though the two have never been directly paired.

These measures are dissociable, are facilitated by different neural circuitry (Cardinal, Parkinson, Hall, & Everitt, 2002; Saunders & Robinson, 2013) and can be measured in several specific ways in a typical autoshaping paradigm (Crombag, Badiani, Maren, & Robinson, 2000; Kawa, Bentzley, & Robinson, 2016; Uslaner, Acerbo, Jones, & Robinson, 2006; Yager & Robinson, 2015):

- *CS approach frequency*: Number of times the CS is approached (which includes moving to the general CS area or interaction with the CS)[5].

- *CS approach latency*: The time it takes to approach the CS from the moment of CS onset.

- *Instrumental responding*: How hard an animal will work (by interacting with the response manipulandum [Tomie, 1996] via nose pokes, lever presses etc.) to be presented with the CS (conditioned reinforcement) or US (conditioned motivation)[6].

- *US approach frequency*: Number of times the US (or US area) is approached or interacted with when the CS is presented.

- *US approach latency*: The time is takes to approach the US (or US area) from the moment of CS onset.

[5] '*Conditioned orientation'* (as opposed to explicit interaction) towards CSs has been shown not to be a reliable method of distinguishing sign-trackers from goal-trackers (Yager & Robinson, 2013). This again may be largely due to experimental setup (White & Naeem, 2017).

[6] Many studies use the terms conditioned reinforcement and conditioned motivation interchangeably. Here, I shall use 'conditioned reinforcer' to refer to cues which elicit approach both towards CSs and USs (or which promotes self-administration of the US). Whether a CS or US is sought will be specified.

- *Psychomotor activity/sensitisation*: The ability of a psychostimulant to produce locomotor activity or drug-paired CS to promote locomotor activity (termed 'cross-sensitisation'). This can be acute (*activity*) or prolonged and progressive after repeated administration (*sensitisation*), the latter being suggested as a form of neurobiological plasticity hypothesised to play a role in addiction.

- *Incentive-sensitisation:* The ability of a substance to elicit progressive demand from an individual, even in the face of increased effort for diminishing returns or even aversive consequences (e.g., an electrified floor must be crossed to obtain the drug or even the drug-related cue).

1.3.3 Correlates of Sign-Tracking and Goal-Tracking

Much of the research on tracking behaviour – and especially the individual differences related to tracking – has focussed on sign-tracking in a single sample, without any contrast with goal-tracking in a comparative group. Thus, section 1.3.3.1 will outline findings from preclinical studies which did *not* explicitly distinguish sign-trackers from goal-trackers before testing them under autoshaping procedures, but rather is an overview of research which simply correlated general sign-tracking with individual differences. Section 1.3.3.2 presents evidence of individual differences *between* tracking groups.

1.3.3.1 Correlates of Sign-Tracking

Drugs

This section will review the evidence for the association between sign-tracking in a general animal population and drug consumption, the propensity to drug seek and vulnerability for substance sensitisation.

In perhaps the earliest experimental investigation into whether sign-tracking CRs are related to drug consumption, researchers found that autoshaping procedures resulted in high rates of alcohol consumption when ethanol was paired with a saccharine solution, though was maintained when saccharine was faded out (Tomie, di Poce, Derenzo, & Pohorecky, 2002). In a similar setup, Tomie's group replicated these findings, with rats consuming both water and (sweetened and unsweetened) ethanol during CS presentation, though the ethanol group consumed significantly more overall (Tomie, Sparta, et al., 2002; Tomie, Wong, Apor, Patterson-Buckendahl, & Pohorecky, 2003). Other studies have shown CS-induced instrumental responding for sweetened and unsweetened ethanol when that CS was previously paired with ethanol (Krank, 2003; Krank, O'Neill, Squarey, & Jacob, 2008), and others have shown that the level of sweetened ethanol consumption is predictive of the extent of sign-tracking (Tomie, Festa, Sparta, & Pohorecky, 2003). Further work has shown that cues paired with unsweetened ethanol can rapidly become incentivised (Cunningham & Patel, 2007; Srey, Maddux, & Chaudhri, 2015). Recent research has solidified the positive correlation between sign-tracking and ethanol-seeking and/or intake (R. I. Anderson & Spear, 2011; Maddux & Chaudhri, 2017). In addition, discrete ethanol-paired cues can invoke greater ethanol-seeking in alcohol-paired contexts than in non-alcohol contexts (Sciascia, Reese, Janak, & Chaudhri, 2015).

An early study using cocaine as a reward in an autoshaping paradigm showed that, unlike other paired rewards, a cocaine CS failed to elicit a sign-tracking response (Kearns & Weiss, 2004). However, more recent work has shown that discrete cues paired with intravenous

cocaine administration do elicit sign-tracking approach behaviours towards them, and with increasing rapidity over time (Uslaner et al., 2006). Cocaine cues also act as effective conditioned reinforcers, prompting an increase in cocaine seeking (Yager & Robinson, 2013). Research has also shown a direct correlation between sign-tracking and cocaine self-administration (Beckmann, Marusich, Gipson, & Bardo, 2011), with a recent study showing that a cocaine-paired cue elicited sign-tracking and was able to promote cocaine-seeking in Rhesus monkeys (Reilly, Berndt, & Woods, 2016). Amphetamine studies employing similar procedures have shown that rats more vulnerable to amphetamine sensitisation are also more likely to sign-track (M. J. F. Robinson, Anselme, et al., 2015).

Finally, though not a drug, it is worth noting that evidence suggests that the tendency to sign-track is also correlated with increased effort to obtain food-paired cues (Tomie, Aguado, Pohorecky, & Benjamin, 2000). Recent work has shown that rats susceptible to developing a sign-tracking CR were also susceptible to developing obesity, and these same obese rats who sign-tracked showed an increased willingness to work for the presentation of a sucrose-paired cue (M. J. F. Robinson, Burghardt, et al., 2015). Overall, these studies suggest that sign-tracking propensity in a general animal population is associated with increased substance seeking, consumption and sensitisation (when exposed to a reward-associated cue).

Personality Characteristics

Several experiments have acquired data on how sign-tracking relates to non-drug-related individual differences in ‘personality’ or behavioural proclivities in animals. These associations cover traits and states such as impulsivity, inattention, and variability in stress response.

In an early investigation, rats from two populations were compared on their sign-tracking CRs. Rats from the 'sensitive group' were more impulsive and more flexible in their behavioural responses than were members of the 'insensitive group'. Results revealed that members of the sensitive group were more likely to perform sign-tracking CRs, with more impulsive individuals acquiring sign-tracking in fewer trials (Tomie, Aguado, Pohorecky, & Benjamin, 1998). In a more recent study, selectively bred high-responder rats (bHRs) and low-responder rats (bLRs) (rats which show either high locomotor activity or are inhibited in response to a novel environment, respectively) were exposed to a typical sign-tracking paradigm. The results revealed that bHRs, but not bLRs, attributed incentive value to a food- or cocaine-related cue, with bHRs also showing less impulsivity on a measure of 'impulsive choice', but were more impulsive on a measure of 'impulsive action' (i.e., they showed difficulty withholding a response to receive a reward, an animal equivalent of behavioural disinhibition) (Flagel, Robinson, et al., 2010). This result was replicated in animals strictly classified as STs and GTs (Lovic, Saunders, Yager, & Robinson, 2012). Perhaps related to such disinhibition, sign-tracking was found to be inversely correlated with attention as measured on a sustained attention task (SAT). That is, the greater the sign-tracking, the lower the attentional performance (Paolone, Angelakos, Meyer, Robinson, & Sarter, 2013).

In addition to sign-tracking studies on impulsivity, research has also measured sign-tracking's association to novelty preference. In one study researchers tested rats on novelty place preference and inescapable novelty tasks (measure of novelty-seeking) as well as a pavlovian approach task (autoshaping paradigm) for a food-paired cue. Results revealed that the extent to which rats attributed incentive salience to the food-paired cue (i.e., sign-tracked) was positively correlated with novelty-seeking (Beckmann et al., 2011). In a later study using larger, highly diverse mouse populations, sign-tracking and novelty reactivity were found to be genetically correlated (though only in males) (Dickson et al., 2015). Finally, in

autoshaping paradigms in which stress response was also measured, rats who more quickly developed a sign-tracking CR showed higher stress-induced corticosterone release (Tomie et al., 2000). A later study suggested that corticosterone release is a physiological endocrine pavlovian CR induced by autoshaping procedures and may be indicative of general arousal rather than fear or stress specifically. However, in this study corticosterone release was not correlated with the extent of sign-tracking behaviours (Tomie, Silberman, Williams, & Pohorecky, 2002). Similar results were also obtained by the same group a couple of years later, with the additional finding that epinephrine (adrenaline) is also induced by the autoshaping/sign-tracking paradigm (Tomie, Tirado, Yu, & Pohorecky, 2004); however, see the authors' discussion for issues with interpretation of these results. Overall, these results suggest that sign-tracking in general animal populations is associated with impulsive action, inattention, novelty-seeking and a heightened stress response; all of which have been implicated in addiction-related tendencies.

1.3.3.2 Individual differences between tracking groups: Sign-Trackers vs. Goal-Trackers

This section will outline individual differences between STs and GTs.

Drugs

Studies which attempt to investigate how drugs affect the different tracking phenotypes employ a range of procedures, though these can be briefly summarised. First, individuals are characterised into STs or GTs based on a typical pavlovian autoshaping paradigm employing food as a response-independent US and a typical discrete cue as the reward-paired CS (e.g.,

light). Second, an additional autoshaping procedure is completed, this time using a different CS (e.g., lever) and a drug as the US (response dependent or independent, depending on the particular procedure and measurements carried out). During this second round of pavlovian conditioning, researchers measure some or all of the following: I) the ability of the drug-paired CS to a) elicit approach, b) to maintain or promote drug seeking or self-administration (i.e., to act as a conditioned reinforcer), c) to promote reinstatement of drug use after extinction, or II) whether tracking phenotypes differ in their vulnerability to drug sensitisation. Experimental studies employing sign-tracking drug paradigms have been performed since at least 2009, mostly using cocaine as its relatively short half-life means that repeated CS-US pairings can be conducted more efficiently (Meyer, Cogan, & Robinson, 2014). However, studies have also administered ethanol, nicotine, and opioids.

In perhaps the first study to distinguish between tracking phenotypes before assessing drug responsivity, researchers found that GTs were more sensitive than STs to the acute locomotor activating effects of cocaine, while STs showed a higher tendency for psychomotor sensitisation upon repeated administration (Flagel, Watson, Akil, & Robinson, 2009). Another study showed that, even though groups did not differ in the acquisition of cocaine self-administration, removal of a cocaine-paired CS significantly reduced cocaine self-administration in STs – by up to 50% – but not GTs (Saunders & Robinson, 2010). Additionally, the extent of sign-tracking in STs was strongly positively correlated with the influence of the CS over their cocaine consumption. A subsequent study showed that rats classified as STs worked nearly twice as hard (via repeated nose pokes) as GTs to obtain a cocaine reward, even in the absence of a discrete CS (Saunders & Robinson, 2011). This indicates that STs may generally be more motivated to obtain rewards even in the absence of an incentivised cue. The authors also found that STs primed with an injection of cocaine showed more robust reinstatement of cocaine-seeking after extinction training than GTs, and

that this was strongly positively correlated with how hard STs worked to acquire cocaine in a previous portion of the study. These results suggest that STs are not only more likely to be motivated to obtain further cocaine rewards by discrete, exteroceptive cues, but also by unconditioned, interoceptive cues (i.e., cocaine effects).

Research has also shown that localised cocaine-paired CSs elicit greater CS approach and effectively act to reinstate drug-seeking during extinction procedures (i.e., act as conditioned reinforcers) in STs but not GTs (or at least in STs to a much greater degree) (Yager & Robinson, 2013). More recent data has shown that sign-tracking is the first known behavioural predictor of increased cocaine choice (over food) in rats (Tunstall & Kearns, 2015), and STs are more motivated than GTs to take cocaine after limited drug exposure, which may increase their vulnerability for incentive-sensitisation (Kawa et al., 2016).

In a slightly different experimental setup aiming to explain such findings, researchers found that STs, but not GTs, showed a conditioned place preference for a floor type (grid versus hole) previously paired with the administration of cocaine (Meyer, Ma, et al., 2012)[7]. Importantly, STs produced more frequency-modulated ultrasonic vocalisations (USVs) than GTs following a single injection of cocaine, as well as during the overall cocaine conditioning period. These vocalisations indicate heightened euphoria, which means that the preferences of STs for cocaine-paired CSs may be driven by greater levels of unconditioned reward (i.e., 'liking'), relative to GTs. More recent results have replicated this finding, with STs producing 5–24 times more cocaine-induced USVs than GTs, a response which became sensitised only in STs with repeated cocaine injections (Tripi, Dent, & Meyer, 2016).

[7] This may appear to be a contextual cue [*place* preference], but the salient feature of this CS was the tactile nature of the floor which is a specific feature of the environment, much like the colour or location of a light CS or the shape and size of a lever CS.

In support of the idea that sign-tracking persists despite negative consequences, researchers initially trained rats to self-administer cocaine, before curtailing self-administration by requiring the rats to cross an electrified floor to obtain the reward (although the reward was not given). They found that the presentation of a noncontingent, discrete, cocaine-paired CS motivated STs to cross the floor to acquire cocaine to a significantly greater extent than GTs (Saunders et al., 2013). Importantly, STs and GTs do not differ in their sensitivity to the pain of shocks. The authors concluded that drug-associated stimuli have the power to induce substantial "craving" in STs, enough to maintain drug-seeking despite aversive consequences. More recent data support the idea that the sign-tracking CR is almost never truly extinguished. Even when physical interaction with the reward-paired cue is reduced, more subtle approach behaviours take their place (e.g., attentional orienting), indicating that the incentive salience of the cue remains (Chang & Smith, 2016; White & Naeem, 2017).

The final cocaine-related studies covered here are ones that used contextual, non-localised cues rather than discrete cues. In the first study, GTs showed greater conditioned hyperactivity than STs, as well as a trend towards greater psychomotor sensitisation when placed in a cocaine context (Pitchers et al., 2017). More importantly, though both tracking groups showed context-induced renewal of cocaine seeking, GTs' renewal was more robust and the strength of the renewal behaviour among GTs was significantly correlated with their previous goal-tracking behaviour. In a second study, a non-localised auditory-CS was paired with cocaine. Presentation of this CS reinstated drug-seeking equally in STs and GTs after extinction (such results may vary given specific aspects of the auditory cue, such as localizability). These results suggest that GTs may be as motivated to obtain drugs by contextual cues as STs are by discrete cues. Indeed, evidence suggests that the power of discrete versus contextual cues to influence behaviour is largely determined by an animal's

specific neural circuitry (Khoo, Gibson, & Prasad, 2017; T. E. Robinson et al., 2014; Saunders et al., 2014).

Similar autoshaping paradigms using different drugs have found mixed results. For ethanol, the only study which seems to match the cocaine studies described above in procedure found no differences between STs and GTs in ethanol consumption across five experiments. However, they did find that ethanol-paired CSs elicited approach and acted as effective conditioned reinforcers in STs (in two out of four tests) but not GTs (Villaruel & Chaudhri, 2016). Another important finding of this study was the observation that many animals initially classified as GTs were reclassified as STs over time due to changes in their behaviour (i.e., changes in their attribution of incentive salience towards the alcohol cue). As the authors note, this is in accordance with the incentive-sensitisation framework which suggests that repeated exposure to addictive substances can lead to the maladaptive attribution of incentive salience (there were no cases in which STs became GTs) (T. E. Robinson & Berridge, 1993).

For nicotine, contrary to that found in cocaine and ethanol, discrete nicotine-paired cues were found to be equally attractive (i.e., were approached to the same extent) in STs and GTs. However, when the nicotine CS's ability to act as a conditioned reinforcer was tested, it was found that it was a more effective reinforcer in STs than GTs (though only when nicotine infusions were of a sufficiently high dose), consistent with studies using other drugs (Yager & Robinson, 2015). The authors attribute this difference to nicotine's ability to act as an *incentive amplifier* when consumed (i.e., it increases the incentive value of associated cues). More recent data have replicated this finding, with STs showing greater drug-seeking reinstatement in response to a nicotine-paired cue compared to GTs (Versaggi, King, & Meyer, 2016). This indicates that both tracking groups highly regarded the nicotine CS during

nicotine infusion (and thus approached it), but in nicotine's absence the associated CS was more likely to act as a reinforcer in STs than GTs as, at baseline, STs incentivise discrete cues more than GTs.

As for ethanol, only one study has investigated the effect of opioids in a sign-tracking paradigm[8]. The study found that STs approached an opioid-CS more readily than GTs, and in a test of conditioned reinforcement STs worked harder for access to the CS than GTs (Yager et al., 2015). Overall, findings have revealed that cocaine, ethanol, nicotine and opioids, as well as the discrete cues paired with such drugs, are more often approached, sought after and consumed (to varying extents across drug types) in STs compared to GTs.

Personality Characteristics

In addition to tracking groups differing across measures of drug craving, liking, sensitisation, seeking and consumption, and cue reactivity, the phenotypes also differ in 'personality' characteristics. As in earlier sections, 'personality' is used as a proxy term for trait and state measures which differ between animals that are not drug- and alcohol-related (e.g., impulsivity, stress response etc.). Here, differences in such characteristics between sign-trackers and goal-trackers are discussed.

Group differences in fear and stress responses have been examined in several studies. In one study, although tracking groups did not differ in their acquisition of a conditioned freezing (fear) response, fear incubation – that is, an increase in fear over time – was found in

[8] More studies exist which utilise ethanol, opioids and amphetamine in sign-tracking paradigms, but the procedures and outcome measures do not fit our discussion here. Instead, such studies are detailed in section 1.5.4.

STs but not GTs (Morrow et al., 2014). Interestingly, this seems to have had less to do with fear increasing over time than the inhibition (suppression) of fear behaviour dissipating gradually. Further, an earlier study showed that STs do in fact show greater acute fear conditioning than GTs (Morrow, Maren, & Robinson, 2011), though in the later Morrow et al. (2014) study the authors suggest that this discrepancy is most likely due to different experimental procedures, such as the intensity/duration of the fear conditioning period. Furthermore, contrary to previous findings (Tomie, Aguado, Pohorecky, & Benjamin, 2000), recent work found only a statistically non-significant trend of increased sensory stress response (loud music, physical restraint) in STs compared to GTs (M. J. F. Robinson, Anselme, et al., 2015). However, there are potential problems with both studies. Tomie et al. (2000) cut the tails off of the rats before final measures of the stress-induced hormone corticosterone were taken, which very likely contributed to heightened levels (for discussion see Tomie, Silberman, Williams, & Pohorecky, 2002). In the Robinson et al. (2015) study, the type of stress measured was *sensory* stress and thus the extent of stress inducement was relatively mild, as indicated by the mild degree of stress sensitisation. However, another explanation could be that developed sign-tracking (incentive sensitisation) may be controlled by a separate neural system than psychomotor sensitisation (physiological and/or behavioural responses to, in this case, stress) (Robinson & Berridge, 2008).

Attentional and impulsivity differences have also been found between tracking groups. Researchers have found that STs perform significantly worse than GTs on a sustained attention task (SAT), with STs' performance fluctuating between periods of good to near-chance success (Paolone et al., 2013). A more recent study from this group found the same pattern of results on the SAT, but only for STs with larger sign-tracking scores (Pitchers et al., 2017). In addition to attentional deficits, tracking group differences in impulsivity – and related concepts such as disinhibition – have also been found. Though there were no group

differences in reaction times, STs made more premature responses than GTs on a choice reaction time (CRT) task, an indicator of response disinhibition (King et al., 2016). Further, STs display smaller prepulse inhibition of an acoustic startle response than GTs, suggesting they possess reduced inhibitory control (Lopez, Karlsson, & O'Donnell, 2015). Important findings also suggest that STs suffer from behavioural inflexibility compared to GTs, which may have important implications for how the attribution of incentive value to reward-associated cues may underlie vulnerability for addiction (e.g., once salience is ascribed to a reward-paired cue, such inflexibility may impair STs' ability to ignore or disengage) (Ahrens, Singer, Fitzpatrick, Morrow, & Robinson, 2015; Nasser, Chen, Fiscella, & Calu, 2015).

Overall, across the domains of drug and 'personality' characteristics, evidence suggests that STs are more prone to cue-elicited drug-seeking and consumption, psychomotor sensitisation, incentive-sensitisation, heightened stress responses, attentional deficiencies (or perhaps aberrant attentional allocation), impulsivity (perhaps response disinhibition, specifically) and behavioural inflexibility. However, all of this must be interpreted whilst being mindful that the vast majority of studies have employed discrete, localised reward cues (such as lights and levers), rather than global, non-localised cues (such as entire cages), and the few studies that have employed the latter have found reverse outcomes (T. E. Robinson et al., 2014).

1.4 Sign-Tracking & Goal-Tracking: Humans

This section covers the research to date focusing on tracking behaviour in humans. Given that the second chapter of this thesis describes the tasks used throughout my PhD, only outlines

will be provided here where necessary. Please see Chapter 2 for a full description of the Additional Singleton Task (AST).

Attentional Bias

Before detailing the tasks used to measure tracking behaviours in humans, it is first important to explain the use and validity of attentional bias measures in obtaining results. Attentional bias (AB) describes the process whereby reward-associated stimuli acquire incentive salience and accrue greater attentional resources than neutral stimuli. Studies of AB typically use methods such as the Stroop and Visual Probe tasks, using either direct (eye-tracking) or indirect (button response) measures of attention, which are gathered via reaction time (RT) and/or gaze dwell time (GDT). Such procedures have shown that users and/or abusers of alcohol, cannabis, tobacco, opiates and cocaine generally show greater AB towards substance-related cues than do non-users (Field et al., 2016; Field & Cox, 2008; van Hemel-Ruiter, de Jong, Ostafin, & Oldehinkel, 2015).

Thus, much in the same way that animals' consistent *physical* approach behaviours towards the CS or US designate them as STs or GTs, respectively, whether humans show consistent *attentional* approach behaviours towards CSs or USs also allows such classification. In fact, some researchers have claimed that AB in humans and conditioned motivation in animals is very likely linked (Saunders & Robinson, 2013; Saunders et al., 2013). The measurement of human sign-tracking can take numerous forms, but always involves discrete, reward-associated, response-irrelevant stimuli drawing attention (indicating acquired salience), thus mirroring the preclinical literature relatively well (B. A. Anderson, 2013; Le Pelley, Mitchell, Beesley, George, & Wills, 2016). Regarding the validity of AB, the

studies detailed in this thesis predominantly employ direct, eye-tracking measures of AB, which have been shown to be more internally reliable than indirect measures (Christiansen, Mansfield, Duckworth, Field, & Jones, 2015).

1.4.1 Autoshaping procedures: Cognitive Tasks

Additional Singleton Task (AST)

Theeuwes's (1991, 1992) additional singleton task (AST, and subsequent variations of it; for examples, see Anderson, Laurent, & Yantis, 2011; Anderson & Spear, 2011; Le Pelley, Pearson, Griffiths, & Beesley, 2015) has widely been used to explore attentional capture in humans, with results consistently demonstrating human sign-tracking behaviours. Typically the task employs a training and test phase. In the training phase participants respond to a cue of a certain colour or shape, while in the test phase this colour or shape is employed as a distractor. A description of the task is given in the Chapter 2, General Methods. However, there are a number of possible variations, a few of which will be described here to enhance interpretation of this thesis's results.

Variations in AST training phase: Slight variations in training phases can prevent the development of sign-tracking (Sha & Jiang, 2015), and can moderate learning rates (as measured by instrumental learning tasks) and thereby moderate sign-tracking (Jahfari & Theeuwes, 2016). Sign-tracking emerges even when the test phase is undertaken one week after the training phase (MacLean & Giesbrecht, 2015).

Variations in AST perceptual features: Using shape orientation rather than shape colour weakens the effect of sign-tracking, suggesting perceptual features matter (Laurent, Hall,

Anderson, & Yantis, 2014), and the use of reward-associated auditory cues in conjunction with visual cues can increase the magnitude of sign-tracking, providing evidence of cross-modal stimulus interaction in human sign-tracking (B. A. Anderson, 2016d; Miranda & Palmer, 2014).

Variations of AST reward: Sign-tracking is observed when AST reward is specific currency ('£', '$'), displayed in either text or pictures (Camara, Manohar, & Husain, 2013; Roper & Vecera, 2016), and when CSs are paired with cues of a negative valence (Wentura, Müller, & Rothermund, 2014), including when CSs are paired with painful stimuli (electric shock) (L. J. Schmidt, Belopolsky, & Theeuwes, 2015). Sign-tracking is seen when CSs are paired with either positive or negative social information (happy or sad cartoon faces) (B. A. Anderson, 2016a, 2016c), though sign-tracking is only ever observed when the CSs contain unique predictive information about reward magnitude (Sali, Anderson, & Yantis, 2014).

Variations in detecting the importance of reward: Reward-associated CSs break through the 'inhibitory surround' (region of attention where information processing is normally supressed) (Wang, Duan, Theeuwes, & Zhou, 2014). Reward magnitude is also more important than perceptual cue features (though the more salient the cue, the greater the attentional capture) (Stankevich & Geng, 2015; Wang, Yu, & Zhou, 2013). Finally, reward captures attention even when participants are made aware of *which* cue (high- or low-value) is coming up and even *where* it is about to be presented (Becker, Hemsteger, & Peltier, 2015; MacLean, Diaz, & Giesbrecht, 2016).

In the adaptation employed throughout this thesis – referred to as the Additional Singleton Tracking Task (ASTT) – there is no training phase. Instead, participants are explicitly instructed about, and implicitly learn, the reward contingencies in the 'test phase' (the only phase). On each trial participants are presented with several grey circles, one grey

diamond and one of two coloured CSs (red or blue), which indicate different reward types given an outcome target (OT) response. One colour predicts high-value monetary rewards, the other low-value (counterbalanced). Sign-tracking is indicated by slower responses towards the OT and by more omissions on high-value compared to low-value trials. Goal-tracking is seen in low levels of distraction across trial types. See Figure 2.1 for a pictorial demonstration of the ASTT. There are now several comprehensive reviews which utilise variations of the AST to explain various realms of cognition (B. A. Anderson, 2013, 2015a; Belopolsky, 2015; Le Pelley et al., 2016; Sali, Anderson, & Courtney, 2016; Theeuwes, 2010).

Multi-Target Tracking Task (MTTT)

This novel task created for use in Study 1 (Chapter Three) also attempts to identify tracking behaviours via a paradigm not seen before, thus potentially allowing for greater variability in the way in which sign-tracking is measured. Briefly, three coloured circles (CSs: pink, green, yellow) were paired with three different reward types (USs: alcohol, chocolate and a grey rectangle), which were linked to a specific spatially distinct OT. Participants had to attend to a specific OT dependant on the CS that appeared (e.g. if a pink CS appeared the participant should respond to the left OT). Sign-tracking should be observable in slower disengagement from the CSs. See Chapter Three and Figures 3.1, 3.2 and 3.3 for a pictorial demonstration.

Pavlovian-to-Instrumental Transfer task (PIT)

Pavlovian-to-Instrumental Transfer (PIT) tasks broadly assess the ability of distinct pavlovian cues (CS+; paired with reward) to influence instrumental responding for rewards (e.g.,

alcohol), compared to cues paired with no reward (CS−). Therefore it provides a test of the "discriminative control function of a stimulus" (Hogarth, Maynard, & Munafò, 2014). PIT effects are found in both animals and humans, with human studies showing that a CS+ can increase instrumental responding for drug and alcohol rewards, and it is suggested that PIT effects may underlay a phasic transition from drug use to dependence (Hogarth, Balleine, et al., 2013). PIT also correlates with neuroimaging (e.g., functional magnetic resonance imaging: fMRI) and neurophysiological activity (e.g., Electroencephalography: EEG) (Cartoni et al., 2016; Corbit & Janak, 2016; Garbusow et al., 2014; Martinovic et al., 2014; Talmi et al., 2008).

It is worth noting that general PIT effects and sign-tracking reflect a transition from goal-directed to model-free (or habitual) learning, and thus may in some cases be modelled as similar effects (Garbusow et al., 2014; Hogarth, Field, et al., 2013). A recent PIT study concluded that, like sign-tracking, PIT effects have a negative relation to model-based learning, with both effects instead possessing the hallmarks of model-free learning (Sebold et al., 2016). A recent study measured sign-tracking during a PIT task and assessed how strongly PIT effects influenced STs as compared to GTs (Garofalo & di Pellegrino, 2015). STs selected reward-associated stimuli more than GTs when in the presence of the CS+, indicating that the mere presence of reward-paired cues increased responding for reward (i.e., conditioned reinforcement) in STs compared to GTs. See Figures 6.1, 6.2 and 6.3 were this task is used.

1.4.2 Influence of Task Setup on Outcomes

Before briefly reviewing the tracking responses found in humans, it is necessary to explain some of the fundamental psychological concepts underlying the variations of the additional singleton task, the predominant measure of tracking.

Attention

In humans, attentional bias (AB) can be observed using a range of cognitive tasks (for reviews of AB in relation to addiction and/or obesity, see Field et al., 2016; Field & Cox, 2008). This thesis focuses on attentional aspects of conditioning, with traditional models of attentional control suggesting that attention is driven by both endogenous (top-down processes regulated by internal factors, e.g., goal-driven selection) and exogenous (bottom-up processes, driven by external factors, e.g., stimulus salience) control factors (for reviews of these topics see Awh, Beloposky, & Theeuwes, 2013; Chelazzi, Perlato, Santandrea, & Della Libera, 2013). However, Awh et al. (2013) highlight that there are at least two forms of selection phenomena not explained by such models (and which are important for our purposes, here): *selection history* and *reward history*. These may have been overlooked in previous research, perhaps being mistaken as part of generic top-down processing (Awh et al., 2013). In order to parse such mechanisms, some important attentional features shall be described next.

Selection and Reward History

Selection history describes how behaviour may be biased by past choice. Wolfe, Butcher, Lee and Hyle (2003) employed a target-finding task wherein participants had to find a target possessing a specific perceptual feature (e.g., colour, orientation). During some blocks the perceptual feature remained consistent (e.g., always respond to the blue target), while during

other blocks the perceptual feature varied (e.g., respond to the blue target on some trials and the square target on others). They found slower RTs on the varied, compared to the consistent blocks, and concluded that general endogenous processing (e.g., goal-driven selection) is hindered when having to focus on more than one feature for selection. However, these findings can alternatively be explained by selection history: a bias towards previously-selected stimuli, regardless of one's current goals. This suggests that pure, consistent trials produce an invariable selection history which negates any potential conflict between previously-selected target stimuli and current target stimuli, thereby reducing RT. Conversely, varied trials (sometimes) produce conflict between selection-history and one's current goal-driven selection state, thus inflating RT. Data supporting a selection-history interpretation have been found (Maljkovic & Nakayama, 1994; Theeuwes & Van der Burg, 2011).

Regarding reward history, Thorndike (1911) described in his Law of Effect that if multiple responses are made in the same situation, those rewarded will be most likely to recur. Though Thorndike applied this law exclusively to overt behavioural responses, recent research shows it can also be applied to habitual selection biases, as demonstrated by both behavioural (Hickey, Chelazzi, & Theeuwes, 2010 *a*; Kyllingsbaek, Schneider, & Bundesen, 2001; KyllingsbÃ¦k, Van Lommel, SÃ¸rensen, & Bundesen, 2014; Libera & Chelazzi, 2009) and neural responses (Hickey, Chelazzi, & Theeuwes, 2010 *b*; Kiss, Driver, & Eimer, 2009; Small et al., 2005), as well as in the responses of animals (Ikeda & Hikosaka, 2003; Peck, Jangraw, Suzuki, Efem, & Gottlieb, 2009). When a *previously-rewarding* target of high value is shown in subsequent trials (when it is no longer rewarding), the now-irrelevant target continues to slow RT to a greater extent than when an identical procedure is conducted with low-value targets (Anderson, Laurent, & Yantis, 2011). Such results show that previous stimuli reward associations are paramount to visual selective attention.

It is therefore imperative that sign-tracking as measured by the ASTT – the task employed throughout this thesis – cannot be explained merely by response habituation (selection history) or by stimulus-response (instrumental) reward history. The influence of such effects can be avoided by presenting variable trials (selection history) and ensuring that responses to CSs (or CS features) were never at any point rewarded (reward history), but rather are *always* response-irrelevant.

Task Relevance

In the majority of human sign-tracking studies (in particular those using the AST) the distractor (CS) contains a feature (e.g., colour) that was previously response-relevant (e.g., participants were previously rewarded for responding to said feature in a training phase), therefore accommodating selection- and reward-history effects (B. A. Anderson et al., 2011a, 2011b; Chelazzi et al., 2013; Donohue et al., 2016; Failing & Theeuwes, 2014, 2015; Kiss et al., 2009; Le Pelley et al., 2015; Theeuwes, 2010; Theeuwes & Belopolsky, 2012). There have however been a handful of studies which have observed sign-tracking towards stimuli which have *always* been response-irrelevant[9] and have never been instrumentally paired with reward but which are still associated with value (Failing, Nissens, Pearson, Le Pelley, & Theeuwes, 2015; Le Pelley et al., 2015; Pearson, Donkin, Tran, Most, & Le Pelley, 2015). This shows that attentional capture can be elicited by cues which have *never* been response-relevant. This effect can likely be explained by CS value altering individuals' endogenous, top-down state, causing them to involuntarily attend to cues that cannot aid them in their task

[9] 'Response-irrelevant' is used instead of "task-irrelevant", used by others in the literature, as this is a misnomer in many versions of the task. The CSs are clearly task relevant as they signify how much participants can win on a given trial. However, in the versions of Le Pelley et al. (2015) and in the version used in this paper, the CSs *are* always 'response-irrelevant'.

performance. Indeed, it has been shown that even automatic (involuntary) attentional shifts are contingent on 'attentional control settings', or endogenous goal-driven states (Folk, Remington, & Johnston, 1992). This was in contrast to contemporary theories which suggested the primary, in some cases only, factors governing involuntary AB were the properties of exogenous stimuli (e.g., the colour of the CS).

A final note on task relevance in addition to response-relevance must also be made, as important findings in the literature show that higher order cognitions can also influence sign-tracking. Specifically, evidence suggests that both context and semantic content are partial determinants of value-modulated attentional capture (VMAC; here, unless specified, VMAC is used interchangeably with sign-tracking). In one study, a discrete stimulus feature (e.g., the colour red) either did or did not capture attention depending on whether it had been rewarded within the context in which it was presented (where context refers to the background scene: a forest versus a city landscape) (B. A. Anderson, 2014). The author noted that "the experience of a particular context evokes its own unique set of value priors, which can be independently updated with learning and automatically bias attention when activated." (p. 754). In another study, researchers conditioned participants to associate one context (e.g., forest scene) with high reward and another (e.g., mountain scene) with low reward and found that such scenes also capture (nonspatial) attention (Failing & Theeuwes, 2015). However, in a second experiment these researchers went further and, after initially conditioning participants as described above, tested the extent to which images which had never been presented before but which shared a semantic category with conditioned images still captured nonspatial attention. They found that the never-before-seen images which shared a semantic category with the high-reward scenes captured attention at a higher rate than the images sharing a semantic category with the low-reward scenes. Others have replicated this with other semantic categories (e.g., cars, trees and people) (Hickey, Kaiser, & Peelen, 2015). This finding

suggests that VMAC may not be constrained by simple stimuli (or stimuli feature) associations with reward, but that the value ascribed to a stimulus may be generalised to other stimuli of the same semantic category. In human terms, this could plausibly extend to alcohol consumers who have had positive experiences in a single pub generalising such positive associations to other pubs.

Prediction-Driven versus Value-Modulated Attentional Capture

The distinction between a cue's predictive value and its reward value is also important. Through pavlovian conditioning, stimuli develop predictive power and provide information concerning current and future environments (for reviews, see Le Pelley, 2004; Pearce & Mackintosh, 2010 [in Mitchell & Le Pelley]). Not only do (accurately) predictive stimuli become conditioned at a quicker rate than non-predictive stimuli, but evidence suggests that predictive stimuli can also induce involuntary oculomotor capture (Le Pelley, Oakeshott, Wills, & McLaren, 2005; Le Pelley, Vadillo, & Luque, 2013; Livesey, Harris, & Harris, 2009). On the other hand, value-driven attentional capture – described by Thorndike's (1911) Law of Effect – explains how highly-rewarded responses (such as responses to a particular stimulus) are more likely to recur than responses which result in the acquisition of fewer rewards, via instrumental conditioning. Both the value and the predictive utility of stimuli can determine how much attention they capture (see Le Pelley et al., 2015).

Thus, it is important that the ASTT present CSs which possess *neither* predictive utility nor instrumental value. Specifically, it is not that CSs should not be predictive of the US (it appears they have to be to be imbued with salience), but rather CSs should not predict what

kind of response should be employed or what kind of stimuli should be responded to[10], as this would prevent us from distinguishing between sign-tracking towards a CS that was produced because it has incentive value rather than because it has predictive value. Likewise, CSs should not reward responses elicited towards them as this would bring into play the effects of instrumental reinforcement. Controlling for these underlying mechanisms is important for identifying the cause of persistent, maladaptive behaviour (sign-tracking) and when developing procedures to alter it (e.g., treatment). Other potentially important factors shall be discussed in the *Introduction* sections of relevant chapters.

1.4.3 Tracking Responses in Humans

Research employing the AST has shown that humans produce several sign-tracking behaviours analogous to those seen in various animal species. Specifically, Le Pelley et al. (2015) have shown that discrete, reward-paired CSs produce slower RTs towards the OT for both direct (eye-tracking) and indirect (button response) measures, with high-value CSs impeding RT to a greater extent than low-value CSs. Additionally, they showed that high-value CSs produced significantly more overt attentional/oculomotor capture than low-value CSs, with trials containing either type of CS producing more capture than trials with no CS. Finally, Le Pelley et al. (2015) also found that, as in nonhuman animals, sign-tracking responses were developed in the absence of any response contingency and were maintained in the face of aversive consequences (*negative automaintenance*), a pattern which seems to be explained by sign-tracking's apparent automaticity (Pearson et al., 2015).

[10] Predictive utility is, unfortunately, unavoidable in the Multi-Target Tracking Task. However, as the predictive value of all types of CSs is counterbalanced (i.e., the contingencies between reward types and response types is alternated between participants), predictive utility in this instance should not be problematic.

1.4.3.1 Correlates of Sign-Tracking & Goal-Tracking: Humans

Though dozens of studies have examined human responses in cognitive autoshaping paradigms (with most exploring how subtle differences in task setup influence responses), few have investigated how tracking performance relates to individual difference factors such as impulsivity or drug use. First, as with nonhuman animal findings earlier, findings from human studies shall first look at *within*-subject correlates of tracking behaviour (section 1.4.3.1.1), before looking at any differences between tracking groups (1.4.3.1.2).

1.4.3.1.1 Correlates of Sign-Tracking

Drugs

Only two studies at the time of writing have investigated the potential relationship between human sign-tracking and substance use. The first discussed here compared 17 opioid-dependent patients undergoing methadone-maintenance treatment to 17 healthy controls on a variation of the AST (B. A. Anderson, Faulkner, Rilee, Yantis, & Marvel, 2013). The authors observed that opioid-dependent patients showed greater levels of sign-tracking (via slowed target responses on high-valued CS trials compared to CS-absent trials) compared to control participants. Thus the authors showed, for the first time, that individuals with a history of drug dependence show greater VMAC towards a nondrug (monetary) reward cues than those without a history of addiction.

In a subsequent study from the same research group, researchers tested 24 immunodeficiency virus positive (HIV+) patients on the AST (B. A. Anderson, Kronemer,

Rilee, Sacktor, & Marvel, 2016). Crucially, patients were also asked to give a detailed history of lifetime drug and alcohol exposure (drug testing ruled out current drug users, with the exception of cigarette smokers). In addition to finding a general sign-tracking effect among the sample (with greater attentional capture by the high-value CS compared to the low-value and absent CSs), they also found that HIV+ patients with an additional history of substance dependence showed greater sign-tracking than HIV+ patients with no prior substance dependence. This suggests that there may potentially be a unique association between sign-tracking and substance dependence, given that this link is observed even within populations already known for their risk-taking and sensation-seeking behaviours.

A third study covered here did not measure sign-tracking or VMAC specifically, rather a PIT task was used. However, PIT assesses model-free learning and sign-tracking is the quintessential model-free (or habitual) learning process, therefore some argue that PIT has key parallels with sign tracking (Garbusow et al., 2014). The authors investigated whether any differences existed between Alcohol Use Disorder (AUD) patients and controls in their propensity to succumb to PIT effects. Results showed that AUD patients were more likely than controls to show general PIT effects. However, while AUD patients showed a stronger negative PIT effect to aversive cues (conditioned suppression) than controls, there was no group difference in appetitive PIT (conditioned approach). Overall, however, these results tentatively indicate that AUD may be associated with model-free learning on a PIT task, which has major parallels with sign-tracking.

Overall, this evidence suggests that substance use disorders may be associated with sign-tracking in humans. Anderson and colleagues (2016) suggest that the combined results of the first two studies is consistent with heightened susceptibility to VMAC being a trait-like characteristic that is not contingent upon active drug use and its acute effects on the brain.

However, it is important to note that these studies cannot tell us whether substance users' and abusers' greater sign-tracking preceded their drug use or whether it was a result of cognitive changes brought on by prolonged use (or both). Future research employing longitudinal follow-up designs may offer elucidation.

Personality Characteristics

Following the same pattern as the drug-related studies outlined above, relatively few studies have examined whether potential links exist between human attentional tracking and personality factors. Again, 'personality' here refers to trait and state measures which differ between individuals that are not drug- and alcohol-related behaviours (e.g., impulsivity, risk-taking, sensation-seeking, working memory etc.). As has been found in animals, human studies have identified an association between sign-tracking (VMAC, more generally) and impulsivity (all studies cited here measured impulsivity via the Barratt Impulsivity Scale–11 or Behavioural Inhibition System/Behavioural Activation System scale [BIS/BAS]). Several studies have now found a positive association between sign-tracking (as measured via the AST) and trait impulsivity (B. A. Anderson et al., 2011b; Hickey et al., 2010b; Pearson et al., 2015), with a further study finding that the severity of non-planning impulsiveness (a BIS–11 subscale) leading up to a HIV+ diagnosis was correlated with sign-tracking, suggesting a possible link between VMAC and HIV-associated risk (B. A. Anderson, Kronemer, et al., 2016). However, at least one study has published results showing no link between sign-tracking and impulsivity (both BIS–11 total and subscale scores) in a sample of opioid-dependent patients (B. A. Anderson et al., 2013).

Several studies have now also found a link between sign-tracking and visual working memory (VWM). Anderson and Yantis (2012) showed that individuals with relatively low VWM were more susceptible to VMAC (i.e., sign-tracking) on the AST, compared to those with comparatively high VWM. Similarly, Anderson et al (2011b) found a negative relationship between sign-tracking and VWM capacity, a finding which has been replicated in clinical samples of both HIV+ patients (link found in an initial lab visit, but not at follow-up) and opioid-dependent patients (link found in patients but not the control group) (B. A. Anderson et al., 2013; B. A. Anderson, Kronemer, et al., 2016). In a study which simultaneously assessed working memory and visual selective attention, findings showed that higher memory load resulted in greater distractor effects (though distractors were not reward-paired in this study). This supports previously-cited results showing that working memory (and perhaps VWM in particular) is negatively associated with visual selective attention (and perhaps VMAC in particular) (de Fockert, Rees, Frith, & Lavie, 2000).

In a deeper investigation into how sign-tracking and VWM are related, a recent electroencephalography (EEG) study has shown that individuals with high VWM capacity are better able to suppress salient distractors on the AST (as opposed to better VWM enabling superior target detection) (Gaspar, Christie, Prime, Jolicœur, & McDonald, 2016). In the same vein, an fMRI study found that, while there was no relationship observed between VMAC and VWM, Blood-Oxygen-Level-Dependent (BOLD) activity was correlated with VMAC, but only under high working memory load (de Fockert & Theeuwes, 2012). Due to such consistent and seemingly robust findings, some researchers suggest that working memory provides goal-directed control over visual selective attention (Lavie & de Fockert, 2005). However, there is evidence to the contrary that VWM explains variance in VMAC. One study in particular compared adolescents (aged 13–16) to adults (aged 20–35) on the AST and found that while adolescents sign-tracked to a greater extent and for longer (VMAC

persisted into later blocks of the task) than adults, these differences were not accounted for by developmental differences in VWM capacity (Roper, Vecera, & Vaidya, 2014).

Using the AST, one study found a strong positive correlation between attentional capture by a high-value distractor and *trait reward-seeking* as measured by the Behavioural Activation System$_{drive}$ subscale (Hickey et al., 2010b). This may suggesting that, like animals, some humans may possess a trait-like tendency to sign-track. Further, the authors suggest that BAS$_{drive}$ reflects incentive sensitisation theory's 'wanting' component, which is the aspect of the theory describing how drug-seeking can be motivated by incentivised cues, regardless of drug valuation (i.e., whether the drug is 'liked' or not) (Berridge, Robinson, & Aldridge, 2009). Future studies directly investigating any association between tracking behaviours and 'wanting' or 'liking' should treat these two components as dissociable.

Studies on patients have also revealed that clinical disorders (excluding substance use disorders) correlate with sign-tracking. In a study of depression sufferers it was found that while sign-tracking was found in a control group, depressed patients showed no VMAC. (B. A. Anderson, Leal, Hall, & Yassa, 2014). Further, patients' depression scores negatively correlated with the magnitude of VMAC. These result may indicate either that depressed patients don't find such cues rewarding, or that depression is accompanied by differences in how the attentional system processes reward information (or both).

The final studies covered here relate to human sign-tracking as measured across time. For example, in one study which monitored brain activity via fMRI, participants completed a passive viewing task which included exposure to stimulus-reward pairings, where the 'reward' was erotic pictures and 'no reward' was fractal images. The researchers found that BOLD activation in the ventral striatum (which the authors used as a proxy for pavlovian conditioning) predicted financially-costly approach behaviour on an active choice task 2–4

months later (Chumbley, Tobler, & Fehr, 2014). The authors concluded that they have presented tentative evidence that variations in ventral striatal activity may partially cause model-free learning (i.e., sign-tracking) and its consequences (financially risky behaviour in this context) (Sebold et al., 2016). However, it should be noted that this study possesses many components, and thus may not be a clear-cut measure of strict sign-tracking behaviour.

In the final study of this section, findings revealed that individuals tested on the AST for only the second time after a 7–9 month interval had retained their attentional approach behaviour towards noncontingent, response-irrelevant, but previously reward-associated CSs (B. A. Anderson & Yantis, 2013). Crucially, even though no participants reported any memory of which colour was associated with high value and which with low, the colours' effects on performance were statistically significant, suggesting that conscious awareness of reward contingencies is not necessary for incentivised CSs to influence behaviour. In terms of how this relates to the individuals, the findings suggest that one session of autoshaping (via the AST) is enough to subconsciously alter peoples' attentional orienting towards differently valued cues over a period of months. Crucially, this suggests that single events in which individual, discrete cues become incentivised can cause such cues to subsequently attract attention. This is potentially important given evidence that attention correlates with subjective reports of craving and may even predict relapse in abstinent users and addicts (Field, Munafò, & Franken, 2009; Marissen et al., 2006; Waters et al., 2003).

1.4.3.1.2 Individual differences between human tracking groups: Sign-Trackers vs. Goal-Trackers

This section will outline individual differences between human participants classified as STs and GTs. Only two studies at the time of writing have assessed individual differences in humans classified into tracking groups. However, neither of these studies investigates STs' or GTs' relationships with drugs, therefore, the section below is a general overview of individual differences observed between human tracking groups.

STs vs. GTs: Individual Differences

The first study employed a PIT task similar to that of Garbusow et al. (2014), reviewed above. Garofalo and di Pellegrino (2015) designed a PIT task which first presented an instrumental conditioning task, then a pavlovian conditioning task, before a PIT task assessed how much influence (if any) pavlovian cues exhibited over instrumental responding for reward-associated stimuli. Participants were classified as STs or GTs based on their CRs during the pavlovian conditioning phase. Individuals whose attention was biased towards the CS+ were classified as STs, and those whose attention was consistently drawn to the region of US (reward) delivery were classified as GTs. They found that STs, but not GTs, were more likely to choose the reward-response option when the CS+ was displayed compared to the CS– (even though rewards were no longer available). This indicates an influence of a noncontingent, discrete cue on STs' reward choices even in extinction. Furthermore, it seems that in the last block of the PIT choice task, regardless of which CS was displayed, STs chose more rewards than GTs. Finally, in a replication of animal studies, the authors found that STs were significantly more impulsive than GTs, as reported on the BIS–11.

In another study, 64 lean and 88 obese adults viewed food-related, pleasant, neutral and unpleasant images while EEG recordings were taken (Versace, Kypriotakis, Basen-Engquist,

& Schembre, 2015). Late positive potentials (LPP) were taken as a measure of cue-related incentive salience for each category and were used to categorise participants into tracking groups. Participants classified as STs were those whose LPP responses to food-related cues were of the same magnitude as those towards other highly arousing stimuli, whereas participants classified as GTs presented with LPP responses to food cues that were indistinguishable from responses to neutral cues. The results showed that obese individuals were significantly more likely than lean individuals to be classified as STs – 40% of the obese sample versus 23% of lean participants. Further analysis revealed that obese individuals designated as STs had a greater proclivity for maladaptive eating behaviours, shown by higher self-reports of emotional eating and food cravings, coupled with greater feelings of loss of control and positive outcome expectancies.

Taken together, the evidence of associations to different tracking phenotypes attained so far in humans suggests that I) STs' reward choices may be more influenced by discrete, reward-associated cues, II) that STs may choose rewarded options more often even in the absence of the influence of reward-associated cues, III) STs may be significantly more impulsive than GTs, IV) obese individuals may be more likely to imbue food-related cues with incentive salience (i.e., sign-track), and V) obese sign-trackers may have increased rates of maladaptive eating patterns.

1.5 Aetiology of Tracking Behaviours

These final sections cover the evidence concerning the possible causes and/or factors which may potentiate the development of tracking behaviours. (It should be noted that the sections below cover broad aetiologies, and do not cover the large influence of experimental setup in

autoshaping, which is covered in sections 1.3.2.3 [nonhuman animals] and 1.4.2 [humans].) The areas covered here are genetics (1.5.1), neurobiology (1.5.2), the influence of early life experiences (1.5.3) and the influence of drugs (1.5.4).

1.5.1 Genetics

Animals

Several preclinical studies have investigated the role of genetics in influencing tendencies to sign-track versus goal-track. These studies typically expose different rat strains to identical autoshaping procedures and assess the emergent prevalence of tracking behaviours across the different groups. In perhaps the earliest study to do this, Lewis (LEW) and Fischer (F344) rats – the former of which are known to possess higher impulsivity and more readily self-administer drugs – were exposed to a food-paired lever-CS in an autoshaping paradigm and assessed for levels of sign-tracking (Kearns, Gomez-Serrano, Weiss, & Riley, 2006). The results revealed that LEW rats acquired a sign-tracking CR more rapidly and sign-tracked to a greater extent than the F344 rats. The authors concluded that this may be due to physiological components such as hypothalamic–pituitary–adrenal axis activity, which influences psychological traits such as impulsivity, drug consumption and (possibly) sign-tracking.

A study conducted a year later applied similar procedures using mouse strains and ethanol and saline as the reward (US). Mice were injected with ethanol or saline before being tested for sign-tracking via exposure to the appropriate reward-paired cue (Cunningham & Patel, 2007). Results revealed that both NZB/B1NJ mice and DBA/2J sign-tracked to almost identical degrees for the CS paired with saline, but only NZB/B1NJ showed a sign-tracking CR for the ethanol-paired CS and an acquisition curve (i.e., a progressive increase in sign-

tracking over time). A more recent study using a food-paired CS and utilising Sprague-Dawley (SD) rats and Heterogeneous Stock (HS) found that female SD rats acquired a sign-tracking CR faster than male SD rats, but that there was no sex difference in HS rats (Pitchers et al., 2015). In a study using a large sample, researchers found that rates of ST and GT differed in rats obtained from different vendors and from different colonies within vendors. (Christopher J. Fitzpatrick et al., 2013). Although environmental variables are impossible to discount, this suggests that genetics are a determining factor.

Highly genetically and behaviourally diverse mouse populations show significant sign-tracking differences, with such differences showing correlations with novelty-seeking (Dickson et al., 2015). Further, rats bred for novelty-seeking are more likely to show behavioural disinhibition and sign-tracking (Flagel, Robinson, et al., 2010), as are mice bred for lower serotonin 5-HT function (Campus, Accoto, Maiolati, Latagliata, & Orsini, 2016). Chemogenetic manipulations which cause disruption to ventral pallidum neurons have also been found to impair sign-tracking, leaving goal-tracking unaffected (Chang, Todd, Bucci, & Smith, 2015). Furthermore, one study has shown CS-induced c-fos (proto-oncogene) mRNA (messenger ribonucleic acid) expression in corticostriatal regions only in those who imbue said CSs with incentive salience (i.e., sign-trackers) (Flagel, Cameron, et al., 2011). Crucially, Dickson et al. (2015) estimate that the heritability – the proportion of variance in a given population that can be accounted for by genetic factors – of sign-tracking and goal-tracking is between .32 and .41, suggesting moderate heritability in these populations.

Before ending this section, it is worth outlining the reason sign-tracking may have evolved, given that it can be such a costly behaviour (i.e., is associated with cue-induced drug-seeking, is persistently maladaptive in the face of aversive consequences etc.). It is possible that these behaviours are a side-effect of heuristics which are evolutionarily

advantageous on average, with such quick, automatic and low-level pavlovian learning having benefits for the organism, suggesting evolutionary origins are likely (Hickey et al., 2015; Hickey & van Zoest, 2013). However, in certain situations (e.g., autoshaping paradigms, specifically crafted choice tasks, exposure to addictive substances etc.), these heuristics can be exploited and often result in unwanted and/or inappropriate behaviours. These heuristics aid both bottom-up and top-down learning, but also appear to be automatic, and so awareness does not offer protection from maladaptation (Awh et al., 2013).

Humans

There are no studies measuring the genetic influence on the sign-tracker and goal-tracker phenotypes in humans. However, many of the traits that are related to tracking behaviours in the preclinical literature (e.g., impulsivity, risk-taking, sensation-seeking etc.) and in some human studies (e.g., self-reported impulsivity, loss of control and obesity) have been shown to be highly heritable in humans (Anne & Paul, 2014; Locke et al., 2015; Polderman et al., 2015). Thus, given that tracking-related traits are highly heritable in animals and that all human behavioural traits are heritable (Turkheimer, 2000), it seems very likely that human variance in sign-tracking will also be at least partly heritable.

1.5.2 Neurobiology

Animals

The preclinical literature on the neurobiological underpinnings and correlates of sign-tracking is vast, with neurochemical features ranging from dopaminergic and GABAergic

involvement to the influence of designer drugs on designer receptors, and neuroanatomical regions ranging from cortical structures (e.g., the frontal cortex) to the evolutionarily old subcortical structures (e.g., the amygdalae and striatum).

The most implicated neurotransmitter in sign-tracking research is dopamine (DA). Dozens of studies suggest that DA and specific dopaminergic receptors play a key role in the attribution of incentive salience (Fraser, Haight, Gardner, & Flagel, 2016). In the first study to examine this directly in subgroups of STs and GTs, researchers found that STs exhibited higher levels of the D1 DA receptor (DRD1) mRNA relative to GTs on the first day of testing (Flagel et al., 2007). Further, low and moderate doses of typical and atypical antipsychotics (which work at D2 DA receptors, DRD2) attenuate sign-tracking, with goal-tracking only being affected at a maximal dose (Danna & Elmer, 2010). Similarly, bred high-responder rats (bHRs; bred for novelty) who also score highly on impulsivity and sign-tracking show DA super-sensitivity and a greater proportion of $DRD2^{high}$ receptors compared to bred low-responders (bLRs; who are more likely to goal-track) (Flagel, Robinson, et al., 2010).

A body of evidence using different techniques has shown that DA function is involved in the acquisition (Chow, Nickell, Darna, & Beckmann, 2016; Darvas, Wunsch, Gibbs, & Palmiter, 2014; Flagel, Clark, et al., 2011; Scülfort, Bartsch, & Enkel, 2016; Yau et al., 2016), maintenance (DiFeliceantonio & Berridge, 2016; Christopher J. Fitzpatrick, Creeden, Perrine, & Morrow, 2016; Lopez et al., 2015; Saunders & Robinson, 2012; Singer, Guptaroy, et al., 2016; Soares, Cardoso, Malato, & Messias, 2017; Yager et al., 2015) and modulation (Aitken, Greenfield, & Wassum, 2016; Peciña & Berridge, 2013; Saunders et al., 2013) of sign-tracking. However, there are nuances to the research highlighting DA as a key component in sign-tracking. For example, amphetamine (a DA agonist) can both magnify sign-tracking and cause some STs to goal-track (DiFeliceantonio & Berridge, 2016).

Similarly, in an autoshaping procedure using contextual, rather than discrete cues (perhaps best called a goal-tracking paradigm), DA antagonism blocked cocaine-context induced hyperactivity, suggesting that DA might also modulate goal-tracking in environments conducive to producing a goal-tracking (as opposed to a sign-tracking) CR (Saunders et al., 2014). However, overall, researchers have concluded that "sign-tracking behaviour is more heavily controlled by dopamine than goal-tracking" (Lopez et al., 2015, p. 2096).

Regarding other neurotransmitters, glutamatergic receptors in various forms have been shown in several studies to be related to tracking behaviours; the ones covered here are all ionotropic glutamate receptors (NMDA, AMPA, Kainate). First, photoinhibition of general glutamatergic receptors has been shown to significantly impair goal-tracking CRs during CS presentation (in a paradigm which only promoted goal-tracking) (Yau et al., 2016). For NMDA (N-Methyl-D-Aspartate) receptors (NMDARs), the research is mixed. NMDAR antagonists have been shown to both enhance (DeAngeli et al., 2015) and reduce (Milton et al., 2012) sign-tracking towards ethanol-paired cues. A further study found a loss of NMDARs in DA neurons did not affect the expression of sign-tracking at all (James, Pennington, Tran, & Jentsch, 2015). For AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) and kainite receptors, one study found that an AMPAR antagonist in the basolateral amygdala, but not the caudate putamen, diminished cue-evoked alcohol seeking by a discrete CS (Sciascia et al., 2015). Another found that an AMPA/Kainate antagonist in the nucleus accumbens core, but not the shell, reduced cue-induced cocaine-seeking by a discrete CS even when an NMDA antagonist did not (Di Ciano & Everitt, 2001). The authors concluded that NMDA and AMPA/Kainate effects are dissociable.

There is further evidence that serotonin, opioid, acetylcholine and DREADD (Designer Receptor Exclusively Activated by Designer Drugs) receptors are also involved. For

serotonin, STs possess lower levels of 5-HIAA and lower 5-HIAA/5-HT turnover (Tomie et al., 2000), and 5-HT depletion increases sign-tracking (Campus et al., 2016). For mu opioid receptors, agonists increase sign-tracking (DiFeliceantonio & Berridge, 2016) and receptor stimulation enhances vulnerability for conditioned reinforcement (i.e., the ability of reward-paired CSs to elicit drug-seeking) (Peciña & Berridge, 2013). For acetylcholine (ACh), STs possess lower levels (which seems to moderate their poor attentional control) (Paolone et al., 2013), and sign-tracking towards an alcohol cue is enhanced by nicotine injections into ACh receptors (Maddux & Chaudhri, 2017). Further, photoinhibition of cholinergic inputs during CS presentation can impair goal-tracking (Yau et al., 2016). Finally, for DREADDs, activation of inhibitory DREADD receptors which disrupt ventral pallidum neurons impairs the acquisition of sign-tracking, but not goal-tracking, nor the expression of sign-tracking once the CR is acquired (Chang et al., 2015).

Brain regions of interest have been largely omitted in the review of neurotransmitters above. Due to the consistency in the regions of note in the literature, it is more efficient to list them and their relation to specific neurotransmitters. The majority of work has discovered the areas important for tracking behaviours to be: the striatum (*dorsal:* caudate and putamen; *ventral:* nucleus accumbens [NAcc]), the ventral tegmental area (VTA), thalamus, amygdala, hippocampus, and ventral pallidum. These areas roughly correlate to the basal ganglia and limbic system, areas which regulate emotion, movement, reward learning and attention (among other things).

There is now a large evidence base that dopamine activity in the NAcc core (and mixed evidence for the shell) is vital in the development and expression of sign-tracking behaviours (Aitken et al., 2016; Christopher J. Fitzpatrick, Creeden, et al., 2016; Christopher J. Fitzpatrick, Perrine, Ghoddoussi, Galloway, & Morrow, 2016; Flagel, Clark, et al., 2011;

Flagel, Robinson, et al., 2010; Flagel et al., 2007; Peciña & Berridge, 2013; Saddoris, Wang, Sugam, & Carelli, 2016; Saunders & Robinson, 2012; Saunders et al., 2013; Singer, Guptaroy, et al., 2016; Tomie et al., 2000; Yager et al., 2015), while some evidence suggests that that DA NAcc functioning is also involved in goal-tracking when reward-associated contexts are employed, rather than discrete CSs (Saunders et al., 2014). Dopaminergic anatomy and function in the striatum generally is also related to sign-tracking (Darvas et al., 2014; Flagel, Robinson, et al., 2010); the dorsolateral quadrant of the neostriatum (DLS) is related to increases in sign-tracking in STs and goal-tracking in GTs (DiFeliceantonio & Berridge, 2016). Crucially, the dorsomedial and dorsolateral striatum mediate the shift between goal-directed and habitual action, respectively (Gremel & Costa, 2013; Murray, Belin, & Everitt, 2012). Further brain regions related to sign-tracking via dopamine signalling include the VTA (Flagel et al., 2007), ventral (but not dorsal) hippocampus (Christopher J. Fitzpatrick, Creeden, et al., 2016; Christopher J. Fitzpatrick, Perrine, et al., 2016; Lopez et al., 2015), putamen (Tomie et al., 2000) and the general cortico-limbic and amygdalo-striatal-thalamic circuits (Lopez et al., 2015; Yager et al., 2015).

Regarding regions in which the other neurotransmitters work, the evidence again suggests consistency. For glutamatergic (NMDA, AMPA, Kainate) activity, these receptors and transmitters function at the NAcc (Di Ciano & Everitt, 2001; Madayag, Stringfield, Reissner, Boettiger, & Robinson, 2017), VTA (Yau et al., 2016), hippocampus (DeAngeli et al., 2015), and amygdala (Sciascia et al., 2015). For serotonin, activity in the VTA (Tomie et al., 2000) and medial prefrontal cortex (mPFC) (Campus et al., 2016) is related to sign-tracking. Further, mu opioid receptors at the NAcc (Peciña & Berridge, 2013) are related to sign-tracking, while opioid receptors at the DLS are related to both sign-tracking and goal-tracking (DiFeliceantonio & Berridge, 2016). Cholinergic activity operating at the inputs from the mesolimbic system, including the VTA, also appear to regulate sign-tracking

(Maddux & Chaudhri, 2017; Paolone et al., 2013; Yau et al., 2016). Finally, DREADD receptors operating in the ventral pallidum play a crucial role in the acquisition of sign-tracking (Chang et al., 2015).

Research not employing any specific receptor agonist/antagonist, but which rather lesion brain regions or utilise electrophysiological recordings have also found sign-tracking to be at least partly dependent on or regulated by the NAcc (Chang, Wheeler, & Holland, 2012; Guercio, Schmidt, & Pierce, 2015; Haight, Fuller, Fraser, & Flagel, 2017), VTA (Mahler & Aston-Jones, 2012), amygdala (Chang et al., 2012; Haight et al., 2017; Mahler & Aston-Jones, 2012; M. J. F. Robinson, Warlow, & Berridge, 2014; Ross et al., 2016), thalamus (Haight, Fraser, Akil, & Flagel, 2015; Haight et al., 2017), and ventral pallidum (Ahrens, Meyer, Ferguson, Robinson, & Aldridge, 2016; Mahler & Aston-Jones, 2012; Richard et al., 2016). All of these results suggest that dopamine, glutamate and various other neurotransmission in the limbic and basal ganglia substructures (chiefly the NAcc, VTA, thalamus, amygdala and ventral pallidum) are key neurobiological structures involved in sign-tracking (Flagel & Robinson, 2017; Fraser & Haight, 2016).

Humans

There are several human studies which have extended the results of the preclinical literature. This section will first review fMRI (functional Magnetic Resonance Imaging) studies which employed variations of the additional singleton task (AST), as these are most relevant to this thesis. PET (Positron Emission Tomography), EEG (electroencephalography) and tRNS (transcranial random noise stimulation) studies using the AST will then be covered.

In the earliest of the fMRI AST studies, distractors were perceptually salient and irrelevant, but *not* reward-associated (de Fockert, Rees, Frith, & Lavie, 2004). Interference from the salient feature was found (versus no feature present), with activation in the bilateral superior parietal lobe and the left lateral precentral gyrus. Interestingly, a strong negative correlation was found between the strength of the neural signal in the frontal cortex and the magnitude singleton distractor interference (singleton targets showed much smaller effects). A replication from the same group using an identical sample size found identical results (Lavie & de Fockert, 2006). In a replication which also measured working memory (WM) load, the presence (vs. absence) of colour singletons is associated with neural activity in the right inferior frontal gyrus, but only under high WM load (de Fockert & Theeuwes, 2012). These findings suggest neural responses related to distraction detection (inferior frontal gyrus), the allocation of spatial attention (superior parietal cortex) and attentional selection between multiple stimuli for action (frontal cortex).

The problem with the studies above, however, is that the salient features were not associated with reward, and as such only the attentional processing of irrelevant neutral cues was investigated, not sign-tracking. Recent studies have bridged this gap. In the first, 18 participants displayed sign-tracking when an irrelevant distractor contained a feature (red colour) which had previously been paired with monetary reward (B. A. Anderson, Laurent, & Yantis, 2014). Sign-tracking was linked to activity in the caudate tail (known to represent object identity and location), intraparietal sulcus (attentional control), inferior frontal gyrus (distraction detection, behavioural disinhibition), middle frontal gyrus (contingency awareness) and the striatum (reward anticipation). Crucially, in a second experiment (14 participants) some of these modulations in neural response (caudate tail and striatum, specifically) were not seen for equally familiar distractors which were *not* paired with reward, suggesting that these brain regions are specific to *value*-modulated attentional control. In the

most recent fMRI AST study, although no sign-tracking effect was observed, the *value-driven attention network* – which includes the caudate tail, intraparietal sulcus, lateral occipital complex and the early visual cortex – was activated by high-value distractors compared to those of low-value or no value (B. A. Anderson, 2016b).

In addition to fMRI work, a recent PET AST study revealed that attentional capture by reward-associated distractors positively correlated with dopamine (D2/D3) release in the right caudate and posterior putamen (both substructures of the striatum), areas known to underscore habit learning and the expression of habitual behaviours (B. A. Anderson, Kuwabara, et al., 2016). These results comport with both the human fMRI and the preclinical results. In the realm of EEG research, event-related potentials (ERPs) were evoked by reward-associated distractors during an AST, but not by equally familiar, non-reward-associated distractors (Qi, Zeng, Ding, & Li, 2013). Other work has shown that P1 ERPs – reliable indicators of early visual selective attention – are evoked by reward-paired distractors, even when participants are tested one week after reward contingency training (Maclean & Giesbrecht, 2015). In an EEG study which classified obese and lean individuals based on their neural responses to emotionally salient stimuli, obese individuals were significantly more likely to be classified as sign-trackers (Versace et al., 2015). Importantly, STs showed similar LPP (late positive potential) ERPs – indicators of attentional reactivity to emotional stimuli – to food stimuli as they did towards emotionally salient stimuli (e.g., erotica), while GTs' LPPs to food was similar to that produced towards neutral stimuli. Obese individuals classified as STs based on their neural responses also showed the most maladaptive eating patterns of all the groups. Finally, in a study which utilised tRNS during the training phase of an AST, tRNS applied to the occipital cortex (which houses the visual cortex) produced a sign-tracking effect while the tRNS frontal cortex and sham tRNS groups

did not (Van Koningsbruggen, Ficarella, Battelli, & Hickey, 2016). The authors concluded that neural plasticity can contribute to value-modulated attentional capture.

The brain regions identified in the sign-tracking literature are also involved in general reward processing and have been linked to differential functioning in hard drugs users and addicts. For example, dysfunction of D2 receptors in the ventral striatum (where the NAcc is located) may contribute to the attribution of incentive salience for alcohol-paired cues and subsequent cue-evoked craving (Heinz et al., 2004). Further, D2 receptor activity in the dorsal striatum (caudate and putamen) is reduced when exposed to cocaine cues, and this is related to subjective craving (Volkow et al., 2006). Similarly, D2 receptor occupancy in the putamen correlates with cue-elicited craving (Wong et al., 2006). Moreover, methamphetamine addicts show reward-evoked activation in the striatum, with abstinent addicts showing increased activation in the putamen and caudate compared to relapsed addicts (Gowin, Ball, Wittmann, Tapert, & Paulus, 2015). Finally, a review of the data suggests the ventral pallidum is a key structure in encoding incentive and hedonic stimuli, as well as in the motivation to attain such stimuli (Smith, Tindell, Aldridge, & Berridge, 2009), and a meta-analysis of 142 studies concluded that reward outcome significantly activates the NAcc and amygdala (Liu, Hairston, Schrier, & Fan, 2011). All of these data taken together suggest a link in the neurological underpinnings of sign-tracking in humans and nonhuman animals, as well as a link to aberrant outcomes (such as drug dependence).

1.5.3 Influence of Early Life Experiences

Animals

In addition to biological factors, preclinical work has shown that environmental factors influence sign-tracking development. The studies covered here span three areas of influence: I) the impact of drugs during adolescence, II) the impact of food restriction and inadequate social experience during childhood and adolescence, and III) the impact of exposure to pavlovian autoshaping (sign-tracking) paradigms in adolescence. The first two factors in particular are important as they have been associated with increased risk of substance use disorders in humans (Dube, Anda, Felitti, Edwards, & Croft, 2002; Meier et al., 2016).

Beginning with exposure to autoshaping, adolescent rats exposed to an autoshaping procedure demonstrated larger sign-tracking in adulthood compared to control rats tested only in adulthood (R. I. Anderson & Spear, 2011). Further, adolescent autoshaping pre-exposure increased ethanol consumption in adult sign-trackers. This is the only study to assess the impact of mere exposure to autoshaping procedures in adolescence on behaviour in adulthood.

Three studies have investigated the influence of inadequate early life socialisation on adult sign-tracking. The first found that artificially reared (AR) rats – rats deprived of maternal and sibling interaction – were more likely to develop sign-tracking behaviours than maternally reared (MR) rats (Lomanowska et al., 2011). Rats who received some tactile stimulation during their social deprivation (AR + STM) developed sign-tracking behaviours intermediate to that of AR and MR rats. A second study revealed that food restriction promoted sign-tracking among socially isolated adolescent rats, while promoting goal-tracking in pair-housed (social) adolescent rats, revealing an interaction between social and food deprivation (R. I. Anderson et al., 2013). Food restriction in adults increased both sign-tracking and goal-tracking behaviours (in members of each respective phenotype) *regardless* of their social housing situation. The third study found that rats reared in isolated

environments (small, hanging cages with no novel objects or social cohorts) predominantly became STs, while rats reared in enriched environments (large cages, novel objects and social cohorts) became GTs (Beckmann & Bardo, 2012). These findings suggest that social environment during early life is maybe important in the development of sign-tracking.

Turning to how consumption of drugs in adolescence influences the development of sign-tracking, the earliest study conducted found that, although amphetamine increased sign-tracking, it did so with no observable differences between age groups (Doremus-Fitzwater & Spear, 2011). Studies using alternative substances have found different results. Ethanol-treated adolescents sign-track significantly more in adulthood than control-treated adolescents (McClory & Spear, 2014). Crucially, these effects were not seen in rats exposed to ethanol only in adulthood, suggesting that ethanol exposure *during adolescence* is key. Additionally, intermittent ethanol exposure in adolescence increased sign-tracking and blunted goal-tracking in adulthood (Madayag et al., 2017). Finally, adolescent cocaine exposure increased goal-tracking in low-responder rats ('addiction-resilient'), but caused no change in high-responders ('addiction-prone'), a surprising result given the findings of cocaine influence on adult sign-tracking (see section 1.5.4) (García-Fuster, Parsegian, Watson, Akil, & Flagel, 2017).

Overall, the literature on the influence of early life experience suggests that food deprivation and social isolation in adolescence and childhood can (separately and in conjunction) elevate sign-tracking in adulthood. Further, the evidence on the influence of drug consumption during adolescence suggests that, depending on the substance and population used, adolescent drug exposure can increase adult sign-tracking and perhaps goal-tracking. However, these results should be interpreted with caution as most of the cited studies did not include an appropriate adult control group. Finally, mere exposure to an

autoshaping paradigm has been shown in one study to elevate ethanol consumption in rats prone to sign-tracking, perhaps indicating that stimulus-reward learning in adolescence may enhance the effects of reward-seeking in later life, but only for those who sign-track.

Humans

Though there is evidence of a relationship between reward-related attentional bias in adolescence and substance use years later, such studies have not measured sign-tracking (van Hemel-Ruiter et al., 2015). However, one study has attempted to investigate the interaction of age and sign-tracking in humans. In this study, 40 adolescents and 40 adults were tested on a typical AST. Although both groups demonstrated sign-tracking, the effect was exacerbated and persisted longer in the adolescents (Roper et al., 2014). Visual working memory (VWM) was also measured in both groups, with results showing that – contrary to other studies in adults (B. A. Anderson, Kronemer, et al., 2016; B. A. Anderson & Yantis, 2012) – developmental differences in VWM capacity did not account for differences in sign-tracking.

These results provide evidence that younger people sign-track to a greater extent, but provide no insight as to why this is the case. It is also of note that these results conflict with work in animals showing that adult rats sign-track to a greater degree than adolescents (R. I. Anderson et al., 2013; R. I. Anderson & Spear, 2011; Doremus-Fitzwater & Spear, 2011). However, without knowing the mechanism of the human finding, the reasons for this conflict are unknown. No study has investigated whether sign-tracking is linked to childhood trauma, though the latter is a known precursor for later substance abuse (Dube et al., 2002). Future work could explore the possible relationship between early trauma, enhanced attribution of incentive salience to irrelevant reward cues (sign-tracking), and substance use.

1.5.4 Influence of drugs

Animals

In addition to the studies reviewed above showing how age and drug consumption interact, studies have investigated how substances alter tracking behaviours more generally. These studies can be likened to human priming studies which assess the influence of acute alcohol consumption on various cognitive measures such as attentional bias (see 'Humans', below) (Rose, 2013). The preclinical literature has explored the effects of the following: amphetamine, cocaine, ethanol, flupenthixol, ketamine, nicotine and opioids.

Amphetamine's influence on sign-tracking has the largest evidence base. Excluding an early study (Holden & Peoples, 2010), research has shown that rats that have undergone amphetamine sensitisation show enhanced sign-tracking relative to controls (M. J. F. Robinson, Anselme, et al., 2015). Further, acute amphetamine injection into the dorsolateral quadrant of the neostriatum (DLS) of STs selectively enhances their approach toward a reward-paired lever-CS (DiFeliceantonio & Berridge, 2016). Acute amphetamine exposure also increases sign-tracking towards a light-CS, with presentation of the CS inducing activity in the nucleus accumbens (NAcc) (Wan & Peoples, 2008). Similarly, amphetamine injection into the NAcc core enhances incentive motivation for a reward-paired lever-CS in STs, but not GTs (Singer, Guptaroy, et al., 2016). In addition to the result that amphetamine injection enhances sign-tracking in STs, DiFeliceantonio and Berridge (2016) found that the same injection in GTs enhanced goal-tracking. It even enhanced goal-tracking in some STs (though to a minor extent). Accordingly, amphetamine appears to promote the reinforcing effects both of a lever-CS in STs and of a tone-CS in GTs (Meyer et al., 2014). Thus, there is consistent

evidence that amphetamine can enhance both sign-tracking and goal-tracking, though this depends on experimental setup, the brain region targeted and maybe the rat strain tested.

In the first cocaine study, in addition to finding that cocaine-paired CSs (exteroceptive cues) influenced STs more than GTs, it was also found that STs were primed to a greater extent to approach cocaine paired-cues than were GTs after cocaine exposure (an interoceptive cue) (Saunders & Robinson, 2011). Thus, certain interoceptive cues (e.g., cocaine) may have the ability to enhance the motivational value (incentive salience) of exteroceptive cues (cocaine-paired CSs). A more recent study replicated these results (Saddoris et al., 2016).

For ethanol studies, early research showed that all ethanol doses – daily pre-session intraperitoneal injections – increased sign-tracking (rapid acquisition of a sign-tracking CR towards a lever-CS) compared to saline, but only moderate (0.5–0.7 g/kg) and not low or high (0.25 g/kg, 1 g/kg) doses enhanced sign-tracking *statistically significantly* towards a food-related cue in an inverted-U shape dose effect curve (Tomie, Cunha, et al., 1998). Similar results were obtained by the same group some years later (Tomie, Festa, et al., 2003). In a more recent study using similar procedures, however, Tomie's results were not replicated – the data showed a 0.7 g/kg dose of ethanol *reduced* sign-tracking as opposed to increasing it (Versaggi et al., 2016). This could be due to a variety of reasons including the Tomie et al. (1998; 2003) results being spurious (while ethanol increased sign-tracking over saline, it did not do so above a no injection control group), or plausibly due to different rat strains being used (see section 1.5.1). Thus, the findings on alcohol priming are so far mixed. Further work with adequate control groups and controlling for animal strain, administration procedure, and dose is needed.

The antipsychotic drug and dopamine receptor antagonist flupenthixol has been shown to markedly impair the expression of sign-tracking, but not goal-tracking CRs (Saunders & Robinson, 2012). Flupenthixol has also been found to reduce conditioned approach behaviour, but not conditioned orienting (Yager et al., 2015). The authors of both studies conclude that flupenthixol may reduce sign-tracking by altering the core of the NAcc's dopaminergic system. The only study to assess the influence of ketamine on tracking behaviours found that a subanesthetic dose decreased sign-tracking and increased goal-tracking in STs, while leaving GTs unaffected (C. J. Fitzpatrick & Morrow, 2016). Ketamine may therefore reduce attribution of incentive salience to reward-paired cues – and thereby reduce the influence of such cues – via NMDA receptor antagonism (see section 1.5.2).

Regarding nicotine, one study found that nicotine pre-treated rats across multiple experiments increased sign-tracking towards a light-CS, effects which lasted beyond the pharmacological effects of the drug itself (Palmatier et al., 2013). Similarly, nicotine enhances sign-tracking towards a food-paired lever-CS, but not goal-tracking (Versaggi et al., 2016). Nicotine also enhanced the conditioned reinforcing properties of the food-paired cue. Nicotine may therefore enhance sign-tracking by either facilitation of incentive attribution of reward-paired cues, or via an acute effect of nicotine on incentive value (with evidence more strongly in support of the latter).

Finally, research on opioid influence of tracking behaviours dictate that rather than injecting opioids into the animal, mu opioid receptors are instead directly stimulated or targeted via direct opioid agonists. Data have shown that DAMGO microinjections into the central amygdala enhances sign-tracking in STs and goal-tracking in GTs (DiFeliceantonio & Berridge, 2012; Mahler & Berridge, 2009). Additionally, DAMGO microinjections into the DLS enhances sign-tracking in STs and goal-tracking in GTs, while also causing STs to work

harder to earn presentation of the reward-paired lever-CS (DiFeliceantonio & Berridge, 2016). Interestingly, when the lever-CS was moved to a new (further away) location, STs tracked the CS following mu opioid receptor stimulation.

Humans

To date, there are no studies examining whether acute drug consumption affects tracking behaviours in humans. Only two studies have looked at drug use and sign-tracking in humans. These studies show that opioid-dependent patients display greater sign-tracking compared to a control group and that substance abuse history correlates with current sign-tracking behaviour (B. A. Anderson et al., 2013; B. A. Anderson, Kronemer, et al., 2016). However, these studies don't assess causality; addicted individuals may have always possessed greater sign-tracking CRs which may have contributed to their addiction, chronic substance use/abuse may have elevated sign-tracking, a third factor may exacerbate both, or all of these causal pathways may be true. Future studies could follow the alcohol priming literature in which varying doses of alcohol are consumed by participants before completing a cognitive task (e.g., an attentional bias task). Such studies show that acute consumption of varying alcohol doses can increase AB towards reward-paired cues (on an inverted-U curve) in a non-sign-tracking paradigm (Rose, 2013). Given the link between AB, craving and consummatory behaviour, as well as findings that AB is larger in drugs users versus non-users (Field et al., 2016), studies investigating the acute effects of drugs (e.g., alcohol) on sign-tracking and related craving and further *ad libitum* consumption may be useful.

1.5.5 Sign-Tracking: What are the Causes?

Overall, tracking behaviours possess both biological and environmental causes. Using evidence from a variety of pathways (selective breeding, employing rats from different colonies, chemogenetic manipulation etc.), it is now clear that tracking phenotypes are at least moderately heritable and can be strongly genetically influenced (via specific manipulations). Further, while there is no direct genetic evidence of sign-tracking in humans, related traits (such as risk-taking and novelty-seeking) do possess a genetic basis, and thus it seems very likely (especially given that all human behavioural traits are heritable) that human tracking behaviours are influenced by genetics.

Regarding the neurobiology of tracking, the preclinical evidence for the role of dopamine in acquisition, expression (maintenance) and the modulation of related behaviours is overwhelming. Serotonin may help to regulate sign-tracking (with depletion increasing sign-tracking), while stimulation of mu opioid receptors amplifies sign-tracking. The evidence for the role of the other neurotransmitters is as yet too tentative to make firm conclusions. These transmitters and their related receptors primarily act at the striatum (NAcc, caudate and putamen), amygdalae, VTA, thalamus, hippocampus and ventral pallidum. Additionally, human neuroscientific sign-tracking studies have shown that activity in the striatum, amygdalae, inferior frontal gyrus, intraparietal sulcus and visual cortex are associated with the presence of response-irrelevant high-reward CSs (compared to low-value or no CS), and that this activity is likely linked to dopaminergic midbrain function.

The preclinical evidence base for the influence of early life experience is mixed. Although there is relatively strong evidence that social isolation and food deprivation in adolescence can increase sign-tracking behaviours, the evidence for the influence of adolescent drug use and early life exposure to autoshaping paradigms on adult sign-tracking is quite poor (studies investigating both questions lacked appropriate controls). For humans, a

single study has provided evidence that adolescents sign-tracking to a greater extent and for longer than adults, though contrary to other studies in animals and human adults, this difference was not accounted for by differences in working memory. Amphetamine, cocaine, nicotine, and opioids appear to enhance sign-tracking in animals, while antipsychotics and ketamine impairs the sign-tracking CR. The preclinical evidence for the influence of ethanol is mixed. There are no studies to date assessing acute substance administration on sign-tracking in humans, though there is some evidence that drug abuse/dependence is associated with increased sign-tracking (though there is the problem of causal interpretation). Procedural setup when assessing sign-tracking also plays a large role in the type of tracking CR observed.

1.6 Summary & Aims

The preceding discussion has outlined sign- and goal-tracking within a learning theory framework. Evidence from pre-clinical and human research has been presented to highlight what is known about ST and GT, and also to identify existing questions. Understanding the behavioural, cognitive and neural signature of sign-tracking may further our understanding of the development of substance use disorders, identify risks for harmful substance use, and inform future treatments. The general aim of this thesis is to build on previous work in human sign-tracking (B. A. Anderson, 2016b; B. A. Anderson, Kronemer, et al., 2016; Garofalo & di Pellegrino, 2015; Le Pelley et al., 2015) and extend findings to investigate I) whether sign-tracking effects hold up using larger samples than have been used previously, II) whether sign-tracking is driven by pavlovian conditioning, III) how variations of the AST may alter sign-tracking, IV) how the AST compares to alternative methods of measuring sign-tracking, V) whether acute alcohol exposure influences sign-tracking, VI) whether the neuroscientific

results obtained so far can be replicated and extended, and VII) whether sign-tracking is associated with other individual difference measures (such as alcohol consumption and impulsivity).

Chapter Three: Investigated human sign-tracking using a variation of the AST (ASTT) on the largest sample to date. The mechanism via which sign-tracking develops (namely pavlovian learning) was assessed. Further, individual difference measures (weekly alcohol consumption, impulsivity, childhood trauma) were obtained and associations with sign-tracking assessed – these potential associations were measured in every study.

Chapter Four: Investigated the influence of two different doses of alcohol administration (0.3 g/kg vs. 0.6 g/kg) on sign-tracking expression across two experiments.

Chapter Five: Investigated the influence on sign-tracking of an ASTT which employed three (rather than the usual two) noncontingent, reward-associated distractors.

Chapter Six: Compared sign-tracking responses across three different task setups: I) ASTT (eye-tracking), II) ASTT (button-box), and III) a Pavlovian-to-Instrumental Transfer (PIT) task.

Chapter Seven: Investigated sign-tracking on the ASTT (button-box) in an fMRI design. Participants were recruited from previous studies and the stability of sign-tracking across time was assessed.

Chapter Eight: Supplementary analyses investigating the influence of potential covariates and confounds on sign-tracking.

Chapter Nine: An examination of ASTT outcome measures (e.g., a statistical assessment of whether different outcome measures correlate).

Chapter Two

General Methods

This chapter will overview equipment hardware and task and analysis software. It will detail the variation of the additional singleton task and questionnaires used throughout the thesis.

2.1 Cognitive Tasks

Multiple cognitive tasks were used across the six experiments; however, variations of the same task – the additional singleton tracking task (ASTT) – were used across all experiments. The basic version is detailed here and is referred to throughout the thesis.

2.1.1 Hardware/Software for Eye-Tracking Tasks

Inquisit 3.0.6.0: Inquisit (Millisecond Software, 2011) was used to program all tasks. Font style and size for on-screen instructions (Arial, 14pt), feedback text (Arial, 4.79% of screen size) and fixation crosses (Arial, 64pt) were kept consistent across trials, participants and tasks. All other details (unless specified) were also maintained across tasks, including the number of trials (300 per task; M. Le Pelley, personal communication, December 5th, 2013). All trials were displayed against a black background.

Eye-Tracker: In order to accurately monitor participants' eye movements, the Eye-Trac D6 (Applied Science Laboratories, Bedford, MA) was used. The sampling rate was 120Hz. Gaze direction was measured in degrees, once every 8.5ms, dwell times were defined as eye movements stable to within 1° of the visual angle for at least 100ms, and all measures were taken only in relation to areas of the screen housing the predictive CSs and OTs (i.e., the areas of interest). The ASTT and Multi-Target Tracking Task (MTTT) utilised the feedback capabilities of the eye-tracker; responses were made via eye movements, registered in real time and used to supply participants with their performance feedback after each trial.

SPSS: Various versions (versions 19.0, 22.0 and 24.0) of the Statistical Package for the Social Sciences (IBM Corp.) were used to analyse data.

Picture Editing: The creation, manipulation or customisation of the images and stimuli used in the tasks throughout this thesis were done via Paint software (Microsoft Windows, version 6.1).

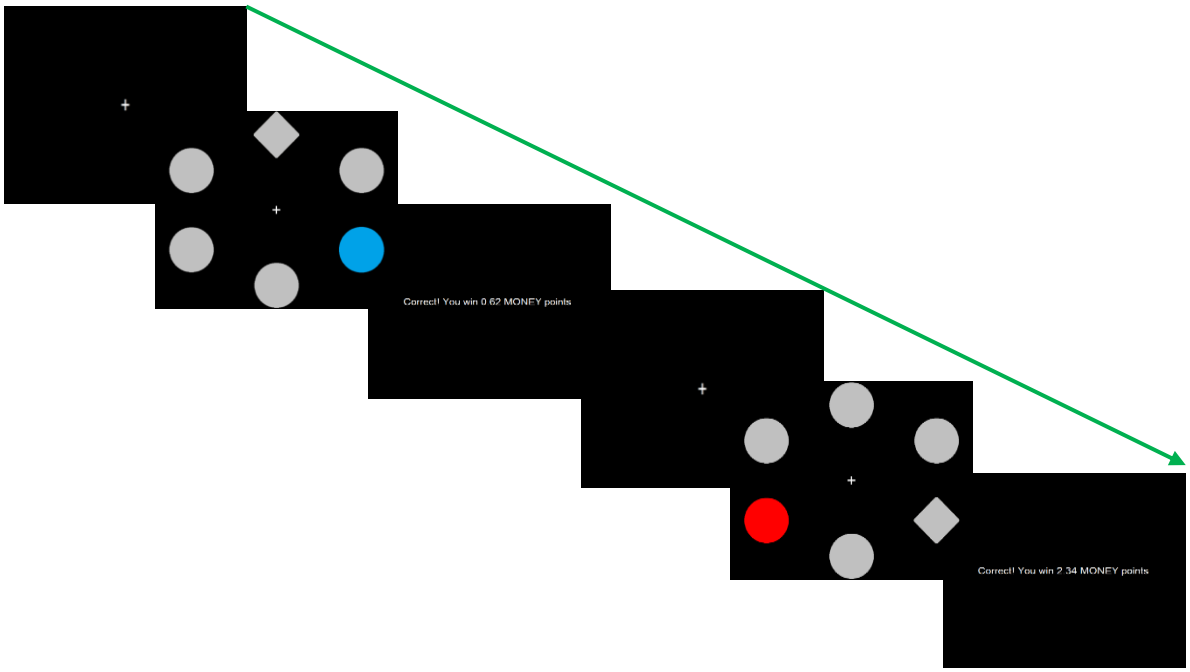
2.1.2 Additional Singleton Tracking Task (ASTT)

The ASTT is an adaptation of the additional singleton task (AST) (Theeuwes, 1991, 1992, 2010). Each trial presents a fixation cross in the centre of the screen for the entire trial; after 800ms six shapes (all 240×240 pixels) appear in a circular formation around the screen's outer edge and remain for 2000ms or until a response is recorded. On each trial, participants are instructed to look for the single grey diamond shape (outcome target; OT) while ignoring the circles. No button-pressing is required during the task, responses are given solely via eye gaze. Of the circles, four are grey and one is coloured (red or blue; conditioned stimuli, CSs). The coloured circles are paired with either high or low reward. That is, they alert the

participant to how many points can be earned on that trial (if they correctly respond to the OT). However, CSs confer a loss of points if looked at directly. Participants are motivated to locate the diamond OT quickly and ignore the circles. Looking at the grey circles slows their RT to the OT, reducing potential points gained. Looking at either of the CSs results in point deductions. Participants are told their points tally upon task completion is converted into extra voucher rewards.

It is important to note that most (if not all) prior research using a variant of the AST first trains participants to associate colours with rewards by having them explicitly orient their attention towards those colours in order to gain reward (B. A. Anderson, 2013, 2015a; Le Pelley et al., 2016). After this training phase the test phase requires participants to ignore these colours and focus on finding the shape singleton (or some other feature). That is, previous target colours are now acting as distractors. These versions are in contrast to the version used throughout this thesis (the ASTT). The ASTT never uses a training phase to instil associations and participants are *never* required to respond to the coloured CSs. Instead, explicit instructions are given and implicit associations are learned over time via the feedback participants receive on trials containing different distractors (high- versus low-value). See Figure 2.1 for a representation of the ASTT.

Figure 2.1 Pictorial demonstration of two consecutive trials of the ASTT (one low-value [blue], one high-value [red])



Fixation cross = 0-2000ms; shape stimuli (OT [diamond], CSs [red/blue] and neutral [grey] distractors) = 800-2000ms (or until participant response); feedback trials = 2000-4200ms. *Note.* Here, blue trials = low-value trials and red trials = high-value trials.

Correct responses triggered the immediate end of the trial and were met with positive feedback "*Correct! You win xxx MONEY points*" (where "xxx" represents a numeric value) on a continuous scale, calculated via the following formula

$$(1000 - RT) \times .002 \times \textit{reward value}$$

where *RT* is reaction time (in milliseconds) and *reward value* equals 1 or 10 (depending on trial type – low [e.g., blue CS] or high [e.g., red CS]). On high-value trials participants could win a maximum of 20.00 'money points', while this was reduced to 2.00 'money points' for low-value trials. Responses to the coloured distractors (CSs) also triggered the end of the trial but produced negative feedback "*Incorrect! You lose 5 MONEY points*", while responses to the grey circles produced no immediate feedback, but failure to make any subsequent OT

response again produced negative feedback. Feedback was presented for 1500ms[11]. CS colour-reward contingencies were counterbalanced across participants and six practice trials were completed prior to three-hundred experimental trials. The task lasts 21 minutes.

Sign-tracking is inferred from I) slower responses to the OT on high-value compared to low-value trials, and II) greater omissions (CS responses) on high-value compared to low-value trials. See Appendix A for calculations of outcome variables.

2.2 Questionnaires

The same questionnaire pack was used across all six experiments (with some alterations, see footnotes). Therefore, each self-report questionnaire is described below. These questionnaires were chosen based on previous research (animal and human) suggesting links between tracking behaviours and various individual differences (e.g., substance use habits [including risky substance use], impulsivity, early trauma etc.) (B. A. Anderson et al., 2013; B. A. Anderson, Kronemer, et al., 2016; Belin, Belin-Rauscent, Everitt, & Dalley, 2016; Flagel, Akil, et al., 2009; Garofalo & di Pellegrino, 2015; T. E. Robinson et al., 2014; Tomie et al., 2008).

TimeLine FollowBack (TLFB; Sobell & Sobell, 1992)

Using a diary format, the TLFB measures daily alcohol consumption over the previous two weeks. Daily estimation methods have been shown to offer a range of advantages over

[11] The ASTT used in Study 1 (Chapter Three) differs from the rest with respect to the duration of feedback trials. The Study 1 ASTT presented feedback trials for 1500ms, however all subsequent ASTTs presented feedback for 2200ms (to ensure the participant had adequate time to process the information).

Quantity-Frequency estimates (Sobell & Sobell, 1995 [in Allen & Columbus]), and the TLFB itself is a well-established measure of past consumption (Sobell, Maisto, Sobell & Cooper, 1979; Sobell, Sobell, Khajner, Pavon & Basian, 1986). Evidence suggests that the general public has poor awareness of how many alcohol units their drinks contain (Das et al., 2014; White et al., 2005; YouGov survey, 2008 [in House of Commons Health Committee, 2010, p. 59]). Participants were therefore asked to write down, as accurately as possible, every alcoholic drink they had consumed over the previous fortnight, including the brand wherever possible (to determine Alcohol By Volume, ABV). An online alcohol unit calculator (Drinkaware, 2013) was used to compute mean weekly alcohol unit consumption (1 unit = 8 g alcohol) and binge frequency (≥8 units for men and ≥6 units for women per drinking episode) (Reinert & Allen, 2007)[12]. A 'typical week' measure was also taken when participants struggled to remember the previous fortnight or when consumption during this time period was atypical (i.e., unusually heavy or light).

Alcohol Use Questionnaire (AUQ; Mehrabian & Russell, 1978)

The AUQ is a quantity-frequency index of alcohol consumption. The version employed here utilising only some aspects of the AUQ, including questions regarding units consumed per hour, age at first drink, age at which regular drinking began, total number of times being drunk in the previous six months ('drunk frequency'), and the estimated percentage of drinking occasions in which one gets drunk ('drunk percentage').

[12] Note that in the United Kingdom these recommendations have recently been changed, with a binge now considered to be the consumption of >6 alcohol units in one occasion for both men and women (Department of Health, 2016). However, all studies have analysed binge scores based on the old criteria (≥8 units for men, ≥6 units for women).

The Alcohol Use Disorders Identification Test (AUDIT; Saunders, Aasland, Babor, De la Fuente & Grant, 1993)

Originally developed as a clinical tool, the AUDIT is a ten-item scale. The first three questions relate to quantity and frequency of alcohol use, and the remaining 7 assess behaviours associated with drinking and its consequences. Scores range from 0 (minimum) to 40 (maximum). In men, a score of 8 or above is used to signify hazardous alcohol use, while a score of 5 or above is used for women. The AUDIT has good internal consistency as a single factor when used in university students (Cronbach's α = .82, Shields, Guttmanova & Caruso, 2004), and in more broad populations a meta-analysis by Reinert and Allen (2007) showed that it possesses good internal reliability (median reliability coefficient = .83), test-retest reliability (mean interclass correlation coefficient, ICC = .860), as well as construct and criterion validity.

Modified Drinking Motives Questionnaire – Revised (Modified DMQ-R; Grant, Stewart, O'Connor, Blackwell, & Conrod, 2007)

A self-report questionnaire consisting of 28 items, this version is a compilation of Grant et al's five-factor *Modified Drinking Motives Questionnaire* and Cooper's (1994) *Drinking Motives Questionnaire: Revised* (M DMQ-R). Grant et al (2007) found that their social subscale (Cooper, Russell, Skinner and Windle, 1992) is less reliable than Cooper's revised version (Cooper, 1994), thus recommend a combined version of the scale. The scale is divided into 5 factors: *Social*, *Conformity*, *Coping-anxiety*, *Coping-depression* and *Enhancement* motives for alcohol use. Higher scores on a particular subscale indicate greater motivations to drink for that particular reason. The questionnaire's subscales perform well on measures of internal

consistency (ranging from α = .61 to α = .91) and test-retest reliability (ICC = .610 to .780; Grant et al., 2007). Furthermore, various subscales have been shown to predict alcohol-related behaviours (Grant et al., 2007; Mezquita et al., 2011). Each item is assessed on a five-point frequency scale (*Almost Never/Never*, *Some of the time*, *Half of the time*, *Most of the time*, *Almost Always/Always*)[13].

The Brief Young Adult Alcohol Consequences Questionnaire (B-YAACQ; Kahler, Strong, & Read, 2005)

A self-report questionnaire consisting of 24 items designed to assess a full range (from low severity to high) of alcohol-related problems in the past year. For example, it assesses significant alcohol consequences, including regretted experiences (impulsive acts, social misbehaviour), highly risky experiences (significant blackouts, driving while impaired), impaired functioning (missed classes, loss of energy), and difficulty limiting drinking. The remaining seven items reflect increased social impairment (poor work/school performance, neglected obligations, interpersonal problems), significant longer-term physical consequences of drinking (being overweight from drinking, worse physical appearance), and finally indications of significant physiological dependence (e.g., needing a drink upon wakening; Kahler et al., 2005).

Higher scores indicate an increased tendency towards high risk situations regarding alcohol use. Item-severity estimates ranged from -3.16 to 2.50, suggesting that items cover a comprehensive spectrum of severity of alcohol problems. The B-YAACQ also highly

[13] It should be noted that in Study 1 (Chapter Three) a four-point scale was used (*Never/Almost Never, Sometimes, Often, Almost Always/Always*). Some of the items were also worded slightly differently (e.g., item 7 in the Grant et al. (2007) paper reads "To be sociable", while item 7 in Study 1 read "Because it makes social gatherings more fun"). These updates were made in subsequent studies.

correlates with its larger parent form, the YAACQ (r = 0.95), has similar internal consistency (α = .83 vs α = .89) and is similarly associated with frequency of alcohol consumption (r = .350 and r = .360; Kahler et al., 2005). The B-YAACQ is rated dichotomously (yes/no)[14].

Alcohol Purchase Task (APT; Murphy & MacKillop, 2006)

A behavioural-economic questionnaire that assesses individuals' demand for alcohol consumption at the moment of the task. Participants are asked to imagine 'one drink' as a typical pint of beer, glass of wine, shot of spirit (with/without mixer) before being instructed to "*Imagine that you and your friends are at a bar from 9 p.m. to 2 a.m. to see a band. The following questions ask how many drinks you would purchase at various prices.*" (Murphy & MacKillop, 2006, p. 221).

The scale consists of 25 items (as opposed to the 14 items of the original) and price ranges extend from *£0* to *£15* (Amlung, Acker, Stojek, Murphy & MacKillop, 2012). The construct of relative reinforcing efficacy (RRE) is used to assess alcohol demand via 5 metrics: (a) *Breakpoint*: first price at which consumption is zero; (b) *Intensity of demand – Observed*: consumption at minimum price (i.e., free); (c) *Elasticity of demand*: sensitivity/change in demand as price increases; (d) P_{max} – *Observed*: price of each drink at O_{max} (i.e., price at which drink expenditure is maximised); (e) O_{max} – *Observed*: maximised total expenditure on a single purchase.

[14] The version of the B-YAACQ employed in Study 1 (Chapter Three) rated responses on a four-point scale (Never/Almost Never, Sometimes, Often, Almost Always/Always) rather than dichotomously. This rating scale has been shown to be less reliable (Kahler et al., 2005). Additionally, the B-YAACQ instructional set asks participants to respond only if they have experienced the situations *in the past year*; the version used in Study 1 did not include this instruction. These updates were made in subsequent studies.

For (c) *Elasticity of Demand*, values were calculated using the equations below (Hursh, Raslear, Shurtleff, Bauman, & Simmons, 1988; Hursh & Silberberg, 2008)

$$1n\ Q = 1n\ L + b(1n\ P) - aP,$$

where *1n* equates to a log transformation, *Q* is quantity consumed, *L* is consumption at "unrestricted access" (i.e., free), *b* is the declining slope of the demand curve after a miniscule increase in price (in this case, the difference in consumption between unrestricted access [free] and the first increase in price [£0.01]), *P* is price, and *a* is the rate of decline of consumption (*b*) as a function of *P* (for every unit increase). Elasticity (*e*) can then be derived via:

$$e = b - aP$$

Thus, *b* and *a* are fixed parameters for each demand curve, meaning that *e* changes as a linear function of *P*. Individual elasticity is derived for each price, and an overall measure of *e* is calculated as the mean of these values for each participant, with greater negative values indicative of greater price sensitivity/elasticity (Jacobs & Bickel, 1999).

Finally, APT indices seem to be reliably associated with actual alcohol use behaviours and characteristics. In a study of nearly 5000 people, Intensity of Demand was found to be correlated with alcohol use, alcohol use disorder (AUD) criteria, and number of consequences. O_{max} was also correlated with alcohol use (Bertholet, Murphy, Daeppen, Gmel, & Gaume, 2015). Additionally, a recent meta-analysis has shown APT measures are correlated with alcohol-related problems and drinking behaviours, with the Intensity of

Demand index predictive of heavy alcohol use and predictive of alcohol use disorder symptoms (Kiselica, Webber, & Bornovalova, 2016)[15].

Barratt's Impulsivity Scale (BIS–11; Patton, Stanford & Barratt, 1995)

A self-report questionnaire comprised of 30 items assessing trait-like impulsivity. Each item is assessed on a four-point frequency scale (*Never/Rarely, Occasionally, Often, Almost Always*) and scores range from 30 to 120, with higher scores indicating higher impulsivity. Scores below 52 indicate overly-controlled individuals, while scores above 71 indicate highly impulsive individuals. The BIS–11 contains 6 first-order factors (attention, motor, self-control, cognitive complexity, cognitive instability, and perseverance) and 3 second-order factors (motor, attentional, and non-planning impulsiveness). Throughout this thesis, only a total score and second-order factors are used. A review of the literature in which the majority of participants were university students revealed a robust internal consistency (α = .83) and test-retest reliability (r_s = .83) (Stanford et al., 2009).

Impulsive Sensation-Seeking Scale (ImpSS; Zuckerman, Kuhlman, Joireman, Teta, & Kraft, 1993)

A subscale of the Zuckerman-Kuhlman Personality Questionnaire III (ZKPQ III) which assesses sensation seeking and impulsivity traits. The version employed here utilises a four-point rating scale (*Very False for Me, Somewhat False for Me, Somewhat True for Me, Very*

[15] Alcohol Purchase Task measures were only included in Study 1 (Chapter Three) as all subsequent studies obtained questionnaire measures online before participants attended the laboratory. Given this, APT measures may not be validly associated with task (ASTT) measures as they are temporally distal.

True for Me) for each of the 19 items. The scale consists of 11 sensation-seeking items and 8 impulsivity items. The items on sensation seeking assess 4 components: *Thrill and Adventure Seeking* (TAS: desire to engage in [physically] risky activities), *Experience Seeking* (ES: tendency for novelty seeking*)*, *Disinhibition* (Dis: propensity to seek sensation via activities such as attending parties, social drinking and sex*)*, and *Boredom Susceptibility* (BS: intolerance for repetitive activities of any kind) (Zuckerman, 1994). Across multiple experiments, the ImpSS scale acquired an average internal consistency of α = .80 (rounded up; Zuckerman et al., 1993).

Child Abuse and Trauma Scale (CATS; Kent & Waller, 1998; Sanders & Becker-Lausen, 1995)

A self-report questionnaire that assesses negative childhood experiences, especially in relation to parental (and general familial) abuse. Each of the 38 items is measured on a five-point frequency scale (*Never*, *Rarely*, *Sometimes*, *Very Often*, *Always*) ranging from 0-4. Sanders and Becker-Lausen (1995) identified 3 subscales: negative home environment and/or neglect (14 items), punishment (6 items) and sexual abuse (6 items). Subsequently, Kent and Waller (1998) identified another subscale: emotional abuse (7 items). The internal reliability of the subscales ranges from α = .61 to α = .88, with the overall scale producing α = .90. Finally, the CATS correlates with ratings of depression (r = .36) and anxiety (r = .409; Kent & Waller, 1998).

2.3 Additional Research Aspects

There are aspects of work undertaken that will not be discussed in the remainder of the thesis. However, they are briefly outlined here as they formed part of the PhD process and give context to some aspects of the thesis.

2.3.1 Equipment Maintenance and Repair

The running of experiments throughout this thesis required familiarity with technologies to the point of being able to setup and maintain the equipment, while also repairing any hardware or software problems that arose. All experiments except one utilised eye-tracking technology. The ASL Eye-Trac D6 (Applied Science Laboratories, Bedford, MA) was employed in five of the six studies contained in this thesis. Six months in total (spread over two years) was spent improving the performance of, maintaining and repairing the Eye-Trac D6.

The only experiment which did not use eye-tracking technology was Study 6 (Chapter Seven). Repair of the previously defunct ASL Eye-Trac 504 with Long Range Optics (R-LRO6 – XG) (Applied Science Laboratories, Bedford, MA) for use inside an fMRI scanner took three months. However, though the equipment now works, the spatial and temporal resolution of the eye-tracker was still too poor for use on the ASTT. Thus, for Study 6 a button-box was used to record responses. The Gazepoint GP3 Desktop eye-tracker (Gazepoint Research Inc., Canada) was also set up, but not used for various reasons.

2.3.2 Study 7

Given the importance of determining whether ST and GT are differentially associated with AUDs, a study was developed to compare ASTT performance between patients diagnosed with an alcohol use disorder with an age- and gender-controlled sample of social drinkers. The process of setting the study up (including obtaining NHS ethical approval and arranging recruitment procedures with the Alcohol Service department of the Royal Liverpool University Hospital) took approximately fourteen months. However, there was continued difficulty in recruiting patients, and after several months only one patient had been tested. Given that the study required a sample of 30 patients and 30 matched controls, a decision was made to cancel the study. This provided the opportunity to run studies 4 and 5 (Chapters Five and Six), which focus on testing predictions made based on earlier findings (Study 4) and to replicate previous research and ensure the methodological rigor of the ASTT (Study 5).

Chapter Three

Human Sign-Tracking: A Large-Scale Investigation in Social Drinkers

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3.1 Abstract

Background: Research has noted similarities between sign-tracking – valuing conditioned stimuli (CS) as if they were unconditioned stimuli (US) – and indicators of substance use in animals. Goal-tracking – utilising CSs only for their predictive value – has also been linked to excessive consumption. *Aims:* To identify associations between tracking outcomes (measured via validated and novel eye-tracking tasks) and independent outcome measures (e.g., drinking habits). *Methods:* Social drinkers (N = 98) completed the tasks, in which CSs predicted whether high- or low-value USs were available, and were instructed to locate the US and ignore CSs. Individual measures of drinking behaviours, outcomes, and risk factors for hazardous consumption were measured via questionnaires. *Results:* Tracking behaviours were identified only via the validated task. Sign-tracking was indicated by slower RTs to the US and greater omissions on high-value compared to low-value trials. Tracking was not associated with individual differences. *Conclusions:* Using translational methods, human sign-tracking was distinguished from goal-tracking in the largest study to date. However, predictions of an association between tracking and individual differences were unsupported. This may highlight differences across preclinical and human research, and suggests a complex relationship between value attribution and behaviour.

Keywords: Sign-tracking, Goal-tracking, Alcohol, Attentional bias, Eye-tracking

3.2 Introduction

Sign-tracking (the attribution of incentive salience towards noncontingent, discrete conditioned stimuli [CSs]) and goal-tracking (using such CSs to predict the onset of reward, attributing incentive value only to contextual cues) have been associated with substance-use behaviour in animals. Although it is unclear how these learned behaviours may be associated with alcohol consumption in humans, it has been suggested that the value attributed to a stimulus is important (Field et al., 2016; Rose, Brown, Field, & Hogarth, 2013). It is also known that stimuli which individuals value attract greater attention, which can be observed via eye-tracking paradigms that measure attentional bias (AB) (Field & Cox, 2008). General substance AB measures are associated with self-reported craving and impulsivity (Field et al., 2009; Leung et al., 2017) and may be clinically relevant for certain groups (Luijten, Field, & Franken, 2014; Marissen et al., 2006). In the wider, non-clinical population, substance users also show enhanced AB towards substance-related stimuli compared to nonusers (Field et al., 2016). Taken together, AB seems to provide a measure of current value. It is therefore reasonable to assume that eye-tracking tasks can be utilised to determine whether the incentive value (as measured by AB) of either irrelevant discrete CSs (sign-tracking) or outcome targets (OTs) (goal-tracking) is associated with heavier drinking and/or risk factors for hazardous use.

Preclinical studies using a range of paradigms have shown that a variety of species sign- and goal-track and that this tracking behaviour is associated with various traits, states and outcomes, including risk factors for substance misuse (Meyer, Lovic, et al., 2012; T. E. Robinson et al., 2014; Saunders & Robinson, 2013; Tomie et al., 2008). In humans, various cognitive tasks have been used to investigate sign-tracking, typically by measuring participants' propensity to attend to response-irrelevant, discrete cues which have been paired

with reward outcome. The assumption is that humans attend to stimuli that hold incentive value, and the literature showing the effect of value on attention is now quite large (B. A. Anderson, 2013, 2015a, B. A. Anderson et al., 2013, 2011a, 2011b; B. A. Anderson, Kronemer, et al., 2016; B. A. Anderson & Yantis, 2012, 2013; Bucker, Silvis, Donk, & Theeuwes, 2015; Bucker, Belopolsky, & Theeuwes, 2014; Bucker & Theeuwes, 2014; Failing & Theeuwes, 2014, 2015; Hickey et al., 2010b; Hickey, Chelazzi, & Theeuwes, 2014; Jahfari & Theeuwes, 2016; Le Pelley, Mitchell, & Johnson, 2013; Le Pelley et al., 2015; Munneke, Hoppenbrouwers, & Theeuwes, 2015; Pearson et al., 2015; Roper et al., 2014; Sali et al., 2014; Theeuwes, 2010; Theeuwes & Belopolsky, 2012; Wang et al., 2014).

Although several theoretical links have been made between sign-tracking and addiction (Garofalo & di Pellegrino, 2015; Le Pelley et al., 2016, 2015; Tomie et al., 2008), only two studies so far have explored this link in humans. The first administered the additional singleton task (AST) to a group of opioid-dependent patients and a group of healthy controls (B. A. Anderson et al., 2013). They found that, even though all participants actively sign-tracked towards the discrete, response-irrelevant CSs, patients' sign-tracking was significantly greater than controls'. Furthermore, patients scored significantly higher on impulsivity measures than controls, a characteristic believed to be a risk factor for harmful drinking (Verdejo-García, Lawrence, & Clark, 2008) (though this was not significantly correlated with sign-tracking). The second study again administered the AST, this time to a sample of HIV+ individuals (B. A. Anderson, Kronemer, et al., 2016). The authors found that sign-tracking was related to substance abuse history and non-planning impulsiveness in the year leading up to patients' HIV+ diagnosis.

Several preclinical studies have also investigated the link between sign-tracking and alcohol. Some studies show a positive relationship between sign-tracking and consumption (R. I. Anderson & Spear, 2011; Tomie, Sparta, et al., 2002; Tomie, Wong, et al., 2003),

others show that alcohol consumption reduces sign-tracking (Versaggi et al., 2016), and others still that sign-trackers (STs) do not consume more alcohol than goal-trackers (GTs) but that an alcohol CS acts as an effective conditioned reinforcer in STs but not GTs (Villaruel & Chaudhri, 2016). No study has performed a similar experiment concerning alcohol use in humans. The current study will investigate – for the first time – whether any link exists between sign-tracking and alcohol use in humans. This study will therefore supply original translational data, bridging the gap between the animal and human literatures.

The most prolific tasks used to measure sign-tracking in humans are variants of the AST (Theeuwes, 1991, 1992). In a training phase, participants are instructed to attend to certain colours, with different colours associated with different levels of reward. In a subsequent test phase, these colours are used as distractors, impeding participants' new goal of finding the outcome target (typically a shape or colour which has not been paired with reward). Sign-tracking is identified via slower responses to the OT and a greater number of omissions (mistaken responses to the CSs) on trials containing a high-value CS as opposed to a low-value CS (or compared to trials containing no CS). The ability of reward-associated cues of different value to manipulate attention to different extents is referred to here as value-modulated attentional capture (VMAC) (Le Pelley et al., 2016). In a series of three experiments, Le Pelley et al. (2015) showed that high-value CSs elicit more omissions and slower OT responses than low-value singletons, that these attentional responses are automatic (as they are in direct conflict with goal-driven selection), and that these findings are most plausibly explained by pavlovian conditioning (as omissions were never rewarded). However, as the authors themselves acknowledge, alternative interpretations allow for an instrumental conditioning aetiology.

The vast majority of studies employing the AST (B. A. Anderson et al., 2011a, 2011b; Chelazzi et al., 2013; Donohue et al., 2016; Failing & Theeuwes, 2014, 2015; Kiss et al.,

2009; Le Pelley et al., 2015; Theeuwes, 2010; Theeuwes & Belopolsky, 2012) succumb to the potentially confounding effects of selection and reward history effects, in that the CSs were previously response-relevant (*selection history*) and CS responses directly resulted in a rewarding outcome (*reward history*). Due to these factors, pure sign-tracking effects cannot be obtained. Only three studies have removed these confounding factors using an altered version of the AST with no training phase, and all studies still observed a sign-tracking effect (Failing et al., 2015; Le Pelley et al., 2015; Pearson et al., 2015). However, all of these studies contained the alternative problem of providing categorical – rather than continuous – rewards. This is an issue because, as noted by Le Pelley et al. (2015), this allows for the opportunity of 'covert distractor shifts' towards the CS, before an 'overt' shift towards the OT is made, which still results in a rewarding outcome. This means that attentional shifts towards the CS are indirectly rewarded via superstitious conditioning (Skinner, 1948)[16]. It is also important to know that in the studies above, overt oculomotor capture by the CSs only resulted in no rewards being gained – no rewards were ever rescinded.

In the current study (and throughout the thesis) a novel variant of the AST – henceforth the additional singleton tracking task (ASTT) – is used. In the ASTT, participants only ever respond to the OT, and on every trial one of two coloured CSs predict high or low reward given an OT response. Both selection and reward history effects are prevented by using CSs which participants are never instructed to respond to, and which are never rewarded. Further, the use of continuous (rather than categorical) rewards which are tied to OT reaction times (RTs) means that covert distractor shifts result in a loss of rewards, and are therefore deterred (importantly, participants are told this explicitly in the instructions, as well as learning via experience and feedback). Thus, this study is investigating automatic oculomotor capture

[16] However, as Le Pelley et al. (2015) observe, such a *'covert bias produces oculomotor bias' argument'* is vulnerable to a negative feedback loop, whereby instrumentally-driven covert distractor-shifts would in turn be instrumentally extinguished when overt oculomotor capture by the CS inevitably occurred.

towards CSs which have *always* been response-irrelevant, which incur a direct loss of rewards when attended to, and which can therefore only be plausibly produced by pavlovian – not instrumental – conditioning.

In addition to the ASTT, a second, novel task, termed the multi-target tracking task (MTTT) is used. This task also utilises eye-tracking and requires participants to first learn a series of CS-US (colour-reward) contingencies for a range of rewards (chocolate, alcohol, nothing [control]), before being instructed as to the CS-OT (colour-target) contingencies. Participants are then presented with each CS in the presence of multiple OTs and are instructed to disengage from the CS as quickly as possible and find the *corresponding* OT (e.g., focus on the left OT when presented with the chocolate CS, the right OT when shown the alcohol CS etc.). Sign-tracking should be observed via slower initial disengagement from the reward CSs compared to the control CS as well as a greater number of CS reengagements.

We hypothesised that sign-tracking and goal-tracking tendencies would be measurable via task performance. For the ASTT, we predicted that high-value CSs would capture more attention (as shown by slowed OT RTs and increased CS omissions) than low-value CSs. For the MTTT, we predicted that reward-associated cues would capture more attention (indicated by slowed RT to disengage from the CS and increased reengagement with the CS) than neutral cues. Given previous pre-clinical results showing links between risk factors for harmful drinking (e.g., impulsivity, early trauma etc.) and sign-tracking, we also hypothesised that sign-tracking would positively correlate with self-report measures of drinking, impulsivity and childhood trauma. Finally, we hypothesised that individuals' extent of sign-tracking would correlate between tasks.

3.3 Method

Participants

One-hundred and three participants were recruited via opportunistic sampling, many via university and social media (e.g., Facebook) advertisements. Of 103 participants, 3 were excluded due to missing data and 2 were removed due to lack of ability to follow task instructions; 98 (55 female) remained for analysis. All remaining participants were aged between 18 and 35 years (M = 23.61, SD ± 4.22). The inclusion criteria were regular consumption of alcohol (10 units or more per week) and chocolate (consumed at least once per week), and normal or corrected-to-normal vision. Self-reported past or present alcohol or drug use problems were exclusions. All participants provided written informed consent before taking part in the study, and were debriefed upon completion. The study was approved by the University of Liverpool Research Ethics Committee. All were debriefed upon completion.

Materials

Questionnaires

The questionnaires used in this study are described in detail in General Methods (Chapter Two). The following questionnaires are used here to measure I) *Drinking habits*: TimeLine FollowBack (TLFB), Alcohol Use Questionnaire (AUQ) and the Alcohol Use Disorders Identification Test (AUDIT), II) *Motivations to drink*: Modified Drinking Motives Questionnaire – Revised (M DMQ-R), III) *Consequences of drinking*: Brief Young Adult Alcohol Consequences Questionnaire (B-YAACQ), IV) *Baseline relative reinforcing effect of alcohol (i.e., demand for alcohol)*: Alcohol Purchase Task (APT), V) *Impulsivity:* Barratt's Impulsivity Scale – 11 (BIS-11) and Zuckerman's Impulsive/Sensation-seeking Scale (ImpSS), VI) *Childhood trauma*: Childhood Abuse and Trauma Scale (CATS).

Cognitive Tasks

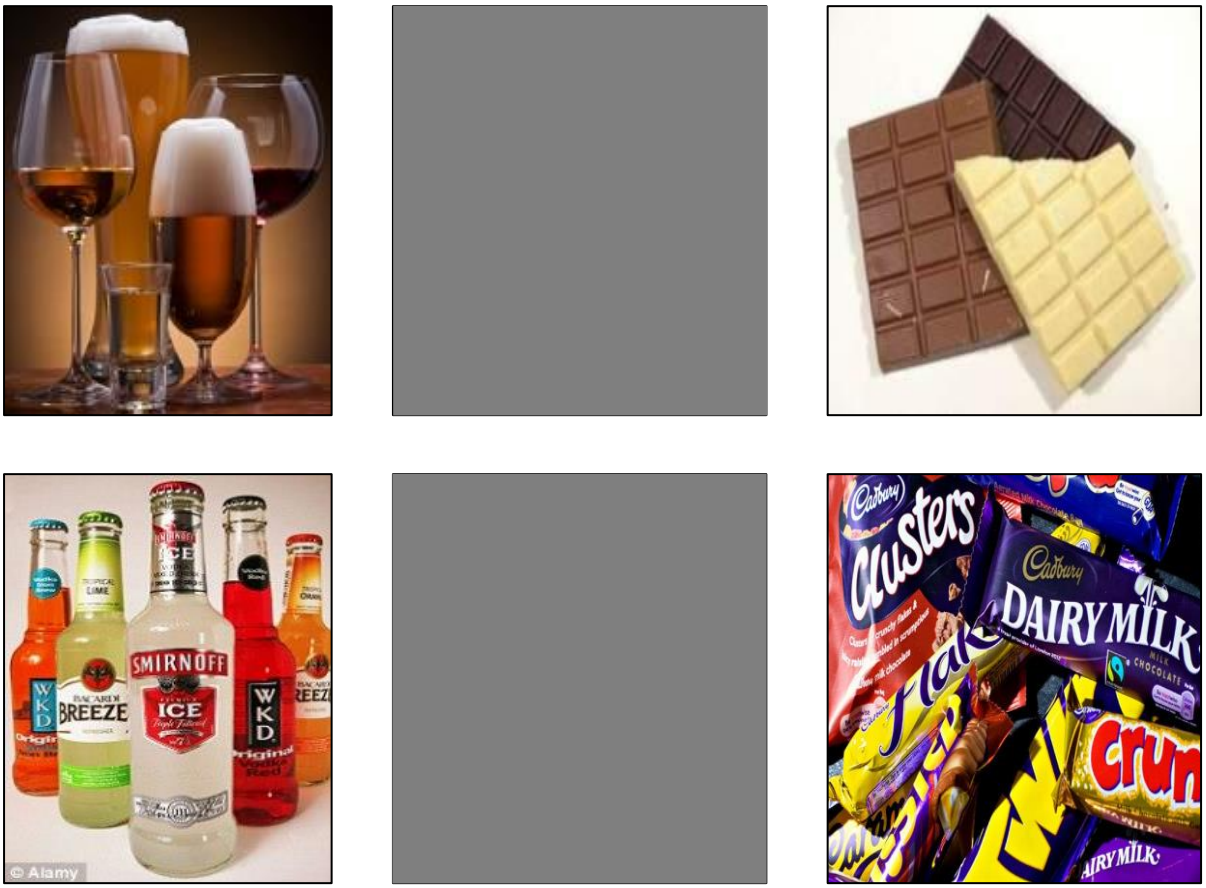
Additional Singleton Tracking Task (ASTT): The ASTT is described here only briefly, for further details, see Chapter Two (General Methods). The 2 CSs (coloured circles; red and blue) were chosen so as to not contaminate any previous, or subsequent, colour associations formed in the MTTT. The task was developed by Theeuwes (1991, 1992), adapted for use in previous experiments (Gaspar & McDonald, 2014; Le Pelley et al., 2015), and is adapted still further here to produce the variant referred to as the ASTT. Six practice trials were completed prior to 300 true trials. Each trial presented a fixation cross in the screen's centre for the entire trial. After 800ms, six shapes appear in a circular formation around the screen's outer edge and last for 2000ms or until a response is recorded. Feedback lasted 1500ms. Participants' goal was to find the diamond shape and ignore the five circles (one of which was red or blue). Engaging the coloured CSs resulted in a deduction of points. High-value trials rewarded correct responses with up to 20 'money' points, low-value trials with up to 2 'money' points (See Chapter Two for further details on feedback calculation and presentation). The task took approximately 21 minutes to complete.

Sign-tracking was measured as I) RTs towards the OT being slower on high-value trials relative to low-value trials and II) omissions (or overt oculomotor capture by the CS) being higher on high-value trials relative to low-value trials. It was hypothesised that I) sign-trackers and goal-trackers could be distinguished based on task performance, and II) sign-tracking would positively correlate with self-report measures.

Multi-Target Tracking Task (MTTT)

Conditioning Phase: Three CSs (pink, yellow and green circles; *visible size*: 165×175, given in pixels) were constructed. These colours were chosen so as not to conflict with the colours used in the ASTT (red and blue). Twenty images from the internet were adjusted for size, shape and other attributes – images presented in portrait were 235×300 (300×235 for landscape) – and were split equally between reward types (i.e., 10 alcohol-related images, 10 chocolate-related). The final image was a grey rectangle (neutral stimulus, 400×224). It should be noted that, though the pixel sizes of the reward/neutral and CS stimuli are different, they appear perceptually identical on screen. The images were chosen due to their potential for widespread appeal. That is, most images contained multiple kinds of each reward type (e.g., alcohol: various beers, wines, and spirits; chocolate: white, dark, bars and cakes. See Figure 3.1). This was done in an attempt to present participants with at least one reward they desired in each category. Finally, reward images were divided into a 50:50 ratio of 'unbranded' – alcohol already poured into a glass, chocolate already unwrapped – and 'branded' – presented in branded wrappers and receptacles – rewards. The distance between the centre points of paired images was 130mm.

Figure 3.1 Examples of the reward stimuli used in the Conditioning Phase of the MTTT

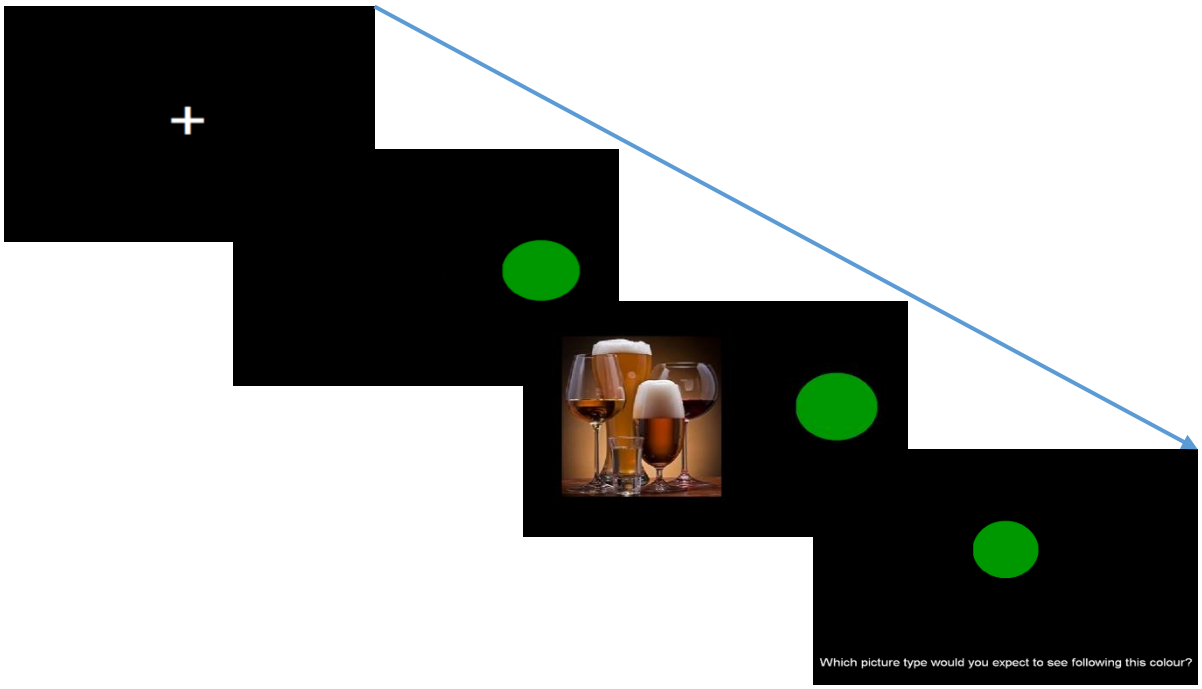


Top: unbranded; *bottom*: branded. *Left*: alcohol, *centre*: neutral; *right*: chocolate.

Participants were instructed to pay careful attention to the colour-reward contingencies as they would be questioned on them at the end of the task (contingencies were counterbalanced between participants). This stage contained 60 trials: 10 images of alcohol, 10 of chocolate and 10 of the neutral stimulus in a random order, each paired with a different coloured CS. Each individual reward picture was presented twice, each time in a different way: I) presented side-by-side with the CS, and II) located behind the CS (only appearing after the CS had vanished). These two pairing techniques were used to avoid unintentionally training participants to look towards or away from CSs when reward stimuli were presented, as this would mimic tracking behaviour and thus may have affected responses on the task.

Each trial lasted 6000ms – a fixation cross was presented in the screen's centre for 1000ms before the CS was presented, followed 1000ms later by the reward stimulus. In all, the CS-reward pair was presented for 4000ms. At the end of this phase participants were presented with three trials, each presenting a CS and asking which reward type they would expect to be shown next (contingency-awareness check). Answers were recorded – if participants answered incorrectly, they would be asked the questions again verbally, and this was repeated until all answers were correct. This phase lasted 5 minutes; see Figure 3.2 for a pictorial demonstration of the Conditioning Phase.

Figure 3.2 Pictorial demonstration of the Conditioning Phase of the MTTT



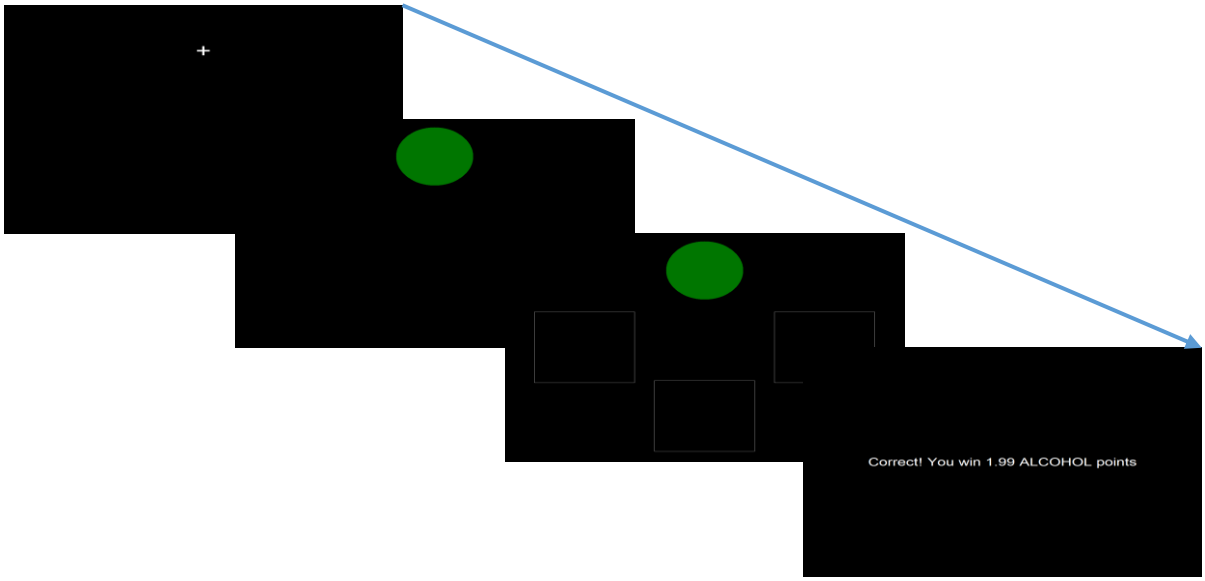
Fixation cross = 0-1000ms; CS = 1000-2000; reward stimulus = 2000-6000. In all, the stimulus pair is present for 4000ms. The trial depicts a green CS paired with alcohol. The final trial depicts one of three questions asked at the end of the Conditioning Phase (contingency-awareness test). (Trials where reward images appear *behind* CSs are not shown.)

MTTT Testing Phase: The 3 CSs used in the Conditioning Phase were used again, except the images were slightly larger (250×264) to cater for the different onscreen setup. A fixation cross was used, as well as a black square with a white outline (328×320) which functioned as the outcome target (OT); this square was duplicated to produce 3 spatially distinct but identical OTs. This task was developed by the authors (as was the Conditioning Phase).

Participants completed 9 practice trials, before 300 true trials; the task was divided into three sections: I) main task (150 trials), II) contingency booster session (30 trials), and III) main task (150 trials). The booster session was integrated to ensure that participants' awareness of the contingencies was still in place, and consisted of a repeat of the Conditioning Phase (with only half the number of trials), including the contingency-awareness check. In the main task, participants' aim was to respond as quickly as possible to the presentation of the CS by looking at the appropriate OT. First, a fixation cross was shown for 500ms before being replaced by the CS. Then, 300ms after the onset of the CS, three OTs appeared for 2200ms. The CS and OTs remained on screen for 2200ms while eye-movements were recorded. Feedback trials lasted 1500ms (see Figure 3.3).

For some participants, a green CS required them to look to the bottom-centre OT, a yellow CS to the bottom-left, and a pink CS to the bottom-right, while others received different instructions based on counterbalancing procedures. The positioning of the CS and OTs were also counterbalanced – half of participants were presented with the CS at the top and OTs at the bottom (as in Figure 3.3), while the other half viewed the reverse. OTs were spatially staggered so as to avoid unnecessary errors from eye-tracker calibration discrepancies – staggering the OTs creates greater spatial distinction, thereby reducing mistaken "omissions" caused by stimuli being too near together. All trials lasted 3000ms, regardless of participants' responses.

Figure 3.3 Pictorial demonstration of a single trial of the MTTT



Fixation cross = 0-500ms; CS = 500-800; OTs = 800-3000. In all, the CS-OT pair is present for 2200ms.

Participants were told that points earned could be exchanged for real alcohol and chocolate which was on display in the lab. After each trial participants were given feedback – correct responses elicited "*Correct! You win xxx ALCOHOL/CHOCOLATE points*" (where "xxx" represents a numeric value from 0-2.00). Incorrect responses (i.e., looking at the wrong OT, or at no OT) triggered "*Incorrect! You lose 5 ALCOHOL/CHOCOLATE points*" (reward name was dependent on trial type). Feedback after neutral trials presented participants' speed: "*Correct, Your Reaction Time was yyy*" (where "yyy" represents speed in milliseconds), or "Incorrect!" after incorrect responses. All feedback was presented in plain, white text and feedback points were calculated as

$$(1000 - RT) \times .002$$

where RT is reaction time on that particular trial (Le Pelley et al., 2015). Feedback was thus continuous and dependent on participants' response times. For this task, sign-tracking

behaviour was inferred from I) slower disengagement from the CS, II) greater fixation duration (gaze dwell time [GDT]) on the CS and less on the OT, and III) greater numbers of individual fixations on the CS (signifying return gazes after previously fixating on the OT or elsewhere). Conversely, goal-tracking was inferred via faster CS disengagement, minimal CS GDT and fewer fixations on the CS. The testing phase lasted approximately 26 minutes.

Regarding rewards specifically, it was expected that I) GDT bias would be greater for reward-paired CSs compared to neutral-paired CSs, that II) RT bias would be greater for reward CSs than neutral CSs (i.e., taking longer to disengage from reward CSs compared to neutral CSs), that III) omission (error) bias (i.e., looking at the wrong target square) would be greater towards reward OTs than the neutral OT. It was hypothesised that I) sign-trackers and goal-trackers would be distinguishable via task performance, and that II) sign-tracking would correlate with self-report measures of drinking behaviour, impulsivity and childhood trauma.

Task design features

As already noted, these tasks must be designed carefully and with the results of past research in mind. Following advice from Awh et al. (2013), both tasks were designed to I) vary stimuli presentation on a trial-by-trial basis to prevent selection history effects (sequential priming), and II) keep target stimuli (OTs) perceptually distinct from CSs in both shape and colour. Crucially, the perceptual features of the CSs are *never* directly implicated in reward; responses towards the CSs (or delayed disengagement from them) cause, at best, reduced reward earnings and, at worst, the subtraction of points from one's tally. Finally, regarding stimuli salience, although all CSs (distractors) are more perceptually salient than all targets, all CSs are counterbalanced between participants and analyses will look to investigate

the influence of physical salience (regardless of value) on attentional capture (see Chapter Eight).

Procedure

All testing took place between the times of 1 p.m. and 8 p.m. in the eye-tracking laboratory of the School of Psychology, University of Liverpool. After reading the Participant Information Sheet and signing the Consent Form, participants were informed that their performance on the tasks determined how many extra payment vouchers (ASTT) or alcohol/chocolate (MTTT) they would receive upon study completion. To make this believable the lab contained alcohol (beers, wines and ciders) and chocolate (Dairy Milk, Mars, Snickers etc.), which were visible to participants. Participants then sat at a chinrest in front of a computer (approximately 23 inches from the monitor) ready to begin the first task. Once eye movements were calibrated participants were given instructions, with further verbal clarification from the researcher if needed. Participants then completed the tasks, taking approximately five minutes in between for a break. Task order was counterbalanced between participants.

Following completion of both tasks, participants completed 8 self-report questionnaires. Given the sensitive and potentially upsetting nature of the *Child Abuse and Trauma Scale* (CATS), this was administered last. Before participants were compensated – £15 in high street shopping vouchers – and debriefed they were asked if they believed they would receive alcohol, chocolate, and extra monetary rewards. Responses were recorded before participants were informed they would not receive any alcohol or extra monetary rewards (but that they may take some chocolate if they wished). Each session lasted approximately 1hr 30m.

3.4 Data Reduction and Analysis

The following are an extension of measures that have been used in previous research in estimating attentional bias and stimulus value (Christiansen, Mansfield, et al., 2015; Field, Mogg, & Bradley, 2005; Rose et al., 2013). For the MTTT, all fixations were defined as a stable eye movement within one degree of the visual angle for 100ms or longer (Jones et al., 2012). For the ASTT all RT responses <80ms and >999ms were recoded as missing data. Latencies of less than 80ms are often regarded as anticipatory in visual perception research (Walker, Walker, David, Husain, & Kennard, 2000), and is the cut-off used in previous studies using an almost identical task (Le Pelley et al., 2015; Pearson et al., 2015). The 999ms upper limit was chosen due to the distractions present during the task (i.e., the CSs), which by design increase RT, and was thought of as less restrictive compared to the upper limit of 500ms used in comparative studies (Le Pelley et al., 2015; Pearson et al., 2015). This was not done for the MTTT as participants may sometimes have, theoretically, been so distracted by the CS that their RT was ≥1000ms. Likewise, some participants may have been so disinterested in the CS that, upon OT onset, their eye movements began not on the opposite side of the screen but very near the OT, making RTs of interest ≤100ms possible.

Task Outcome Measures

MTTT: Due to the novelty of this task, an exploratory approach was taken in its analysis and measures were divided into response frequencies, RTs and gaze dwell times. This resulted in a total of 42 potential outcome measures (see Table A1, Appendix A), 18 of which were used in the final analysis. RTs and gaze dwell times are further divided into bias scores for

statistical analysis. For RT Bias, larger (negative) values indicate greater sign-tracking (for example, slower RTs to the alcohol OT compared to the other OTs, suggests greater distraction by the alcohol CS), while larger (positive) values indicate greater goal-tracking. For GDT Bias, larger (positive) values indicate greater bias – greater OT bias reflects goal-tracking, while greater CS bias indicates sign-tracking.

ASTT: Measures for the ASTT were those used by Le Pelley et al. (2015) and were divided into omissions and RTs (no dwell time calculations were possible as participant responses prompted the immediate end of trials). For both Omission Bias and RT Bias, greater (positive) values indicate sign-tracking (as high-value distractors should induce more errors and slower responses to the OT than low-value distractors; see Table A2, Appendix A for calculations).

3.5 Results

Participant Characteristics

Table 3.1 summarises the sample's average alcohol use characteristics, while Table 3.2 provides an overview of trait and state measures. Men were most likely to binge 2 times per fortnight (30.2% of the sample), women 3 times per fortnight (29.1%). Most participants (84.7%) scored ≥8 on the AUDIT, classing them as at-risk drinkers. Self-reports showed that, overall, the participant population were hazardous drinkers, consuming over recommended weekly guidelines (14 units per week for men and women). A recent meta-analysis on APT indices shows Intensity of Demand (IoD) to be the measure with the largest relation to alcohol consumption and the best predictor of alcohol use disorder symptoms (Kiselica et al., 2016). The average (M = 5.36, SD ± 5.12) for the IoD measure is somewhat smaller than that of

previous work (*M* = 8.68; 7.12) (Bertholet et al., 2015; Murphy & MacKillop, 2006), suggesting that alcohol has a lower reinforcing efficacy in current sample (i.e., the current sample desires less alcohol when the alcohol is free).

A majority (64.3%) of participants scored <5 on the B-YAACQ: Total, with 86.7% scoring <10. Participants with a score of 5 have a 79% chance of having done something embarrassing while drinking, a 23% chance of having done something impulsive that they regret, and a 6% chance that drinking harmed their work life, while the respective numbers are 94%, 56% and 22% for participants with a score of 10 (Kahler et al., 2005). In terms of personality variables, most participants scored within the normal ranges of the scales (e.g., 57.4% scored within the BIS-11 range of normality [scores 52-71]; the ImpSS average was almost identical [*M* = 9.00] to that found previously in undergraduates [*M* = 9.50] [Ball, 1995]). The CATS: Total average (*M* = 0.86) was also similar to that of earlier work in nonclinical samples (*M* = 0.74; 0.77) (Kent & Waller, 1998; Sanders & Becker-Lausen, 1995), and suggests low levels of childhood trauma.

Table 3.1 Alcohol use characteristics (Means ± SD)

Alcohol unit consumption (TLFB)	21.90 (± 13.10)
Binge frequency	2.50 (± 1.60)
AUQ: Units consumed per hour	4.27 (± 2.06)
AUQ: Age at first drink	14.24 (± 2.35)
AUQ: Age at regular drinking	17.28 (± 1.76)
AUQ: Drunk frequency	25.51 (± 19.29)
AUQ: Drunk percentage	58.93 (± 29.53)
AUDIT	12.65 (± 5.58)

Consumption = UK units (1 UK unit = 10 ml or 8 g of pure alcohol); *TLFB* = TimeLine FollowBack, based on an average of the prior two weeks of alcohol consumption; *AUQ* = Alcohol Use Questionnaire; *Binge frequency* = ≥8 units for men, ≥6 units for women per day, based on an average of the prior two weeks of alcohol consumption; *Age at regular drinking* = the age at which regular drinking was undertaken; *Drunk frequency* = number of times individuals have been drunk in the previous 6 months; *Drunk percentage* = percentage of drinking occasions in which individuals become drunk; *AUDIT* = Alcohol Use Disorders Identification Test.

Table 3.2 Trait/State characteristics (Means ± SD)

BIS-11: Total	63.59 (± 12.76)
B-YAACQ: Total	4.23 (± 4.07)
ImpSS	10.05 (± 3.93)
APT: IoD	5.36 (± 5.12)
CATS: Total	0.86 (± 0.50)

BIS-11 = Barratt's Impulsivity Scale; *B-YAACQ* = Brief Young Adult Alcohol Consequences Questionnaire; *ImpSS* = Impulsive Sensation Seeking; *APT: IoD* = Alcohol Purchase Task: Intensity of Demand; *CATS* = Child Abuse and Trauma Scale. *Note.* An *M DMQ-R: Total* variable was not computed as the questionnaire's subscales qualitatively conflict (e.g., coping versus enhancement); thus, a total score would be interpretively useless.

Multi-Target Tracking Task

Response frequencies, RTs and GDTs towards OTs are shown in Table 3.3, while Table 3.4 shows frequencies and GDTs towards the CSs.

Table 3.3 Correct and incorrect OT response frequencies and durations (Means ± SD)

Outcome Measure	*Frequencies*	*RTs*	*Gaze Dwell Time*
Correct alcohol OT responses	170.85 (± 75.67)	226.79 (± 133.33)	1248.64 (± 631.40)
Correct chocolate OT responses	169.78 (± 80.50)	226.72 (± 105.06)	1209.89 (± 619.34)
Correct neutral OT responses	162.03 (± 80.95)	225.72 (± 101.84)	1177.02 (± 700.99)
Error alcohol OT responses	17.66 (± 37.17)	-	23.30 (± 54.85)
Error chocolate OT responses	27.19 (± 56.53)	-	35.40 (± 92.40)
Error neutral OT responses	21.01 (± 34.73)	-	25.38 (± 39.28)

Each outcome measure's fixation frequency, RT and gaze dwell time are shown here. For RTs and gaze dwell time, values are milliseconds. No RT data are given for error responses – the variables were not calculated due to their irrelevance to any measurable tracking behaviour. OT = Outcome Target.

Table 3.4 CS response frequencies and durations (Means ± SD)

Outcome Measure	*Frequencies*	*Gaze Dwell Time*
Alcohol CS responses	52.58 (± 65.98)	252.14 (± 472.41)
Chocolate CS responses	58.96 (± 71.46)	260.20 (± 440.93)
Neutral CS responses	77.99 (± 95.38)	366.10 (± 564.75)

Each outcome measure's fixation frequency, RT and gaze dwell time are shown here. For gaze dwell time, values are milliseconds. No RT data is presented as responses follow a path *from* the CS *to* the OT; thus, RT data can be gleaned from Table 3.3's Correct OT responses. CS = Conditioned Stimulus.

ANOVAs were conducted to assess responses to stimuli for the MTTT. Bonferroni was consistently chosen as a confidence interval adjustment.

Reaction Times: Due to extreme outlying RT values, 7 participants were removed; thus, $N = 91$ for the following analyses. Repeated-Measures ANOVAs showed no differences in RT Bias between the 3 OTs (regardless of whether the response was correct or incorrect). As sphericity was violated, X^2 (2) = 15.99, $p = .001$, the Huynh-Feldt correction was used ($\varepsilon = .87$), $F(1.75, 157.29) = .07$, $p = .92$, $\eta_p^2 = .001$.

Gaze Dwell Time: Regardless of whether gaze responses were correct or incorrect, Repeated-Measures ANOVAs showed no differences in fixation durations between the 3 OTs, $F(2, 194) = .31$, $p = .74$, $\eta_p^2 = .003$ or the 3 CSs, $F(2, 194) = 1.34$, $p = .26$, $\eta_p^2 = .01$.

Frequencies: Regardless of whether responses were correct or incorrect, Repeated-Measures ANOVAs showed no differences in overall fixation frequencies between either the 3 OTs, $F(2, 194) = 1.14$, $p = .32$, $\eta_p^2 = .01$, or the 3 CSs, whose assumption of sphericity was violated, X^2 (2) = 10.12, $p = .006$, forcing the use of the Huynh-Feldt correction ($\varepsilon = .93$), $F(1.85, 179.53) = 2.399$, $p = .10$, $\eta_p^2 = .02$.

Omissions: Repeated-Measures ANOVAs were conducted to assess whether any differences existed in the number of omission fixations made towards specific OTs (e.g., looking at the alcohol OT on a neutral trial). Since sphericity was violated, X^2 (2) = 9.68, $p = .008$, the Huynh-Feldt correction was applied ($\varepsilon = .93$). No differences between reward-specific omission fixations were found, $F(1.86, 180.23) = 1.08$, $p = .34$, $\eta_p^2 = .01$.

No hypotheses regarding the outcomes of the MTTT were supported by these data, suggesting that the MTTT task cannot reliably identify or measure sign-tracking. Further analyses were conducted to evaluate a post-hoc hypothesis as to why the task failed to capture tracking behaviour (see Appendix B).

Additional Singleton Tracking Task

Table 3.5 shows average response frequencies towards the OT and CSs. Analyses investigated whether any RT and/or omission differences existed between high- and low-value trials.

Table 3.5 Response frequencies (Means ± SD)

Outcome Measures	*Frequencies*
OT	282.03 (± 11.61)
High-value distractor	7.13 (± 7.37)
Low-value distractor	3.90 (± 3.41)

Each outcome measure's fixation frequency is presented. OT = Outcome Target. *Note.* Frequencies do not add up to 300 (total number of trials) as these descriptives do not include non-responses.

Reaction Times: A Paired-Samples *t*-test revealed that, on average, RTs were slower on high-value (M = 358.27, SD ± 36.59) compared to low-value trials (M = 353.21, SD ± 35.28), and this difference was statistically significant, $t(97) = 3.19$, $p = .001$, $r = .31$ (1-tailed).

Omissions: A Wilcoxon Signed-Rank test revealed differences in the number of omissions made on high-value versus low-value trials, with significantly more errors being made on high-value (*Mdn* = 5.00, *range* = 0-31) compared to low-value trials (*Mdn* = 3.00, *range* = 0-18), $T = 864.00$, $p < .0001$, $r = .40$ (1-tailed).

Associations with Individual Differences

Correlations were conducted between task outcomes (MTTT and ASTT) and self-report measures (e.g., alcohol consumption, impulsivity etc.). The correlation matrix is presented in Table C1 (Appendix C). After appropriate statistical corrections were applied, of the 407 correlations performed, no analysis reached statistical significance.

Sign-Trackers versus Goal-Trackers

Analyses were performed on participants deemed sign-trackers (STs) and goal-trackers (GTs) in the ASTT. The 25 participants with the largest positive RT Bias and the 25 with the largest negative RT Bias were selected as STs and GTs, respectively. The other 48 participants were designated as members of an intermediate group (intermediate trackers, ITs)[17]. RT Bias scores were used as a metric of tracking behaviour as omissions were rare, potentially making the measure less reliable.

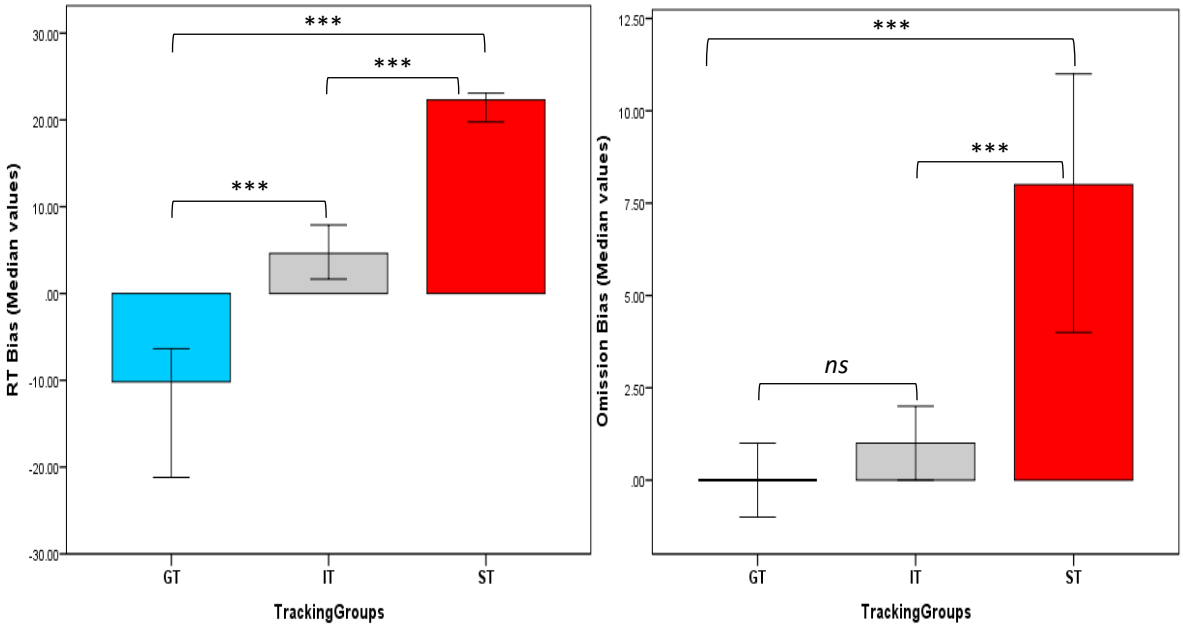
Reaction Times: A Mixed-ANOVA was conducted with trial type (high/low) included as a within-subjects factor and tracking group (STs/GTs) as a between-subjects factor. A main effect of trial type was found, with OT RTs larger on high-value trials (M = 366.42, SD ± 41.91) than low-value (M = 361.25, SD ± 39.55), $F(1, 48) = 14.97$, $p = .0003$, $\eta_p^2 = .24$, but no main effect of tracking group, $F(1, 48) = 0.51$, $p = .48$, $\eta_p^2 = .01$. There was, however, an interaction, $F(1, 48) = 202.17$, $p < .0001$, $\eta_p^2 = .81$. Planned comparisons revealed that, as expected, STs' OT RTs were larger on high-value (M = 379.94, SD ± 45.07) compared to low-value (M = 355.74, SD ± 42.85) trials, $t(24) = 13.17$, $p < .0001$, $r = .94$ (1-tailed). GT's responses showed the converse, with OT RTs higher on low-value (M = 366.75, SD ± 35.98) compared to high-value (M = 352.90, SD ± 34.28) trials, $t(24) = -7.12$, $p < .0001$, $r = .82$ (2-

[17] ITs are not included in analyses here, but are presented via analyses on bias scores shown in Figure 3.4.

tailed). Thus, STs showed a large sign-tracking RT effect in the expected direction (*high* > *low*), and GTs showed an almost equally large effect in the opposite direction (*low* > *high*).

Omissions: Analyses were conducted as above. There was a main effect of trial type, with more omissions on high-value (M = 8.92, SD ± 8.10) compared to low-value (M = 4.42, SD ± 3.47) trials, $F(1, 48) = 22.69$, $p < .0001$, $\eta_p^2 = .32$, but no main effect of tracking group, $F(1, 48) = 3.60$, $p = .06$, $\eta_p^2 = .07$. There was, however, an interaction, $F(1, 48) = 22.29$, $p < .0001$, $\eta_p^2 = .32$. Planned comparisons revealed that, as expected, STs produced more omissions on high-value (M = 12.40, SD ± 8.58) compared to low-value (M = 3.44, SD ± 2.65) trials, $t(24) = 5.51$, $p < .0001$, $r = .75$ (1-tailed). GTs' omission did not differ between high-value (M = 5.44, SD ± 5.93) and low-value (M = 5.40, SD ± 3.94) trials, $t(24) = 0.04$, $p = .97$, $r = .008$ (2-tailed). Thus, STs showed a large sign-tracking omission effect in the expected direction, while GTs showed no effect. Results for both RTs and omissions are graphically summarised via difference (bias) scores in Figure 3.4.

Figure 3.4 Bar charts showing group differences in RT Bias (*left*) and Omission Bias (*right*)



GT = Goal-trackers; IT = Intermediate-trackers; ST = Sign-trackers. ***$p < .0001$, *ns* = non-significant. Medians (95% CI).

Whether STs and GTs differed in their trait and state characteristics was investigated with a series of Welch's *t*-tests[18] and a Chi Square test for gender. After corrections, no differences were found. All analyses are presented in Table C2 (Appendix C).

3.6 Discussion

This study explored whether sign-tracking and goal-tracking – cognitive reward-processing types seen across a range of nonhuman animal species – could be identified in humans in the largest sample to date by using two eye-tracking tasks (one validated, one novel). The study

[18] As opposed to the more typical Independent-Samples *t*-test, Welch's test is much more robust against violations of homogeneity of variance, gives the same results when variances are equal and can be used to investigate samples of different sizes (Ruxton, 2006). Effect size (Cohen's d_s) is calculated by square-rooting the *F* statistic, which gives identical results to calculations which use the commonly used *t* statistic (via an Independent-Samples *t*-test). As such, Welch's *t*-tests shall be used where possible throughout this thesis.

also aimed to determine whether tracking behaviours correlate with alcohol use and risk factors for misuse and dependence. It was hypothesised that the tasks would allow for the identification of sign-tracking and goal-tracking behaviours, and that some individuals would produce such consistent tracking behaviours that they could be categorised into specific tracker types. It was further predicted that sign-tracking would correlate with risk factors for alcohol abuse (e.g., high impulsivity, childhood trauma), as well as with generally higher levels of alcohol consumption and other measures of alcohol use (e.g., AUDIT score, binge frequency etc.)

Results were mixed. The novel Multi-Target Tracking Task (MTTT) was unable to measure sign-tracking and thus will not be discussed further. Conversely, the Additional Singleton Tracking Task (ASTT) allowed for the identification and statistically significant separation of individuals based on their tracking behaviours. However, no task measure significantly correlated with any self-report measure, and no group differences in such measures were observed after *post-hoc* corrections were applied.

The ASTT is a variant of a validated task adapted from Le Pelley et al. (2015), who showed how external reward structures can produce maladaptive behaviours (i.e., behaviours which conflict with one's goals) in student samples. The current study is a conceptual replication of one of their studies (Le Pelley et al., 2015, Experiment 3) with slight alterations to the task. Specifically, the ASTT contained no distractor-absent trials, presented participants with continuous – not categorical – reward feedback, distractors were 100% – not 80% – predictive of reward type, and omissions caused a deduction of points rather than simply negating the winning of points. Despite these differences their results were replicated here. The changes were implemented to narrow the theoretical interpretations of results; specifically, these alterations prevent selection and reward history effects from confounding

interpretations of the sign-tracking effect. The possibility of sign-tracking resulting from instrumental conditioning was also constricted by removing any potential rewarding outcome for attentional capture by distractors (including covert distractor shifts). The current study therefore provides additional support for pavlovian conditioning being responsible for the development of sign-tracking, as opposed to response-driven, instrumental learning. Specifically, this replicated previous results which show that the important aspect of a stimulus in such paradigms is the extent to which it *signals* reward/value, not the extent to which it allows one to *acquire* rewards (Failing et al., 2015; Le Pelley et al., 2015; Pearson et al., 2015).

The findings that RTs were slower on high-value compared to low-value trials and that omissions followed the same pattern – even though both CSs captured saccadic RTs with the same 'force' (see Chapter Nine) – also replicated the work of Le Pelley et al (2015). This suggests that CSs which predict higher available rewards can capture attention even when this means the reward will not only be lost, but also when points previously earned are actively deducted. Another result replicated here was that of RTs in relation to response type: omission (CS) RTs were significantly quicker than correct (OT) RTs (see Chapter Nine). This indicates that omissions are more likely the result of automatic, reflexive saccades, and that correct responses are the result of top-down, conscious deliberation. This result may reveal a distinction between endogenous and exogenous influences on attention (i.e., goal-driven versus stimulus salience).

Effect sizes (ESs) between current results and that of Le Pelley et al. (2015) differed slightly; they found mostly large effect sizes and the current study mostly medium-to-large. Given the calculation of Cohen's *dz* (Pearson's *r* was used in the current study),

$$dz = t/\sqrt{n}$$

where *t* is the t value and *n* the sample size, if ESs are converted this study still produces a much more modest effect size estimate (d_z = .33). However, the generated effect size would have been more comparable (d_z = .65) if our sample size (*N* = 98) had been equal to Le Pelley et al's (*N* = 24). Using a common language effect size, the current data suggest that after controlling for individual differences, the likelihood that a person will produce slower OT RTs on high-value trials compared to low-value trials is 63%. It is also worth noting that, while the average difference in OT RT between high- and low-value trials in this study was 5ms, a gap of 13ms was found in Le Pelley et al's (2015).

Contrary to preclinical (Meyer, Lovic, et al., 2012) and previous human results (B. A. Anderson, Kronemer, et al., 2016), sign-tracking did not correlate with self-reported measures of alcohol use or any other trait/state variables associated with hazardous drinking behaviour. This could be due to the high quantity of correlations which, after familywise corrections, rendered the alpha levels too low to accommodate the effect sizes that would have been expected. It could also be due to the likelihood that humans (compared to animals who have been bred specifically for experimental purposes) are less likely to show robust phenotypes. As there is theoretical rationale for testing these associations – and given future studies within this body of research will test these associations in different samples – this series of studies will retain the questionnaires used.

Tracking types were determined by selecting participants with the highest (STs) and lowest (GTs) RT Bias scores. This method was chosen over using Omission Bias due to the infrequency of omissions across the sample (*Mdn* = 4.00, *range* = 0-19.50, out of 300 trials). Additionally, the moderate-large positive association found between both bias types (see Figure 9.1, Chapter Nine) indicates that either type of bias may be a reasonable basis for selecting STs and GTs. Notably, this bias correlation was larger for the tracking groups than

in the general sample (r_s = .56 versus r_s = .47, respectively), suggesting that increased sign-tracking occurs via both slowed RTs and greater omissions towards high-value distractors.

Regarding the comparison of tracking groups, GTs (*M* = 2105.90) were more successful (earned more points) than STs (*M* = 2015.40), as one would expect. While no differences were found in *overall* RTs (ruling out any fundamental speed differences between them), differences between groups in OT RTs were found on high-value trials, with STs being slower than GTs, but not on low-value trials. This finding extends observations in the animal literature showing STs to be significantly more distracted by reward-paired cues (Flagel, Robinson, et al., 2010; Flagel et al., 2007; Tomie et al., 2008), as well as human studies showing that the value of such cues is integral to their ability to distract (Le Pelley et al., 2013; Le Pelley et al., 2015). Additionally, current results replicate those in the animal literature showing that the presence of an irrelevant, discrete, reward-paired CS (in this case, the high-value CS) can increase OT/US latency in some individuals (STs) while decreasing it in others (GTs) (Meyer, Lovic, et al., 2012). Moreover, while tracking groups did not differ in their omissions rates towards low-value CSs (or in the number of overall omissions), STs did make significantly more high-value CS omissions than GTs. This finding also has support from the animal literature: ST animals make more CS (lever/light) contacts than GT animals, even when the actual reward (US/OT) is concurrently available (Meyer, Lovic, et al., 2012).

Interestingly, the pattern of omission results on low-value trials trends towards significance in the *opposing* direction. That is, STs (*Mdn* = 3.00) actually produced only half the number of omissions as GTs (*Mdn* = 6.00) on low-value trials. The most plausible explanation for this finding appears to have nothing to do with GTs being any more distracted on low-value trials than high value. Rather, it seems that STs are much *less* distracted on low value compared to high-value trials (while GTs' levels of distraction are maintained across

trials) that this difference becomes statistically significant. This is borne out by the data which show that GTs' omissions stay quite constant across trial types (high value: *Mdn* = 4.00; low value: *Mdn* = 6.00), while ST's omissions drastically inflate from low- (*Mdn* = 3.00) to high-value trials (*Mdn* = 12.00). This pattern is also reflected in OT RTs given STs' (*Mdn* = 344.95) inclination to be quicker than GTs (*Mdn* = 367.08) on low-value trials. This suggests that STs' attention is captured even *less* than GTs' on low-value trials, effectively making their behaviour appear goal-oriented – relative to GTs – in situations where the potential outcome (US) is low and so the predictive cue (CS/distractor) is also considered to be of low value.

Furthermore, STs (*Mdn* = 275.25) and GTs (*Mdn* = 290.29) did not significantly differ in their RTs towards CSs in general. This is contrary to findings in the animal literature which show that STs produce faster 'omissions' (i.e., approaches towards the CS) than GTs, essentially reversing findings of RT responses towards the OT (Flagel et al., 2010, 2007). However, it should be noted that these results are in line with human studies of sign-tracking (Le Pelley et al., 2015). The null findings, however, could simply be a result of the lack of possible CS RT variability, given that preclinical CS periods last a lot longer (typically around 8s) than human participants' reactions in the ASTT allow (typically <1s). One way to test whether STs produce faster omissions towards CSs of different value is by using a task which employs more than two CSs of value. This would allow for greater potential variability in responses (See Study 4 [Chapter Five] in which this hypothesis is tested).

The current study contains several potential limitations, as well as differences to preclinical studies, which could explain the lack of associations between tracking and individual differences. The reasons could lie either with the sample, or the questionnaires. Regarding the sample, participants were mostly university students with weekly drinking

habits ranging between 1-7 drinking episodes per week, binges between 0-4 times per week and weekly unit consumption ranging from 4-92[19]. Self-reports showed that, overall, the participant population were hazardous drinkers, consuming over recommended weekly guidelines (14 units per week for men and women). Though the majority of participants displayed hazardous drinking, it is possible that an even more risky population (e.g., patients with alcohol use disorders [AUDs]) would be needed to observe an association between tracking and alcohol consumption (see below). Most participants fell within the normal ranges of consequences of drinking, impulsivity and childhood trauma measures, which again may display a lack of extreme traits necessary to observe the link between tracking and individual differences.

One major difference between investigating these associations in human versus nonhuman animals is that preclinical paradigms often breed specimens for study over several generations. This selective breeding is used to magnify the traits of study and thus are likely to amplify not only tracking behaviours, but also any related traits (such as impulsivity). This is especially true given that tracking phenotypes are heritable, meaning that tracking and any associated traits may be genetically linked (Campus et al., 2016; Flagel, Clark, et al., 2011; Meyer, Lovic, et al., 2012; Pitchers et al., 2015). Analogous work in humans which recruited individuals from populations which tend to show extreme traits (e.g., HIV+ patients) has found links between value-modulated attentional capture (VMAC), non-planning impulsiveness and visual working memory capacity (B. A. Anderson, Kronemer, et al., 2016). Additionally, work has also shown that opioid-dependent patients show greater VMAC than controls, and this VMAC was also negatively associated with visual working memory

[19] Note that the lower end of this range (4) is lower than the study's lower limit for alcohol consumption in the inclusion criteria (10). This criteria cannot apply to every single week since participants began drinking alcohol. Thus, some participants (9.8%) happened to have consumed fewer than 10 units in one or both of the weeks prior to testing, despite typically consuming ≥10.

capacity (though not with impulsivity) (B. A. Anderson et al., 2013). More work in this area and with larger sample sizes is needed. Alternatively, other paradigms could be utilised to assess consumption in the laboratory, allowing for the direct correlation between controlled ad-lib consumption (e.g., Jones, Cole, Goudie, & Field, 2011) and tracking behaviours.

Regarding the questionnaires used, there were several oversights concerning the wording of some questions and scales (e.g., for the M DMQ-R a four-point scale was used instead of the five-point used in previous research). This was due to older versions being used, and all subsequent studies use the most recent versions (details can be found in General Methods, Chapter Two, section 2.2). However, it should be noted that analyses revealed that these discrepancies did not significantly alter the internal consistency of the questionnaires, nor did they significantly alter participant responses, both of which were comparable to outcomes found in previous research. These results indicate that the differences in questionnaire construction are unlikely to be the cause of the lack of association between self-report and tracking measures. More likely, it is due to the sheer number of correlations (in addition to the possibility that there are no real associations to find).

In summary, most previous research regarding human sign-tracking and goal-tracking has focussed primarily on the cognitive and theoretical frameworks underpinning the phenomenon of tracking. The current study aimed to help widen the scope of such research by directly assessing whether tracking in humans is related to alcohol use and risk factors for misuse. Our results replicate previous work showing attentional capture by response-irrelevant stimuli (sign-tracking) in humans, as well as providing robust evidence that such capture is automatic/reflexive, is in opposition to one's goal-driven state, and is resistant to aversive consequences. We also provide further support that sign-tracking is driven not by instrumental conditioning, but by pavlovian processes. Our predictions that tracking would be

correlated with self-reported drinking behaviours and risk factors for harmful use (such as impulsivity) were unsupported. However, this may be because the sample tested (mainly university students) do not show extreme enough traits or behaviours (e.g., impulsivity and alcohol use). Utilising more extreme populations (e.g., AUD patients) may be more useful in examining any potential relationships there may be between tracking behaviours and alcohol use in humans.

Chapter Four

Sign-Tracking is Amplified by Acute Alcohol Consumption for Lower, but not Higher, Doses

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4.1 Abstract

Background: Sign-tracking – the persistent attribution of incentive value to discrete reward-related cues – has been demonstrated in animals and humans. Moreover, preclinical work has revealed that acute drug doses can enhance the motivational value of reward-related cues (which can be measured via attention and craving), perhaps contributing to drug-related behaviour. *Aims:* Alcohol's effect on sign-tracking was investigated in humans for the first time. *Methods:* Two experiments employed a within-subjects alcohol priming paradigm to assess if 0.3 g/kg (Exp. 1) and/or 0.6 g/kg (Exp. 2) doses of alcohol altered sign-tracking behaviour, compared with a soft drink control. Social drinkers ($n \approx 30$) were tested on two separate days during which they completed an additional singleton task, while their eye movements were monitored. *Results:* Sign-tracking was observed in all conditions across both experiments. The magnitude of sign-tracking was increased after ingestion of 0.3 g/kg of alcohol (relative to control), but was unaffected by the higher 0.6 g/kg dose. *Conclusions:* Acute administration of 0.3 but not 0.6 g/kg doses of alcohol amplifies sign-tracking in social drinkers. Sign-tracking priming paradigms may be a new avenue through which to investigate the link between incentive salience and alcohol use.

Keywords: Sign-tracking, Alcohol priming, Incentive salience, Attentional bias, Eye-tracking

4.2 Introduction

Sign-tracking (ST) develops when discrete, response-irrelevant reward-related cues (conditioned stimuli [CS]) are imbued with incentive value, while goal-tracking (GT) occurs when the same CS is used solely to predict the onset of reward (unconditioned stimuli [US]). Both ST and GT have been linked to substance-use behaviours and risk factors associated with substance use (e.g., impulsivity and risk seeking) in preclinical studies, and it has been suggested that both phenotypes confer vulnerability for compulsive behavioural disorders, such as addiction (Flagel, Akil, & T. E. Robinson, 2009). However, sign-tracking in particular has been given special attention due to the ability of discrete cues imbued with value to subsequently influence behaviour. For example, compared with GTs, ST rats exposed to a response-noncontingent cocaine-paired cue were more willing to cross an electrified floor to gain access to the cue, even in the absence of the cocaine reward (Saunders et al., 2013). Discrete, alcohol-paired cues have also been shown to act as conditioned reinforcers in STs but not GTs, with STs motivated to work harder to be presented with the alcohol-paired cue (Villaruel & Chaudhri, 2016). Further, alcohol exposure has also been shown to amplify sign-tracking in rats (Madayag et al., 2017; McClory & Spear, 2014), though results are mixed (Versaggi et al., 2016).

Sign-tracker and goal-tracker subgroups appear across a range of species (Breland & Breland, 1961), with preclinical work revealing that STs are more impulsive, show greater novelty- and sensation-seeking behaviours, poorer executive control and are more driven to seek rewards by the presence of discrete reward-paired cues than are GTs (Meyer, Lovic, et al., 2012; T. E. Robinson et al., 2014). On the other hand, GTs imbue *contextual* cues with value (e.g., the use of different cages), with such cues better suited to motivating the reinstatement of cocaine seeking in GTs compared to STs (Saunders et al., 2014). Recent

research has revealed that humans also sign-track, as measured by a variety of tasks gauging value-modulated attentional capture (VMAC) (Anderson, Laurent, & Yantis, 2011; Anderson & Yantis, 2012, 2013; Le Pelley, Mitchell, & Johnson, 2013; Le Pelley, Pearson, Griffiths, & Beesley, 2015). Importantly, due to the differences in animal and human selection for measuring tracking propensity, it is highly unlikely that tracking phenotypes of the type found in animals will be found in human lab studies. Human tracking is likely better viewed on a continuum alongside traits such as impulsivity. However, we may still be able to alter human tracking responses through various manipulations, such as alcohol priming.

The most widely used tasks to date are typically variations of the additional singleton task (AST) (Theeuwes, 1991, 1992, 2010), in which individuals respond to a target (e.g., a diamond) whilst ignoring or avoiding responses to a stimulus that was previously associated with reward (e.g., a coloured circle; CS). In a recent study similar to the one used here, participants were trained to associate one coloured circle with high reward and another with low reward. Subsequently, these circles were presented as distractors in successive trials in which participants were instructed to locate a shape singleton (a diamond) (Le Pelley et al., 2015). They found that oculomotor capture by the CS previously associated with the high-value reward was greater than for the CS associated with low reward, and this persisted despite distractor capture resulting in rewards being omitted. Such capture also occurred under shorter durations – and thus via faster saccades – than did target (diamond) responses, indicating that distractor capture was an automatic (bottom-up) process. Such sign-tracking responses also persist despite punishment and are maintained over a period of months without the need for continued reinforcement (Anderson & Yantis, 2013), which could be viewed as a similar potential risk factor for the kind of cue-modulated reward seeking seen in Pavlovian-to-Instrumental Transfer studies (Cartoni et al., 2016; Hogarth et al., 2014). Finally, human participants designated as STs (via a median split) engage in greater CS-driven reward

seeking and have higher levels of self-reported impulsivity compared to GTs (Garofalo & di Pellegrino, 2015).

In an important study, researchers compared opioid-dependent patients to healthy controls on an AST and found that, while sign-tracking was evident across the entire sample, the magnitude of sign-tracking was significantly larger in the patient group, indicating amplification of sign-tracking in addiction (B. A. Anderson et al., 2013). Results from the same group have further shown that substance abuse history is positively associated with sign-tracking (Anderson, Kronemer, Rilee, Sacktor, & Marvel, 2016). However, in both of these studies causality is impossible to ascertain; did the propensity to sign-tracking contribute to the addiction, or do the drugs enhance sign-tracking (or both)?

It is well-established that social and dependent users of alcohol and other substances show an attentional bias (AB) towards user-specific substance-related stimuli, compared to nonusers/non-consumers (for a review, see Field & Cox, 2008). These biases appear to develop over time as users learn to associate various cues (e.g., branding symbols) with reward (e.g., alcohol consumption), giving cues incentive-motivational properties that are evident in attentional processing. However, a recent critical review of AB theories suggests that perhaps the most robust (albeit weak) association to AB is an individual's current motivational state (Field et al., 2016). For instance, craving is positively correlated with AB (both of which fluctuate) for substances. Perhaps such within-subject fluctuations (e.g., before or after a priming dose) represent current incentive value and are more important than between-group differences (e.g., individuals with and without an alcohol use disorder [AUD]).

Interestingly, however, although AB and craving have been linked, alcohol priming appears to affect the two measures differently, with alcohol preloads increasing craving dose-

dependently, while affecting AB via an inverted-U association (Field, Schoenmakers, & Wiers, 2008). A recent field study – which observed a greater range of doses than had been observed previously – also showed that AB and craving respond differently to an alcohol prime. Craving was positively predicted and AB negatively predicted by alcohol dose in participants who had been binge drinking (Schoenmakers & Wiers, 2010).

Some modern theories of conditioned responding to reward-related cues focus on the attribution of incentive salience. For example, incentive sensitisation theory posits that prolonged exposure to potentially addictive substances can cause the brain's reward circuitry to become hyper-sensitised, leading to substance-related stimuli gaining motivational value and attracting attention (i.e., becoming 'wanted') (T. E. Robinson & Berridge, 2008). This sensitisation may be related to aberrant cognitive processing such as poor attentional control (as measured by visual working memory tasks) and high impulsivity, both of which are associated with increased AB towards reward-related stimuli – an account which has support in both pre-clinical and human studies (Anderson et al., 2013, 2015; Flagel et al., 2009; Tomie, Aguado, Pohorecky, & Benjamin, 2000).

Substance priming (enhanced motivation following an initial dose) promotes attentional orienting towards substance-specific (e.g., cocaine and nicotine) cues in rats (Frenk, Martin, Vitouchanskaia, Dar, & Shalev, 2017; Kawa et al., 2016) and rhesus monkeys (Reilly et al., 2016). However, preclinical studies also suggest that priming can increase incentive salience for rewards (and reward-related stimuli) more generally, known as *cross-priming*. For example, data reveal that ethanol (Tomie et al., 1998; Tomie, Festa, Sparta, & Pohorecky, 2003; however, for recent contrasting results, see Versaggi, King, & Meyer, 2016), nicotine (Palmatier et al., 2013; Versaggi et al., 2016), opiates (DiFeliceantonio & Berridge, 2012, 2016; Mahler & Berridge, 2009) and amphetamine (DiFeliceantonio & Berridge, 2016; cf. Holden & Peoples, 2010) can all prime rodents to increase sign-tracking behaviours towards

food-related CSs. Similar low-dose effects have also been reported for barbiturates and benzodiazepines (Bordi & Matthews, 1990). Importantly, recent work has also shown that nicotine injections in rats augments sign-tracking towards alcohol-related cues (i.e., it increased alcohol-seeking behaviour), while a nicotinic acetylcholine receptor antagonist blocked this effect (Maddux & Chaudhri, 2017).

In humans, Field, Mogg and Bradley (2005) found that a 0.4 g/kg dose of alcohol increased AB towards smoking cues in smokers, which is suggestive of cross-priming. Further, studies have also shown that alcohol primes can increase AB for cocaine cues in cocaine users (Montgomery et al., 2010) and increase high-calorie food intake (Caton, Ball, Ahern, & Hetherington, 2004; Christiansen, Rose, Randall-Smith, & Hardman, 2015; Schrieks et al., 2015; Yeomans, 2010), though others give a more nuanced take (Rose, Hardman, & Christiansen, 2015). Overall, these results suggest that alcohol (and other substances) may prime individuals for reward in general, rather than in a substance-specific way.

The current experiments combined the areas of attentional bias, sign-tracking and cross-priming to assess the extent to which sign-tracking persists and potentially increases following low (0.3 g/kg; Exp. 1) and moderate (0.6 g/kg; Exp. 2) doses of alcohol, compared to control beverages. The two doses were chosen as they have previously shown some contrasting results in the literature: low-moderate priming doses (e.g., 0.3-0.4 g/kg) have been found to increase AB towards reward cues (typically alcohol), while moderate-high doses (e.g., 0.6 g/kg+) do not (Adams, Ataya, Attwood, & Munafò, 2012; Christiansen, Rose, Cole, & Field, 2013; Duka & Townshend, 2004; Fernie, Christiansen, Cole, Rose, & Field, 2012; Schoenmakers, Wiers, & Field, 2008; Weafer & Fillmore, 2013); however, see (Schoenmakers & Wiers, 2010). Additionally, using low and moderate doses (with one twice the ‘strength’ of the other) also allows for the observation of how craving is affected and,

finally, how craving and AB are linked (or not) after each priming dose. It is worth noting that the studies which have shown no increase in AB after moderate-high doses typically present stimuli which correspond to the prime itself (e.g., AB towards alcohol pictures is measured after alcohol consumption), and none have yet (to our knowledge) investigated an alcohol prime's influence on AB for monetary reward.

Here we report two experiments wherein participants attended two separate laboratory sessions, during which they consumed either lemonade (control) or vodka and lemonade (alcohol). After consumption, participants completed an adaptation of the additional singleton task – the additional singleton tracking task (ASTT) – in order to assess the extent of sign-tracking. We also investigated the associations between sign-tracking (on control and priming days) and individual differences (e.g., alcohol use, impulsivity etc.). We predicted that sign-tracking would persist across all conditions (control and alcohol) in both experiments. Specifically, given the dose-dependent effects found in both human and animal research, we hypothesised that in Experiment 1 (0.3 g/kg) sign-tracking would be amplified after a priming dose of alcohol, relative to a control drink. However, no directional hypothesis was made for Experiment 2 (0.6 g/kg). Finally, exploratory analyses were conducted to further investigate the association between sign-tracking and individual differences.

4.3 General Methods

Both studies received ethical approval from the University of Liverpool's Research Ethics Council and participants provided informed consent to all parts of each study (online and laboratory).

Materials

Questionnaires

The same questionnaire pack used in study 1 was given to all participants to assess drinking habits (TLFB, AUDIT), drinking motives (Modified DMQ-R), drinking consequences (B-YAACQ), impulsivity (BIS-11, ImpSS) and childhood trauma (CATS) (see Chapter Two [General Methods] for full descriptions). In addition, scales were also used to assess subjective intoxication and desire for alcohol, before and after consuming all beverages.

Subjective Intoxication Scales (SIS; Duka, Tasker & Stephens, 1998): The SIS consists of 6 100mm VAS assessing subjective feelings of being 'light headed', 'irritable', 'stimulated', 'alert', 'relaxed' and 'contented'.

Desire for Alcohol Questionnaire – brief version (DAQ; Love, James & Willner, 1998): The DAQ consists of 14 items rated on a scale of 1 to 7, with higher scores indicating greater craving. Based on a recent Principal Components Analysis three factors are evident: 1) strong desires/intention to drink, 2) negative reinforcement, and 3) positive reinforcement + ability to control drinking (Kramer et al., 2010). Total scores are also calculated.

Cognitive Task

Additional Singleton Tracking Task (ASTT): The task employed was identical to the task used in study 1 (Chapter Three, see Chapter Two [General Methods] for full description), and is an adaptation of the singleton task developed by Theeuwes (1991, 1992, 2010). Sign-

tracking is inferred from I) slower responses to the OT on high-value compared to low-value trials, and II) greater omissions (CS responses) on high-value compared to low-value trials.

4.4 Experiment 1

Low-moderate priming doses of alcohol can increase attentional bias towards alcohol-related cues (Adams et al., 2012; Duka & Townshend, 2004; Fernie, Christiansen, Cole, Rose, & Field, 2012; Schoenmakers et al., 2008). The aim of the first experiment (Study 2) was to extend these findings to assess, for the first time, whether a 0.3 g/kg dose of alcohol magnifies attentional sign-tracking towards discrete, noncontingent CSs, compared to a control beverage.

4.4.1 Method

Participants

Thirty-four social drinkers were recruited through opportunistic sampling, via internal university and social media advertisements. Of these, one was excluded due to not understanding the instructions of the task, one due to an adverse reaction to the priming dose of alcohol, and three due to attrition. The remaining 29 participants (16 female) were aged 18-31 years (M = 21.66, SD ± 2.86). The inclusion criteria were I) regular consumption of alcohol (≥10 units per week) to ensure that all participants were familiar with drinking alcohol, would be unlikely to have an adverse reaction to the dose given, but also provided a large pool of drinking habits from which to recruit, II) normal or corrected-to-normal vision and III) the provision of a breath alcohol reading of 0.0 mg/l before study commencement.

Exclusion criteria I) were self-reported past or present alcohol or drug use problems, II) colour-blindness, III) recent or current cold and flu symptoms, IV) currently taking medications which may be affected by alcohol, V) aversion to lemonade or vodka, VI) pregnancy or breastfeeding and VII) refusal to answer questions regarding childhood trauma (due to the upsetting nature of some of the questionnaires given).

Design

This study used a within-subjects design, which took place over two sessions at least three days apart. In one session participants were administered alcohol (0.3 g/kg), in the other session they received lemonade. In both sessions participants were fully aware which beverage they were receiving, and thus the experiment consisted of an alcoholic drink and a control, not a placebo. This decision was made in order to create an ecologically valid test in which participants knew what they were drinking. However, due to the design any conclusions cannot separate out the pharmacological effects of alcohol from its anticipated effects (Christiansen et al., 2013). Regarding the task, participants were also aware of the colour-reward contingencies as, though research shows human sign-tracking persists regardless of conscious awareness (see Le Pelley et al., 2015), no study has yet tested this after a priming dose of alcohol. Both session order and colour contingency (red or blue/high or low CS) were counterbalanced across participants.

Beverage Administration and Breath Alcohol Concentration

Before alcohol administration, participants were breathalysed (Lion 500 Alcometer, UK) and only those with a 0.0 mg/l breath alcohol reading were permitted to continue. Participants

were then weighed and the researcher calculated the amount of alcohol to be given, based on a 0.3 g/kg dose (equating to approximately 2.5 units for a 61 kg person). The alcohol used was Smirnoff Red vodka (37.5% alcohol by volume [ABV]). The total dose was separated equally via an enteral syringe into three glasses, before Schweppes lemonade was added at a ratio of 3:1 (for a 61 kg person, this equates to approximately 62 ml of vodka and 186 ml of lemonade [split over three glasses]). Participants were given each glass in turn and guided in a semi-structured fashion; they consumed each drink within a 4 minute period, giving a total consumption time of 12 minutes. This was followed by an absorption period lasting 20 minutes during which participants were simply asked to relax. Participants were breathalysed for a second time before commencing with the task (which lasted approximately 21 minutes). Participants provided a third, final breathalyser reading upon task completion. Control sessions were conducted identically, except that a commensurate volume of lemonade was administered *in lieu* of alcohol.

Procedure

The experiment consisted of three parts: I) online questionnaires, II) session 1, and III) session 2 (three or more days after session 1). Potential participants who met the criteria to participate completed the online questionnaire pack, providing measures of drinking habits and motives, impulsivity and trauma (TLFB, AUDIT, M DMQ-R, B-YAACQ, BIS-11, ImpSS, CATS) via Qualtrics (Provo, UT, 2015). Those who fulfilled the criteria were invited to attend the laboratory sessions. Sessions took place between 1 p.m. and 6 p.m. in the eye-tracking laboratory of the School of Psychology, University of Liverpool. During both sessions, participants completed a baseline desire for alcohol questionnaire (DAQ) and the subjective intoxication scale (SIS) before they were administered their beverages (alcohol or

control). After the consumption (12 min) and subsequent absorption (20 min) periods, participants once again completed the SIS and DAQ (5 min), before completing the ASTT (21 min). Participants were told that any earned points would be converted to additional monetary rewards which would be provided at the end of session 2. Participants were always asked to remain in the lab until their BrAC reached half that of the UK driving limit (0.17 mg/l or below). Upon conclusion of session 2, participants were asked if they knew the study aims and believed whether they believed their task performance affected how many vouchers they received.

Participants received either course credits or £20 in 'Love2Shop' vouchers as compensation for their travel expenses and time. During the debriefing it was explained that they would not receive any extra vouchers based on their task performance, and that this was a necessary deception. Each session lasted approximately 1hr 15m. If participants refused to remain in the lab while their BrAC levels fell to ≤0.17 mg/l, they were required to sign a waiver.

4.4.2 Data Reduction and Analysis

The following are an extension of measures that have been used in previous research in estimating attentional bias and stimulus value (Field & Cox, 2008; Rose, Brown, Field, & Hogarth, 2013). As in Study 1, all RT responses on the ASTT <80ms and >999ms were recoded as missing data.

Additional Singleton Tracking Task: Outcome Measures

Measures for the ASTT were those used by Le Pelley et al (2015) and were divided into omissions and RTs. For both Omission and RT Bias, greater (positive) values indicate sign-tracking (as high-value distractors should induce more errors and slower responses to the OT than low-value distractors). See Table A2 (Appendix A) for calculations.

4.4.3 Results

Participant Characteristics

Table 4.1 summarises the sample's average alcohol use characteristics, while Table 4.2 provides an overview of trait and state measures. Men were more frequent binge drinkers (23.1% binged 3-4 times p/fortnight) than women (26.7% binged once p/fortnight). Most participants (66.6%) scored ≥8 on the AUDIT, classing them as at risk drinkers. Self-reports showed that, overall, the participant population were hazardous drinkers, consuming over recommended weekly guidelines (14 units per week for men and women). Contrary to the sample of Study 1, only 7.7% of participants scored ≤5 on the B-YAACQ: Total, with 30.6% scoring between 6 and 10 and 38.4% scoring between 11 and 15. A score greater than 5 is associated with increased likelihood of risky drinking (e.g., experiencing impulsivity, embarrassment, regret and/or harm as a result of drinking) (Kahler et al., 2005). In terms of personality variables, most scored within the normal ranges of some personality scales (e.g., 75% scored within the BIS-11 range of normality [52-71]; the ImpSS average was almost identical [M = 9.96] to that found previously in undergraduates [M = 9.50] [Ball, 1995]). The CATS: Total average (M = 0.65) was similar to that of earlier work in nonclinical samples (M = 0.74; M = 0.77) (Kent & Waller, 1998; Sanders & Becker-Lausen, 1995), and suggests a low level of childhood trauma.

Table 4.1 Alcohol use characteristics (Means ± SD)

Alcohol unit consumption (TLFB)	26.75 (± 13.28)
Binge frequency	3.79 (± 2.83)
AUQ: Units consumed per hour	4.42 (± 2.83)
AUQ: Age at first drink	13.83 (± 1.58)
AUQ: Age at regular drinking	16.69 (± 1.63)
AUQ: Drunk frequency	44.14 (± 14.63)
AUQ: Drunk percentage	66.39 (± 26.74)
AUDIT	8.36 (± 3.68)

Consumption = UK units (1 UK unit = 8g of pure alcohol); *TLFB* = Timeline FollowBack, based on an average of the previous two weeks of drinking; *AUQ* = Alcohol Use Questionnaire*; Binge frequency* = ≥8 units for men, ≥6 units for women per day, based on an average of the prior two weeks of alcohol consumption; *Age at regular drinking* = the age at which regular drinking was undertaken; *Drunk frequency* = number of times individuals have been drunk in the previous 6 months; *Drunk percentage* = percentage of drinking occasions in which individuals become drunk; *AUDIT* = Alcohol Use Disorders Identification Test.

Table 4.2 Trait/State characteristics (Means ± SD)

BIS-11: Total	60.70 (± 9.65)
B-YAACQ: Total	11.67 (± 4.31)
ImpSS	9.93 (± 4.41)
CATS: Total	0.65 (± 0.31)

BIS-11 = Barratt's Impulsivity Scale; *B-YAACQ* = Brief Young Adult Alcohol Consequences Questionnaire; *ImpSS* = Impulsive Sensation Seeking; *CATS* = Child Abuse and Trauma Scale. *Note.* An *M DMQ-R: Total* variable was not computed as the questionnaire's subscales qualitatively conflict (e.g., coping versus enhancement); thus, a total score would be interpretively useless.

Additional Singleton Tracking Task

Tables 4.3 and 4.4 provide descriptive statistics for the ASTT, showing average response frequencies and RTs for OTs and CSs. It is clear that participant responses were

overwhelmingly directed towards the OT, and that high-value distractors attracted more responses than the low value. Further, latencies towards the OT on high-value trials are greater than on low-value trials across both sessions.

Table 4.3 Response frequencies (Means ± SD)

	Frequencies	
	Alcohol session	Control session
OT	285.38 (± 7.97)	282.83 (± 9.67)
High-value distractor	7.55 (± 5.63)	9.14 (± 8.25)
Low-value distractor	3.17 (± 3.70)	2.83 (± 2.66)

Each outcome measure's fixation frequency is presented. OT = Outcome Target. *Note.* Frequencies do not add up to 300 (total number of trials) as these descriptives do not include non-responses.

Table 4.4 RTs (Means ± SD)

	Reaction Times	
	Alcohol session	Control session
OT responses on high-value trials	369.08 (± 36.96)	364.91 (± 40.84)
OT responses on low-value trials	355.36 (± 38.63)	356.14 (± 40.19)

Each outcome measure's RT (milliseconds) on both high-value and low-value trials are presented. OT = Outcome Target.

Reaction Times and Omissions

Reaction Times: A 2 (drink: alcohol vs control) × 2 (value: high vs low) Repeated-Measures ANOVA containing session order as a between-subjects factor (to rule out practice or boredom effects) was conducted. Importantly, there was no main effect of session order,

$F(1, 26) = 0.09$, $p = .77$, $\eta_p^2 = .003$ (2-tailed), nor were there any significant order interaction effects (*ps* > .10). Results revealed a main effect of value, $F(1, 26) = 26.19$, $p < .0001$, $\eta_p^2 = .50$, with latencies towards OTs slower on high-value ($M = 368.28$, $SD \pm 37.54$) versus low-value ($M = 356.34$, $SD \pm 38.94$) trials. Further, while there was no effect of drink, $F(1, 26) = 0.17$, $p = .69$, $\eta_p^2 = .006$ (2-tailed), there was an interaction between drink and value, $F(1, 26) = 3.33$, $p = .04$ $\eta_p^2 = .11$ (1-tailed)[20].

Post-hoc Paired-Samples *t*-tests revealed the effect of value across both alcohol and control conditions. Alcohol condition: latencies were higher in high-value ($M = 370.19$, $SD \pm 37.14$) compared to low-value ($M = 355.45$, $SD \pm 39.33$) trials, $t(27) = 5.67$, $p < .0001$, $r = .74$ (2-tailed). Control condition: high-value latencies ($M = 366.37$, $SD \pm 40.81$) were again higher than low-value latencies ($M = 357.23$, $SD \pm 40.48$), $t(27) = 3.23$, $p = .002$, $r = .53$ (1-tailed).

Post-hoc Paired-Samples *t*-tests were conducted to assess responses within trial types across drink conditions. There were no differences in responses to the OT on high-value trials between the alcohol ($M = 370.20$, $SD \pm 37.14$) and control conditions ($M = 366.40$, $SD \pm 40.81$), $t(27) = 0.95$, $p = .35$, $r = .09$. There were no response differences in low-value trials between alcohol ($M = 355.40$, $SD \pm 39.33$) and control ($M = 357.20$, $SD \pm 40.48$) conditions, $t(27) = -0.54$, $p = .59$, $r = -.05$ (both 2-tailed). Results suggest VMAC, as measured here with sign-tracking RT Bias, occurs after both control and alcohol beverages. Further, though there were no differences in responses on high- or low-value trials between drink conditions, there was found to be a statistically significant interaction between drink condition and trial value. This reflects a small (not statistically significant) increase in latency on high-value trials and

[20]The main effect analysis of condition was non-directional as we did not predict that conditions would significantly alter responses *overall*, only that condition would alter responses in a specific manner; i.e., alcohol would increase sign-tracking (the response gap between high and low trials).

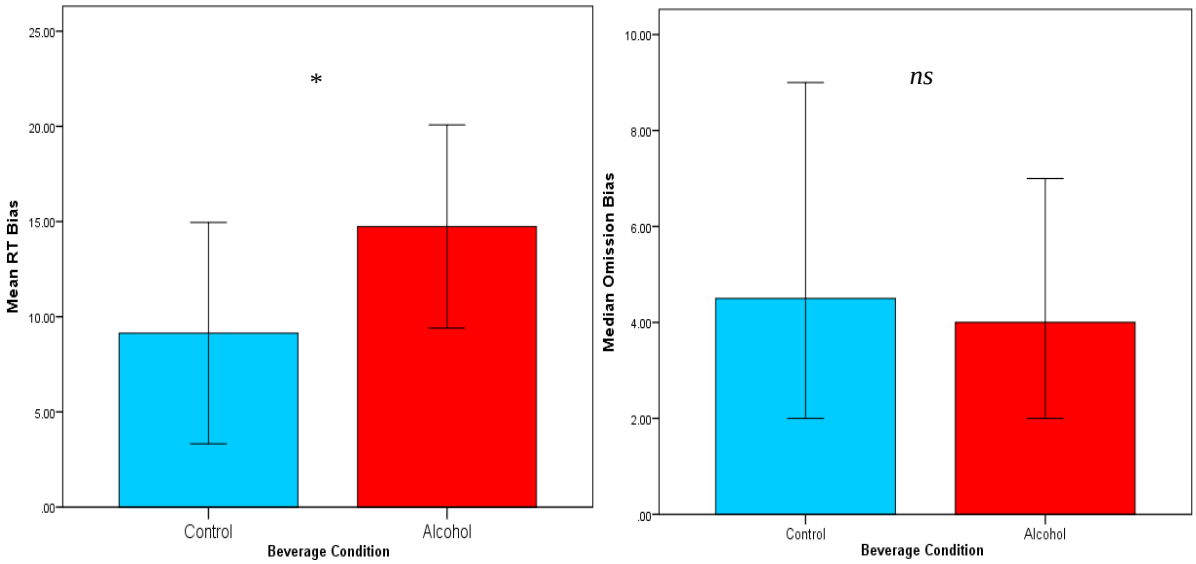
the decrease in latency on low-value trials for the alcohol condition compared to control. Given that the effect size for the difference between OT responses on high- versus low-value trials was larger in the alcohol condition, it seems that alcohol consumption is driving this difference.

Omissions: A Related-Samples Two-Way Friedman's ANOVA revealed statistically significant differences between omissions across high- versus low-value trial types, $\chi^2(3) = 26.89$, $p < .0001$. Wilcoxon Signed-Rank tests were conducted to investigate where these differences lay. Analyses revealed statistically significant differences in responses between trial types in both alcohol and control conditions. In the alcohol condition, there were a greater number of omissions on high-value (*Mdn* = 6.50, *range* = 0-23) compared to low-value trials (*Mdn* = 2.00, *range* = 0-10), *T* = 20.00, *p* = .0001, *r* = .51. In the control condition, there were again a greater number of omissions on high-value (*Mdn* = 6.50, *range* = 0-28) compared to low-value trials (*Mdn* = 2.00, *range* = 0-11), *T* = 19.50, *p* = .0002, *r* = .50. No differences in responses were found within trial type, or across drink condition. There was no difference in high-value omissions between the alcohol (*Mdn* = 6.50, *range* = 0-23) and control (*Mdn* = 6.50, *range* = 0-28) conditions, *T* = 147.00, *p* = .47, *r* = .10. There was also no difference in low-value omissions between the alcohol (*Mdn* = 2.00, *range* = 0-10) and control (*Mdn* = 2.00, *range* = 0-11) conditions, *T* = 145.50, *p* = .90, *r* = .02. Thus, while no difference were found between responses within trial types across drink conditions, sign-tracking effects (differential responses on high- versus low-value trials) as measured via omissions were found within both alcohol and control conditions. These effects were almost identical in size.

Whether overall RT and Omission Biases (difference scores between high- and low-value trials) differed across sessions was also investigated (Figure 4.1). Paired-Samples *t*-tests

revealed that RT Bias was larger in the alcohol session (M = 14.74, SD ± 13.77) compared to the control session (M = 9.14, SD ± 14.99), $t(27) = 1.89$, $p = .04$, $r = .34$, while no such difference was found for Omission Bias, $t(27) = -1.06$, $p = .15$, $r = .20$. These results suggest that alcohol amplified sign-tracking as measured by RT Bias, relative to a control drink.

Figure 4.1 Bar charts showing comparisons of RT Bias (*left*) and Omission Bias (*right*) between alcohol and control conditions



*$p < .05$ (1-tailed); *ns* = non-significant. Values are means (*left*) and medians (*right*) (error bars: 95% CI).

Associations with Individual Differences

Correlations were conducted between RT and Omission Biases (across alcohol and control conditions) and participant characteristics (e.g., alcohol consumption, impulsivity etc.). The correlation matrix is presented in Table D1 (Appendix D). After appropriate statistical corrections were applied, of the 148 correlations performed, no associations reached statistical significance.

Effects of alcohol

Desire for Alcohol Questionnaire (DAQ)

Two (drink) × two (time) Repeated-Measures ANOVA were conducted to assess changes in desire for alcohol. Each of the four DAQ measures were assessed in turn. For 'desire', there was a main effect of drink condition, with desire larger in the alcohol session (M = 18.11 SD ± 4.04) compared to the control session (M = 15.98, SD ± 4.65), $F(1, 27) = 7.41$, $p = .01$, $\eta_p^2 = .22$, but no effect of time (pre-post), $F(1, 27) = 0.80$, $p = .38$, $\eta_p^2 = .03$, and no interaction, $F(1, 27) = 2.12$, $p = .16$, $\eta_p^2 = .07$. For 'pos + control' (positive reinforcement and ability to control drinking), there was no main effect of drink condition, $F(1, 26) = 2.08$, $p = .16$, $\eta_p^2 = .07$, no main effect of time, $F(1, 26) = 0.01$, $p = .91$, $\eta_p^2 = .0005$, and no interaction, $F(1, 26) = 0.20$, $p = .66$, $\eta_p^2 = .008$. For 'negative' (negative reinforcement), again there were no main effects of drink condition, $F(1, 26) = 3.59$, $p = .07$, $\eta_p^2 = .12$ or time, $F(1, 26) = 3.90$, $p = .06$, $\eta_p^2 = .13$, and no interaction, $F(1, 26) = 0.29$, $p = .59$, $\eta_p^2 = .01$. Finally, for total DAQ scores, there was a main effect of drink condition, with total scores higher in the alcohol session (M = 43.20, SD ± 8.88) than in the control session (M = 38.34, SD ± 10.27), $F(1, 27) = 7.13$, p = .01, $\eta_p^2 = .21$. There was no main effect of time, $F(1, 27) = 0.03$, $p = .87$, $\eta_p^2 = .001$, and no interaction, $F(1, 27) = 1.95$, $p = .17$, $\eta_p^2 = .07$.

Post-hoc Paired-Samples t-tests were conducted for 'desire', comparing before control versus before alcohol (i.e., at baseline) and after control versus after alcohol (all 2-tailed). Results showed no difference in total scores at baseline, $t(27) = -1.82$, $p = .08$, $r = .33$, though revealed that 'desire' was significantly higher after alcohol (M = 18.64, SD ± 5.34) compared to after control (M = 15.89, SD ± 5.15), $t(27) = -2.88$, $p = .008$, $r = .48$. The same analyses

were conducted for total DAQ scores. While the baseline comparison did not reach statistical significance $t(27) = -2.05$, $p = .051$, $r = .37$, total scores after the alcohol drink were significantly higher ($M = 43.82$, $SD \pm 10.86$) than after control ($M = 37.86$, $SD \pm 11.33$), $t(27) = -2.81$, $p = .009$, $r = .48$.

Overall results reveal that two out of four DAQ measures (desire and total score) were significantly higher post-alcohol compared to post-control, although pre-alcohol and pre-control scores did not differ. However, there were no pre-post consumption differences in either drink condition. Alcohol's priming of craving cannot therefore be reasonably inferred.

Subjective Intoxication Scale (SIS)

Given that SIS measures were used in an exploratory fashion and were of secondary import, these analyses are located in the appendices (Appendix D). Briefly, 'light-headedness', 'stimulation', and 'relaxation' showed a pre-post alcohol (priming) increase, with 'alertness' showing the converse ($ps < .05$). No changes were found for 'irritable' or 'contented' measures ($ps > .05$).

Sign-tracking and Craving and Intoxication measures

To investigate any associations between sign-tracking and experimental alcohol measures, correlational analyses included change scores for any craving (DAQ: 'desire' and 'total') and intoxication (SIS: 'alertness', 'stimulation', 'relaxation' and 'alertness') measure which showed either a drink condition or time effect. Breath alcohol concentration (BrAC) was also included for analysis. After corrections were applied, no statistically significant

correlations were found between sign-tracking, DAQ and SIS change scores or BrAC measures (see Tables D2, D3 and D4 in Appendix D, respectively).

4.4.4 Discussion

Study 2 replicated the findings of Study 1 (Chapter Three): sign-tracking – as indicated by both RT and omission differences in responding between high- and low-value trials – was found in social drinkers when sober. This experiment extended these findings to show, for the first time, that sign-tracking (as indicated by both RTs and omissions) is also present after social drinkers consume a low dose (0.3 g/kg) of alcohol. Importantly, a statistically significant interaction was found between condition (drink type) and trial type (CS value). However, *post-hoc* tests found no statistically significant differences between responses across conditions within the same trial type (i.e., responses on high-value trials were not statistically different after alcohol compared to control, as was also the case for low-value trials). Rather, the descriptive statistics show that alcohol increased RT on high-value trials while decreasing RT on low-value trials (both compared to control), though neither to a statistically significant degree. This suggests that any amplification of sign-tracking by alcohol may not occur solely through an increase in attentional capture by high-value CSs nor through a decrease in perceived value (and thus reduced capture) of low-value CSs, but rather via small changes in both pathways. This is supported by a statistically significant difference in RT Bias between alcohol and control conditions. Although this finding must be interpreted with caution, it is possible that sign-tracking in human social drinkers may be magnified by a low dose of alcohol. However, due to the non-significant *post-hoc* tests, a larger sample size may be required than this experiment possesses. Sign-tracking as measured by omissions did not significantly alter after a low dose of alcohol.

Analyses of the visual analogue scales revealed that two of the four DAQ measures – 'desire' and total score – showed significant increases after alcohol compared to after control. However, there was no pre-post differences for alcohol (nor control) consumption, which indicates a lack of a priming effect. Indeed, previous work has shown that higher doses than 0.3 g/kg are needed to prime craving as measured by the DAQ (Rose & Duka, 2006). Visual inspection of the current data revealed that this may have been due to an anticipatory priming effect, with DAQ measures being higher before alcohol consumption than before control consumption (though this difference did not reach statistical significance). This anticipation, coupled with a possible ceiling effect of 0.3 g/kg dose's maximum impact on subjective desire, may have been responsible for the lack of a priming effect. For the SIS, 'light-headedness', 'stimulation', and 'relaxation' increase post-alcohol, while an alcohol (priming) 'alertness' decreased. The 'irritable' and 'contented' measures were unaffected. These results suggest that participants' subjective feelings of intoxication were altered by alcohol, even though their subjective craving was not. No DAQ, SIS or BrAC measures were significantly correlated with any sign-tracking measure, suggesting that an individual's tendency to attend to cues of higher incentive value is unrelated to any other individual difference.

4.5 Experiment 2

Alcohol priming research shows that enhanced motivation to drink following initial consumption may be dose dependent. For example, Rose and Duka (2006) found a priming effect on self-reported craving after 0.6 g/kg of alcohol but not 0.3 g/kg, compared to placebo. The higher 0.6 g/kg dose shows a robust priming effect of craving in the literature, and several papers suggest that this priming effect may work via increasing the positive reinforcing effects of alcohol (i.e., increasing its value) (Rose & Duka, 2006; Rose &

Grunsell, 2008). However, alcohol doses appear to affect attentional bias differently. Previous research has shown that more extreme alcohol doses (both low and high; e.g., doses ≤0.13 g/kg and doses ≥0.6 g/kg) (Adams et al., 2012; Duka & Townshend, 2004; Weafer & Fillmore, 2013) do not increase AB towards alcohol-related stimuli, unlike moderate doses (~0.2-0.4 g/kg) (Adams et al., 2012; Fernie et al., 2012; Field & Duka, 2002; Schoenmakers et al., 2008). Further, one recent pre-clinical study found that a 0.7 g/kg dose in rats – the human dose equivalent of approximately a 1.04 g/kg dose for a 60 kg person (for dose calculations, see Reagan-Shaw, Nihal, & Ahmad, 2007; Shin, Seol, & Son, 2010) – actually *reduced* sign-tracking for food cues, while increasing goal-tracking (Versaggi et al., 2016; cf. Tomie et al., 1998; Tomie et al., 2003). The aim of this experiment was to build on this research (as well as the findings of Study 2) to explore whether a 0.6 g/kg alcohol prime would significantly alter sign-tracking AB towards discrete, reward-independent CSs (particularly those of high value, relative to low value).

4.5.1 Method

Participants

Thirty-three social drinkers were recruited through opportunistic sampling and recruited via internal university and social media advertisements. Of these, one was excluded due to not being able to remain still during the task after the alcohol prime, one due to not being able to consume all of the drinks in the time set, and one due to too much missing data. The remaining 30 participants (18 female) were aged 18-31 years (M = 22.47, SD ± 4.52). Inclusion and exclusion criteria were identical to Study 2.

Design

The design and procedure were identical to those of Experiment 1. The only difference was the dose, which was increased from 0.3 g/kg (Study 2) to 0.6 g/kg (Study 3).

4.5.2 Results

Participant Characteristics

Table 4.5 summarises the sample's average alcohol use characteristics, while Table 4.6 provides an overview of trait and state measures. Men showed a narrower range of binge drinking (25% binged once p/fortnight) than women (~16.7% binged 0 to 6 times p/fortnight). Most participants (70%) scored ≥8 on the AUDIT, classing them as at risk drinkers. Self-reports showed that, overall, the participant population were hazardous drinkers, consuming over recommended weekly guidelines (14 units per week for men and women). Twenty-three percent of participants scored ≤5 on the B-YAACQ: Total, with 53.3% scoring between 6 and 10 and 23.3% scoring between 15 and 20. A score greater than 5 is associated with increased likelihood of risky drinking (e.g., experiencing impulsivity, embarrassment, regret and/or harm as a result of drinking) (Kahler et al., 2005). In terms of personality variables, most scored within the normal ranges of some personality scales (e.g., 63.2% scored within the BIS-11 range of normality [52-71]; the ImpSS average was similar [M = 8.57] to that found previously in undergraduates [M = 9.50] [Ball, 1995]). The CATS: Total average (M = 0.92) was slightly higher than that of earlier work in nonclinical samples (M = 0.74; M = 0.77) (Kent & Waller, 1998; Sanders & Becker-Lausen, 1995), though is still below the average typically found in clinical samples.

Table 4.5 Alcohol use characteristics (Means ± SD)

Alcohol unit consumption (TLFB)	26.37 (± 11.91)
Binge frequency	2.97 (± 1.94)
AUQ: Units consumed per hour	3.23 (± 1.80)
AUQ: Age at first drink	13.92 (± 2.42)
AUQ: Age at regular drinking	16.97 (± 1.83)
AUQ: Drunk frequency	26.53 (± 19.72)
AUQ: Drunk percentage	52.03 (± 28.67)
AUDIT	10.53 (± 4.08)

Consumption = UK units (1 UK unit = 8g of pure alcohol); *TLFB* = Timeline FollowBack, based on an average of the previous two weeks of drinking; *AUQ* = Alcohol Use Questionnaire; *Binge frequency* = ≥8 units for men, ≥6 units for women per day, based on an average of the prior two weeks of alcohol consumption; *Age at regular drinking* = the age at which regular drinking was undertaken; *Drunk frequency* = number of times individuals have been drunk in the previous 6 months; *Drunk percentage* = percentage of drinking occasions in which individuals become drunk; *AUDIT* = Alcohol Use Disorders Identification Test.

Table 4.6 Trait/State characteristics (Means ± SD)

BIS-11: Total	61.47 (± 10.37)
B-YAACQ: Total	9.37 (± 5.20)
ImpSS	8.57 (± 4.05)
CATS: Total	0.93 (± 0.40)

BIS-11 = Barratt's Impulsivity Scale; *B-YAACQ* = Brief Young Adult Alcohol Consequences Questionnaire; *ImpSS* = Impulsive Sensation Seeking; *CATS* = Child Abuse and Trauma Scale. *Note.* An *M DMQ-R: Total* variable was not computed as the questionnaire's subscales qualitatively conflict (e.g., coping versus enhancement); thus, a total score would be interpretively useless.

Additional Singleton Tracking Task

Tables 4.7 and 4.8 show average response frequencies and RTs for the OT and CSs. Participant responses were overwhelmingly directed towards the OT, followed by the

distractors (CSs), with the high-value distractor drawing more responses than the low value. Furthermore, latencies towards the OT on high-value trials are larger than on low-value trials across both sessions.

Table 4.7 Response frequencies (Means ± SD)

	Frequencies	
	Alcohol session	Control session
OT	282.03 (± 12.90)	279.93 (± 13.23)
High-value distractor	6.30 (± 4.68)	8.70 (± 6.16)
Low-value distractor	3.57 (± 3.85)	6.17 (± 8.18)

Each outcome measure's fixation frequency is presented. OT = Outcome Target. *Note.* Frequencies do not add up to 300 (total number of trials) as these descriptives do not include non-responses.

Table 4.8 Reaction Times (Means ± SD)

	Reaction Times	
	Alcohol session	Control session
OT responses on high-value trials	393.95 (± 38.99)	364.03 (± 28.02)
OT responses on low-value trials	388.20 (± 38.75)	359.65 (± 28.83)

Each outcome measure's RT (milliseconds) on both high-value and low-value trials are presented. OT = Outcome Target.

Reaction Times and Omissions

Reaction Times: A 2 (drink: alcohol vs control) × 2 (value: high vs low) Repeated-Measures ANOVA with session order as a between-subjects factor (to rule out practice/boredom effects) was conducted. Results revealed a main effect of value, $F(1, 28) =$

5.97, $p = .02$, $\eta_p^2 = .18$ (2-tailed), with higher latencies towards OTs on high-value (M = 378.99, SD ± 36.89) compared to low-value (M = 373.92, SD ± 36.79) trials. Results also revealed a main effect of drink, $F(1, 28) = 33.74$, $p < .0001$, $\eta_p^2 = .55$ (2-tailed), with higher latencies towards OTs in the alcohol condition (M = 391.07, SD ± 38.65) than the control condition (M = 361.84, SD ± 28.27). There was no interaction observed between value and drink, $F(1, 28) = 0.11$, $p = .74$, $\eta_p^2 = .004$ (2-tailed). However, there was an interaction effect between drink and session order, with higher RTs in the alcohol condition (M = 404.82, SD ± 25.84) compared to control (M = 352.64, SD ± 25.10) in the *alcohol → control* order, and higher RTs in the alcohol (M = 379.04, SD ± 43.71) compared to control (M = 369.89, SD ± 27.74) condition in the *control → alcohol* order, $F(1, 28) = 16.61$, $p = .0003$, $\eta_p^2 = .37$ (2-tailed).

Post-hoc Paired-Samples *t*-tests revealed a sign-tracking effect between high- and low-value trials within both drink conditions. In the alcohol condition, latencies were higher on high-value (M = 393.95, SD ± 38.99) compared to low-value (M = 388.20, SD ± 38.75) trials, $t(29) = 2.18$, $p = .04$, $r = .37$ (2-tailed), as they also were in the control condition (high value: M = 364.03, SD ± 28.02; low value: M = 359.65, SD ± 28.83), $t(29) = 1.67$, $p = .05$, $r = .30$ (1-tailed).

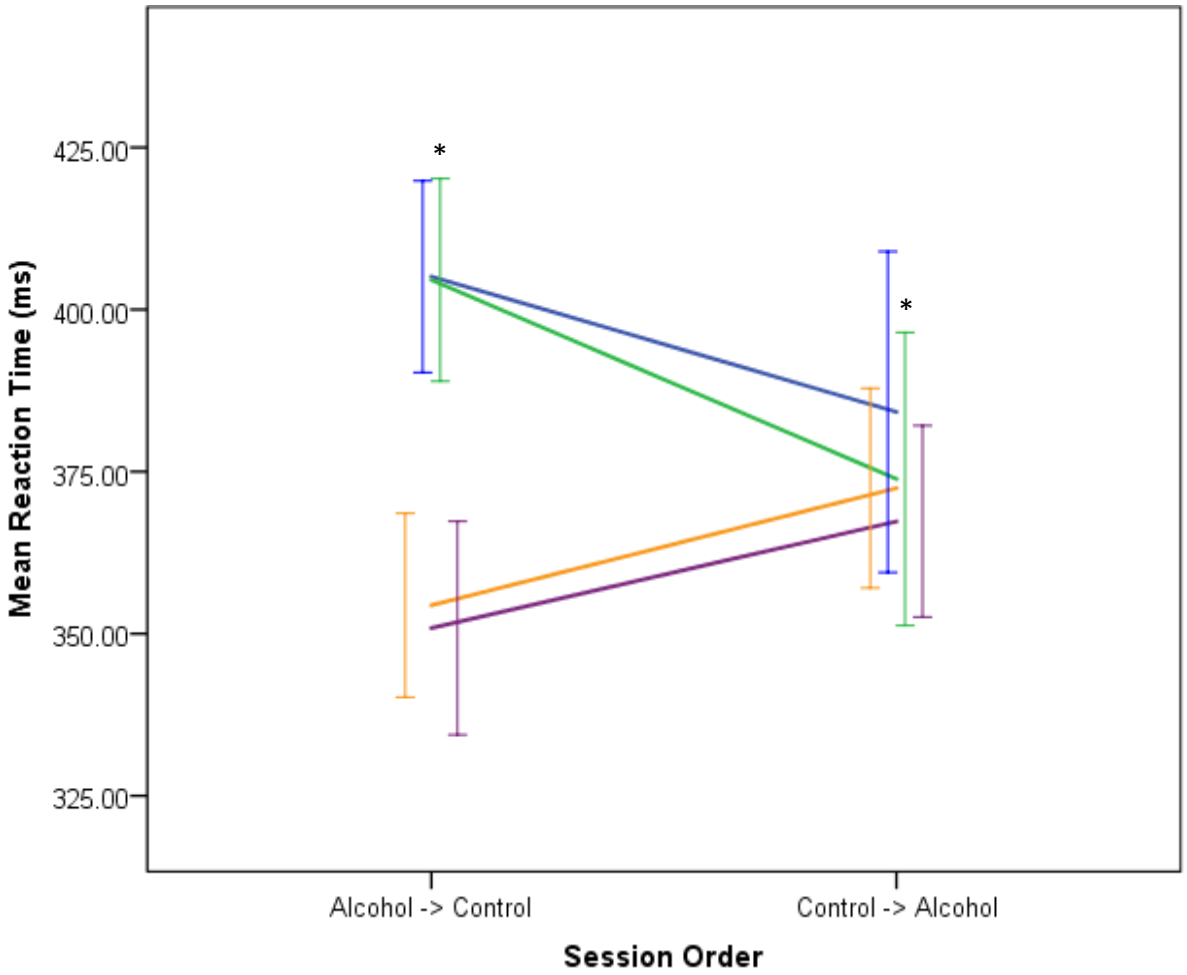
Inspecting the main effect of drink, Paired-Samples *t*-tests revealed that OT latencies were slower on high-value trials in the alcohol condition (M = 393.95, SD ± 38.99), compared to the control condition (M = 364.03, SD ± 28.02), $t(29) = 4.53$, $p < .0001$, $r = .64$, with the same pattern observed for low-value trials (alcohol: M = 388.20, SD ± 38.75; control: M = 359.65, SD ± 28.83), $t(29) = 4.15$, $p = .0003$, $r = .61$ (both 2-tailed). This means that participants were slower to respond to the OT on alcohol versus control days (regardless of trial type), and that the effect of trial type (CS value) was present on both alcohol and control

days. Together, these results suggest sign-tracking effects are present when sober and intoxicated, but that the extent of sign-tracking is not affected by alcohol consumption.

Turning to the interaction between session order and drink condition. In order to explore this interaction Welsh's *t*-tests were run on the entire sample with OT responses by trial type (high/low) and drink condition (alcohol/control) as the dependent variables and session order as the independent factor. The only difference in responses lay in low-value OT responses in the alcohol condition, $F(1, 25.77) = 5.72$, $p = .02$, $r = .43$ (2-tailed). Specifically, participants who consumed alcohol in session 2 were faster to respond to the OT on low-value trials than participants who consumed control (soft) drinks during their second session ($M = 373.87$, $SD \pm 42.42$, versus $M = 404.56$, $SD \pm 27.07$, respectively) (see Figure 4.2).

A reasonable interpretation may suggest that participants who received alcohol in session 2 were already conditioned to the value contingencies (in the prior control session) and so could more easily ignore distractors of low value compared to participants who completed the task for the first time under the influence of alcohol (and with no prior conditioning). That is, prior conditioning when sober may help participants reflexively ignore low-value cues when subsequently intoxicated and exposed to the same stimuli.

Figure 4.2 Interaction plot showing mean OT RTs on high- and low-value trials across drink conditions and session orders



Blue = Alcohol: High-value; Green = Alcohol: Low-value; Orange = Control: High-value; Purple = Control: Low-value. *Left:* alcohol session followed by control session; *right:* control session followed by alcohol session. Error bars are 95% CIs.

Omissions: A Related-Samples Two-Way Friedman's ANOVA revealed statistically significant differences between omissions across high- versus low-value trial types, $\chi^2(3) = 15.98$, $p = .0006$. Wilcoxon Signed-Rank tests were conducted to investigate where these differences lay. Analyses revealed statistically significant results for drink condition affecting omission rate for both high- and low-value CSs (*ps* < .05). Omissions on both high- and low-value trials were greater in the control, as opposed to the alcohol, condition. These results were in the opposite direction to those predicted and so the null hypothesis is accepted.

Further, while an effect of CS value was found in the alcohol condition, with more omissions in the high-value (M = 6.30, SD ± 4.68) compared to the low-value (M = 3.57, SD ± 3.85) trials, $t(29) = 2.56$, $p = .008$, $r = .43$ (2-tailed), no such difference was found in the control condition (high-value: M = 8.70, SD ± 6.16; low-value: M = 6.17, SD ± 8.18), $t(29) = 1.59$, $p = .06$, $r = .38$ (1-tailed). This indicates that drink type did not significantly affect sign-tracking omissions, though value-modulated omissions were only found in the alcohol condition.

Associations to individual differences

Correlations were conducted between RT Bias, Omission Bias (across alcohol and control conditions) and self-report measures (e.g., alcohol consumption, impulsivity etc.). The correlation matrix is presented in Table E1 (Appendix E). After appropriate statistical corrections were applied, of the 148 correlations performed, no associations between task outcomes and individual differences were found.

Effects of alcohol

Desire for Alcohol Questionnaire (DAQ)

Two (drink) × two (time) Repeated-Measures ANOVA were conducted to assess changes in desire for alcohol. Each of the four DAQ measures were assessed in turn. For 'desire', there was a main effect of drink condition, with desire larger in the alcohol session (M = 15.39 SD ± 4.84) compared to the control session (M = 13.36, SD ± 4.69), $F(1, 28) = 8.23$, $p = .008$, $\eta_p^2 = .23$, but no effect of time, $F(1, 28) = 3.38$, $p = .08$, $\eta_p^2 = .11$. There was an interaction between drink and time, $F(1, 28) = 10.01$, $p = .004$, $\eta_p^2 = .26$. For 'pos +

control' (positive reinforcement and ability to control drinking), there was a main effect of time, with increases found after consumption (M = 13.51, SD ± 5.01) compared to before (M = 12.24, SD ± 4.07), $F(1, 28) = 4.41$, $p = .05$, $\eta_p^2 = .14$. There were no effects of drink condition, $F(1, 28) = 2.93$, $p = .10$, $\eta_p^2 = .10$, and no interaction effect, $F(1, 28) = 3.83$, $p = .06$, $\eta_p^2 = .12$. For 'Negative' (negative reinforcement), there was no main effect of drink condition, $F(1, 28) = 3.93$, $p = .06$, $\eta_p^2 = .12$, no main effect of time, $F(1, 28) = 0.02$, $p = .88$, $\eta_p^2 = .001$, and no interaction, $F(1, 28) = 2.07$, $p = .16$, $\eta_p^2 = .07$. For DAQ total scores, there was a main effect of drink condition, with higher scores in the alcohol (M = 38.27, SD ± 11.45) condition than the control condition (M = 33.55, SD ± 11.55), $F(1, 29) = 9.33$, $p = .005$, $\eta_p^2 = .24$. There was no main effect of time, $F(1, 29) = 3.07$, $p = .09$, $\eta_p^2 = .10$, but there was an interaction effect, $F(1, 29) = 7.36$, $p = .01$, $\eta_p^2 = .20$.

Post-hoc Paired-Samples *t*-tests were conducted for the statistically significant effects, comparing before control versus before alcohol (i.e., at baseline) and after control versus after alcohol (all 2-tailed). For 'desire', there was no condition difference at baseline, $t(28) = -0.56$, $p = .58$, $r = .10$. There was a difference after consumption, with 'desire' higher after alcohol (M = 16.67, SD ± 6.69) compared to after control (M = 12.93, SD ± 4.92), $t(29) = -4.10$, $p = .0003$, $r = .61$. The ordinal interaction effect is driven by desire significantly increasing after alcohol (M = 16.76, SD ± 6.79) compared to before (M = 14.03, SD ± 4.33), $t(28) = -2.56$, $p = .02$, $r = .44$, while no such pre-post change occurs in the control condition, $t(29) = 1.29$, $p = .21$, $r = .23$. These results suggest an alcohol priming effect. For 'pos + control', this measure was higher after alcohol compared to before, $t(28) = -2.41$, $p = .02$, $r = .42$. There was no pre-post difference in the control condition, $t(29) = -0.65$, $p = .52$, $r = .12$. This results suggests an alcohol priming effect. For total DAQ scores, there was no difference before consumption (i.e., at baseline), $t(29) = 0.76$, $p = .45$, $r = .14$. At post consumption, total DAQ scores were higher after alcohol (M = 41.10, SD ± 15.68) compared to after control (M = 33.03, SD ±

12.05), $t(29) = 3.77$, $p = .001$, $r = .57$. The ordinal interaction effect is driven by total scores significantly increasing after alcohol consumption ($M = 41.10$, $SD \pm 15.68$) compared to before ($M = 35.43$, $SD \pm 10.22$), $t(29) = -2.34$, $p = .03$, $r = .40$. No such pre-post difference is found in the control condition, $t(29) = 1.25$, $p = .22$, $r = .23$. These results suggest an alcohol priming effect after consumption of 0.6 g/kg of alcohol with respect to total DAQ scores, desire and positive reinforcement.

Subjective Intoxication Scale (SIS)

Given that SIS measures were used in an exploratory fashion and were of secondary import, these analyses are located in the appendices (Appendix E). Briefly, 'light-headedness', 'stimulation', 'relaxation' and 'contentedness' showed a pre-post alcohol (priming) increase, with 'alertness' showing a decrease after consumption of the control drink but not alcohol ($ps < .05$). No change in the 'irritable' measure was found ($p > .05$).

Sign-tracking and Craving and Intoxication measures

As in Study 2, correlational analyses were conducted on the change scores for craving (DAQ: 'desire', 'pos + control' and 'total') and intoxication (SIS: 'light-headedness', 'stimulation', 'relaxation', 'contentedness' and 'alertness') measures which showed either drink condition or time effects, to investigate if there was any association to sign-tracking. Breath alcohol concentration (BrAC) was also included for analysis. Results showed that DAQ: Desire (pre-post control consumption change) was significantly negatively correlated with RT Bias (control condition) ($r_s = -.45$). However, no other DAQ measure, and no SIS or

BrAC measure statistically significantly correlated with sign-tracking after corrections were applied (see Tables E2, E3 and E4, Appendix E).

4.5.3 Discussion

Study 3 partially replicated the findings of study 1 (Chapter Three) and Study 2. Sign-tracking was found in social drinkers, as indicated by RT differences across drink conditions and omission differences in the alcohol condition between high- and low-value trials. However, unlike Study 2, sign-tracking was not amplified by the alcohol dose compared to a control drink. This is in line with a recent preclinical study showing that higher doses of ethanol may actually reduce sign-tracking in rats (Versaggi et al., 2016), as well human studies showing that higher and lower doses are less likely to affect AB than are moderate doses (e.g., 0.2-0.4 g/kg) (Adams et al., 2012; Duka & Townshend, 2004; Fernie et al., 2012; Field & Duka, 2002; Schoenmakers et al., 2008; Weafer & Fillmore, 2013).

There was an interaction of session order and drink condition. This suggested that participants who undertook the alcohol session second found it easier to ignore low-value distractors (perhaps as they had already been conditioned whilst sober), compared to participants who underwent initial conditioning while intoxicated in session 1. The lack of influence of session order in Study 2 likely reflects the much lower dose of this earlier study. That is, in Study 2 participants who completed the ASTT after alcohol in session 1 may still have found it relatively easy to ignore the low-value distractors given the low dose. The lack of omissions differences between high- and low-value trials in the control condition is a first across these three studies, and may again reflect the relative instability and insensitivity of the omission measure.

Analyses revealed that three out of four DAQ measures were primed by alcohol consumption. 'Desire' was increased post-alcohol compared to both pre-alcohol and post-control consumption. 'Pos + control' (positive reinforcement) showed a pre-post alcohol consumption increase. Total DAQ scores again showed an increase post-alcohol compared to both pre-alcohol and post-control consumption. For the SIS, 'light-headedness', 'stimulation', 'relaxation' and 'contentedness' showed a pre-post alcohol (priming) increase, while 'alertness' showed a decrease after consumption of the control drink but not alcohol, and 'irritable' showed no change. These results suggest that most measures of subjective craving and intoxication were altered (mostly increased) by consuming 0.6 g/kg of alcohol, supporting previous findings (Rose & Duka, 2006; Rose & Grunsell, 2008).

Finally, after correcting for familywise error, no individual difference measure was statistically significantly correlated with measures of sign-tracking. Only DAQ: Desire (pre-post control consumption change) was significantly negatively correlated with RT Bias in the control condition. However, it is unclear what could have prompted this increase in craving and thus the association with sign-tracking is difficult to interpret. No other DAQ, SIS or BrAC measures were significantly correlated with any sign-tracking measure, suggesting that an individual's tendency to attend to cues of higher incentive value is unrelated to any other individual difference.

4.6 Results Synthesis

In order to assess whether the samples of experiments 1 and 2 (studies 2 and 3) differed in the extent of their sign-tracking after alcohol, compared to their respective control conditions, the two samples were pooled for statistical analysis ($N = 58$). Welch's *t*-test analyses revealed

that the majority of measures (including age, gender and psychological questionnaire measures) did not significantly differ between experimental groups (*ps* > .05). Craving (DAQ) scores showed differences mainly before consumption, with 'desire' (before alcohol), 'desire' (before control) and DAQ total score (before alcohol) all higher in Study 2 than Study 3. The only significant difference *after* consumption was 'desire' (after control), which was again higher in Study 2. No post-alcohol differences were found. This seems to suggest that the alcohol doses did not differentially affect craving between the two samples. All measures which were found to be statistically different between experimental samples are shown in Table 4.9.

Table 4.9 Differences in self-reports between samples (Studies 2 and 3) (Means ± SD)

	Experimental sample		*p*-value
	Exp. 1	Exp. 2	
Drunk frequency	44.00 (± 14.88)	26.53 (± 19.72)	<.001
MDMQ-R: Enhancement	3.65 (± 0.70)	3.11 (± 0.79)	.007
CATS: Punishment	1.10 (± 0.44)	1.84 (± 0.49)	.004
CATS: Total	0.65 (± 0.31)	0.93 (± 0.40)	.001
DAQ: Desire (before alcohol)	17.57 (± 3.52)	14.03 (± 4.33)	.001
DAQ: Desire (before control)	16.07 (± 4.54)	13.40 (± 4.67)	.03
DAQ: Desire (after control)	15.89 (± 5.15)	12.93 (± 4.92)	.03
DAQ: Total (before alcohol)	42.57 (± 8.13)	35.43 (± 10.22)	.005
SIS contented (after alcohol)	57.04 (± 27.64)	70.20 (± 19.33)	.04
Pre-BrAC	0.19 (± 0.02)	0.32 (± 0.09)	<.001
Post-BrAC	0.14 (± 0.04)	0.33 (± 0.05)	<.001

All analyses are 2-tailed. *M DMQ-R* = Modified Drinking Motives Questionnaire – Revised; *CATS* = Childhood Abuse Trauma Scale; *DAQ* = Desire for Alcohol Questionnaire; *SIS* = Subjective Intoxication Scale; *Pre-BrAC* = BrAC taken before ASTT; *Post-BrAC* = BrAC taken after ASTT.

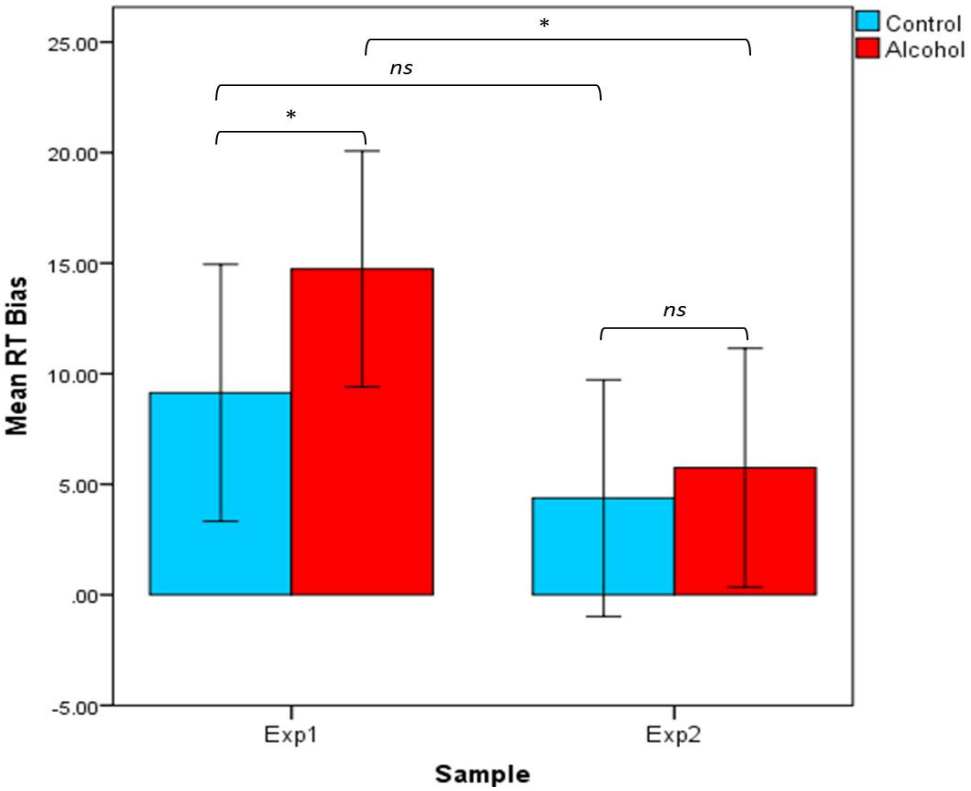
Next, analyses were performed to investigate whether sign-tracking biases (RT and Omission) differed between samples.

Reaction Time Bias: A Welch's *t*-test was conducted, with experimental sample as the between-subjects factor and RT Biases (alcohol and control) as dependent variables. First, no difference was found in RT Bias between the samples in their respective control conditions, $F(1, 55.26) = 1.53$, $p = .22$, $r = .16$ (2-tailed). However, a difference in RT Bias was found

between experimental samples for the alcohol condition, with the 0.3 g/kg sample showing greater RT Bias (M = 14.74, SD ± 13.77) than the 0.6 g/kg sample (M = 5.75, SD ± 14.46), $F(1, 55.98) = 5.88$, $p = .02$, $r = .31$ (2-tailed). These results suggest that, though the samples did not differ in the extent of their sign-tracking in the control condition, the sample receiving a 0.3 g/kg dose of alcohol sign-tracked to a greater extent than the sample receiving a 0.6 g/kg dose (see Figure 4.3).

Omission Bias: Identical analyses were ran as above. No difference was found in Omission Bias between the samples in their respective control conditions, $F(1,55.87) = 3.68$, $p = .06$, $r = .25$ (2-tailed). Unlike for RT, no difference in Omission Bias was observed between samples in the alcohol condition, $F(1, 55.88) = 2.44$, $p = .12$, $r = .20$ (2-tailed).

Figure 4.3 Bar chart comparing RT Bias across samples for alcohol and control conditions



Values are means (error bars: 95% CI). *$p < .05$; *ns* = nonsignificant.

4.7 General Discussion

Using the ASTT, two experiments were conducted to assess whether small and moderate priming doses of alcohol (0.3 g/kg and 0.6 g/kg, respectively) increased sign-tracking behaviours in social drinkers relative to a control drink. Questionnaires also gathered information on drinking habits and other individual differences which have been associated with sign-tracking behaviour in preclinical studies, such as impulsivity and trauma (Belin et al., 2016; Flagel, Akil, et al., 2009; Tomie et al., 2008). Results from both experiments replicated that of Study 1 (Chapter Three) and previous research (Le Pelley et al., 2015), demonstrating that humans sign-track towards discrete, noncontingent reward-CSs (under non-primed conditions). Specifically, value-modulated attentional capture (VMAC) is greater towards high-value CSs than towards low-value CSs. Additionally, we showed for the first time in humans that sign-tracking is maintained after both a 0.3 g/kg and 0.6 g.kg dose of alcohol. Perhaps a more important finding was that the 0.3 g/kg dose of alcohol amplified sign-tracking, compared to a control beverage, while the 0.6 g/kg dose did not. Furthermore, the extent of the OT RT sign-tracking effect in experimental sample 1 (0.3 g/kg) was significantly greater than in experimental sample 2 (0.6 g/kg), with a medium estimated effect size. Analyses on change scores from both experiments showed mixed findings with regard to alcohol priming. For craving (DAQ), while it cannot be said that there was any strict priming in Study 2 (craving after alcohol was higher than after control, but there was no pre-post alcohol difference), three out of four DAQ measures increased following alcohol consumption, suggesting a priming effect in Study 3. Almost all SIS measures showed an effect of drink across both studies (see Appendices D and E for more information). However, the DAQ craving effects were not significantly dose-dependently affected by alcohol

consumption, as no difference was found in craving between the two samples after the alcohol preload (for reviews, see Field et al., 2008; Rose, 2013).

In Experiment 1, no correlation with individual differences (TLFB, BIS-11 etc.), craving (DAQ), intoxication (SIS) or BrAC was statistically significant after familywise error corrections were applied. In Experiment 2, again no correlation with individual differences, SIS or BrAC was statistically significant after familywise error corrections were applied. For craving, DAQ: Desire (pre-post control consumption) was significantly negatively correlated with RT Bias (control), indicating that decreased desire following control drink consumption was associated with higher sign-tracking in the control condition (as measured by RT Bias). The lack of a relationship between sign-tracking and individual difference measures across both experiments contrasts with more stable findings in the preclinical literature (Flagel, Akil, et al., 2009; Tomie et al., 2008), as well as the specific links between sign-tracking and impulsivity previously found in humans (B. A. Anderson, Kronemer, et al., 2016; B. A. Anderson et al., 2011a), though results are mixed (B. A. Anderson et al., 2013).

The data contained in this paper do not accord to meta-analytic results showing that AB to reward cues is associated – albeit weakly – with craving measures (Field et al., 2009). However, given the continued mixed results of this effect since the meta-analysis (Adams et al., 2012; Schoenmakers & Wiers, 2010), the small effect that was found, and the evidence suggesting AB and craving are differentially affected by alcohol preloads (Field et al., 2008), it is perhaps unsurprising that no strong and/or consistent associations with craving were found in this study. Another possible reason could be the existence of individual differences in the way in which alcohol priming manifests differently when comparing explicit self-report measures (such as craving and perceived intoxication) to implicit cognitive processing (Schoenmakers et al., 2008). A final possibility relates to the recent theoretical synthesis

which suggests that AB and subjective craving may be discrete measures of value (Field et al., 2016).

The amplification of sign-tracking found in Experiment 1 is supported by some preclinical work with alcohol (Tomie et al., 1998, 2003), though findings are mixed (Versaggi et al., 2016). Studies using other substances (e.g., amphetamine, nicotine etc.) have been more consistent (Bordi & Matthews, 1990; DiFeliceantonio & Berridge, 2012, 2016; Mahler & Berridge, 2009; Palmatier et al., 2013; Versaggi et al., 2016). The pooling of data from experiments 1 and 2 revealed that sign-tracking was similar in the two control groups, but was significantly greater following consumption of the 0.3 g/kg alcohol dose compared to the 0.6 g/kg dose (0.6 g/kg did not differ from control). This finding of increased sign-tracking suggests that low doses of alcohol can amplify VMAC, even when cues are irrelevant and attention to them is not only not rewarded, but actively punished. Tomie et al. (1998) suggest that alcohol may increase sign-tracking via effects on the dopaminergic system. This hypothesis has gleaned support, with recent human data showing that magnitude of sign-tracking across individuals is associated with changes in available D2/D3 dopamine receptors in the right caudate and posterior putamen (substructures of the striatum) (B. A. Anderson, Kuwabara, et al., 2016). Omission Bias was unaffected by the alcohol priming dose, though this is perhaps unsurprising given that omissions occurred rarely (~2% across trial types) in both beverage conditions, making it a relatively insensitive measure of sign-tracking.

In humans, most of the priming literature has focussed on findings showing that administration of specific substances (e.g., alcohol) increases incentive salience (as measured by increased AB) for cues relating to that same substance (Adams et al., 2012; Duka & Townshend, 2004; Schoenmakers & Wiers, 2010; Schoenmakers et al., 2008). However,

studies have also shown that acute alcohol consumption can increase AB for arbitrary features of a cue (e.g., colour) previously paired with low doses of alcohol (Field & Duka, 2002), as well as for other rewards (e.g., smoking cues) (Field et al., 2005). Here, Experiment 1 showed that a 0.3 g/kg alcohol dose amplified AB towards discrete, response-irrelevant cues associated with a monetary reward. This supports the hypothesis that alcohol can induce a reward-general increase in incentive salience, rather than one that is reward-specific. Moreover, the results suggest that this enhanced attribution of incentive salience is modulated by reward cues' relative value.

Experiment 2 aimed to explore the effects of a higher dose (0.6 g/kg) on sign-tracking. Although sign-tracking was again found after alcohol consumption, sign-tracking biases (both RT and Omission) were not statistically significantly different from biases found after the control drink. That is, while there was no inflation of sign-tracking after the 0.6 g/kg dose, the sign-tracking CR remained (at a magnitude no different to responses after the control drink). (Note that an Omission Bias effect was absent after the control drink, likely due to the general insensitivity of the measure.) Further, though there was found to be an effect of condition (alcohol or control) on ASTT performance, this merely reflected a slowing down of overall responses regardless of trial type. This may mirror results found previously showing that ≥0.6 g/kg doses of alcohol can lead to transient impairments in executive cognitive functioning (Christiansen et al., 2013). This may be particularly important given the link between human sign-tracking and working memory (B. A. Anderson et al., 2013, 2011b; B. A. Anderson & Yantis, 2012).

These results extend those of the priming literature showing that AB in social drinkers can be manipulated by low-moderate doses of alcohol (e.g., 0.2-0.4 g/kg), but that such manipulations are less susceptible to more extreme (low and high) doses (e.g., 0.1 g/kg or

>0.6 g/kg). For example, Duka and Townshend (2004) found that AB towards alcohol-related stimuli in a dot-probe task increased after a 0.3 g/kg dose, but not after a 0.6 g/kg dose. Similarly, Schoenmakers et al. (2008) found that a 0.3 g/kg dose increased AB on a visual probe task compared to placebo, while Weafer and Fillmore (2013) found that heavy drinkers showed a dose-dependent *decrease* in AB from placebo to 0.45 g/kg to 0.65 g/kg. Finally, Adams et al. (2012) found that AB on a visual probe increased after a 0.4 g/kg dose, but not after a 0.13 g/kg dose. The current data are thus in line with previous research showing an inverse-U relationship between the amount of alcohol consumed and changes in AB, as suggested by Duka and Townshend (2004) (cf. a recent naturalistic study by Schoenmakers & Wiers, 2010, who report AB manipulations up to a much higher dose than seen in the lab).

Overall, given the preclinical findings that substances of various doses affect sign-tracking, and that human studies show the alteration of attentional processing is also dose-dependent, it would seem reasonable to tentatively conclude that human sign-tracking may also be dose-dependently influenced by alcohol. Implications for addiction are apparent; acute consumption of small amounts of alcohol can (implicitly) increase the value of reward-associated cues, with cues that were already rewarding to begin with (e.g., alcohol, food and other substances) becoming even more greatly valued *relative* to other, less valued rewards (e.g., healthy food/drink options, fulfilling specific obligations etc.). It is possible that higher doses may influence other cognitive processes and influence substance use through, for example, decreased inhibitory control and increased risk taking (Christiansen, Rose, et al., 2015; Rose, Jones, Clarke, & Christiansen, 2014).

Future work should aim to assess a wider variety of doses, preferably within the same sample, to plot a dose response curve and better establish the relationship between acute alcohol effects and sign-tracking. A placebo drink could also be utilised in order to assess the

anticipated effects of alcohol on sign-tracking, as has been done for various other cognitive processes (Christiansen et al., 2013). Additionally, to directly investigate whether alcohol increases incentive salience in a reward-general – rather than a reward-specific – way, the ASTT could be adapted to present cue-contingent feedback which is reward specific (e.g., CS1 = alcohol, CS2 = food, etc.), the responses to which could then be compared. (Note: such an adaptation would need to control for perceived reward value, so that the effects of reward *type* and reward *value* can be disentangled.) Moreover, future work must be mindful of the issue of adequate power. Though a statistically significant effect was found here in Experiment 1, a power analysis (G*Power 3.1.9; (Erdfelder, Faul, & Buchner, 1996) based on the OT RT effect size of Study 1 indicates that an *N* of 58 was necessary to achieve 80% power, a criterion which should be met in any replication attempts. Finally, future research should also consider directly investigating what cognitive mechanisms moderate this the effect of alcohol on sign-tracking.

In summary, these studies are the first to explore the effects of alcohol on social drinkers' propensity to sign-track towards discrete, noncontingent reward cues of differing value. We showed that sign-tracking biases (both RT and Omission Bias) remained at both a 0.3 and 0.6 g/kg dose of alcohol, using an adapted version of the additional singleton paradigm. We also found increased sign-tracking RT Bias – but not Omission Bias – at the 0.3 g/kg dose. However, there was no increase in either type of sign-tracking at the 0.6 g/kg dose. The data suggest that acute alcohol consumption at low-moderate doses may affect reward-based processing of discrete cues, increasing the salience of already valuable rewards, as measured by attentional bias. However, this alteration of cognitive bias seems largely unconnected to changes in subjective craving and other self-report measures. Acute alcohol consumption may affect processing of reward-associated cues, which in turn may contribute to excessive substance use.

Chapter Five

Is Sign-Tracking maintained in a Singleton Task with more than Two Distractors? A First Look

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5.1 Abstract

Background: All versions of the additional singleton task in the literature use two or fewer CSs. *Aims:* This study aimed to answer questions based on the results of Study 1 (Chapter Three): when there are more than two distractors of value in the ASTT, I) do distractors of differential value pull with differential force, and II) does sign-tracking remain? *Methods:* A within-subjects design was employed. Thirty social drinkers completed an adaptation of the ASTT containing three distractors instead of two. Participants also completed questionnaires to provide individual difference measures (e.g., alcohol consumption, impulsivity etc.). *Results:* RTs towards CSs were not affected by value. For the first time, no statistically significant difference was found in target RTs between high- and low-value trials. However, a difference was found between high- and medium-value trials. Omission differences were found between high- and medium-value trials, and high- and low-value trials. Evidence of associations between sign-tracking and individual differences was weak. *Conclusions:* Research into human sign-tracking must expand its methods in order to investigate how sign-tracking may change as individuals are exposed to more complex environments (e.g., when the number of discrete, reward-associated distractors exceeds two).

Keywords: Sign-tracking, Goal-tracking, Attentional bias, ASTT

5.2 Introduction

Sign-tracking and goal-tracking are phenotypes found across a range of species (Flagel, Akil, et al., 2009; Tomie et al., 2008). Sign-trackers (STs) attach salience to discrete, response-irrelevant conditioned stimuli (CSs) which have been associated with reward, while goal-trackers (GTs) use such CSs as indicators of reward availability. The difference between the tracking groups is observed in both the attentional resources they devote to discrete CSs (STs show an attentional bias [AB] while GTs do not), as well as in their associations with impulsivity, distractibility, risk-taking, novelty-seeking, tendency to succumb to the influence of reward-associated CSs, and higher consumption (or consumption *risk* via greater acquisition, reinstatement, sensitization or resistance to extinction) of alcohol, drugs and/or food (Ahrens et al., 2015; R. I. Anderson & Spear, 2011; King et al., 2016; Meyer, Lovic, et al., 2012; Olshavsky et al., 2014; Saunders & Robinson, 2010, 2011; Versaggi et al., 2016; Villaruel & Chaudhri, 2016; Yager et al., 2015; Yager & Robinson, 2015).

These associations to sign-tracking – many of which also correspond to goal-tracking in different contexts (T. E. Robinson et al., 2014) – have made these phenotypes interesting to the study of human issues such as drug addiction (Saunders & Robinson, 2013). In fact, recent work has shown that human sign-trackers also show similar traits and associations. Studies have shown that opioid-dependent patients (B. A. Anderson et al., 2013), obese individuals (Versace et al., 2015) and adolescents (Roper et al., 2014) all sign-track to a greater extent than nondrug, non-obese, adult controls. Additionally, in HIV+ patients sign-tracking was positively correlated with premorbid non-planning impulsiveness, negatively correlated with visual working memory capacity, and patients who also possessed a history of drug abuse showed greater sign-tracking than patients who showed no history of abuse. Thus,

these phenotypes may hold great interest to researchers studying a variety of human disorders and conditions.

The vast majority of studies investigating sign-tracking in humans have employed variations of the additional singleton task (AST) (B. A. Anderson, 2015a; Le Pelley et al., 2015; Theeuwes, 1991, 1992, 2010), though other cognitive measures have also been used (Garofalo & di Pellegrino, 2015). Fundamentally, the AST presents participants with various shapes and colours, and initially pairs certain colours with certain levels of reward (low, high or none). Participants must then quickly locate the colours in order to win rewards[21]. After this initial training phase participants are then instructed to find a shape (e.g., a diamond in an array of circles) in order to win rewards. However, during this test phase some (or all) trials contain circles of the colour previously associated with reward and the previous targets of attention. These previously reward-associated stimuli now act as distractors to participants' current goal of locating the diamond. Studies 1, 2 and 3 in this thesis all employed a variant of the AST, called the additional singleton tracking task (ASTT). The ASTT uses no training phase, and thus participants are *never* rewarded for responding to the colours. This setup reduces any likelihood that instrumental factors drive sign-tracking, instead allowing for narrower interpretations of a pavlovian cause (see Study 1, Chapter Three, for further discussion of this topic).

One finding in the studies conducted so far shows that STs' omission RTs are no quicker than GTs', which conflicts with the animal literature (Flagel, Robinson, et al., 2010; Flagel, Watson, et al., 2009; Meyer, Lovic, et al., 2012). In Study 1 (Chapter Three) it was suggested that this null finding might be symptomatic of a lack of RT variability, given that preclinical

[21] Most variations of the AST do not instruct participants to respond to the colour specifically, but rather to a feature of the shape presented (e.g., the single horizontal bar presented amongst an array of vertical bars). Researchers simply pair this feature most often with a certain colour. Thus, an implicit association is drawn between the colour and the level of reward.

trial periods last a lot longer (typically around 8s) than human participants' reactions in the ASTT (typically <1s). It was proposed that one way to overcome this limitation is to use a task which employs more than two CSs of differing value. This change would not alter the timing structure of the ASTT (which is difficult to do given the task setup and has the added shortcoming of introducing confounds which could make interpretation difficult); however, by potentially increasing variability in CS (omission) RTs, it may be possible to determine whether STs' CS RTs are quicker than GTs' (both in general and across CSs of different value). Relatedly, previous human research has shown that while CSs of differing value capture attention to different extents, the 'pull' or 'force' with which they do so is equal across CS value (Le Pelley et al., 2015). That is, while high-value CSs slow down RTs to the target more than low-value CSs (as well as causing more omissions), the speed with which attention is drawn to each of the CSs during omission responses is equivalent. This finding was replicated in Studies 1, 2 and 3 (see Chapter Nine).

Using an increasing number of reward-associated cues is also important in order to assess how robust value-modulated attentional capture (VMAC) is when applied to more complex environments (i.e., the presence of more stimuli and additional associations). The consistent results in paradigms which use only two reward-associated cues may not be applicable to paradigms whose cue quantity exceeds two. Indeed, as others have suggested, "*It would be informative for future studies to place differently valued distractors in direct competition with one another.*" (B. A. Anderson & Yantis, 2012, p. 1651). By presenting participants with three reward-associated cues, rather than two, the current study aims to test these outstanding questions: I) do STs show quicker CS RTs than GTs when CS RT variability is increased, and II) do CS RTs (in the general sample) differ between CSs of different value when the quantity of CSs exceeds two (i.e., when CS RT variability is increased)? The primary hypotheses of the previous studies will also be tested in the context

of this new task variant. Given the robust result of this thesis so far (and of the literature in general), it is hypothesised that the value-dependent effects observed with two CSs, will also be observed with three CSs. That is, attentional capture will be greatest on high-value trials, lowest on low-value trials, and somewhere in between on medium-value trials.

5.3 Method

Participants

Thirty participants (18 female) were recruited through opportunistic sampling. Participants were aged between 18 and 26 years (M = 19.93, SD ± 1.95). The inclusion criteria were regular consumption of alcohol (≥10 units per week) and normal or corrected-to-normal vision. Self-reported past or present alcohol or drug use problems were exclusions. All participants provided written informed consent before taking part in the study, which was approved by the University of Liverpool Research Ethics Committee.

Materials

Questionnaires

The same questionnaire pack used in Study 1 was given to all participants to assess drinking habits (TLFB, AUDIT), drinking motives (Modified DMQ-R), drinking consequences (B-YAACQ), impulsivity (BIS-11, ImpSS) and childhood trauma (CATS) (see Chapter Two [General Methods] for full descriptions).

Cognitive Task

Additional Singleton Tracking Task: Plus (ASTT+): The task used is almost identical to the ASTT used in Studies 1, 2 and 3 (see Chapter Two [General Methods] for full description), and is an adaptation of the additional singleton task developed by Theeuwes (1991, 1992, 2010). This version employs three, rather than two, noncontingent discrete reward-associated cues, corresponding to high, medium and low monetary reward (red, blue and green singletons, counterbalanced). Sign-tracking is inferred from I) slower responses to the OT on higher-value compared to lower-value trials, and II) greater omissions (CS responses) on higher-value compared to lower-value trials. Note that this applied to all three trial types (e.g., high-value trials should induce the slowest OT responses, followed by medium-value trials, followed by low-value trials). The maximum feedback for low, medium and high-value trials (following correct responses) was 2.00, 20.00 and 60.00 'MONEY' points, respectively. Feedback was calculated via the following formula

$$(1000 - RT) \times .002 \times \textit{reward value}$$

where *RT* is reaction time (in milliseconds) and *reward value* equals 1, 10 or 30 (depending on trial type). Given the extra trial type, the ASTT+ contains 450 trials, compared to the ASTT's 300 trials (in order to retain power). The task lasted approximately 32 minutes.

Procedure

All testing took place between the times of 12 p.m. and 6 p.m. in the eye-tracking laboratory of the School of Psychology, University of Liverpool. Before attending the lab, every participant completed an online questionnaire pack (TLFB, AUDIT, DMQ-R, B-YAACQ, BIS-11, ImpSS, CATS) via Qualtrics (Provo, UT, 2015). Those who fulfilled the criteria were invited to attend the laboratory session. All participants provided informed

consent before both the online questionnaire and lab portions of the study. During the lab session, participants completed the ASTT+ after being told that extra vouchers were available based on their task performance. Participants received either course credits or £10 in 'Love2Shop' vouchers as compensation for their travel expenses and time. During the debriefing it was explained that they would not receive any extra vouchers based on their task performance, and that this was a necessary deception. Each session lasted approximately 30 minutes.

5.4 Data Reduction and Analysis

The following are an extension of measures that have been used in previous research in estimating attentional bias and stimulus value (Field & Cox, 2008; Rose, Brown, Field, & Hogarth, 2013). As in previous studies, all RT responses <80 ms and >999 ms were recoded as missing data.

Additional Singleton Tracking Task: Outcome Measures

Measures for the ASTT were those used by Le Pelley et al (2015) and were divided into omissions and RTs. For both RT and Omission Biases, greater (positive) values indicate sign-tracking (as higher-value distractors should induce more errors and slower responses to the OT than lower-value distractors). See Table A2 (Appendix A) for calculations.

5.5 Results

Participant Characteristics

Table 5.1 summarises the sample's average alcohol use characteristics, while Table 5.2 provides an overview of trait and state measures. Men binged more (41.7% binged 4 times p/fortnight) than women (27.8% binged 3 times p/fortnight). One-hundred percent of participants scored ≥8 on the AUDIT, classing them as at risk drinkers. Self-reports showed that, overall, the participant population were hazardous drinkers, consuming over recommended weekly guidelines (14 units per week for men and women). On the B-YAACQ: Total, 16.7% of participants scored ≤5, with 23.3% scoring between 6 and 10, 33.3% scoring between 11 and 15 and 26.6% scoring between 16 and 24. A score greater than 5 is associated with increased likelihood of risky drinking (e.g., experiencing impulsivity, embarrassment, regret and/or harm as a result of drinking) (Kahler et al., 2005). In terms of personality variables, most scored within the normal ranges of some scales (e.g., 63.3% scored within the BIS-11 range of normality [52-71]; the ImpSS average was almost identical [*M* = 9.43] to that found previously in undergraduates [*M* = 9.50] [Ball, 1995]). The CATS: Total average (*M* = 0.79) was comparable to earlier work in nonclinical samples (*M* = 0.74; *M* = 0.77) (Kent & Waller, 1998; Sanders & Becker-Lausen, 1995), suggesting low levels of childhood trauma.

Table 5.1 Alcohol use characteristics (Means ± SD)

Alcohol unit consumption (TLFB)	32.25 (± 16.51)
Binge frequency	4.10 (± 1.86)
AUQ: Units consumed per hour	4.39 (± 2.36)
AUQ: Age at first drink	14.32 (± 1.65)
AUQ: Age at regular drinking	17.18 (± 1.86)
AUQ: Drunk frequency	45.20 (± 16.28)
AUQ: Drunk percentage	69.10 (± 26.55)
AUDIT	23.53 (± 6.17)

Consumption = UK units (1 UK unit = 10 ml or 8 g of pure alcohol); *TLFB* = Timeline FollowBack, based on an average of prior two weeks of alcohol consumption; *AUQ* = Alcohol Use Questionnaire; *Binge frequency* = ≥8 units for men, ≥6 units for women per day, based on an average of prior two weeks of alcohol consumption; *Age at regular drinking* = the age at which regular drinking was undertaken; *Drunk frequency* = number of times individuals have been drunk in the previous 6 months; *Drunk percentage* = percentage of drinking occasions in which individuals become drunk; *AUDIT* = Alcohol Use Disorders Identification Test.

Table 5.2 Trait/State characteristics (Means ± SD)

BIS-11: Total	65.38 (± 11.11)
B-YAACQ: Total	11.79 (± 6.01)
ImpSS	10.05 (± 3.93)
CATS: Total	0.80 (± 0.35)

BIS-11 = Barratt's Impulsivity Scale; *B-YAACQ* = Brief Young Adult Alcohol Consequences Questionnaire; *ImpSS* = Impulsive Sensation Seeking; *CATS* = Child Abuse and Trauma Scale. *Note.* An *M DMQ-R: Total* variable was not computed as the questionnaire's subscales qualitatively conflict (e.g., coping versus enhancement); thus, a total score would be interpretively useless.

Table 5.3 presents descriptive statistics for the ASTT, showing average response frequencies for the OT and CSs. Table 5.4 reveals the range of CS RT responses across all studies thus far. This is important as the aim of employing the ASTT+ containing an extra distractor was to increase CS RT response variability. The data show that Study 4 (ASTT+) has produced the largest range of CS RT responses, compared with Studies 1, 2 and 3

(ASTT). A One-Way ANOVA was conducted to investigate if the variance of CS RTs in the current study was significantly different to that of CS RTs in studies 1-3. Levene's test statistic showed a violation of the assumption of homogeneity of variance between studies, $F(3, 363) = 5.97$, $p = .001$, while the analysis of variance test also showed a significant difference in variance, $F(3, 366) = 3.69$, $p = .01$. However, planned contrasts showed no significant difference between CS RTs in the current study and studies 1-3, $t(147.63) = 0.13$, $p = .45$, $r = .01$ (1-tailed). This suggests that, although the ASTT+ increased the variability of CS responses compared to studies 1-3, it did not do so to a statistically significant degree. Whether this nonsignificant increase is sufficient to alter participant responses is examined below.

Table 5.3 Response frequencies (Means ± SD)

Outcome Measures	*Frequencies*
OT	422.73 (± 18.63)
High-value distractor	8.23 (± 9.44)
Medium-value distractor	4.83 (± 3.54)
Low-value distractor	5.35 (± 4.29)

Each outcome measure's fixation frequency is presented. OT = Outcome Target. *Note.* Frequencies do not add up to 450 (total number of trials) as these descriptives do not include non-responses.

Table 5.4 CS RT response ranges

Studies	*Min. – Max. (Range)*
Study 1	91.00 – 474.33 (383.33)
Study 2	216.75 – 864.00 (647.25)
Study 3	142.00 – 606.00 (464.00)
Study 4	153.00 – 917.00 (764.00)

Studies 1, 2 and 3 all employed an ASTT using only two CSs; Study 4 uses the ASTT+, which contains three CSs. Values are taken from raw response scores across CS types. The CS RT range for Studies 1-3 refer to RTs towards high- and low-value CSs combined; Study 4 ranges apply to high, medium and low-value CS RTs combined. *Note.* The data from Studies 2 and 3 are taken from the 'control' session, not the 'alcohol' session.

Analyses were first run to investigate the central question of this study: do RTs towards CSs of different value significantly differ?

High-value CS vs. Medium-value CS vs. Low-value CS: A Friedman test revealed no statistically significant difference in RT, indicating similar pull or 'force' (Le Pelley et al., 2015) between high- (*Mdn* = 311.09, *range* = 240.43 – 574.33), medium- (*Mdn* = 295.00, *range* = 222.25 – 917.00) and low-value (*Mdn* = 289.75, *range* = 153.00 – 418.67) CS RTs, $\chi^2(2) = 2.08$, $p = .35$ (2-tailed).

Given that one of the predictions, based on preclinical results, is that sign-trackers should show quicker CS RTs than goal-trackers given the increased CS variability, a median split was conducted on participants' RT Bias scores to create tracking groups (each group, $n = 15$).

High-value CS vs. Medium-value CS vs. Low-value CS (STs vs. GTs): Kruskal-Wallis analyses revealed no difference between tracking groups in RTs towards high-value, $\chi^2(1) = 2.68$, $p = .10$, medium-value, $\chi^2(1) = 0.76$, $p = .38$, or low-value CSs, $\chi^2(1) = 0.52$, $p = .47$ (all

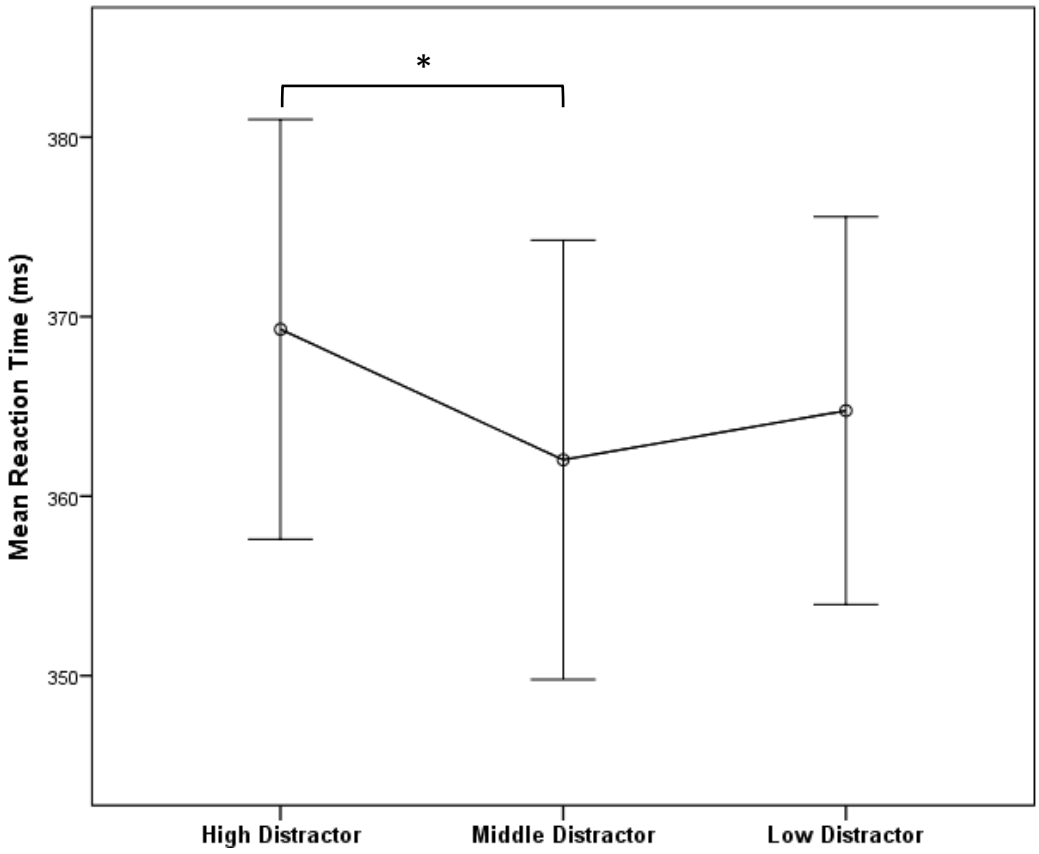
2-tailed). This suggests that CSs of different value attract STs' and GTs' RT responses with the same magnitude.

Overall CS RT differences in STs vs. GTs: A Mann-Whitney U test was used to investigate whether group differences existed in RTs towards CSs overall, regardless of value. No difference between STs (*Mdn* = 296.93, *range* = 250.08 – 341.42) and GTs (*Mdn* = 300.00, *range* = 225.69 – 565.17) were found, $U = 112.00$, $p = .98$ (2-tailed).

Next, whole-sample analyses were run to investigate whether OT RT and/or omission differences existed between high, medium and low-value trials.

Reaction Times: A Repeated-Measures ANOVA revealed a main effect of distractor type on RTs towards the target (OT), $F(2, 58) = 3.99$, $p = .02$, $\eta_p^2 = 0.12$. Pairwise comparisons show that, after a Bonferroni correction, the only statistically significant effect found was that of higher latencies on high-value ($M = 369.30$, $SD \pm 31.32$) compared to medium-value trials ($M = 362.03$, $SD \pm 32.76$), $p = .02$, $r = .43$. Contrary to previous results in ASTTs using only two distractor types there was no significant difference found between high-value and low-value ($M = 364.76$, $SD \pm 28.92$) trials, $p = .37$. There was also no difference between medium-value and low-value trials, $p = .58$ (see Figure 5.1).

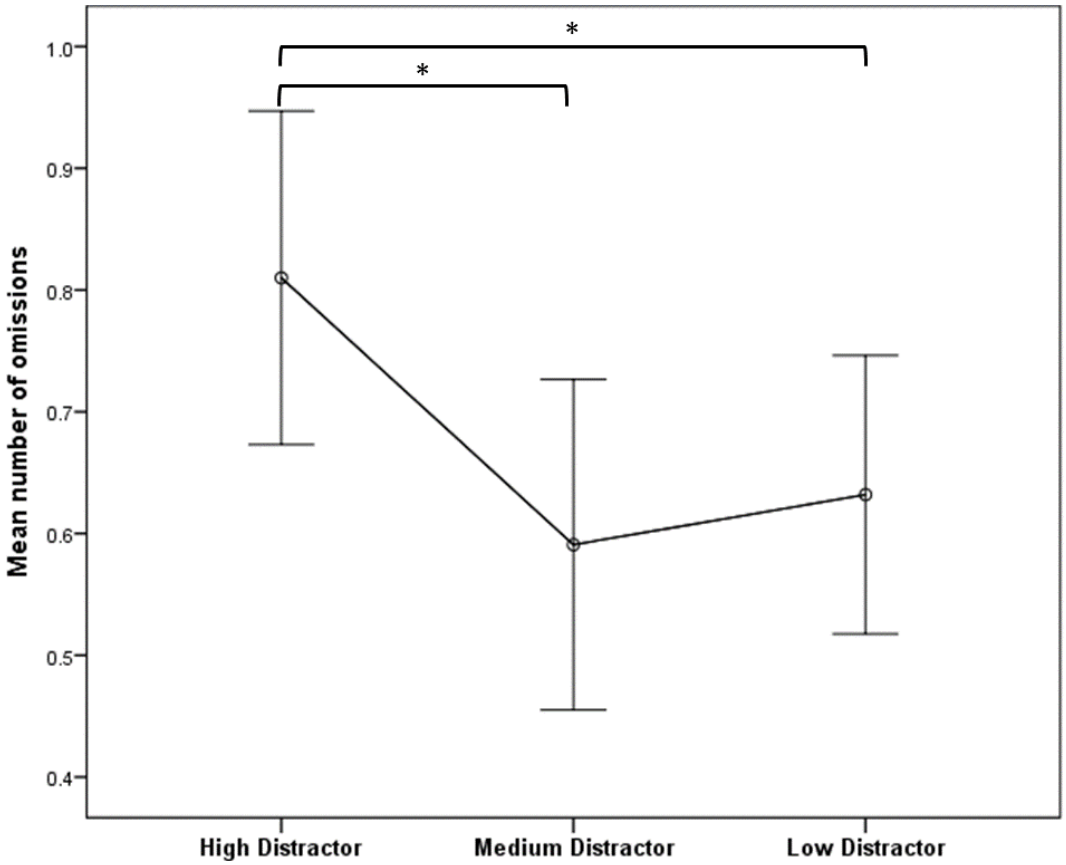
Figure 5.1 Error bar chart depicting mean OT RT differences between CSs (entire sample)



Mean reaction times are in milliseconds. *$p < .05$. Error bars = 95% CI.

Omissions: Due to the omission data being highly skewed, the data were log-transformed before analysis. A Repeated-Measures ANOVA was also conducted for omission frequencies across trial types. There was a significant main effect of trial type on the number of omissions, $F(2, 50) = 6.72$, $p = .003$, $\eta_p^2 = 0.21$. Pairwise comparisons using a Bonferroni correction revealed that there were significantly more omissions on high-value trials (M = 0.81, SD ± 0.34) compared to low-value trials (M = 0.63, SD ± 0.28), $p = .01$, $r = .53$. Likewise, there were significantly more omissions on high-value trials relative to medium-value (M = 0.59, SD ± 0.34) trials, $p = .01$, $r = .47$. No difference in omission frequency was found between medium- and low-value trials, $p = 1.00$ (see Figure 5.2).

Figure 5.2 Error bar chart depicting mean omission differences between CSs (entire sample)



Omission data for all trial types have been log-transformed. *$p \leq .01$. Error bars = 95% CI.

Associations with Individual Differences

Correlations were conducted between task outcomes and self-report measures (e.g., alcohol consumption, impulsivity etc.). The correlation matrix is presented in Table F1 (Appendix F). After appropriate statistical corrections were applied, of the 111 correlations performed, only a correlation between *Omission Bias 2* (difference score between high- and low-value trials) and the CATS: Sexual Abuse subscale reached statistical significance (r_s = .52, p = .007; 2-tailed). This suggests that higher levels of omissions (as measured as a

difference in errors between high- and low-value trials) is associated with higher levels of self-reported sexual abuse.

5.6 Discussion

Based on findings from studies 1-3 and research recommendations within this field (B. A. Anderson & Yantis, 2012), the current study sought to investigate – for the first time – how sign-tracking responses may be altered on the ASTT by including three response-irrelevant, reward-associated distractors, rather than the usual two. Results revealed no statistically significant difference in CS RT responses, either in the sample as a whole, or when tracking groups were compared. These results applied to CSs of every value, as well as to CSs as a whole, regardless of value. Analyses further showed that RTs towards the OT were higher on high-value trials compared to medium-value trials; however, no differences were found between high- and low- or medium- and low-value trials. Greater numbers of omissions were also found on high-value compared to medium- *and* low-value trials, although no difference between medium- and low-value trials was found. Finally, the only correlation between sign-tracking measures and individual differences that reached statistical significance was between 'Omission Bias 2' (difference score between high- and low-value trials) and the Childhood Abuse and Trauma Scale (CATS) Sexual Abuse subscale.

The question of how sign-tracking may be altered by an increased number of CSs was posed after the results of Study 1 (Chapter Three), which showed that the entire sample (as well as STs and GTs, individually) produced RTs of similar magnitude towards distractors (CSs) of differing value (as well as towards distractors overall, regardless of value). This is in accordance with previous human studies (Le Pelley et al., 2015) but contrasts with the

preclinical literature, which shows that STs produce faster omissions than GTs (Flagel, Robinson, et al., 2010; Flagel, Watson, et al., 2009; Meyer, Lovic, et al., 2012). Thus, the current study aimed to investigate this discrepancy further by employing an adapted version of the ASTT – termed the ASTT+ – which utilised three distractors of value in order to increase the variability in CS RT responses. This method was used as the ASTT paradigm does not lend itself to the extended trial durations of the kind found in the animal literature, and so increased CS number was introduced as an alternative way to study CS response variability. It should be noted that although the ASTT+ did show greater CS RT variability than all other studies using the ASTT (see Table 5.4), it did not do so to a statistically significant degree. Further, we cannot be certain that this (nonsignificant increase) is attributable to the increased number of CSs. It could instead be due to the increased number of trials (450 vs. 300), or a combination of the two. This would need to be investigated in future studies.

The results did not replicate those of the preclinical literature, but rather, they aligned with those of Studies 1, 2 and 3, as well as with previous human studies. The sample as a whole showed no difference in RTs towards CSs of different value, replicating Le Pelley et al. (2015) who showed that high- and low-value CSs attract attention with the same 'force'. Increasing singleton response variability (though to a statistically nonsignificant degree) by extending distractor number did nothing to alter this seemingly robust finding. STs and GTs (groups created via a median split of RT Bias scores) also did not differ in their RT responses towards CSs of different value[22]. It is important to note that this comparison – of tracking groups' CS RT responses towards CSs (regardless of value) – is the closest human analogue to that of the animal literature, in which animal tracking groups (STs versus GTs) are

[22] Median splits of RT data are not the best way of distinguishing groups (Rucker, McShane, & Preacher, 2015). Ideally, only individuals with more extreme responses would be categorised as STs and GTs (as in Study 1, Chapter Three). However, due to the relatively small sample size, a median split was the only recourse.

compared in how long it takes them to approach a CS. Once again, our findings were contrary to those of the animal literature: human tracking groups did not differ in their overall CS RT responses (as was also found in Study 1, Chapter Three).

Regarding analyses which were primary in previous studies but secondary in this study, results revealed that OT RTs were higher on high-value trials compared to medium-value trials, while no differences were found between high- and low-value or between medium- and low-value trials. Omissions were greater on high-value compared to medium- *and* low-value trials, with no discernible difference between medium- and low-value trials. The finding of no OT RT difference between high- and low-value trials is the first null result of this kind in the thesis so far. Importantly, as stated earlier, this is also the first study in the human literature to employ more than two CSs of differing value, and these results suggest that sign-tracking as measured by latency only manifests between the two most highly valued CSs. Specifically, participants' OT responses on low-value trials failed to be significantly influenced by the CS's value (as indicated by RT responses not being particularly fast or slow, but falling in between that of high and medium trial OT responses). However, such an interpretation may be hampered by study limitations (discussed below).

Finally, analyses were conducted to assess whether sign-tracking measures (both RT and omissions) were associated with individual differences measures. After statistical corrections were applied, only a correlation between *Omission Bias 2* (difference score between high- and low-value trials) and the CATS: Sexual Abuse subscale reached statistical significance. This suggests a positive association between omissions and self-reported sexual abuse. However, given the likelihood of false-positives with so many (one-hundred and eleven) correlations and the lack of association with this particular measure in previous studies, it seems likely that this statistical significance is merely an artefact of running so many

correlational analyses. The findings from the CS RT and OT RT analyses present some predicted, and some unexpected, results. The rest of this discussion will aim to explore the possible reasons for these findings, as well as describing possible methodological limitations which impede some interpretations of the data.

The CS RT findings may be explained several ways. First, the difference in findings between humans and nonhuman animals may simply be one of experimental setup. As stated previously, for preclinical studies a typical trial duration during which the CS is present is around 8 seconds (with animals taking several seconds to move toward the CS), while ASTT trials last 2 seconds (with typical responses averaging several hundred milliseconds). This difference in duration could be one reason for the disparity in CS RTs. A related explanation entails that, although the introduction of an extra CS in the ASTT+ did increase CS RT variability compared to all studies thus far, it is possible that there was still not *enough* variability to allow for what may be a small effect to be found. This explanation is given credence by the lack of a statistically significant difference in CS RT variance between studies. Unfortunately, due to previous null results regarding CS RT difference by CS value, *a priori* effect sizes could not be calculated in order to estimate the necessary sample size for this study.

A further explanation concerns the fact that human and animal studies are using fundamentally different measures of CS value. Although both use approach measures in a broad sense, preclinical studies measure physical movement towards the CS, while human studies measure attentional bias – preclinical studies suggest that this difference may matter even at the level of the brain (Saunders & Robinson, 2013). A solution to all of these issues may require the use of methods which allow for greater trial durations (mimicking durations used in the preclinical literature and increasing response variability to an even greater extent),

as well as the measurement of physical movement towards the CS rather than attentional shifting (e.g., 'action tendencies'). Such methods are already commonplace in the human cognitive and alcohol literature, with tasks such as the Implicit Association Task (IAT), Alcohol Approach Task (AAT) and (Relevant-) Stimulus-Response Compatibility task (R-SRC) (Wiers et al., 2013). In fact, a recent study employed a version of the additional singleton task wherein participants physically reach for the OT and found that distractors associated with high reward actually distracted *less*, which may indicate that different methods of approach are measuring different constructs (Moher, Anderson, & Song, 2016). Only if these explanations are ruled out could we reasonably speculate that there might be qualitative behavioural differences between human and nonhuman animal STs, which cause differential responding towards discrete, reward-associated stimuli. In essence, behavioural measurements of value between humans and nonhuman animals must be sufficiently equated in order to assess whether humans and animals are qualitatively different in this respect.

Regarding the OT RT results (the primary focus of Studies 1, 2 and 3), one explanation for the lack of response differences between high- and low-value trials may be that the values were not differentiated enough. However, this seems unlikely given that the ASTT uses a points divide of 2.00 (low) vs. 20.00 (high), while the current ASTT+ uses 2.00 (low) vs. 20.00 (medium) vs. 60.00 (high). Mathematically, the medium reward is 10 times larger than the low reward, while the high reward is 3 times larger than the medium reward and 30 times larger than the low reward – since the biggest value differences lie between high-low and medium-low trials, a lack of variability or differentiation of values cannot account for RT differences between only high- and medium-value trials. Thus, for RT measures using AST methods, it may be the case that attention is given primarily to the CSs possessing the two highest values, with other, lower value CSs being largely ignored. Regarding sign-tracking as measured via omissions, the predicted patterns of high > medium and high > low were found.

However, no difference between medium- and low-value trials was found. As with RT measures, omission frequency on low-value trials fell in between frequencies on high- and medium-value trials, which further supports the interpretation that participants ignored low-value CSs.

To summarise, this is the first study which has employed a variant of the additional singleton task (AST) that possess more than two singletons/CSs of value. The primary aims were to investigate whether this increased complexity would alter RTs towards CSs of different value, or whether individuals classified as sign-trackers (STs) and goal-trackers (GTs) would respond differentially to CSs overall, regardless of value. We found that CS value did not alter participants' RT responses; that is, CSs, regardless of value, all attracted attention with the same strength, as measured by latency. Similarly, STs and GTs showed no difference in RT responses to CSs, regardless of value. These results support the previous studies of this thesis, as well as the wider human literature, though are at odds with the findings of the preclinical literature. The secondary aims were to investigate OT responses in the context of three value-associated CSs. We found that OT RTs only showed a difference between high-value and medium-value trials – this is the first study not to find a difference between high- and low-value trials. The implication of this may be that, in more complex AST designs, attentional priority is given to the two most highly valued CSs (with the second highest value possibly treated as the de facto 'low-value' cue), with all other CSs being ignored. Omissions were found in greatest frequency in high-value trials, with no difference between medium- and low-value trials being found. No robust evidence of a link between sign-tracking and individual differences was found. Future studies which aim to investigate CS RT responses in a sign-tracking paradigm may wish to employ methods which measure physical approach tendencies, rather than attentional bias.

Chapter Six

A Comparison of Methods for Measuring Human Sign-Tracking

6.1 Abstract

Background: Versions of the additional singleton and alternative tasks measuring sign-tracking have yet to be compared, so it is unclear whether they are measuring the same construct with the same sensitivity. *Aims:* To compare methods of measuring sign-tracking. *Methods:* Social drinkers (N = 25) completed three tasks in one lab session: the Additional Singleton Tracking Task: Eye-Tracker (ASTT [EE]), the ASTT: Button-Box (ASTT [BB]) and a Pavlovian-to-Instrumental Transfer (PIT) task, which also measured sign-tracking. The two ASTTs were virtually identical, except that the ASTT (EE) measured oculomotor responses while the ASTT (BB) measured behavioural (key press) responses. The PIT used a combination of both measures. Participants completed online questionnaires before the lab session assessing alcohol consumption, impulsivity etc. *Results:* No sign-tracking effects were observed in either the ASTT (EE) or ASTT (BB). Though a sign-tracking index was made for the PIT task, no PIT effect was observed, nor were there any differences between STs' and GTs' responses. No task comparisons or correlations to individual differences were performed. *Conclusions:* Given the lack of tracking effects, it is not possible to make any clear conclusions regarding the comparison of tasks. It is possible that completion of three tasks in a single session resulted in cognitive fatigue which impaired performance.

Keywords: Sign-tracking, Pavlovian-to-Instrumental Transfer, Alcohol, Eye-tracking

6.2 Introduction

Sign-tracking and goal-tracking are behaviours found in a variety of species (including humans) and conceptualise the individual differences in responses towards irrelevant, discrete stimuli paired with reward (Tomie et al., 2008). Specifically, sign-trackers (STs) imbue such stimuli (conditioned stimuli; CSs) with value, while goal-trackers (GTs) use CSs merely as predictors of the US. Preclinical studies have shown that animals can reliably be classified into STs or GTs based on their propensity to attribute incentive salience to noncontingent, discrete reward-associated cues (Meyer, Lovic, et al., 2012). The tracking phenotypes have shown links with impulsivity, distractibility, risk-taking, novelty-seeking and higher consumption (or consumption risk) of alcohol, drugs and/or food (Ahrens et al., 2015; R. I. Anderson & Spear, 2011; King et al., 2016; Meyer, Lovic, et al., 2012; Olshavsky et al., 2014; Saunders & Robinson, 2010, 2011; Versaggi et al., 2016; Villaruel & Chaudhri, 2016; Yager et al., 2015; Yager & Robinson, 2015). Human STs show similar traits and associations (B. A. Anderson et al., 2013; Roper et al., 2014; Versace et al., 2015).

The vast majority of studies investigating sign-tracking in humans have employed variations of the additional singleton task (AST), which measure responses via button responses or eye-movements (B. A. Anderson, 2015a; Le Pelley et al., 2015; Theeuwes, 1991, 1992, 2010). Studies 1, 2, 3 and 4 in this thesis have all employed a variant of the AST, called the additional singleton tracking task (ASTT). In every study thus far, the ASTT has measured sign-tracking via oculomotor capture. The ASTT presents participants on every trial with several grey circles and one diamond, and instructs participants to locate the diamond as quickly as possible. On each trial one of the circles is coloured either red or blue, with each colour associated with either high or low reward only when a correct response is made. Sign-tracking is observed when the colour associated with high reward captures

attention and reduces the reaction times (RTs) of correct responses as well as prompting more omissions (errors) compared to low-reward cues.

A recent study has, for the first time, measured sign-tracking during a Pavlovian-to-Instrumental Transfer (PIT) task, which then assessed how strongly PIT effects influenced STs as compared to GTs (Garofalo & di Pellegrino, 2015). PIT refers to the behavioural and psychological phenomenon of increased instrumental (choice) responding for an outcome (e.g., reward) when in the presence of a CS+ (a CS which was separately paired with the same outcome). PIT effects have been found in both animals and humans, with human studies showing that a CS+ can increase instrumental responding for drug and alcohol rewards. This increase in responding (PIT effect) correlates with neuroimaging (e.g., Functional Magnetic Resonance Imaging: fMRI) and neurophysiological activity (e.g., Electroencephalography: EEG) (Cartoni et al., 2016; Corbit & Janak, 2016; Garbusow et al., 2014; Martinovic et al., 2014; Talmi et al., 2008).

In the Garofalo and di Pellegrino (2015) study, participants completed three separate (but related) tasks. The first (*Instrumental Conditioning*) measured participants' top-down selection of cues associated with reward or no reward (rewarded choice versus unrewarded choice). The second (*Pavlovian Conditioning*) measured their bottom-up behavioural and eye-movement responses towards a different set of cues associated with reward or no reward CS+ versus CS−). Participants were also classified as STs or GTs during this stage based on their attentional bias (AB) towards either the CS+ or the location of reward presentation, respectively. The third task (*Pavlovian-to-Instrumental Transfer*) measured the influence of each CS on participants' un/rewarded choice. The results showed that the groups differed in the extent to which their instrumental responding for un/rewarded choice was influenced by the presence of the CS+, with STs responding more towards reward-associated stimuli than

GTs when in the presence of the CS+. That is, reward-paired cues more strongly influenced STs' behaviour than GTs', which in the context of the task lends support to the theory that sign-tracking reflects the attribution of incentive salience towards discrete, response-irrelevant CSs. The authors also found that STs self-reported significantly lower impulse control (as measured by Barratt's Impulsivity Scale–11, Patton et al., 1995) than GTs.

The current study aims to extend the work of Garofalo and di Pellegrino (2015) by producing the first replication of their study whilst also enabling a comparison between their PIT task and the ASTT. Furthermore, to expand our knowledge on the relative merits of various methods of sign-tracking measurement in humans, the current study will employ two different versions of the ASTT – one utilising eye-tracking responses (as has been used in studies 1-4) and one recording behavioural responses via button-box presses. This difference between attentional orienting and motor response has been implicated as an important consideration in animal paradigms (White & Naeem, 2017; Yager & Robinson, 2013), and some data suggest that AB measures as measured via eye-movements are more reliable than those measured via key presses (Christiansen, Mansfield, et al., 2015). Thus, the central concern of this study is methodological: are there multiple ways in which to reliably measure sign-tracking and do they produce similar outcomes? Specifically, I) do all tasks produce sign-tracking effects? II) Does the magnitude of sign-tracking significantly differ between tasks? III) Do the methods possess sufficient sensitivity and specificity to reliably classify the same individuals as STs and GTs across tasks? IV) Do all task outcome measures correlate with individual differences (e.g., alcohol consumption and impulsivity)? It is hypothesised that I) sign-tracking effects (RTs and omissions) will be observed in all three tasks (ASTT [EE], ASTT [BB], PIT task), and II) STs' instrumental responding towards reward-associated stimuli will be influenced by the presence of the CS+ to a greater extent than GTs'.

6.3 Method

Participants

Twenty-five participants (13 female) were recruited through opportunistic sampling. Participants were aged between 20 and 35 years (M = 25.50, SD ± 4.27). The inclusion criteria were regular consumption of alcohol (≥10 units per week) and normal or corrected-to-normal vision. Self-reported past or present alcohol or drug use problems were exclusions. All participants provided written informed consent before taking part in the study, which was approved by the University of Liverpool Research Ethics Committee.

Materials

Questionnaires

The same questionnaire pack used in study 1 was given to all participants to assess drinking habits (TLFB, AUDIT), drinking motives (Modified DMQ-R), drinking consequences (B-YAACQ), impulsivity (BIS-11, ImpSS) and childhood trauma (CATS) (see Chapter Two [General Methods] for full descriptions).

Cognitive Tasks

Additional Singleton Tracking Task: Eye-Tracker (ASTT [EE]): The task employed was identical to the task used in study 1 (Chapter Three, see Chapter Two [General Methods] for

full description), and is an adaptation of the singleton task developed by Theeuwes (1991, 1992, 2010). Sign-tracking is inferred from I) slower responses to the OT on high-value compared to low-value trials, and II) greater omissions (CS responses) on high-value compared to low-value trials.

Additional Singleton Tracking Task: Button-Box (ASTT [BB]): This task was almost identical to the ASTT (EE) task (above). The only difference was the number of stimuli presented on each trial: in the ASTT (EE) there are 6 stimuli (1 diamond [OT], 1 coloured circle [CS], 4 grey circles [valueless distractors]), in the ASTT (BB) there are 8 stimuli presented on each trial (1 diamond [OT], 1 coloured circle [CS], 6 grey circles [valueless distractors]). It should be noted that evidence suggests increased 'display size' (number of stimuli) in additional singleton tasks presenting a coloured distractor increases average response times (Theeuwes, 2010), and so increased stimulus number should not adversely affect the production of sign-tracking. This adaptation was in an effort to mirror as closely as possible the button-box used in Study 6 (Chapter Seven). This was done with the considerable assistance of other researchers and technical support staff at the University of Liverpool: Pawel Jedras and Martin Guest.

Pavlovian-to-Instrumental Transfer Task (PIT): This task was a direct replication of Garofalo and di Pellegrino (2015), and was constructed with the advice of the original study's lead author (S. Garofalo, personal communication, 17th May – 21st July, 2016). As with many of the stimuli used in the Multi-Target Tracking Task (Study 1, Chapter Three), many of the PIT stimuli were acquired from internet searches and customised for use in the task (see 'Fractal Ratings' in Data Reduction and Analysis section).

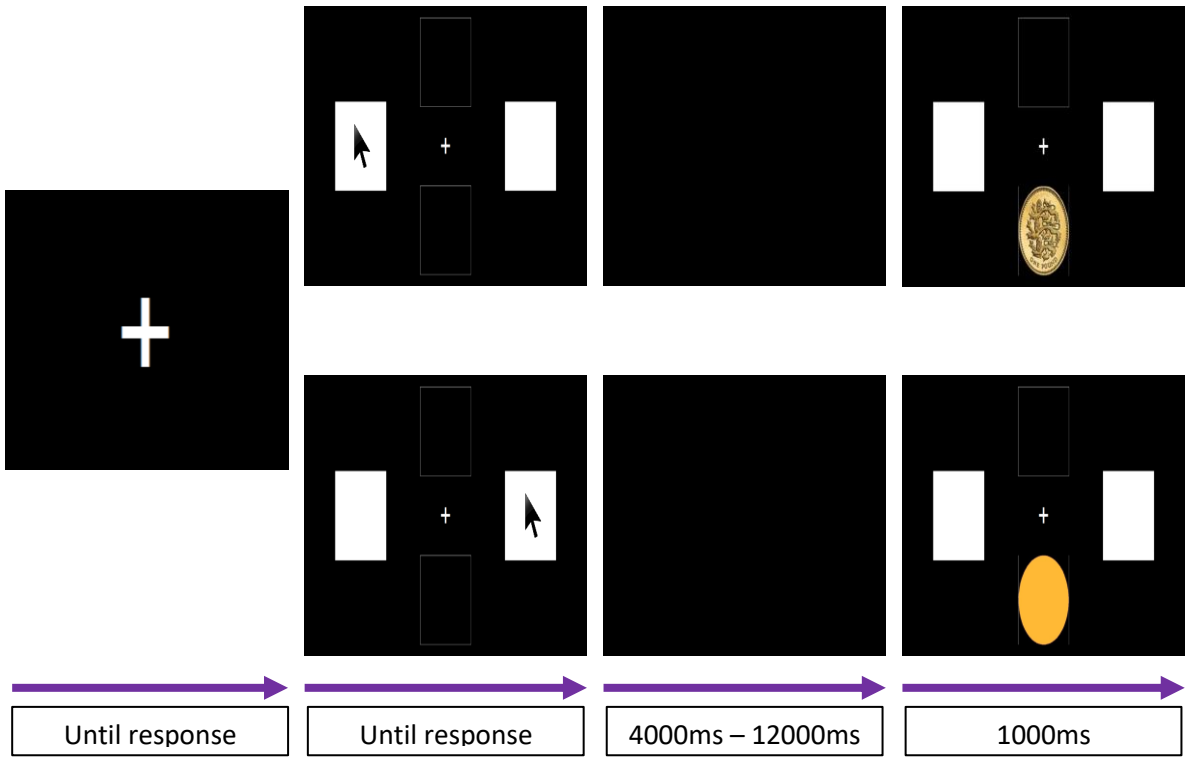
The PIT consisted of three phases: I) Instrumental Conditioning Task, II) Pavlovian Conditioning Task, and III) Pavlovian-to-Instrumental Transfer Task. Participants were again

instructed that they would earn points throughout this task which would later be exchanged for vouchers. It should be noted that the majority of PIT tasks first promote pavlovian conditioning before instrumental conditioning; however, Garofalo and di Pellegrino (2015) opted for the opposite order. Given that the current study is a replication of their work, their methodology is followed closely.

Instrumental Conditioning Task: The first phase of the PIT task requires participants to first select the crosshair in the centre of the screen (Figure 6.1: column one); this ensures participants centre the mouse arrow at the beginning of every trial, so as to prevent a side-selection bias. Next, participants select one of the white boxes (column two). After selection, there is a variable inter-trial interval (ITI) (column three) of between 4000ms and 12000ms (randomised). Finally, participants are presented with feedback (column four), consisting of either a one pound sterling coin (£1) or a plain yellow circle. In the counterbalanced condition, the selection stage is reversed (i.e., left choice = unrewarded, right choice = rewarded). Participants were told that the points they won during this portion would be added to their points tally.

It was expected that participants would adequately learn the difference between the rewarded and unrewarded options, and quickly begin consistently selecting the rewarded stimulus (left white square in Figure 6.1). After the presentation of four practice trials, this stage lasted approximately 6m 30s.

Figure 6.1 Schematic of the Instrumental stage of the PIT task



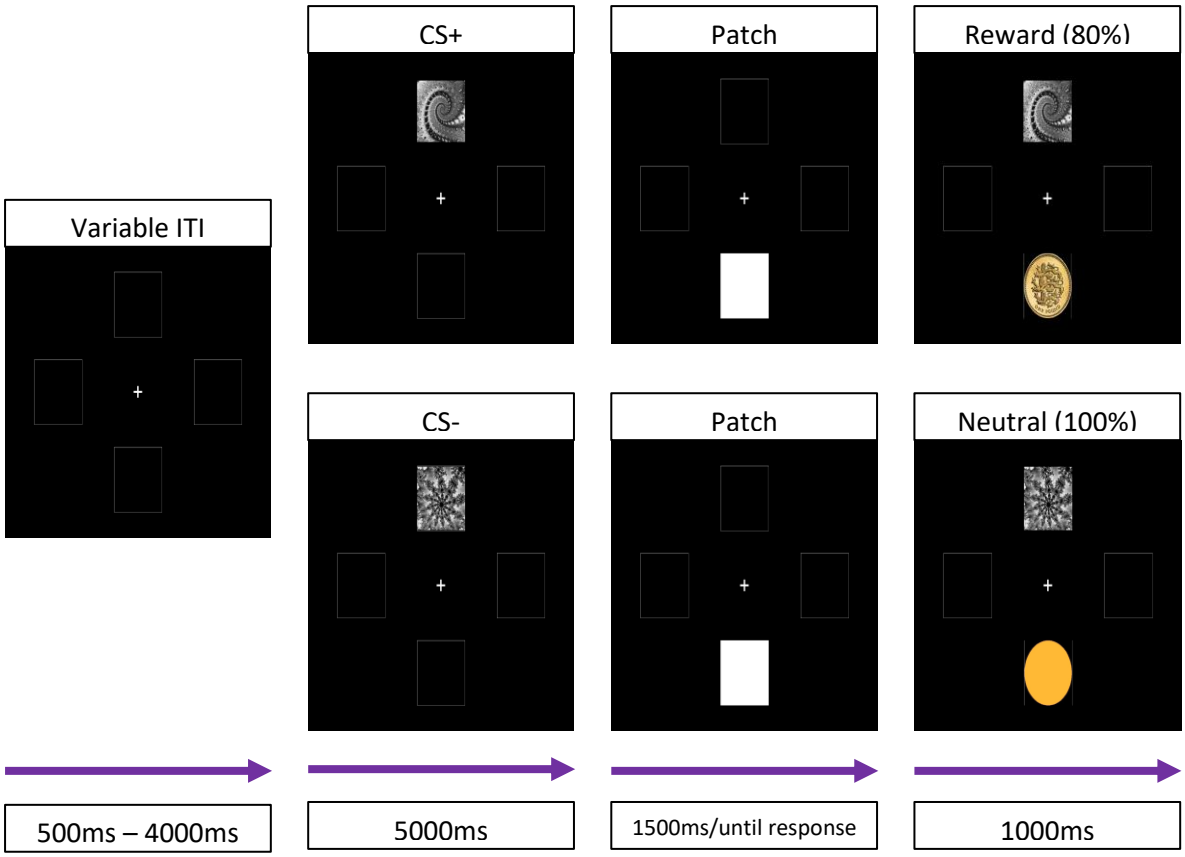
Column one: Forced centralisation; *Column two:* Selection; *Column three:* Inter-trial interval; *Column four:* Feedback. *Top:* Rewarded choice; *Bottom:* Unrewarded choice. *Note.* This schematic shows the 'standard' condition. Purple arrows show duration.

Pavlovian Conditioning Task: In the second stage of the PIT task, participants were first presented with a variable ITI (between 500ms and 4000ms) containing four blank squares (Figure 6.2). Following the ITI participants were presented with one of two fractals in the top square for 5000ms – one of these fractals was associated with reward (CS+), the other with no reward (CS−) (counterbalanced across participants). During CS+ presentation (column two) eye-movement measurements towards the 'sign' (CS+, top-centre square) and 'goal' (bottom-centre square) in the second half of trials *only* (i.e., once contingencies had been learnt) were recorded for analysis and sign-tracker/goal-tracker categorisation. The CS-outcome association was based on a partial reinforcement schedule, wherein the CS− was associated with no reward in 100% of cases, and the CS+ was associated with a reward

outcome in 80% of cases. During the ‘patch’ stage (column three), participants were asked to respond to the onset of the white square (bottom-centre) by pressing the *Ctrl* key (bottom-left corner of keyboard) as quickly as possible. If they did not respond within 1500ms the stage timed out. To prevent instrumental influence on this portion of the PIT task, participants were made aware in the instructions that their responses would *not* influence the reward outcome. However, they were still instructed that the points they received would add to their points tally. Feedback was presented for 1000ms.

It was expected that, if participants correctly learned to discriminate between the two fractals/CSs and their associations, RTs during the patch stage should be quicker on CS+ compared to CS− trials. After two practice trials, forty task trials were completed. This stage lasted approximately 5m 20s.

Figure 6.2 Schematic of the Pavlovian stage of the PIT task

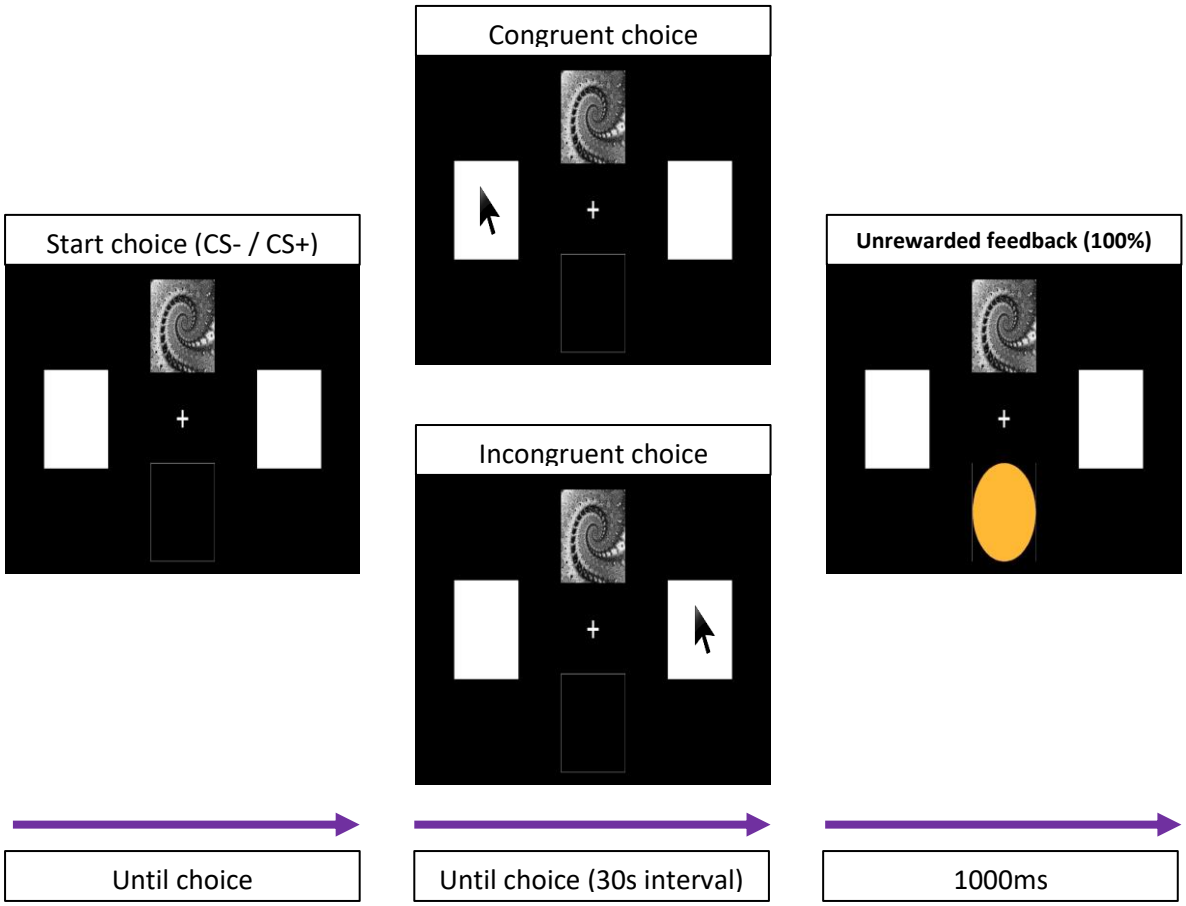


Column one: Variable inter-trial interval; *Column two:* CS+/CS− presentation; *Column three:* participant response; *Column four:* Feedback. *Note.* This schematic shows the 'standard' condition. Purple arrows show duration.

Pavlovian-to-Instrumental Transfer Task: The final stage again involved a choice procedure. Participants were presented with each fractal (CS+ or CS−) in succession for 30 second intervals, during which they were free to choose (again via mouse click) whichever white square they liked, however many times they liked. Figure 6.3 shows a schematic for the 'standard' (not counterbalanced) condition (in the counterbalanced condition the congruent and incongruent choices are reversed). For every selection, participants received neutral feedback for 1000ms 100% of the time, regardless of choice. Extinction procedures are used to assess the influence of pavlovian cues on instrumental responding while removing receipt of reward as a possible confound (Corbit & Janak, 2016; Garofalo & di Pellegrino, 2015;

Talmi et al., 2008). This part of the task ran for 6 minutes at which point it automatically timed out. Every participant received six periods of CS− presentation and six periods of CS+ presentation, in succession, for 30 seconds each time. During this time they were free to perform as many choices as possible without time pressure, and participants were told that the rewards they received throughout this portion would again be added to their points tally. It was expected that CS presentation would influence participant choice, in that the CS+ would increase rewarded choice (left square) and the CS− would have no observable effect (i.e., 50/50 choice). After two practice trials, this stage lasted approximately 6m.

Figure 6.3 Schematic of the Pavlovian-to-Instrumental Transfer stage of the PIT task



Column one: Presentation of either CS− or CS+; *Column two:* Selection; *Column three:* Unrewarded feedback. *Note.* This schematic shows the 'standard' condition. Purple arrows show duration.

Fractal Ratings

The PIT task makes use of several images. Vital among these is the use of two fractals (geometric figures of never-ending patterns). To ensure that participants were influenced by these images only in the way dictated by the task (and not the images' implicit perceptual features), five fractals were acquired via an internet search and were adjusted for size. These were matched on hue, saturation and luminance. Following the method of Garofalo and di Pellegrino (2015), attempts were made to match at least two fractals (to be used in the PIT task) on perceived complexity.

An online pilot study (run via Qualtrics, Provo, UT, 2015) was conducted in which participants (N = 16) were presented with five fractals in sequence (and in a randomised order across participants), each time being asked to rate the fractal on complexity only. Ratings were given via a 7-point Likert scale, ranging from 1 (*Not very complex*) to 7 (*Very complex*). A Friedman's ANOVA tested the null hypothesis of no differences between fractals (1-5). Results revealed a significant effect of fractal type, indicating there were perceived differences in complexity between some or all fractals, $\chi^2(2) = 37.09$, $p < .0001$ (2-tailed).

Wilcoxon Signed Rank *post-hoc* tests (with a Bonferroni correction) revealed that six fractal pairs were significantly different from one another ($ps < .005$). Four pairs were not found to be significantly different from one another ($ps > .07$). A fractal pair was chosen based on this pair having the smallest test statistic (fractal 1: *Mdn* = 3.00, *range* = 2.00-6.00; fractal 2: *Mdn* = 3.50, *range* = 1.00-6.00), $T = 28.50$, $p = .68$, $r = .03$ (2-tailed). These two fractals were chosen for use in the PIT task.

Procedure

All testing took place between the times of 12 p.m. and 6 p.m. in the eye-tracking laboratory of the School of Psychology, University of Liverpool. Before attending the lab, every participant completed an online questionnaire pack (TLFB, AUDIT, DMQ-R, B-YAACQ, BIS-11, ImpSS, CATS) via Qualtrics (Provo, UT, 2015). Those who fulfilled the criteria were invited to attend the laboratory session. All participants provided informed consent before both the online questionnaire and lab portions of the study. During the lab session, participants completed the ASTT (EE), ASTT (BB) and PIT (order counterbalanced) after being told that extra vouchers were available based on their task performance. Participants received either course credits or £10 in 'Love2Shop' vouchers as compensation for their travel expenses and time. During the debriefing it was explained that they would not receive any extra vouchers based on their task performance, and that this was a necessary deception. Each session lasted approximately 1hr 10m.

6.4 Data Reduction and Analysis

Many of the following are an extension of measures that have been used in previous research in estimating attentional bias and stimulus value (Field & Cox, 2008; Rose, Brown, Field, & Hogarth, 2013). This section is broken down by each of the three tasks: ASTT (eye-tracker), ASTT (button-box) and PIT.

ASTT (ET): As in previous studies, RT responses <80ms and >999ms were recoded as missing data.

ASTT (BB): Given the inevitably slower reactions of button-box responses, RTs <150ms and >1199ms were recoded as missing data, as has been done in previous studies using key press measurements (Le Pelley et al., 2015; Roper et al., 2014).

PIT: The data reduction and analysis section follows the methods of Garofalo and di Pellegrino (2015) in all three portions of the task. In the *Instrumental Conditioning task*, the frequency of each kind of choice was measured (left/right choice or rewarded/unrewarded choice). In the *Pavlovian Conditioning task*, RTs in response to the 'patch' presentation were analysed across trials (CS+ versus CS−), as were eye-movement gaze-dwell times (GDTs) towards the top ('sign'/CS) and bottom ('goal'/reward) squares during CS presentation. The eye-tracking parameters (e.g., ≥100ms stable gaze counts as a fixation) were the same as used in other tasks. In the *Pavlovian-to-Instrumental Transfer task*, the frequency of each kind of choice (left/right choice) was analysed across trial types (CS+ versus CS−) in order to assess the potential influence of CS type on choice. All of these analyses were conducted for comparisons of STs and GTs.

Participants were categorised as STs or GTs depending on their oculomotor conditioned response during CS presentation during the *Pavlovian Conditioning task.* A difference score was calculated as the difference between GDTs on the 'sign' (on CS+ trials only) minus GDTs on the 'goal' divided by the total GDT, so

$$(Sign - Goal) \div (Sign + Goal)$$

so that a higher positive value corresponds to a higher GDT towards the 'sign' (i.e., higher sign-tracking) and a lower value corresponds to higher GDT towards the 'goal' (i.e., higher goal-tracking). Given that sign-tracking emerges over time, only the second half of task trials were used for categorisation. Based on the resultant value index, the top and bottom 50% were categorised as STs (eye-gaze index between 0.45 and 1.00) and GTs (index between -1.00 and 0.45), respectively.

Task Outcome Measures

Measures for the ASTT (both ET and BB forms) were those used by Le Pelley et al (2015) and were divided into omissions and RTs. For both Omission RT Biases, greater (positive) values indicate sign-tracking (as higher-value distractors should induce more errors and slower responses to the OT than lower-value distractors). See Table A2 (Appendix A) for calculations. PIT Task outcome measures are covered above but, briefly, consist of correct response frequencies, congruent and incongruent response frequencies, latencies towards CSs of different types and gaze dwell times (GDTs) for various stimuli (e.g., 'sign' versus 'goal'), wherein GDTs are the sum total of all individual fixations within a given region of interest.

6.5 Results

Participant Characteristics

Table 6.1 summarises the sample's average alcohol use characteristics, while Table 6.2 provides an overview of trait and state measures. Women binged more (25% binged 4 times p/fortnight) than men (22.2% binged 0 or 2 times p/fortnight). Most participants (61.9%) scored ≥8 on the AUDIT, classing them as at risk drinkers. Self-reports showed that, overall, the participant population were hazardous drinkers, consuming over recommended weekly guidelines (14 units per week for men and women). For B-YAACQ: Total scores, 28.6% of participants scored ≤5, with 47.6% scoring between 6 and 10 and 23.8% scoring between 12 and 22. A score greater than 5 is associated with increased likelihood of risky drinking (e.g., experiencing impulsivity, embarrassment, regret and/or harm as a result of drinking) (Kahler et al., 2005). In terms of personality variables, most scored within the normal ranges of some personality scales (e.g., 57.4% scored within the BIS-11 range of normality [52-71]; the

ImpSS average was almost identical [*M* = 9.29] to that found previously in undergraduates [*M* = 9.50] [Ball, 1995]). The CATS: Total average (*M* = 0.81) was similar to that of earlier work in nonclinical samples (*M* = 0.74; *M* = 0.77) (Kent & Waller, 1998; Sanders & Becker-Lausen, 1995), suggesting low levels of childhood trauma.

Table 6.1 Alcohol use characteristics (Means ± SD)

Alcohol unit consumption (TLFB)	23.57 (± 15.88)
Binge frequency	2.71 (± 1.95)
AUQ: Units consumed per hour	3.52 (± 1.49)
AUQ: Age at first drink	14.74 (± 2.14)
AUQ: Age at regular drinking	17.95 (± 2.32)
AUQ: Drunk frequency	18.33 (± 21.03)
AUQ: Drunk percentage	37.05 (± 32.28)
AUDIT	10.76 (± 6.24)

Consumption = UK units (1 UK unit = 10 ml or 8 g of pure alcohol); *TLFB* = Timeline FollowBack, based on an average of prior two week's alcohol consumption; *AUQ* = Alcohol Use Questionnaire; *Binge frequency* = ≥8 units for men, ≥6 units for women per day based on an average of prior two week's alcohol consumption; *Age at regular drinking* = the age at which regular drinking was undertaken; *Drunk frequency* = number of times individuals have been drunk in the previous 6 months; *Drunk percentage* = percentage of drinking occasions in which individuals become drunk; *AUDIT* = Alcohol Use Disorders Identification Test.

Table 6.2 Trait/State characteristics (Means ± SD)

BIS-11: Total	59.00 (± 12.23)
B-YAACQ: Total	8.90 (± 6.02)
ImpSS	9.29 (± 3.18)
CATS: Total	0.81 (± 0.43)

BIS-11 = Barratt's Impulsivity Scale; *B-YAACQ* = Brief Young Adult Alcohol Consequences Questionnaire; *ImpSS* = Impulsive Sensation Seeking; *CATS* = Child Abuse and Trauma Scale. *Note.* An *M DMQ-R: Total* variable was not computed as the questionnaire's subscales qualitatively conflict (e.g., coping versus enhancement); thus, a total score would be interpretively useless.

ASTT (Eye-Tracker)

Table 6.3 presents descriptive statistics for the ASTT (EE), showing average response frequencies for the OT and CSs. Analyses were further run to investigate whether any RT and/or omission differences existed between high- and low-value trials.

Table 6.3 Response frequencies (Means ± SD)

Outcome Measures	*Frequencies*
OT	286.40 (± 11.67)
High-value distractor	4.64 (± 6.31)
Low-value distractor	3.08 (± 3.95)

Each outcome measure's fixation frequency is presented. OT = Outcome Target. *Note.* Frequencies do not add up to 300 (total number of trials) as these descriptive do not include non-responses.

Reaction Times: A Paired-Samples *t*-test revealed no difference in RTs towards the OT on high-value (M = 359.48, SD ± 33.56) versus low-value (M = 359.96, SD ± 34.07) trials, $t(24) = -0.23$, $p = .41$, $r = .05$ (1-tailed). This is the first time throughout this thesis a null result for the RT sign-tracking measure has been found.

Omissions: A Wilcoxon Signed-Ranks test revealed no difference in omissions on high-value (*Mdn* = 3.00, *range* = 0-28) versus low-value (*Mdn* = 2.00, *range* = 0-20) trials, $T = 60.50$, $p = .14$, $r = .16$ (1-tailed).

Given that the RT result was in contrast to the moderate-to-large OT RT differences found in studies 1-4, a Welch's *t*-test was conducted with condition (i.e., the order in which participants completed the tasks) as a between-subjects factor. Results were statistically

significant for OT RTs on both high-value, $F(11, 4.74) = 998.36$, $p < .0001$, and low-value trials, $F(11, 4.56) = 52.54$, $p = .0004$. *Post-hoc* comparisons (using Tamhane's T2 correction) revealed a statistically significant difference in high-value OT RTs across two different conditions. Participants in condition 8 (ASTT*c* [ET] → PIT*c* → ASTT*c* [BB]) showed significantly higher RTs ($M = 393.62$, $SD \pm 0.32$) than participants in condition 5 (PIT*s* → ASTT*s* [ET] → ASTT*s* [BB]) ($M = 348.95$, $SD \pm 0.23$), $p = .006$. No *post-hoc* comparisons showed any differences in low-value OT RTs between conditions ($p_s \geq .08$).

To be sure that this difference was not due to *Standard* versus *Counterbalanced* procedures, a Welch's *t*-test with condition (standard or counterbalanced) was conducted. Results revealed no difference in OT RTs between conditions for either high-value, $F(1, 21.61) = 0.56$, $p = .46$, or low-value trials, $F(1, 20.36) = 0.04$, $p = .84$. This suggests that broad standard versus counterbalanced procedures were not responsible for this conditional difference.

ASTT (Button-Box)

Table 6.4 presents descriptive statistics for the ASTT (BB), showing average response frequencies for the OT and CSs. Analyses were further run to investigate whether any RT and/or omission differences existed between high- and low-value trials.

Table 6.4 Response frequencies (Means ± SD)

Outcome Measures	*Frequencies*
OT	296.40 (± 3.35)
High-value distractor	1.40 (± 1.76)
Low-value distractor	1.12 (± 1.72)

Each outcome measure's fixation frequency is presented. OT = Outcome Target. *Note.* Frequencies do not add up to 300 (total number of trials) as these descriptive do not include non-responses.

Reaction Times: A Paired-Samples *t*-test revealed no difference in RTs towards the OT on high-value (M = 510.12, SD ± 50.44) versus low-value (M = 508.20, SD ± 52.37) trials, $t(24) = 0.70$, $p = .25$, $r = .14$ (1-tailed). This replicates the null result for the RT sign-tracking found for the ASTT (EE).

Omissions: A Wilcoxon Signed-Ranks test revealed no difference in omissions on high-value (*Mdn* = 1.00, *range* = 0-6) versus low-value (*Mdn* = 1.00, *range* = 0-7) trials, $T = 30.50$, $p = .25$, $r = .09$ (1-tailed).

PIT Task

Based on the eye-gaze index, STs (n = 12) and GTs (n = 12) were categorised and main analyses were comparisons between tracking groups (one participant was excluded due to only ever selecting the left white square during the Instrumental and PIT phases of the task). First, descriptive statistics for the entire sample across the various areas of interest (AOIs) are presented below. Table 6.5 shows larger gaze dwell times for signs (CSs) compared to goals (USs) across both trial types, without very much difference between GDTs across CS types or across goal types. Table 6.6 shows a similar pattern in which CSs draw a greater number of

fixations (with little difference between CS types) compared to goals (again with little difference between goal types).

Table 6.5 Gaze dwell times within areas of interest (Mean ± SD)

Outcome Measure	*Gaze Dwell Time*
CS+ (Reward sign)	1.09 (± 1.15)
Reward goal	0.66 (± 0.82)
CS− (Neutral sign)	1.04 (± 1.16)
Neutral goal	0.70 (± 0.83)

Reward goal = GDT within the bottom square (goal) during reward-associated (CS+) trials; *Neutral goal* = GDT within the bottom square ('goal') during no-reward (CS−) trials.

Table 6.6 Fixation frequencies towards areas of interest (Mean ± SD)

Outcome Measure	*Fixation Count*
CS+ (Reward sign)	33.92 (± 27.88)
Reward goal	19.79 (± 20.95)
CS− (Neutral sign)	31.42 (± 27.61)
Neutral goal	21.00 (± 20.17)

Reward goal = GDT within the bottom square (goal) during reward-associated (CS+) trials; *Neutral goal* = GDT within the bottom square ('goal') during neutral-associated (CS−) trials.

Instrumental Conditioning Task

Analyses were conducted – both for the sample as a whole and as a comparison of the two tracking groups – to assess participants' choices (mouse clicks) between the left and right white squares, one of which was rewarded, one of which was not. These analyses thus evaluate how well the sample and the tracking subgroups were able to discriminate between rewarded and unrewarded choice options.

Choice (whole sample): A Paired-Samples *t*-test showed greater selection of the rewarded choice (M = 23.19, SD ± 8.59) than the unrewarded choice (M = 11.62, SD ± 8.96), $t(20) = 3.06$, $p = .01$, $r = .56$. This result suggests that the sample as a whole was able to discriminate between the rewarded and unrewarded choices.

Choice (STs vs. GTs): Welch's *t*-tests showed no difference between tracking groups in either the number of rewarded choices (STs: M = 24.09, SD ± 9.35; GTs: M = 23.36, SD ± 8.55), $F(1, 19.84) = 0.04$, $p = .85$, $r = .04$, or unrewarded choices (STs: M = 12.00, SD ± 9.10; GTs: M = 11.27, SD ± 9.25), $F(1, 18.87) = 0.03$, $p = .86$, $r = .04$. This results replicates Garofalo's and di Pellegrino's (2015) finding of no group differences in instrumental choice.

Pavlovian Conditioning Task

First, analyses were conducted to assess if tracking groups showed an overall difference in their GDTs or fixation frequencies towards AOIs.

Gaze Dwell Times: Welch's *t*-tests compared the GDTs of four AOIs (CS+, CS−, reward goal and neutral goal) across tracking groups. Results revealed no group differences in GDTs for either the CS+ ($p = .17$) or the CS− ($p = .26$). However, results did reveal that GTs (M = 1.13, SD ± 0.95) showed significantly longer GDTs towards the Reward Goal compared to STs (M = 0.19, SD ± 0.20), $F(1, 12.02) = 11.26$, $p = .01$, $r = .70$, a pattern also seen for the Neutral Goal (GTs: M = 1.10, SD ± 0.98; STs: M = 0.29, SD ± 0.32), $F(1, 13.26) = 7.49$, p = .02, $r = .60$. These results suggest that GTs show greater fixation durations towards the 'goal' (US) than do STs, regardless of the goal's association with reward. No tracking group differences emerged regarding GDTs towards the 'sign' (either reward or neutral).

Fixation Frequencies: Welch's *t*-tests compared the GDTs of four AOIs (CS+, CS−, reward goal and neutral goal) across tracking groups. Results revealed no group differences in fixation frequencies for either the CS+ (p = .09) or the CS− (p = .14). However, results did reveal that GTs (M = 29.67, SD ± 23.33) showed significantly more fixations towards the Reward Goal compared to STs (M = 9.92, SD ± 12.67), $F(1, 16.97) = 6.64$, p = .02, r = .93, a pattern also seen for the Neutral Goal (GTs: M = 30.17, SD ± 22.78; STs: M = 11.83, SD ± 12.19), $F(1, 16.82) = 6.05$, p = .03, r = .83. These results suggest that GTs perform a greater number of fixations towards the 'goal' (US) than do STs, regardless of the goal's association with reward. No tracking group differences emerged regarding fixations towards the 'sign' (either reward or neutral).

Next, analyses were conducted to assess tracking group comparisons for GDTs and fixation frequencies by hemi-block (first half versus second half of trials).

Gaze Dwell Times: Welch's *t*-tests showed no difference between groups in GDTs towards the CS+ on either the first half (p = .17) or the second half (p = .25) of trials. Similarly, no statistically significant differences were found in GDTs towards the CS− on either the first (p = .40) or the second half (p = .19) of trials. Conversely, GTs showed larger (M = 1.01, SD ± 1.01) GDTs towards the Reward Goal on the first half of trials (hemi-block) compared to STs (M = 0.12, SD ± 0.16), $F(1, 11.53) = 9.12$, p = .01, r = .66. Likewise, GTs showed larger (M = 1.26, SD ± 1.45) GDTs towards the Reward Goal on the second hemi-block compared to STs (M = 0.25, SD ± 0.29), $F(1, 11.90) = 5.54$, p = .04, r = .55. Similarly, GTs showed larger (M = 0.94, SD ± 0.80) GDTs towards the Neutral Goal on the first hemi-block compared to STs (M = 0.21, SD ± 0.27), $F(1, 13.51) = 8.69$, p = .01, r = .63. However, the small difference between tracking groups in GDTs (GTs: M = 1.28, SD ± 1.52; STs: M = 0.36, SD ± 0.42) towards the Neutral Goal on the second hemi-block did not reach statistical

significance, $F(1, 12.66) = 4.06$, $p = .07$, $r = .49$. These results suggest that GTs showed greater fixation durations than STs towards the 'goal' associated with reward across both hemi-blocks, though only greater fixation towards the 'goal' associated with no/neutral reward on the first hemi-block, not the second. No group differences were found in any block for the 'sign' of either association type.

Fixation Frequencies: Welch's *t*-tests showed no difference in fixation frequencies made towards the CS+ in the first ($p = .08$) or second ($p = .18$) hemi-block. Similarly, no statistically significant differences were found in fixations towards the CS− on either the first ($p = .14$) or the second half ($p = .20$) of trials. Conversely, GTs ($M = 12.33$, $SD \pm 11.78$) performed a greater number of fixations than STs ($M = 3.42$, $SD \pm 4.32$) towards the Reward Goal in the first hemi-block, $F(1, 13.90) = 6.06$, $p = .03$, $r = .55$. However, the small difference between GTs ($M = 17.33$, $SD \pm 16.32$) and STs ($M = 6.50$, $SD \pm 9.41$) towards the Reward Goal in the second hemi-block did not reach statistical significance, $F(1, 17.59) = 3.97$, $p = .06$, $r = .43$. For fixations towards Neutral Goals the pattern is similar: GTs ($M = 12.17$, $SD \pm 9.92$) performed greater fixations in the first hemi-block compared to STs ($M = 4.17$, $SD \pm 5.04$), $F(1, 16.33) = 6.21$, $p = .02$, $r = .52$, though the difference between GTs ($M = 18.00$, $SD \pm 15.46$) and STs ($M = 7.67$, $SD \pm 8.16$) in the second hemi-block did not reach statistical significance, $F(1, 16.69) = 4.19$, $p = .06$, $r = .45$. These results suggest that GTs perform a greater number of fixations than STs towards the 'goal' associated with reward on the first hemi-block, but not the second. The pattern regarding fixations towards the 'goal' associated with no/neutral reward was similar, with GTs performing more fixations than STs on the first hemi-block, but not the second. No group differences were found in any block for the 'sign' of either association type.

The final analysis performed for the Pavlovian Conditioning Task assesses RT responses during 'Patch' trials across the presentation of different CSs (CS+ and CS−) both for the sample as a whole, and as a comparison between tracking groups.

Reaction Times (whole sample): A Paired-Samples *t*-test showed that RTs were faster after CS− presentation (M = 363.70, SD ± 64.95) compared to after the CS+ presentation (M = 382.91, SD ± 64.66), $t(23) = 3.13$, $p = .01$, $r = .55$. This result suggests either that prior exposure to the CS− increases participants' RTs during the patch event, or else that pre-exposure to the CS+ slows down RTs. This result contrasts with the finding of Garofalo and di Pellegrino (2015) who showed an effect in the opposite direction.

Reaction Times (STs vs. GTs): Welch's *t*-tests showed no group differences in RTs after presentation of the CS+ (ST: M = 401.12, SD ± 56.56; GT: M = 364.70, SD ± 69.41), $F(1, 21.14) = 1.98$, $p = .17$, $r = .29$. Likewise, no group differences emerged in RTs after presentation of the CS− (ST: M = 379.94, SD ± 60.26; GT: M = 347.47, SD ± 67.92), $F(1, 21.69) = 1.53$, $p = .23$, $r = .26$. This result mirrors the finding of Garofalo and di Pellegrino (2015) of no groups differences in CS RTs.

Pavlovian-to-Instrumental Transfer Task

In order to test for a PIT effect, the number of congruent and incongruent choices during CS+ and CS− presentation were compared. To this end, response indices were created,

CS+ index = *(CS+ congruent choice – CS+ incongruent choice) ÷ Total number of choices*

CS− index = *(CS− congruent choice – CS− incongruent choice) ÷ Total number of choices*

wherein difference scores are created between congruent and incongruent choices before being divided by an overall choice score for each trial type. Higher positive values correspond to a higher probability of making the congruent choice, and lower (and negative) values correspond to a higher probability of making the incongruent choice.

PIT Effect: Welch's *t*-tests revealed no difference between tracking groups in their CS-influenced choice behaviour. In the presence of the CS+, STs (M = 0.03, SD ± 0.11) and GTs (M = -0.01, SD ± 0.36) did not significantly differ, $F(1, 13.05) = 0.21$, $p = .66$, $r = .12$. Similarly, in the presence of CS−, STs (M = -0.02, SD ± 0.14) did not significantly differ from GTs (M = -0.02, SD ± 0.32), $F(1, 14.79) = 0.002$, $p = .97$, $r = .009$. This result contrasts with Garofalo and di Pellegrino's (2015) finding that STs were significantly influenced by the CS+ in comparison to GTs.

Tracking Group Differences in Impulsivity

The final PIT task analysis sought to directly replicate the finding of Garofalo and di Pellegrino (2015) concerning their result that STs possessed significantly greater impulsivity (as measured by the BIS-11) than GTs. In the current sample, a Welch's *t*-test showed no difference between STs (M = 60.40, SD ± 14.01) and GTs (M = 57.70, SD ± 11.49) in BIS-11 total score, $F(1, 17.34) = 0.22$, $p = .64$, $r = .11$.

Comparison of Tasks and Associations with Individual Differences

Given that none of the tasks produced the predicted effects, no comparisons were made and no correlations between task outcomes and self-report measures (e.g., alcohol consumption, impulsivity etc.) were conducted.

6.6 Discussion

This study tested social drinkers on three different tasks – two versions of the ASTT and a PIT task – with the aim of comparing participants' levels of sign-tracking. Specifically, the aim was to assess whether the tasks differed in their ability to elicit sign-tracking, as well as testing whether participants who were categorised as STs or GTs on one task, would also be classified as such on the other two tasks. It was also thought that an increased number of sign-tracking outcome measures from a variety of methods may proffer more utility to the tested associations with self-report measures (alcohol consumption, impulsivity etc.). Unfortunately, this study cannot give any viable information on the questions explored as all of the tasks failed to stimulate the desired effects. Specifically, neither ASTT task produced reliable sign-tracking effects, while the PIT task did not induce any measurable Pavlovian-to-Instrumental Transfer effect. Given these results, there could be no reasonable comparison of the different tasks, nor any correlational analyses between task outcomes and self-reports.

As a result of these widespread failures, and in particular the failure of the ASTT (EE) which has produced robust and reliable effects in the past, the results are uninterpretable. If there was no sign-tracking effect in the ASTT (EE), there would be no reason to suspect measurable effects in the other, lesser used tasks. Thus, this discussion shall be kept brief and will only attempt to address the possible explanations as to why the predicted effects were absent.

Perhaps the most likely cause of the lack of effects was that too many effects were sought. In practical terms, participants were in the laboratory for over an hour, during which time they learned several reward-outcome associations (six in total) during the completion of three cognitive tests which lasted 21m (ASTT [EE]), 21m (ASTT [BB]) and 18m (PIT) (excluding practice trials and instruction pages). This hour-long cognitive battery – which, importantly, many participants reported was fatiguing – may have driven participants to inattention. Ideally, this explanation would be easily verified by an analysis of effects by task order, with participants showing the largest effects in the task they performed first. However, counterbalancing procedures both within ('Standard'/'Counterbalanced') and between (task order) tasks resulted in a total of twelve conditions, leaving only two participants in each condition. Thus, statistical analysis is not possible. Although, it should be noted that this analysis by task order was carried out for the ASTT (EE) and there did appear to be larger effects in participants who performed the task first, but there are too few participants to make a firm conclusion.)

The current study was too ambitious in trying to replicate *and* extend the findings of Garofalo and di Pellegrino (2015). Each participant was in the lab 2.5 times longer than in the Garofalo and di Pellegrino (2015) study, which had the knock-on effect of inducing time constraints that reduced recruitment to just 56% that of the original study (N = 25 versus N = 45). Regarding statistical power, the effect sizes of the main effects (OT RTs) found so far in this thesis offer a broad range of recommendations with regard to sample size (Study 1 suggests an N of 58, Study 2 an N of 19 and Study 3 an N of 69, all for attaining 80% power; G*Power 3.1). This suggests that an average N of around 49 may be the aim in order to reliably detect an effect. However, most of the studies in this thesis so far contained sample sizes smaller than this and still found consistent effects, while the majority of studies using additional singleton (or similar) tasks typically attain robust results with sample sizes in the

mid-teens or twenties (B. A. Anderson, 2015b; B. A. Anderson, Kuwabara, et al., 2016; B. A. Anderson et al., 2013, 2011a; B. A. Anderson, Laurent, & Yantis, 2012; B. A. Anderson, Kronemer, et al., 2016; B. A. Anderson, Laurent, et al., 2014; B. A. Anderson, Leal, et al., 2014; B. A. Anderson & Yantis, 2012, 2013; Bourgeois, Neveu, Bayle, & Vuilleumier, 2017; Bucker et al., 2014; Donohue et al., 2016; Lavie & de Fockert, 2005, 2006; Le Pelley et al., 2015; Theeuwes & Belopolsky, 2012).

The current study may have benefited from changes to its goals. For example, being more selective in which methods were being measured and compared (i.e., comparing participants on just two tasks rather than three) would have reduced testing duration by one third and perhaps prevented cognitive fatigue, boredom effects or any other problems that may have resulted from extended computer testing. The study may have also benefited from changes to its structure. For example, testing participants on one task per day over the course of three days may have also prevented such problems. However, such a change would also come with its own problems such as increased time pressure, participant attrition and so on. Although this study does not offer much in the way of new information regarding ST and GT, it does highlight several methodological factors which should inform future research.

Chapter Seven

Human Sign-Tracking Correlates with BOLD Activity in the Dorsal Striatum

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7.1 Abstract

Background: Neurobiological links to sign-tracking have been shown in both animals and humans. *Aims:* Neural links to sign-tracking were explored using functional magnetic resonance imaging (fMRI). *Methods:* Participants previously classified as sign-trackers (STs), goal-trackers (GTs) or in an intermediate group (ITs) in Studies 1, 2, 3 and 5 were recruited. STs (n = 6), ITs (n = 4) and GTs (n = 10) completed the ASTT (BB) while neural activity was recorded. Participants completed the usual questionnaires online. *Results:* Behavioural data showed the predicted reaction time sign-tracking effect (RT Bias), though the test-retest reliability (from previous to current study) was poor. A general linear model revealed neural activation as a contrast between high-value and low-value trials in regions associated with implicit and reinforcement learning (bilateral putamen), object recognition and object information encoding (right lateral superior occipital cortex). A second *high-value > low-value* contrast with RT Bias included as a moderator showed activity related to appetitive pavlovian conditioning and physical responses to emotive stimuli (amygdala), the processing of rewards of different value (right putamen and pallidum), and attention shifting in tasks involving relative value coding (right superior temporal gyrus). *Conclusions:* Sign-tracking is associated with subcortical functioning, replicating previous results.

Keywords: Sign-tracking, fMRI, Pavlovian conditioning, Visual selective attention

7.2 Introduction

Sign-trackers (STs) attribute incentive value to noncontingent, discrete, reward-paired cues. Goal-trackers (GTs) use such cues to predict the onset of reward. Preclinical studies suggest that STs imbue such cues with the power to drug reinstatement; GTs follow the same pattern for contextual cues (e.g., one cage versus another; entire environments) (T. E. Robinson et al., 2014). Addiction researchers are interested in these phenotypes as they express many of the same maladaptive behaviours as substance-dependent people (compulsiveness, persistence despite negative consequences etc.) and because there is now a large literature showing that sign-tracking in particular seems to be related to typical risk factors for dependence (e.g., impulsivity, risk-taking, sensation-seeking, incentive-sensitisation, cue-induced reward seeking etc.) (Belin et al., 2016; Berridge & Robinson, 2016; Flagel, Akil, et al., 2009; Flagel, Akil, & Robinson, 2010; T. E. Robinson et al., 2014; Saunders & Robinson, 2013; Tomie et al., 2008).

Recent research has provided growing evidence for similar patterns in humans, with sign-tracking found to be associated with self-reported impulsivity, reward-seeking, low working memory capacity, opioid dependence, substance abuse history and self-reported premorbid impulsivity before HIV+ diagnosis (B. A. Anderson et al., 2013, 2011b; B. A. Anderson, Kronemer, et al., 2016; B. A. Anderson & Yantis, 2012; Hickey et al., 2010b; Pearson et al., 2015). Studies have also shown that people classified as STs are more vulnerable to CS-influenced reward behaviours, while obese individuals classified as STs (compared to GTs) have a greater propensity for maladaptive eating behaviour and feelings of a loss of control (Garofalo & di Pellegrino, 2015; Versace et al., 2015).

Much attention in the preclinical literature has been paid to the neurobiological underpinnings of these phenotypes, with evidence indicating that sign-tacking and goal-

tracking may be rooted in different neural circuitry (Flagel & Robinson, 2017; Saunders & Robinson, 2013; Saunders et al., 2013). Preclinical literature suggests that individual variation in CRs to reward-paired cues is largely governed by a 'motive circuit' which includes cortico-striato-pallido-thalamic loops with cortical and subcortical networks converging on the nucleus accumbens (NAcc) (Flagel & Robinson, 2017). In one study, researchers found food-cue induced mRNA expression in STs in the NAcc, dorsal striatum, lateral habenula, lateral septum, orbitofrontal cortex (OFC) and several nuclei of the thalamus (the motive circuit). GTs, by contrast, showed mRNA expression no different to that of unpaired control rats (Flagel, Cameron, et al., 2011). Further, the connectivity in these regions differed between STs and GTs.

The neurotransmitter dopamine (DA) has been found to be important in the acquisition (Scülfort et al., 2016), maintenance (Saunders & Robinson, 2012), and modulation (Peciña & Berridge, 2013) of sign-tracking. In one particular study, rats who eventually developed a sign-tracking CR (STs) (but not a goal-tracking CR; GTs) showed a phasic DA signal transfer in the NAcc from the US to the CS, indicating that reward signalling had shifted from the reward to the reward-paired cue (Flagel, Clark, et al., 2011). The literature on the neurobiology of sign-tracking and goal-tracking is extensive and is outlined in more detail in the Introduction chapter (Chapter One, section 1.5.2); see also the following references for reviews (Flagel & Robinson, 2017; Fraser & Haight, 2016; Huys, Tobler, Hasler, & Flagel, 2014; Pessoa, 2014b; Saunders & Robinson, 2013; Tomie et al., 2008).

Investigations into the underlying neurology of human sign-tracking are also underway. However, the majority of human studies only overlap with the sign-tracking literature, rather than actively exploring it. Nevertheless, such research still has core implications. For example, work using a variety of imaging techniques has shown that the human subthalamic

nucleus encodes the subjective value of reward, the ventral striatum encodes reward preference, and dopaminergic dysfunction in the ventral striatum of alcoholics is associated with greater alcohol cue-induced craving and neural activation (Heinz et al., 2004; O'Doherty, Buchanan, Seymour, & Dolan, 2006; Zénon et al., 2016). One study has also shown that methamphetamine-dependent individuals show differential brain activity in the putamen, caudate and anterior insula to different levels of reward depending on whether they have remained abstinent or not (Gowin et al., 2015). Additionally, in a meta-analysis of 142 neuroimaging studies several brain areas were found to be consistently associated with reward-related decision making, including the NAcc, caudate, putamen, thalamus, OFC, bilateral anterior insula, anterior cingulate cortex (ACC) and posterior cingulate cortex (PCC), with the inferior parietal lobule and prefrontal cortex (PFC) the cognitive control regions (Liu et al., 2011). Crucially, contrast analyses between cues with a positive or negative valence revealed that bilateral NAcc, anterior insula, medial OFC, hippocampus, left putamen and thalamus were more active in response to positive cues than negative; no areas showed more activation by negative cues than positive.

Regarding studies which have directly measured human sign-tracking while simultaneously measuring brain activity, several have employed additional singleton tasks (AST). There are variations in what type of AST is employed in each study, but the salient aspect here is that they have shown clear neural activations in response to high-value cues compared to low-value (or reward-associated cues compared to the absence of such cues). Functional magnetic resonance imaging (fMRI) studies which have employed the AST have shown activation following such a high > low pattern in the extrastriate visual cortex, tail of the caudate nucleus, superior parietal cortex, frontal cortex, inferior frontal gyrus, lateral occipital complex, and intraparietal sulcus (B. A. Anderson, 2016b; B. A. Anderson, Laurent, et al., 2014; de Fockert et al., 2004; de Fockert & Theeuwes, 2012). In a further study

utilising the AST and positron emission tomography (PET), findings revealed that sign-tracking was associated with changes in available D2/D3 DA receptors within the right caudate and posterior putamen (B. A. Anderson, Kuwabara, et al., 2016). Further, DA signalling in the dorsal striatum predicted sign-tracking CRs.

In addition to fMRI and PET, AST studies have also employed electroencephalography (EEG) to monitor neural responses during the task. Such studies have shown that reward-associated distractors can spark brain responses (i.e., capture neural 'attention') before targets do even when they are presented at the same time (Qi et al., 2013). This is supported by evidence suggesting that reward-associated CSs elicit the P1 event-related potential, one of the earliest reliable indicators of visual selective attention (Maclean & Giesbrecht, 2015). They have also found evidence of activation (broadly defined as electrophysiological responses of various kinds) in the anterior cingulate cortex (ACC), matching the work of other scanning techniques (though EEG has far lower spatial resolution) (Hickey, Chelazzi, & Theeuwes, 2010a). In a recent study employing transcranial random noise stimulation (tRNS) prior to the AST, researchers found that stimulation of the occipital cortex (but not the frontal cortex) increased value-modulated attentional capture (VMAC) for a high-value reward-associated cue, suggesting that plasticity in the visual cortex can modulate sign-tracking (Van Koningsbruggen et al., 2016). Finally, in the only study to investigate the neurological responses in human STs versus GTs, researchers recorded EEG responses while lean and obese individuals viewed food-related, pleasant, neutral and unpleasant images (Versace et al., 2015). Results revealed that STs showed late positive potential (LPP) responses to food-related images that were of the same magnitude to LPPs towards other highly emotionally arousing stimuli (e.g., erotica, mutilations), whereas GTs' LPP responses to the food-related images were comparable to those evoked by neutral images. Thus, STs' neurophysiological

responses suggest that such individuals imbue food-related cues with incentive salience to match that of other emotionally salient cues, while this pattern is not seen in GTs.

The present study aims to build on the preclinical and, in particular, the human literature of exploring the neural correlates of sign-tracking. This study is similar in design to Anderson (2016); we employ an event-related fMRI paradigm wherein participants' brain activity is recorded while they complete the additional singleton tracking task (ASTT), a variant of the AST. A secondary aim was to test whether participants who were classified as STs and GTs in a previous study of this thesis (decided by RT Bias in Study 1, Chapter Three) would show similarly robust RT Bias scores in the present study. Specifically, we hypothesised that I) a sign-tracking effect would be found using the ASTT (BB), II) neural activations would replicate areas found in previous work, specifically the striatum and amygdala caudate, and III) such activations would correlate with sign-tracking.

7.3 Method

Participants

Twenty participants (10 female) – all of whom had taken part in a previous study of this thesis – were recruited via a strict selection process based on their RT Bias scores (see *Selective Recruitment*, below). Participants were aged between 19 and 34 years (M = 25.85, SD ± 4.58). The inclusion criteria were regular consumption of alcohol (≥10 units per week), normal or corrected-to-normal vision and righthandedness. Self-reported past or present alcohol- or drug-use problems, brain surgery, crushing head injury, or pregnancy, diagnosis of a neurological disease, psychiatric illness, or anxiety disorder (e.g., claustrophobia, PTSD etc.), and surgery meaning they could not be exposed to the scanner's magnetic field (e.g.

pacemaker, metal implants, body piercings which cannot be removed etc.) were all exclusions. All participants provided written informed consent before taking part in the study, which was approved by the University of Liverpool Research Ethics Committee.

Selective Recruitment

Based on Study 1 (Chapter Three), which possessed the largest sample size and thus was most adequately powered to detect a sign-tracking effect, cut-offs for RT Bias scores were created (GTs: −3.60; STs: 16.58; ITs: everything in between). These bias score cut-offs were applied to participant samples for Studies 1, 2, 3 and 5 (Chapters Three, Four and Six); Study 4 (Chapter Five) was not included due to a different task being used (the ASTT+). Bias scores taken from Studies 2 and 3 were from the control conditions only (not alcohol). Participants within these category bounds who also met the other inclusion/exclusion criteria were recruited. Initial aims were to compare STs to GTs only, so as to compare individuals with only the most extreme scores. However, due to this study taking place up to two years after some participants' previous participation (in the case of Study 1) and with several participants not meeting some of the other inclusion/exclusion criteria, many participants who were contacted could not be recruited. The result of these difficulties was that some participants of previous studies had to be recruited who met the criteria for neither classification as an ST nor GT (i.e., ITs). Based on these factors 10 GTs, 6 STs and 4 IGs were recruited[23].

[23] It should be noted that two participants (one ST, one GT) were recruited from Study 5 (Chapter Six). This is of note as no overall sign-tracking effect was gleaned from this study. However, these two participants' scores did still meet the RT Bias cut-offs described in this section.

Materials

Questionnaires

The same questionnaire pack used in Study 1 was given to all participants to assess drinking habits (TLFB, AUDIT), drinking motives (Modified DMQ-R), drinking consequences (B-YAACQ), impulsivity (BIS-11, ImpSS) and childhood trauma (CATS) (see Chapter Two [General Methods] for full descriptions). An additional scale – the Single Ease Question (SEQ) – was completed after the ASTT. This single question asked participants: *'Overall, how easy or difficult did you find this task? Circle a number below:'* with a 7-point Likert scale from *'very easy'* to *'very difficult'* (Sauro & Dumas, 2009).

Button-Box

The button-box used was constructed by technicians at the Liverpool Magnetic Resonance Imaging Centre (LiMRIC), and it closely mirrored the button-box used in Study 5 (Chapter Six) with a raised button in each corner of the box.

Cognitive Task

Additional Singleton Tracking Task: Button-Box (ASTT [BB]): This task is almost identical to the ASTT (BB) used in Study 5 (Chapter Six). There are 8 stimuli presented on each trial: 1 diamond (OT), 1 coloured circle (CS) and 6 grey circles (valueless distractors). This adaptation was decided upon in order to match it to the task used in Study 5 (Chapter

Six). Given the two extra stimuli presented in each trial (compared to the ASTT [EE]), the stimuli were made slightly smaller (200 × 200 pixels versus 240 × 240 pixels) but were nonetheless perceptually larger due to the larger screen. As noted previously, evidence suggests increased 'display size' (number of stimuli) in ASTs using a coloured distractor increases average response times (Theeuwes, 2010), and so increased stimulus number should not adversely affect the production of sign-tracking. The task was presented on a projector screen parallel to the top of the participant's head (approximately two feet away), which they were able to see via a mirror attached to the scanner's head coil. The task was presented in landscape at a resolution of 1024 × 768.

One of the major differences in the current task was that participants used their right hand (all participants' dominant hand) to make responses, whereas in Study 5 participants used both hands. The other differences concern timings, durations, trial number and trial sequence, all of which were altered compared to previous studies due to the event-related design of the study. In addition to 6 practice trials, there were 160 true trials (80 high value, 80 low value) in a fixed sequence (i.e., the same for all participants), the order of which was determined by a random sequence generator (containing no duplicates) (Haahr, n.d.). Given the time constraints borne of consideration for fMRI scanning (see *'Data Acquisition, Reduction and Analysis',* below), all trials were longer than previously seen in the ASTT and a variable inter-trial interval (ITI) was employed.

Avoiding the technical aspects here (see sections below), the components of task trials ran as follows: fixation trials (null events presenting a fixation cross) lasted 4000ms (randomly staggered, +/− 200ms) before one of the two trials (high/low) was shown for 1000ms, or until a response was registered. Following this, a 2000ms pre-trial pause (black screen) preceded a feedback trial (detailing how many points, if any, were won on the

previous trial) for 6000ms, before a post-trial pause (black screen) was shown for 2000ms. This details a full run-through of one trial (15 seconds in total) and is similar in design to previous fMRI studies employing an AST (de Fockert, Rees, Frith & Lavie, 2004; Lavie & de Fockert, 2006). Task duration was approximately 40 minutes.

Procedure

All testing took place between the times of 9 a.m. and 6 p.m. in the Liverpool Magnetic Resonance Imaging Centre (LiMRIC) at the University of Liverpool. Before attending the lab, participants completed an online questionnaire pack (TLFB, AUDIT, M DMQ-R, B-YAACQ, BIS-11, ImpSS, CATS) via Qualtrics (Provo, UT, 2015). Those who fulfilled the criteria were invited to attend the laboratory session. All participants underwent safety screening, performed by a senior radiographer to confirm their suitability for the session. All participants provided informed consent before both the online questionnaire and lab portions of the study and a standard risk assessment was conducted by the departmental safety coordinator. During the lab session, participants first underwent diagnostic T1 (10 minutes) and T2 (2 minutes) weighted images, before completing the ASTT (BB) whilst undergoing functional scanning (40 minutes). Upon completion of the task, participants completed the SEQ so that their perception of task difficulty could be obtained. Participants received £50 as compensation for their travel expenses and time. It is worth noting that there was no deception in this study regarding the attainment of extra rewards based on task performance as all participants had already undergone such deception in a previous study. Each session lasted approximately 60 minutes.

7.4 Data Acquisition, Reduction and Analysis

7.4.1 Additional Singleton Tracking Task: Outcome Measures

Measures for the ASTT (BB) were those used by Le Pelley et al (2015) and were divided into omissions and RTs. For both Omission Bias and RT Bias, greater (positive) values indicate sign-tracking (as higher-value distractors should induce more errors and slower responses to the OT than lower-value distractors). See Table A2 (Appendix A) for calculations. Given the inevitably slower reactions of button-box responses (compared to eye-movement responses), RTs <150ms were recoded as missing data, as was done in Study 5 (Chapter Six) and as has been done in previous studies using key press measurements (Le Pelley et al., 2015; Roper et al., 2014). Given that stimuli were only presented for 1000ms, no upper cut-off was applied.

7.4.2 Functional Magnetic Resonance Imaging: Data Acquisition and Analysis

Acquisition

Magnetic resonance images were acquired using a whole-body 3 Tesla Siemens Trio MRI imaging system (Siemens, Magnetom, Erlangen, Germany) and an 8-channel head coil. As required by LiMRIC safety protocol, a localiser scan (14s) followed by clinical T1- and T2-weighted anatomical scans were acquired. The first, a high-resolution 3-dimensional T1-weighted image was acquired using a Modified Driven Equilibrium Fourier Transform (MDEFT) sequence (time to repeat [TR] = 7.92ms; time to echo [TE] = 2.48ms; flip angle = 16°; 176 sagittal slices; slice thickness = 1mm; matrix 256 × 240 × 176; in-plane voxel size 1mm × 1mm × 1mm; total acquisition time: 12:50m). The second, T2-weighted image was then acquired (24 axial slices; slice thickness = 5mm; 1.5mm spacing; field of view = 220mm;

TR = 4000ms; TE = 102ms; voxel size = 0.9mm × 0.9mm × 5mm; flip angle = 150°; total acquisition time: 1:50m). These scans were not used for research purposes, but were evaluated by a qualified clinician for medical anomalies or incidental findings that would require further investigation.

Finally, fMRI was conducted whilst participants completed the ASTT (BB) (37 axial slices; 7.4mm spacing; field of view = 192mm; TR = 2200ms; TE = 30ms; voxel size = 3mm × 3mm × 3mm; total acquisition time: 40m). The BOLD (Blood-Oxygen-Level Dependent) signal is acquired here. Briefly, deoxyhaemoglobin in deoxygenated blood possesses paramagnetic properties and attenuates MR signal more than oxyhaemoglobin which is diamagnetic. This difference reflects differential susceptibility to homogenous magnetic fields that subsequently cause the T2-signal intensity changes which can be recorded. BOLD signal intensity reflects the surplus of oxygenated blood in a region and thus regional activation (Kim & Ogawa, 2012).

Analysis

Pre-processing: DICOM (Digital Imaging and Communications in Medicine) data were converted to the NIfTI (Neuroimaging Informatics Technology Initiative) image format and stored and organised in *Total Commander 64 bit* (Ghisler, 2016), before image conversion and spatial pre-processing of functional resting-state data was performed in SPM12 (Statistical Parametric Mapping, Welcome Trust Centre for Neuroimaging, University College London, United Kingdom) running in MATLAB R2016a (MathWorks Inc., Natick, USA, 2016). Functional volumes underwent slice-timing correction, realignment and unwarping, normalisation to MNI (Montreal Neurological Institute) space using the

normalised EPI (Echo Planar Imaging) template image in SPM, and spatial smoothing (5mm full-width at half maximum Gaussian kernel filter).

First-Level Design: A standard event-related design was employed, therefore trials were modelled as events rather than epochs (i.e., delta functions, zero duration). The onset times for high-value trials were input as the first condition, and onset times for low-value trials input as the second condition. A temporal high-pass filter was applied to the time series with a 128 second cut-off to remove slow signal drifts (confounds) > 128s. A Paired-Samples *t*-test was conducted within a general linear model (GLM) to generate a statistical parametric map of the contrast between high-value versus low-value trials for each participant.

Second-Level Design: Two factorial design specifications were created. The first contained age and gender as fixed factors, the second contained the same factors but also included RT Bias as a correlate in a regression. Both GLMs conducted a Paired-Samples *t*-test across all participants to elucidate the group-level differences between high-value and low-value trials based on individual maps. This approach accounts for within- and between-subject variability (Holmes & Friston, 1998; Penny, Friston, Ashburner, Kiebel, & Nichols, 2006).

7.5 Results

Participant Characteristics

Table 7.1 summarises the sample's average alcohol use characteristics, while Table 7.2 provides an overview of trait and state measures. Women (30%) binged 4 times p/fortnight, men either 4 or 14 times p/fortnight (both 20%). Most participants (68.4%) scored ≥8 on the AUDIT, classing them as at risk drinkers. Self-reports showed that, overall, the participant

population were hazardous drinkers, consuming over recommended weekly guidelines (14 units per week for men and women). For B-YAACQ: Total scores, 15.8% of participants scored ≤5, with 21.1% scoring between 6 and 10 and 63.3% scoring between 11 and 20. A score greater than 5 is associated with increased likelihood of risky drinking (e.g., experiencing impulsivity, embarrassment, regret and/or harm as a result of drinking) (Kahler et al., 2005). In terms of personality variables, most scored within the normal ranges of some personality scales (e.g., 53% scored within the BIS-11 range of normality [52-71]; the ImpSS average was almost identical [*M* = 9.58] to that found previously in undergraduates [*M* = 9.50] [Ball, 1995]). The CATS: Total average (*M* = 1.08) was higher to that of earlier work in nonclinical samples (*M* = 0.74; *M* = 0.77) (Kent & Waller, 1998; Sanders & Becker-Lausen, 1995), though was still lower than typical clinical scores.

Table 7.1 Alcohol use characteristics (Means ± SD)

Alcohol unit consumption (TLFB)	22.01 (± 11.48)
Binge frequency	4.85 (± 4.90)
AUQ: Units consumed per hour	3.64 (± 1.13)
AUQ: Age at first drink	13.11 (± 2.02)
AUQ: Age at regular drinking	16.79 (± 1.55)
AUQ: Drunk frequency	21.58 (± 12.61)
AUQ: Drunk percentage	50.58 (± 26.08)
AUDIT	12.79 (± 6.44)

Consumption = UK units (1 UK unit = 10 ml or 8 g of pure alcohol); *TLFB* = Timeline FollowBack, based on an average of prior two weeks of alcohol consumption; *AUQ* = Alcohol Use Questionnaire; *Binge frequency* = ≥8 units for men, ≥6 units for women per day, based on an average of the prior two weeks of alcohol consumption; *Age at regular drinking* = the age at which regular drinking was undertaken; *Drunk frequency* = number of times individuals have been drunk in the previous 6 months; *Drunk percentage* = percentage of drinking occasions in which individuals become drunk; *AUDIT* = Alcohol Use Disorders Identification Test.

Table 7.2 Trait/State characteristics (Means ± SD)

BIS-11: Total	63.68 (± 12.96)
B-YAACQ: Total	11.53 (± 4.96)
ImpSS	9.58 (± 4.66)
CATS: Total	1.08 (± 0.57)

BIS-11 = Barratt's Impulsivity Scale; *B-YAACQ* = Brief Young Adult Alcohol Consequences Questionnaire; *ImpSS* = Impulsive Sensation Seeking; *CATS* = Child Abuse and Trauma Scale. *Note.* An *M DMQ-R: Total* variable was not computed as the questionnaire's subscales qualitatively conflict (e.g., coping versus enhancement); thus, a total score would be interpretively useless.

7.5.1 Behavioural Analysis

Table 7.3 shows average response frequencies for the OT and CSs on the ASTT (BB). Analyses were further run to investigate whether any RT and/or omission differences existed between high- and low-value trials.

Table 7.3 Response frequencies (Means ± SD)

Outcome Measures	*Frequencies*
OT	153.35 (± 5.25)
High-value distractor	1.71 (± 0.95)
Low-value distractor	1.00 (± *)

*No standard deviation could be calculated as only one data point was available. Each outcome measure's fixation frequency is presented. OT = Outcome Target. *Note.* Frequencies do not add up to 160 (total number of trials) as these descriptives do not include non-responses.

Reaction Times: A Paired-Samples *t*-test showed that OT RTs were larger on high-value (M = 625.17, SD ± 68.01) compared to low-value (M = 615.78, SD ± 76.47) trials, $t(19)$ = 1.96, p = .03, r = .41 (1-tailed). This reveals a sign-tracking effect in the predicted direction.

Omissions: There were not enough valid cases for this analysis to be conducted. This may have been due to the extended duration of the trials (due to catering for scanning), which seems likely given that the average reaction time was higher in this study compared to ASTT (BB) RTs in Study 5 (Chapter Six). This indicates that participants were taking their time, perhaps due to the novel situation and increased trial times, and thus were less liable to make mistakes (*RT-accuracy trade-off*). Therefore, omissions will not be analysed further.

Next, participants' RT Bias scores as calculated for both their previous (ASTT [EE]) task completion and their current (fMRI, ASTT [BB]) task completion. Table 7.4 presents both RT Bias scores and tracking group classifications across both time points. Eight out of twenty individuals maintained their tracking group status across time points (3 GTs, 3 STs, 2 ITs). Given the difference in the number of initial GTs (n = 10), STs (n = 6) and ITs (n = 4), this is more accurately viewed as 30% of GTs remained GTs across time, compared to 50% of STs and 50% of ITs (though it should also be noted that the scope of the IT classification is much larger and so maintained classification is *de facto* more likely).

The test-retest reliability of the RT Bias scores was also statistically investigated. An intraclass correlation (ICC) estimate was attained using an average measure (k = 2), consistency type, Two-Way Mixed-Effects model, ICC = .50, p = .07, 95% CI [-0.26, 0.80]. Results indicate poor-to-moderate reliability (Koo & Li, 2016), suggesting that sign-tracking and goal-tracking were not reliably maintained or reliably measured across studies.

Table 7.4 Participant RT Bias scores and tracking rankings across studies

Participant	*RT Bias score: ASTT (EE)*	*RT Bias score: ASTT (fMRI)*	*Subjects' ST/GT classification (previous/current)*
1	−21.91	−21.92	**GT/GT**
2	22.75	3.73	ST/IT
3	−10.44	12.93	GT/IT
4	−3.65	31.63	GT/ST
5	−4.56	0.97	GT/IT
6	27.63	33.06	**ST/ST**
7	57.86	4.42	ST/IT
8	−7.01	−4.31	**GT/GT**
9	−11.67	−1.58	GT/IT
10	16.91	10.07	ST/IT
11	−45.26	−9.10	**GT/GT**
12	−12.01	3.29	GT/IT
13	16.44	−0.71	**IT/IT**
14	6.72	−20.20	IT/GT
15	18.72	37.29	**ST/ST**
16	−0.78	−12.55	IT/GT
17	20.79	57.28	**ST/ST**
18	−9.39	8.01	GT/IT
19	−4.37	46.38	GT/ST
20	−12.16	9.16	**IT/IT**

RT Bias score: ASTT (EE) = Participants' RT Bias score from previous study; *RT Bias score: ASTT (fMRI)* = Participants' RT Bias score from current study; *Subjects' ST/GT classification (previous/current)* = Classification of participants into tracking groups based on previous and current studies (individuals with identical classifications across studies are highlighted in bold). *Note.* Based on cut-off criteria from Study 1 (Chapter Three), individuals with RT Bias scores of 16.58 and above are classified STs, those with −3.60 and below are GTs and any individual with a score in between is categorised an IT.

7.5.2 fMRI Analysis

Brain activity was time-locked to trial onsets in an event-related analysis. Neuromorphometrics was conducted using FSL software (Smith et al., 2004) and locations of brain activations in MNI space are described according to the Harvard-Oxford Cortical and Subcortical Atlases (Behrens et al., 2003; Desikan et al., 2006; Diedrichsen, Balsters, Flavell, Cussans, & Ramnani, 2009; Eickhoff et al., 2005; Frazier et al., 2005; Goldstein et al., 2007; Hua et al., 2008; Lancaster et al., 2000; Makris et al., 2006; Mazziotta et al., 2001). These atlases calculate probability of a given coordinate to be bound within certain neural structures based on T1-weighted structural images of 37 individuals whose scans were then affine-registered to a standard-space MNI52 T1-weighted template, which itself is derived from 152 structural images averaged together. Height and extent-cluster thresholds were set with consideration to previous work and current study setup (sample size etc.) (Bennett, Wolford, & Miller, 2009).

In a first contrast, a whole brain analysis compared high-value and low-value trials, with age and gender specified as fixed factors. Initially, a cluster forming height threshold of T = 3.65 ($p < .001$ uncorrected) was employed but no suprathreshold clusters were found; as a result, this threshold was slightly relaxed. After setting a new height threshold of $T = 2.90$ ($p < .005$)[24] and an extent threshold (k) of 10 voxels, three clusters were observed: right putamen (cluster 1), right lateral superior occipital cortex (extending into the parietal region) (cluster 2) and left putamen (cluster 3). Small volume cluster-level analyses with familywise error (FWE) correction (VOI sphere, 5mm radius) revealed that each cluster was statistically

[24] Note that a height threshold of $p < .005$ is not unusual; in fact, it is the threshold used in a recent fMRI study using the AST (B. A. Anderson, 2016b).

significant at a cluster-FWE corrected level of $p < .05$ (see Table 7.5 and Figures 7.1 and 7.3).

For the second contrast, the difference between high-value and low-value trials was investigated with age and gender as fixed factors. However, this time ASTT (BB) RT Bias was also entered into a regression model as a correlate. At a height threshold of $T = 3.69$ ($p < .001$) and an extent threshold (k) of 10 voxels, three clusters were observed: right putamen (cluster 1), right pallidum and amygdala (cluster 2), and the right superior anterior temporal gyrus and superior posterior temporal gyrus (cluster 3). Small volume cluster-level analyses with FWE-error correction (VOI sphere, 5mm radius) revealed that each cluster was statistically significant at a cluster-FWE corrected level of $p < .05$ (see Table 7.5 and Figure 7.2).

Table 7.5 Regions of activation after a whole brain analysis with age and gender controlled for as fixed factors and RT Bias as a correlate

Region [a]	*MNI Coordinates*			*k*	*T-value*	*p-value*
	x	*y*	*z*			
Main effect of condition (high > low): age & gender entered as fixed factors [b]						
Right putamen	28	12	2	27	4.18	.02
Right lateral superior occipital cortex	32	−72	44	22	3.86	.02
Left putamen	−24	6	−10	13	3.81	.03
Main effect of condition (high > low): age & gender entered as fixed factors and RT Bias as a correlate [c]						
Right putamen	24	18	0	27	5.89	.002
Right pallidum	26	−14	−2	35	5.75	.003
Right amygdala	22	−4	−10		4.07	.01
Right anterior superior temporal gyrus	52	−4	−14	12	4.90	.006
Right posterior superior temporal gyrus						

[a] Neuromorphometrics reported only for structures with probabilities greater ≥ 10% using the *Harvard-Oxford Cortical and subcortical Atlas*. *Note.* Cerebral cortices and white matter were excluded from neuromorphometrics due to their pervasive proximity to all reported structures. *k* = cluster size (voxels); [b] Height threshold: $T = 2.90$ ($p < .005$ uncorrected); Extent threshold: $k = 10$ voxels; Voxel size: 2.0mm × 2.0mm × 2.0mm; [c] Height threshold: $T = 3.69$ ($p < .001$ uncorrected); Extent threshold: $k = 10$ voxels; Voxel size: 2.0mm × 2.0mm × 2.0mm. All reported *p*-values: small volume cluster-level familywise error correction (VOI sphere, 5mm). *Note.* Coordinates 22, −4, −10 are contained within coordinates 26, −14, −2.

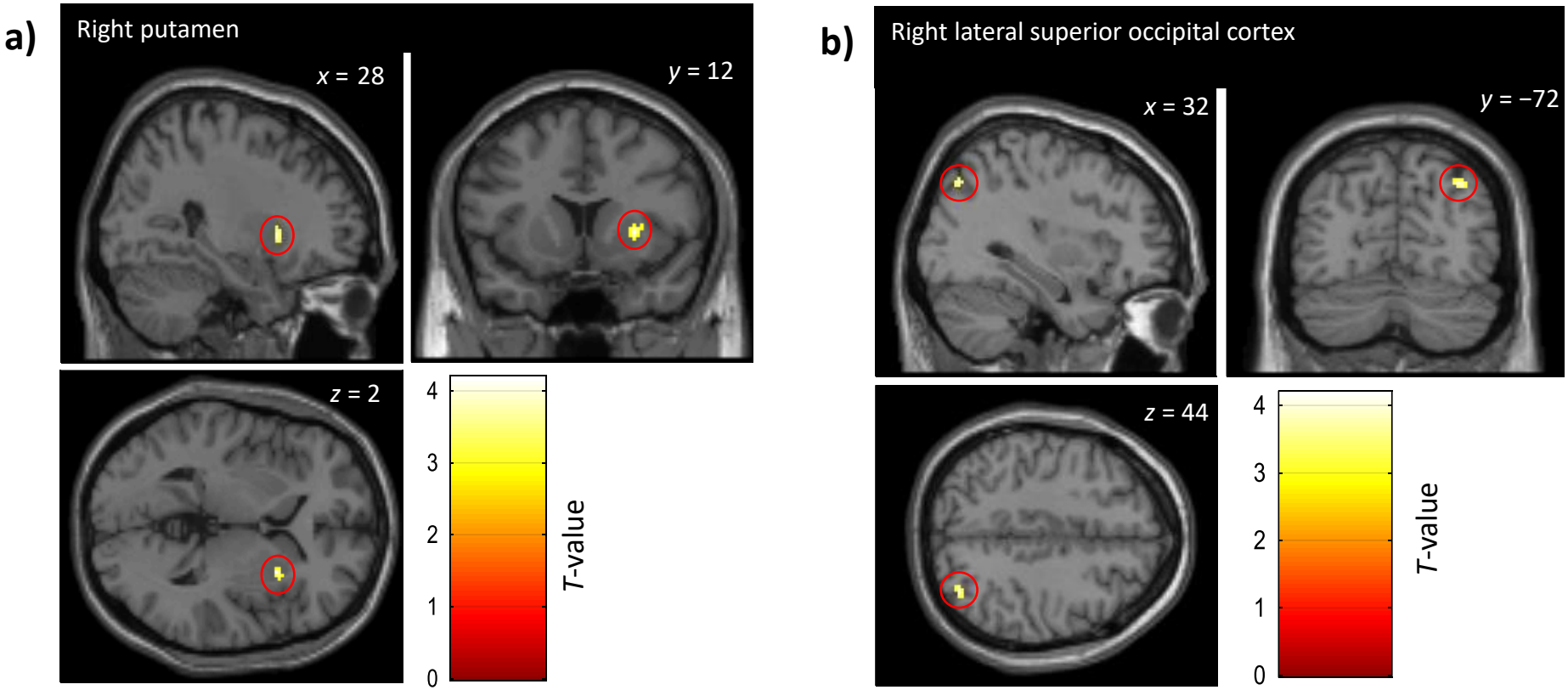


Figure 7.1 BOLD signal representations for the first contrast at *a)* the right putamen (cluster 1) and *b)* the right lateral superior occipital cortex (cluster 2).

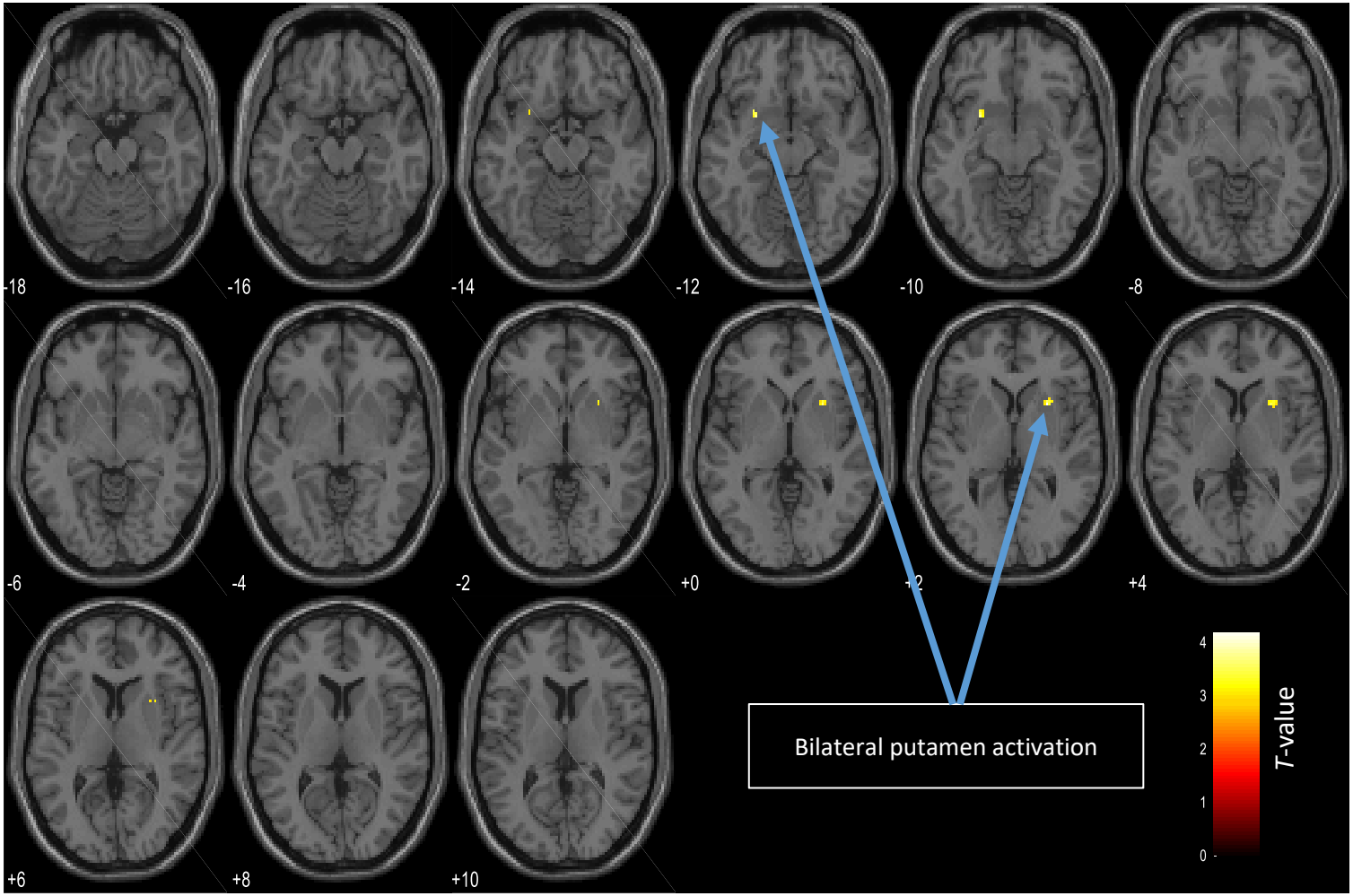


Figure 7.3 Montage showing axial scans (every two slices) revealing the bilateral putamen activation found in the first contrast.

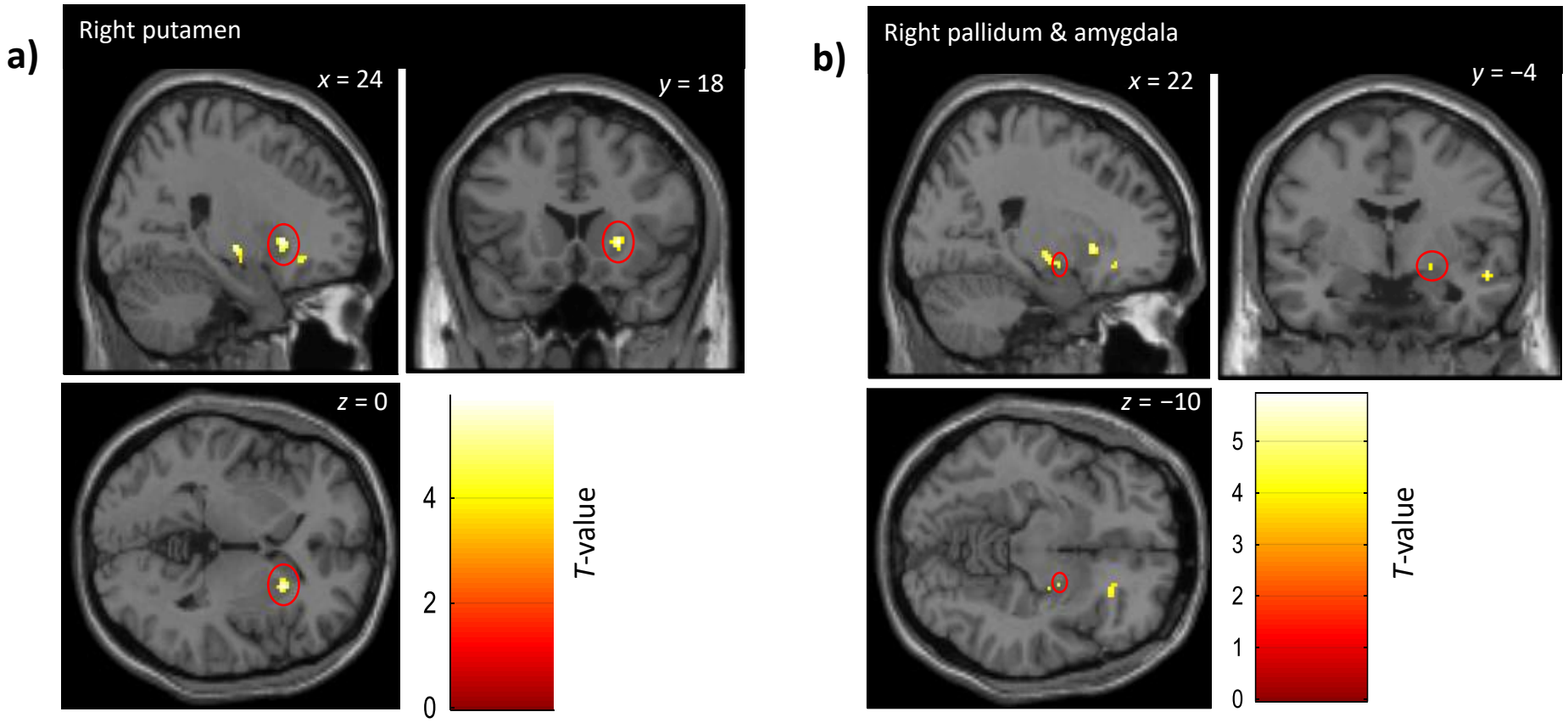
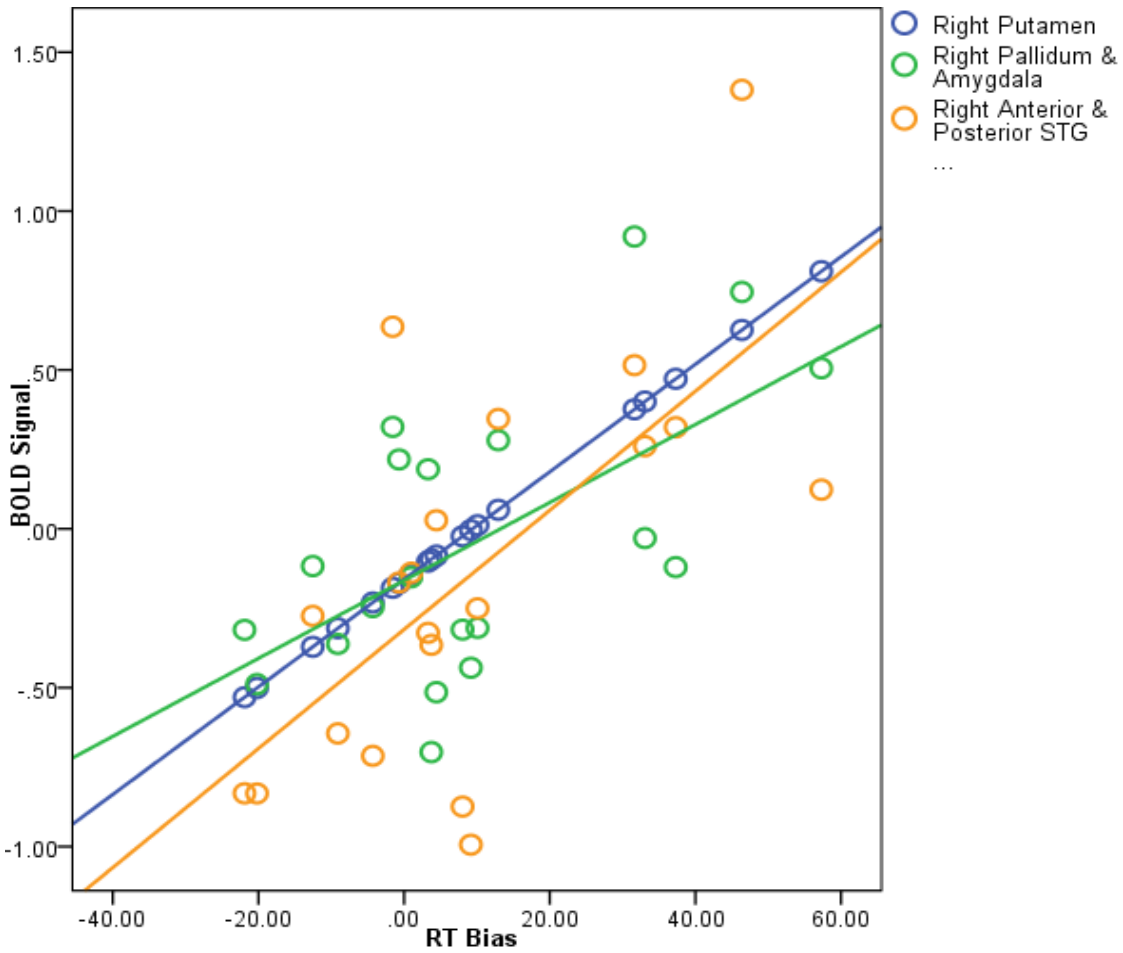


Figure 7.2 BOLD signal representations for the second contrast at *a)* the right putamen (cluster 1) and *b)* the right pallidum and amygdala (cluster 2).

Associations between BOLD signal and RT Bias (Figure 7.4)

In the second contrast which contained RT Bias as a correlate in the regression, a non-adjusted VOI time-series extraction was performed for each of the three clusters in order to extract BOLD signal data for each individual participant, which were then correlated with RT Bias (sign-tracking). Bivariate Pearson correlations revealed statistically significant associations between RT Bias and neural activation in the right putamen (cluster 1), $r = 1.00$, $p < .0001$, the right pallidum and amygdala (cluster 2), $r = .61$, $p = .005$, and right anterior and posterior superior temporal gyrus (cluster 3), $r = .66$, $p = .001$ (all 2-tailed).

Figure 7.4 Pearson correlations between RT Bias and neural activations (BOLD signals)



STG = superior temporal gyrus.

7.6 Discussion

This study employed an event-related fMRI design in which participants – recruited from previous studies and classified as either sign-trackers (STs), goal-trackers (GTs) or else were classed as intermediate trackers (ITs) – completed the ASTT (BB) to measure individual differences in the attribution of incentive salience to discrete, noncontingent reward cues. The study aimed to build on previous work showing that value-modulated attentional capture (VMAC) towards discrete, response-irrelevant cues (sign-tracking) is associated with neural activation in various brain structures and networks. A secondary aim was to assess the test-retest reliability of RT Bias scores on the ASTT. Behavioural results revealed a sign-tracking effect (with slower target responses on high-value versus low-value trials). fMRI analyses from two separate whole-brain GLMs showed significant BOLD signal activation across a variety of cortical and subcortical areas, some of which replicate regions identified by previous research.

This study is only the second in the thesis to use a button-box version of the ASTT. Unlike the previous one (Study 5, Chapter Six), the current button-box ASTT produced an observable sign-tracking effect. (*Note:* The failure of the previous ASTT [BB] was unlikely due to the task itself; the problem was the general procedure of that particular study.) However, even though the current ASTT (BB) produced the predicted effect, the effect size it produced was smaller than has been observed in previous studies[25]. However, this study's effect size is in line with the effect size of the most similar prior study to date with a sample size of 18 (r = .41 versus r = .56, respectively) (B. A. Anderson, Laurent, et al., 2014). The

[25] Even though the effect size is numerically in line with previous effect sizes, this is only because the small sample size in the current study has inflated the estimation (within-subject effect size calculations rely on degrees of freedom, which produce reliably smaller effect size estimates when larger than when smaller). For further discussion of these topics, see (Lakens, 2013; Sellke, Bayarri, & Berger, 2001).

lack of omissions in the present study was likely due to the prolonged trial durations unfortunately no analyses could be conducted with so few data points.

A secondary aim of the current study was to explore, for the first time, whether individuals' RT Bias score on the ASTT was robust over a period of time ranging from 1 month to 2 years and, as a result, whether STs and GTs remained in the same classification over time. Results revealed poor test-retest reliability of RT Bias from the previous to the current study, with only 30% of GTs remaining GTs, and 50% of STs and IGs remaining STs ITs, respectively. In terms of which classification individuals transitioned *into*, of the 12 that shifted, 50% were GTs who transitioned to ITs, 25% were STs into ITs, 16.66% (two people) transitioned from GTs to STs and 8.3% (one person) from IT to GT. This can be summarised as follows: most individuals converted to different tracking groups; of those that maintained their classification, STs were the most robust (as IT is a much larger and more variable group). Of those that transitioned, half were GTs shifting into ITs and a quarter STs into the ITs. Finally, while two individuals transitioned from GTs to STs, the reverse pattern was not observed. Although any interpretations must be treated with extreme caution due to the small sample size, this final result (GT → ST) has precedence in the preclinical literature (Srey et al., 2015). It must also be considered that the poor reliability of sign-tracking may have been due to different tasks being used (ASTT [EE] vs ASTT [BB]). This reliability was investigated in the same sample in the same session in Study 5 (Chapter Six); however, as discussed, no conclusions can be made on the basis of those data.

Moving onto the neuroimaging results, the first GLM contrasting activations across the whole brain for high-value compared to low-value trials, and controlling for age and gender, showed bilateral putamen activation and activation of the right lateral superior occipital cortex. The putamen is associated with implicit and reinforcement learning, behavioural

preferences for some foods over others, contrasting activation on high > low-value reward trials, and the processing of reward-associated distractors, with dopamine release in the putamen also predicting magnitude of VMAC (B. A. Anderson, 2015a; B. A. Anderson, Kuwabara, et al., 2016; Mattfeld, Gluck, & Stark, 2011; O'Doherty et al., 2006; Pollmann, Eštočinová, Sommer, Chelazzi, & Zinke, 2016). Evidence also suggests that the putamen in particular exhibits increasing functional connectivity with other reward- and visual attention-related structures (such as the habenula and frontoparietal regions) as a function of increasing CS value (Lawson et al., 2014; Pessoa, 2014b). Importantly, evidence further indicates that DA activity in the putamen is significantly associated with drug craving in frequent cocaine users (Wong et al., 2006). On a broader view, the dorsal striatum (wherein the putamen resides) maintains reward-related outcomes of particular actions and may oversee the tracking of motivationally salient events (Mattfeld et al., 2011; O'Doherty et al., 2004). Further, DA release in the dorsal striatum has also been linked to cue-induced drug craving (Volkow et al., 2006). Regarding the right lateral superior occipital cortex, evidence suggests that this is a pivotal region in value-modulated attentional priority, and previous studies have shown increased activation on the same *high-value > low-value reward* contrast employed here (B. A. Anderson, 2015a; Pollmann et al., 2016).

In the second GLM, a *high > low* contrast with age and gender as fixed factors was, again conducted, although RT Bias was also entered as a correlate into a regression within the GLM. Results again revealed activation in the right putamen, with additional regional activation in the right pallidum, right amygdala and the anterior and posterior regions of the right superior temporal gyrus. The right pallidum (and putamen) have been associated with reward-seeking behaviours (such as alcohol and drug use), with the ventral pallidum central to reward processing and motivation (Perry et al., 2014; Smith et al., 2009). Given that the pallidum activation appears more ventral than dorsal, it is also important to note that the

ventral pallidum plays a role in pleasure perception (encoding hedonic reward) (Tindell, Smith, Pecina, Berridge, & Aldridge, 2006). Further, the striato-pallidum complex reflects incentive (motivation) levels and has been described as a major reward-related network (L. Schmidt, Lebreton, Cléry-Melin, Daunizeau, & Pessiglione, 2012). The right amygdala has also shown functional connectivity with the right habenula (as did the putamen in the same study), though only as a function of presentation of a CS associated with an electric shock (Lawson et al., 2014). However, evidence does suggest that the amygdala (and the amygdala–ventral striatum complex in particular) is vital in stimulus–reward (incentive) learning, the influence of drug-related cues over behaviour, and the ability of drug cues to evoke rapid, automatic behavioural responses (Bechara & Damasio, 2002). Furthermore, preclinical work indicates that gene (c-fos) expression in the basolateral amygdala differs between STs and GTs (Flagel & Robinson, 2017). The right superior temporal gyrus (rSTG) is another area associated with attention and salience detection, shifting attention in tasks which involve encoding relative value and semantic (but not aesthetic) information (Lim, O'Doherty, & Rangel, 2013; Rapuano, Huckins, Sargent, Heatherton, & Kelley, 2016). A study employing a value-laden Stroop task also showed increased rSTG activation on trials which presented CSs associated with potential reward compared to trials presenting CSs associated with no reward (Krebs, Boehler, Egner, & Woldorff, 2011).

Subsequent to the primary neuroimaging analyses, non-adjusted BOLD signal data were extracted for each participant for each cluster which survived the threshold corrections of the second GLM. These data were then correlated with (fMRI) RT Bias (with higher RT Bias indicating increased sign-tracking). Results revealed statistically significant positive moderate–strong correlations between activation for clusters 2 (right pallidum and amygdala) and 3 (anterior and posterior rSTG), and RT Bias. Cluster 1 (right putamen) showed a perfect positive correlation with RT Bias. This third result flags up a very likely artificial inflation of

the strength of these relationships. In fact, some researchers suggest that the method of analysing neural activations and behavioural responses is pervasively wrong across the field of neuroscience, but such discussion is beyond the scope of this chapter (see Vul, Harris, Winkielman, & Pashler, 2009). However, regardless of the subsequent bivariate correlations conducted to present these associations, the initial GLM still shows a relationship between regional brain activation and RT Bias on the ASTT.

There are several limitations of this study to be discussed. First, as already mentioned, the study's sample size was small, owing in part to time, funding and the general acceptance of small samples in neuroscience (fMRI in particular) (Button et al., 2013). The small sample reduced statistical power and may have overinflated some effects whilst altogether missing others. The study employed the ASTT (BB), whereas most other studies in this thesis used the ASTT (EE). Eye-tracking measures have been shown to be more internally reliable than motor-behavioural responses when assessing attentional bias (Christiansen, Mansfield, et al., 2015)[26]. The recruitment of uneven groups of STs and GTs and small sample size means that interpretation of RT Bias change and tracker classification shift over time is potentially spurious. Finally, the deployment of the ASTT (BB) rather than the ASTT (EE) to measure RT Bias in the current study meant that there was a fundamental mismatch between the methods used across time points. One of the aims of Study 5 (Chapter Six) was to compare RT Bias across both tasks (EE/BB) so that the current fMRI study results could be better interpreted. However, this was not possible due to the failure of all tasks in Study 5 to detect sign-tracking effects. Future studies should aim for larger sample sizes, the utilisation of eye-tracking and the consistent use of task methods and measures over time.

[26] For several months the primary researcher (J.J.D) and multiple lab technicians did attempt to repair an fMRI-compatible eye-tracker for use in this study, but although the equipment was found to be much improved, the spatial resolution was not capable of monitoring attention for this particular task.

In conclusion, this study has replicated previous preclinical and human work showing neural activation in motivation, reward and visual selective attention networks during completion of a variant of the additional singleton task. Participants' brain activations in various regions (such as the putamen and pallidum) was associated with sign-tracking. Overall, these data add to the growing literature on the neural correlates of human sign-tracking. However, the study was likely underpowered and possessed core issues in methodology which makes interpretation of sign-tracking's longevity difficult.

Chapter Eight

Supplementary Analyses

8.1 Background

This chapter is concerned with assessing and ruling out the effects of obvious confounds in all of the analyses previously conducted regarding the ASTT. This chapter investigates whether there are any differences in major outcome variables between I) participants who believed that they would gain additional rewards and those who did not (*deception*), II) *gender*, and III) attentional bias towards the red versus blue stimuli (CSs), regardless of value (*red vs. blue*). All analyses are 2-tailed.

8.2 Study 1 (Chapter Three)

The following analyses concern Study 1, in which a large sample of participants (N = 98) completed the ASTT (the Multi-Target Tracking Task is not included due to null results). No differences were found between believers vs. nonbelievers or males vs. females. However, there were more omissions on blue trials compared to red, regardless of value (Table 8.1).

Table 8.1 Overview of Study 1 analyses

Analysis	Test Statistic	*p*-value	Effect Size (r | Δ)
Deception			
RT Bias	$F = 0.14$	.70	$\Delta = 0.07$
Omission Bias	$U = 965.50$	.23	$r = .12$
Gender			
RT Bias	$F = 0.001$	.97	$\Delta = 0.009$
Omission Bias	$U = 983.50$	.15	$r = .14$
Red vs. Blue			
RTs	$T = 2353.00$	.80	$r = .02$
Omissions	$T = 1112.50$	**.004**	$r = .29$

Deception = difference between those who believed they would receive extra rewards based on task performance and those who did not; *Red vs. Blue* = difference in responses on red vs. blue trials across participants, regardless of each colour's value. 'RTs' and 'Omissions' refer to raw numbers, not bias scores. Test statistic: F = Welch's *t*-test; U = Mann-Whitney U test; T = Related-Samples Wilcoxon Signed-Rank test. Effect size: r = Pearson's r; Δ = Glass's delta[27]. Bold = $p < .05$.

8.3 Study 2 (Chapter Four)

The following analyses concern Study 2, in which participants attended the laboratory over two sessions and consumed either a control drink or alcohol (0.3 g/kg) before completing the ASTT. No differences were found between believers vs. nonbelievers, males vs. females or red vs. blue stimuli (Table 8.2).

[27] Glass's delta (Δ) is used as a Welch's *t*-test effect size (ES). Welch's test gives robust results, even when the standard deviations (SDs) of groups substantially differ (i.e., possess unequal variance) (Delacre, Lakens, & Leys, 2017). However, given that Cohen's *d* (typical ES of Independent *t*-tests) is calculated via pooling the SDs of different conditions, and given that this is not recommended when variance is unequal, Δ is a preferred alternative as it utilises only the SD of one group (typically the control group) (Lakens, 2013). For *deception*, the SD from the nonbelieving group is used (as this group's ES should reasonably be smallest); for *gender*, the SD of females is used (as these are consistently the majority).

Table 8.2 Overview of Study 2 analyses

Analysis	Test Statistic	*p*-value	Effect Size (r | Δ)
Deception			
Control: RT Bias	$F = 4.03$	.056	$\Delta = 1.11$
Control: Omission Bias	$U = 76.00$	.35	$r = .18$
Alcohol: RT Bias	$F = 0.06$	.81	$\Delta = 0.02$
Alcohol: Omission Bias	$F = 2.40$	.14	$\Delta = 0.50$
Gender			
Control: RT Bias	$U = 78.00$	.37	$r = .17$
Control: Omission Bias	$U = 95.50$	.93	$r = .02$
Alcohol: RT Bias	$U = 91.00$	.77	$r = .06$
Alcohol: Omission Bias	$U = 93.00$	.84	$r = .04$
Red vs. Blue			
Control: RTs	$T = 198.00$	.91	$r = .01$
Control: Omissions	$t = 0.18$	.86	$r = .03$
Alcohol: RTs	$T = 185.00$	.68	$r = .05$
Alcohol: Omissions	$T = 159.00$	.47	$r = .14$

Deception = difference between those who believed they would receive extra rewards based on task performance and those who did not; *Red vs. Blue* = difference in responses on red vs. blue trials across participants, regardless of each colour's value. 'RTs' and 'Omissions' refer to raw numbers, not bias scores. Test statistic: F = Welch's t-test; U = Mann-Whitney U test; T = Related-Samples Wilcoxon Signed-Rank test; t = Paired-Samples t-test. Effect size: r = Pearson's r; Δ = Glass's delta. Bold = $p < .05$.

8.4 Study 3 (Chapter Four)

The following analyses concern Study 3, which was identical to Study 2 in all ways except that the alcohol dose was 0.6 g/kg. No differences were found between believers vs.

nonbelievers. However, females showed higher RT Bias in the alcohol condition compared to males, and there were more omissions on blue trials compared to red in the alcohol condition (Table 8.3).

Table 8.3 Overview of Study 3 analyses

Analysis	Test Statistic	*p*-value	Effect Size (r | Δ)
Deception			
Control: RT Bias	U = 109.00	.89	r = .03
Control: Omission Bias	U = 89.50	.34	r = .18
Alcohol: RT Bias	U = 97.00	.52	r = .12
Alcohol: Omission Bias	F = 0.46	.502	Δ = 0.25
Gender			
Control: RT Bias	U = 99.00	.70	r = .10
Control: Omission Bias	U = 94.50	.57	r = .10
Alcohol: RT Bias	U = 59.00	**.04**	r = .38
Alcohol: Omission Bias	U = 85.00	.33	r = .18
Red vs. Blue			
Control: RTs	T = 231.00	.98	r = .004
Control: Omissions	t = .0.04	.97	r = .008
Alcohol: RTs	T = 212.00	.67	r = .05
Alcohol: Omissions	t = .2.31	**.03**	r = .39

Deception = difference between those who believed they would receive extra rewards based on task performance and those who did not; *Red vs. Blue* = difference in responses on red vs. blue trials across participants, regardless of each colour's value. 'RTs' and 'Omissions' refer to raw numbers, not bias scores. Test statistic: F = Welch's t-test; U = Mann-Whitney U test; T = Related-Samples Wilcoxon Signed-Rank test; t = Paired-Samples t-test. Effect size: r = Pearson's r; Δ = Glass's delta. Bold = $p < .05$.

8.5 Study 4 (Chapter Five)

The following analyses concern Study 4, which assessed responses on an updated version of the ASTT – the ASTT+ – employing three CSs rather than two. (*Note:* Omission Bias 1 = *high−medium*; Omission Bias 2 = *high−low*.) No differences were found between believers vs. nonbelievers, males vs. females or red vs. blue stimuli (Table 8.4).

Table 8.4 Overview of Study 4 analyses

Analysis	Test Statistic	*p*-value	Effect Size (r | Δ | η_p^2)
Deception			
RT Bias	$F = 1.47$	.24	$\Delta = 0.39$
Omission Bias 1	$F = 0.52$	.48	$\Delta = 0.24$
Omission Bias 2	$F = 0.06$	.81	$\Delta = 0.10$
Gender			
RT Bias	$F = 1.76$	.20	$\Delta = 0.70$
Omission Bias 1	$F = 1.39$	.25	$\Delta = 0.41$
Omission Bias 2	$F = 0.10$	.76	$\Delta = 0.09$
Red vs. Blue			
RTs	$F = 0.56$	.58	$\eta_p^2 = .02$
Omissions	$F = 0.003$	.99	$\eta_p^2 = .00009$

Deception = difference between those who believed they would receive extra rewards based on task performance and those who did not; *Red vs. Blue* = difference in responses on red vs. blue trials across participants, regardless of each colour's value. 'RTs' and 'Omissions' refer to raw numbers, not bias scores. Test statistic: F = Welch's *t*-test/Repeated-Measures ANOVA. Effect size: Δ = Glass's delta; η_p^2 = Partial eta squared. Bold = $p < .05$.

8.6 Study 5 (Chapter Six)

This experiment investigated potential comparisons between the ASTT (eye-tracker versus button-box) and a PIT task. None of the three tasks elicited sign-tracking, likely due to the procedural setup of the experiment (see the Discussion section in Chapter Six). As a result, supplementary analyses are not conducted for Study 5.

8.7 Study 6 (Chapter Seven)

The following analyses concern Study 6, in which participants who had participated in a previous study from this thesis also participated in this study. Participants completed the ASTT (BB) while undergoing fMRI scanning. Given that participants had already undergone the deception of a previous study, deception analyses were not conducted. Omission analyses were also not conducted due to the virtual absence of omissions. No RT differences were found between males vs. females or red vs. blue stimuli (Table 8.5).

Table 8.5 Overview of Study 6 analyses

Analysis	Test Statistic	*p*-value	Effect Size (r | Δ)
Gender			
RT Bias	$F = 0.26$	.62	$\Delta = 0.31$
Red vs. Blue			
RTs	$t = 1.85$	.08	$r = .39$

Red vs. Blue = difference in responses on red vs. blue trials across participants, regardless of each colour's value. 'RTs' refer to raw numbers, not bias scores. Test statistic: F = Welch's t-test; t = Paired-Samples t-test. Effect size: r = Pearson's r; Δ = Glass's delta. Bold = $p < .05$.

8.8 Conclusions

Overall conclusions for each analysis type are given below.

Deception: No study showed differences in either RT Bias or Omission Bias between those who believed they would receive extra rewards and those who did not. This suggests that belief in reward does not influence sign-tracking. This result is supported by a previous AST study which showed that participants displayed VMAC towards money that they knew they would not receive (i.e., they knew that their performance would not grant them extra rewards) (Roper & Vecera, 2016). This evidence is the first, however, to explicitly investigate this potential confound in the sign-tracking literature.

Gender: Studies 1, 2, 4 and 6 showed no gender differences in either RT Bias or Omission Bias. Study 3 revealed higher RT Bias among women in the alcohol session compared to men, which supports a preclinical study showing that female rats exhibit elevated sign-tracking in an alcohol autoshaping paradigm (Madayag et al., 2017). However, overall there appears to be little evidence of a gender effect on sign-tracking.

Red vs. Blue: Across studies 1, 2, 3, 4 and 6, there was no difference in OT RTs between trials containing red or blue (or green) distractors, regardless of value. However, studies 1 and 3 did show greater omissions on blue trials compared to red (only in the alcohol condition in Study 3). The results suggests that sign-tracking RT effects were not significantly impacted by distractors' physical salience, although sign-tracking as measured by omissions may be more vulnerable to the impact of a stimulus's perceptual properties.

Chapter Nine

Examination of the ASTT

9.1 Background

This chapter is concerned with assessing the validity of the ASTT's measures, as well as replicating specific sign-tracking results found in the human literature. Regarding the replications, two predictions were made: I) reaction times (RTs) towards conditioned stimuli (CSs) will be faster than RTs towards outcome targets (OTs), indicating that CS RTs are produced by automatic, exogenous saccades (Failing et al., 2015), and OT RTs by conscious, endogenous attentional orienting (Theeuwes, 2010), and II) that differently valued CSs will pull with the same 'force', as indicated by no statistical difference between CS RTs (Le Pelley et al., 2015). To assess the validity of ASTT measures, – specifically, whether RT and Omission Biases are broadly measuring sign-tracking – correlations between the two measures were conducted[28]. *Note:* analyses for CS RTs vs. OT RTs are 1-tailed, while high-value CS RTs vs. low-value CS RTs (directionless prediction) and RT Bias-Omission Bias correlations (exploratory) are 2-tailed.

[28] Ideally, Bland-Altman plots would be performed to assess agreement between the two measures (Bland & Altman, 1986). However, bias scores are already difference scores of measures of completely different scales (RTs vs error frequency), the data of which would further need to be transformed before analysis. Multiple levels of difference score creation and data transformation may result in even less interpretable results than standard correlation coefficients.

9.2 Study 1 (Chapter Three)

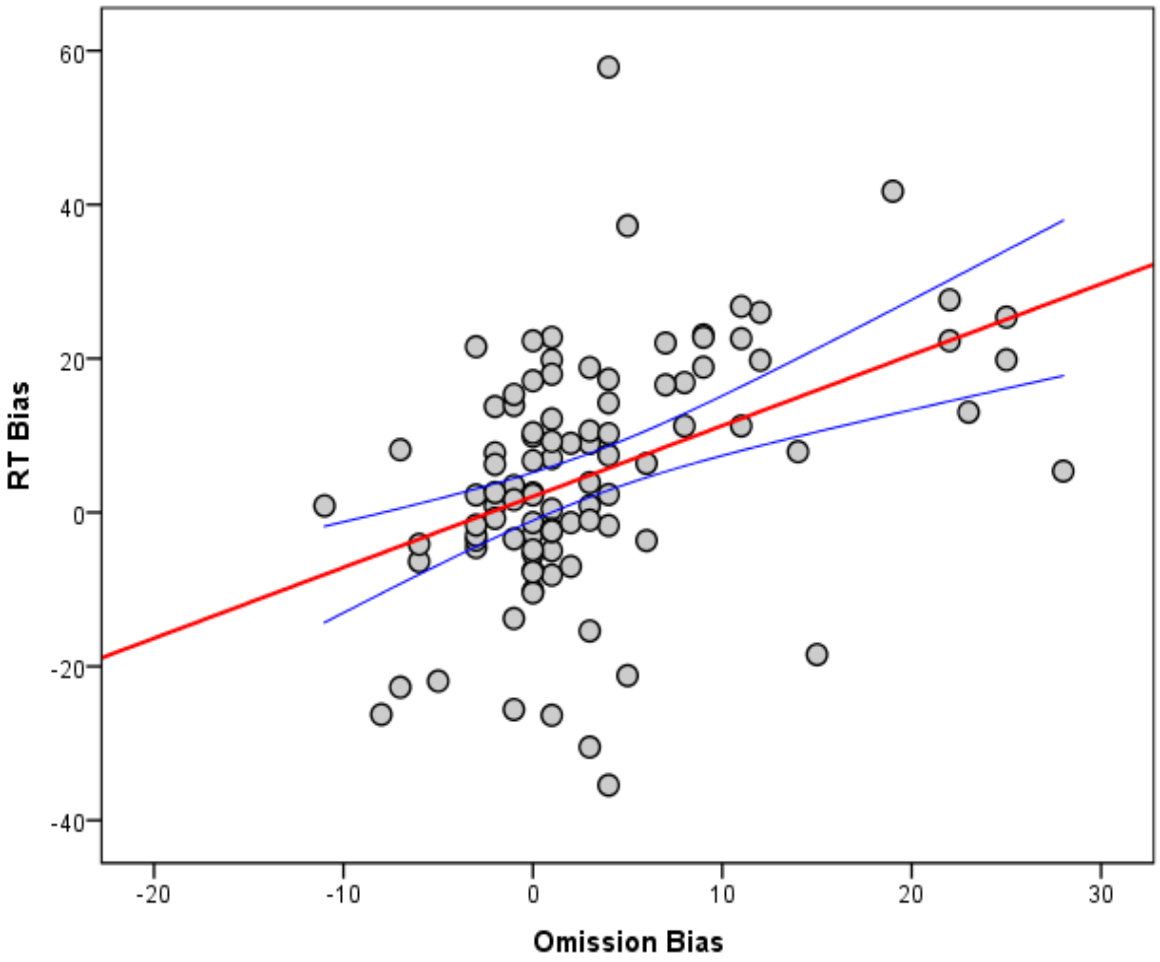
This experiment used a large sample (N = 98) to assess responses on the ASTT.

CS vs. OT: A Wilcoxon Signed-Rank test revealed that RTs to CSs (*Mdn* = 290.23, *range* = 91.00-471.00) were quicker than RTs to the OT (*Mdn* = 351.25, *range* = 293.20-518.39), T = 253.00, $p < .0001$, r = 0.78. This suggests CS RTs are automatic.

High-value CS vs. Low-value CS: When omissions occurred, there was no difference in RTs towards different CSs – indicating similar pull of 'force' (Le Pelley et al., 2015). That is, both low- (*Mdn* = 288.20, *range* = 140.00-469.00) and high-value (*Mdn* = 285.00, *range* = 91.00-474.33) CSs produced omissions of similar speeds, T = 1493.00, p = .97.

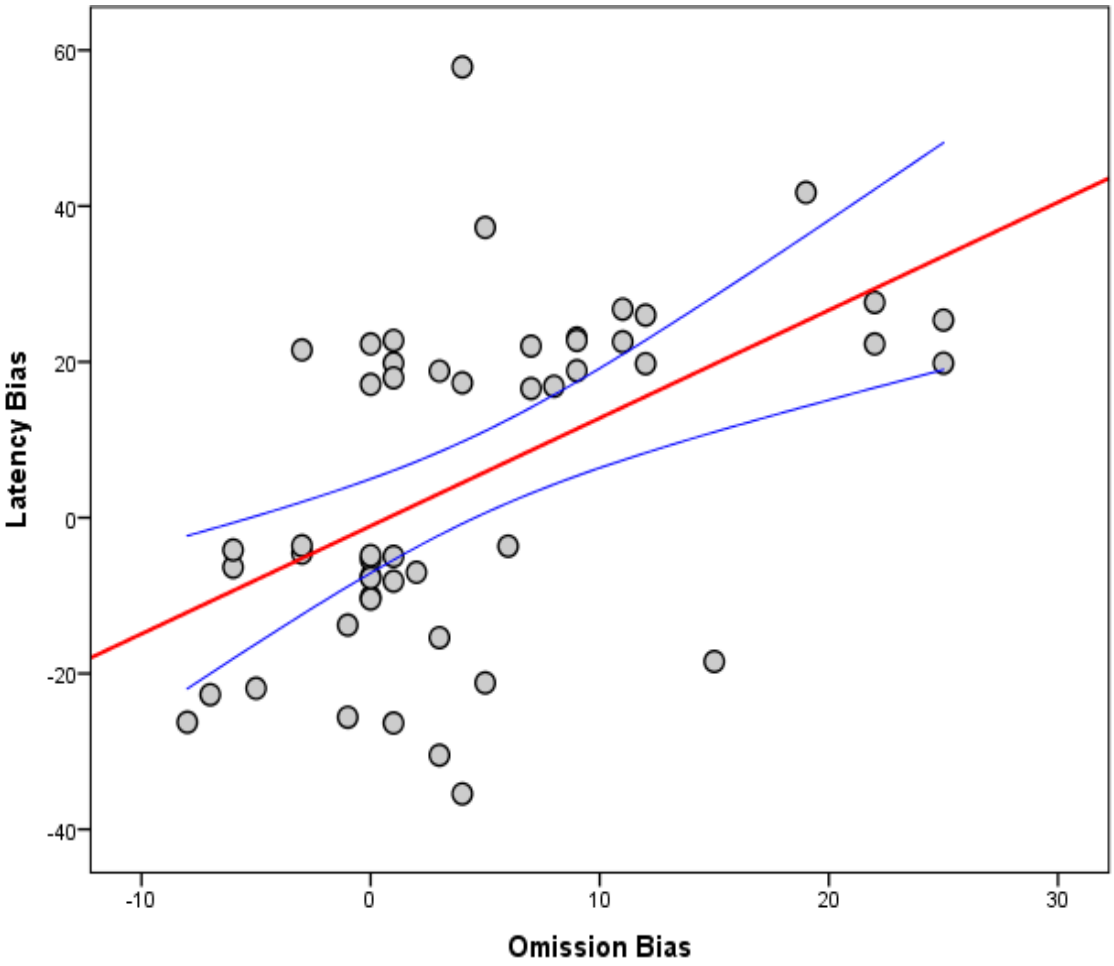
Reaction Time & Omission Biases: Bias scores showed a moderate positive correlation, r_s = .47, $p < .0001$ (see Figure 9.1). When only sign-trackers and goal-trackers were taken into account (i.e., individuals in the top and bottom 25% of RT Bias scores), bias scores showed an even stronger positive correlation than was found in the general sample, r_s = .56, $p < .0001$ (see Figure 9.2). These data lend support to the hypothesis that these scores broadly reflect sign-tracking measurements.

Figure 9.1 Scatterplot showing a positive correlation between bias scores for the ASTT



Blue lines depict mean confidence intervals (95%).

Figure 9.2 Scatterplot showing a positive correlation between bias scores in a sample containing only sign-trackers and goal-trackers



Blue lines depict mean confidence intervals (95%).

9.3 Study 2 (Chapter Four)

This experiment contained two testing sessions with the ASTT, once after the participant had been given a low dose of alcohol (0.3 g/kg) and once after they had been given lemonade (control).

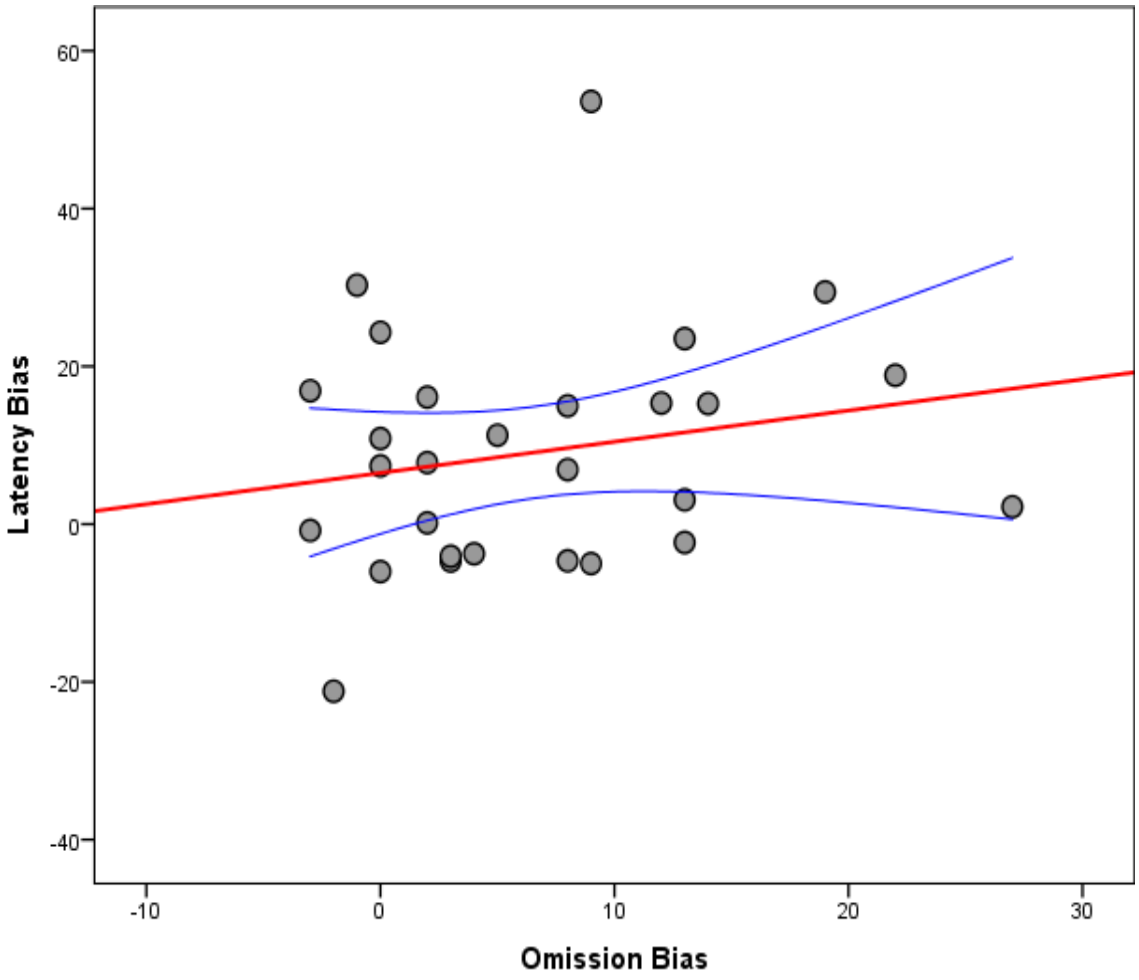
CS vs. OT: A Friedman's ANOVA revealed statistically significant differences in latencies between correct and incorrect responses (OT vs. CS responses, respectively), $\chi^2(3) =$

40.38, $p < .0001$. Wilcoxon Sign-Rank tests were conducted to further investigate these differences. In the alcohol condition, RTs towards CSs (*Mdn* = 288.55, *range* = 189.93) were quicker than towards the OT (*Mdn* = 360.40, *range* = 187.21), $T = 13.00$, $p < .0001$, $r = .58$. Likewise, in the control condition RTs towards CSs (*Mdn* = 299.07, *range* = 421.60) were quicker than towards the OT (*Mdn* = 359.38, *range* = 225.42), $T = 48.00$, $p = .0004$, $r = .39$.

High-value CS vs. Low-value CS: A Friedman's ANOVA (ranking responses by condition and value) revealed, as predicted, no differences in RTs towards CSs between either condition or high-value and low-value cues, $\chi^2(3) = 2.94$, $p = .40$.

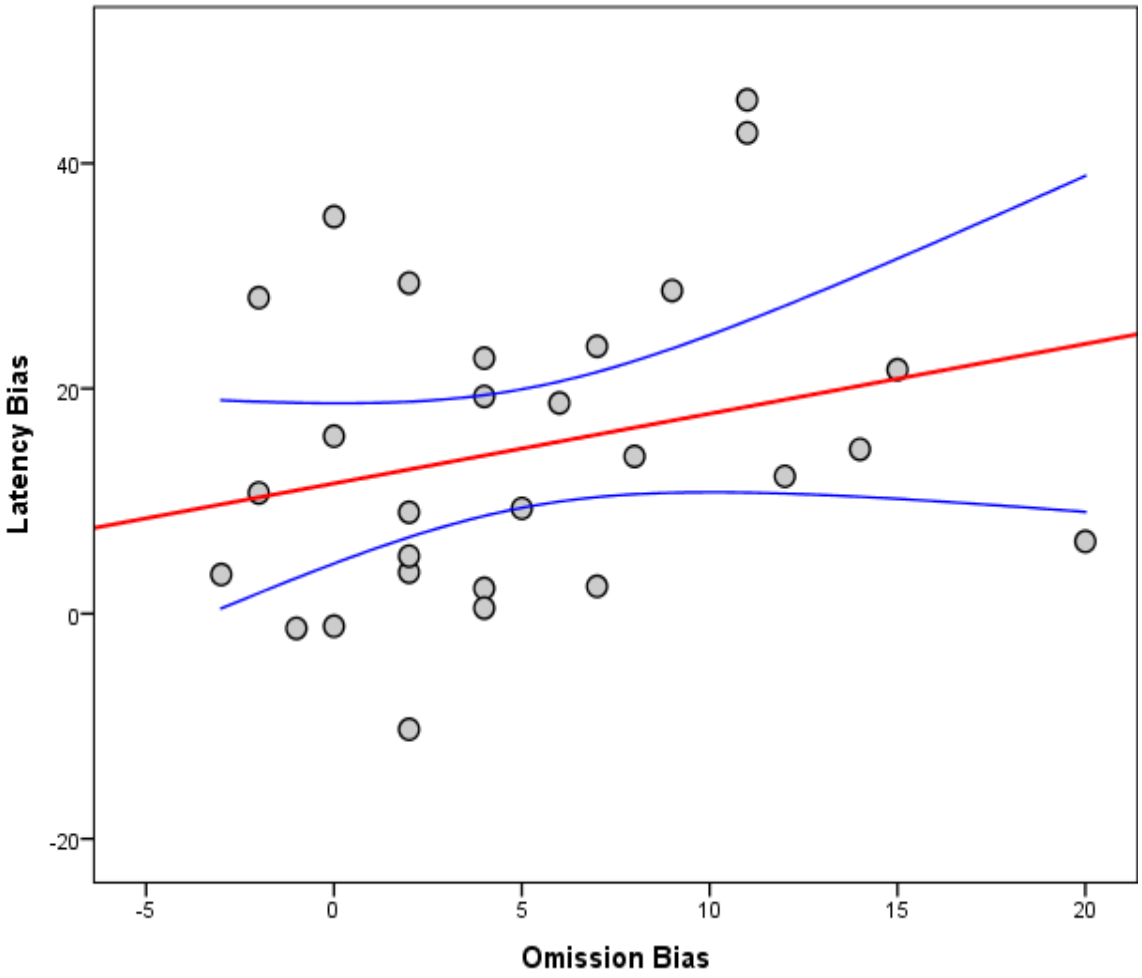
Reaction Time & Omission Biases: Following control consumption, bias scores did not show a statistically significant correlation, $r = .20$, $p = .30$ (see Figure 9.3). Similarly, there was no significant correlation in the alcohol condition, $r = .26$, $p = .19$ (see Figure 9.4). These results may indicate that the measures of sign-tracking are disconnected, or perhaps that there was not enough power to detect an association.

Figure 9.3 Scatterplot showing a nonsignificant correlation between bias scores (control condition)



Blue lines depict mean confidence intervals (95%).

Figure 9.4 Scatterplot showing a nonsignificant correlation between bias scores (alcohol condition)



Blue lines depict mean confidence intervals (95%).

9.4 Study 3 (Chapter Four)

This experiment was identical to Study 2 (above), except that the alcohol dose given to participants was 0.6 g/kg.

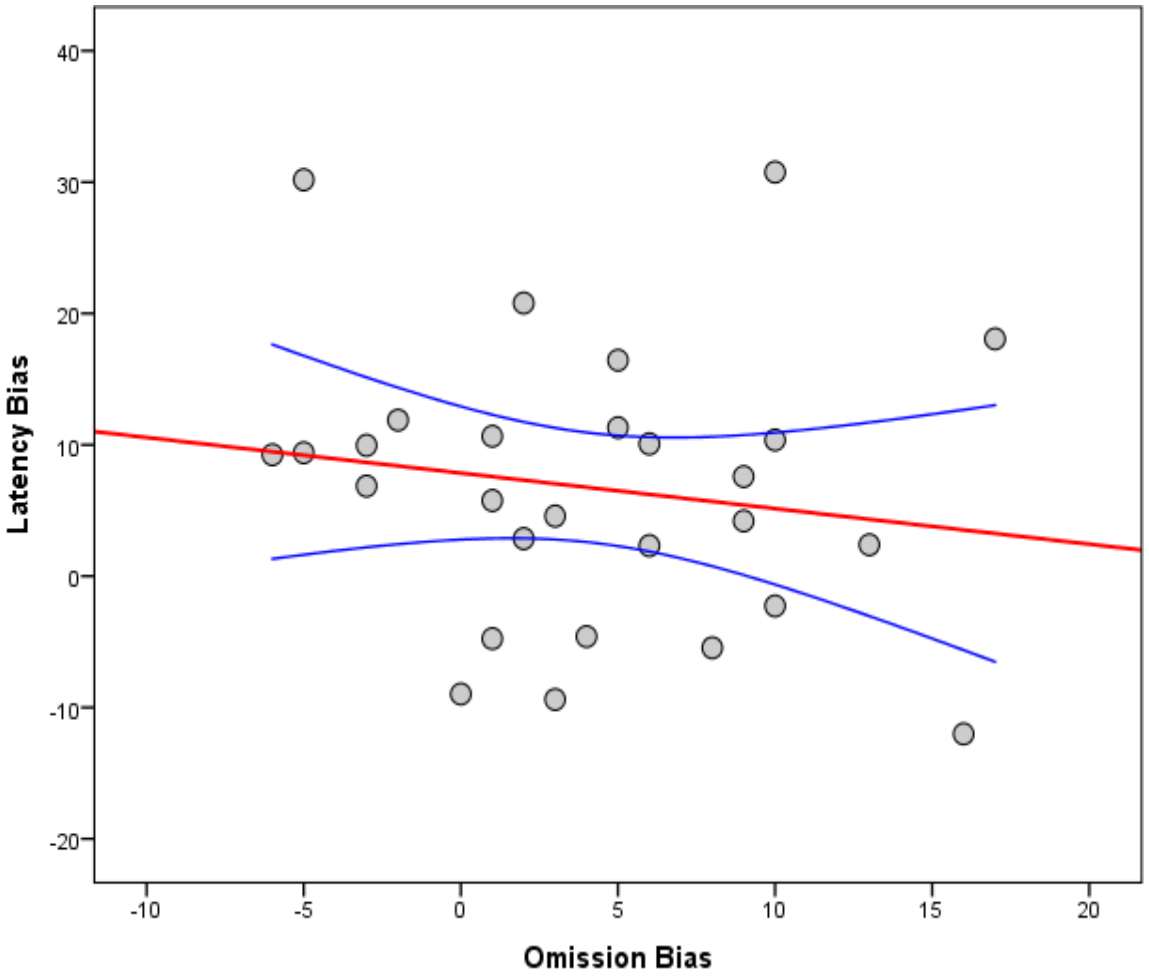
CS vs. OT: A 2 (alcohol vs control) × 2 (OT RT vs CS RT) Repeated-Measures ANOVA revealed a main effect of condition, $F(1, 29) = 7.98$, $p = .008$, $\eta_p^2 = .22$, with RTs in the alcohol condition ($M = 351.57$, $SD \pm 66.70$) slower than in the control condition ($M = 329.66$,

SD ± 44.91). There was also a main effect of stimulus type, $F(1, 29) = 95.37$, $p < .0001$, $\eta_p^2 = .77$, with OT RTs (*M* = 376.37, *SD* ± 36.15) larger than CS RTs (*M* = 304.86, *SD* ± 52.93). There was no interaction between condition and stimulus type. Paired-Samples *t*-tests revealed that, in the alcohol condition, OT RTs (*M* = 391.03, *SD* ± 38.19) were slower than CS RTs (*M* = 312.10, *SD* ± 66.10), $t(29) = 6.90$, $p < .0001$, $r = .79$. An identical pattern was observed in the control condition (OT RTs: *M* = 361.71, *SD* ± 27.49; CS RTs: *M* = 297.62, *SD* ± 34.97), $t(29) = 9.19$, $p < .0001$, $r = .86$. This is again suggestive of OT responses being voluntary and endogenous (top-down processes), and CS responses reflexive and exogenous (bottom-up).

High-value CS vs. Low-value CS: A Two-Way Friedman's ANOVA revealed, as predicted, no difference between CS RTs, $\chi^2(3) = 3.27$, $p = .35$. This again suggests that, across and within conditions, CSs of differing value attract attention with the same 'force'.

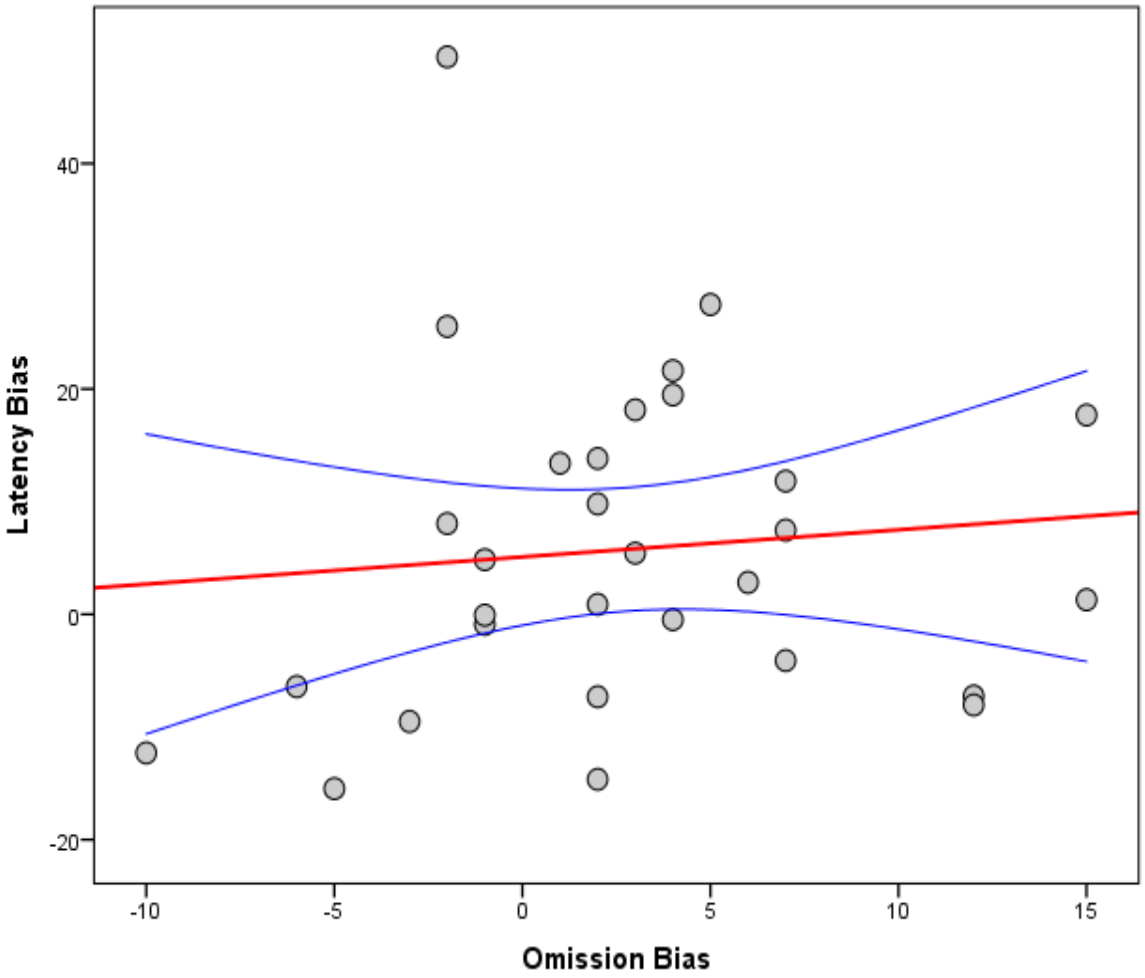
Reaction Time & Omission Biases: Following control consumption, bias scores did not show a statistically significant correlation, $r = -.13$, $p = .51$ (see Figure 9.5). Similarly, there was no significant correlation in the alcohol condition, $r = .10$, $p = .61$ (see Figure 9.6). These results again indicate either that the measures of sign-tracking are disconnected, or perhaps that there was not enough power to detect an association. See the section 'Studies 3 & 4' below in which the samples from these studies were combined.

Figure 9.5 Scatterplot showing a nonsignificant correlation between bias scores (control condition)



Blue lines depict mean confidence intervals (95%).

Figure 9.6 Scatterplot showing a nonsignificant correlation between bias scores (alcohol condition)



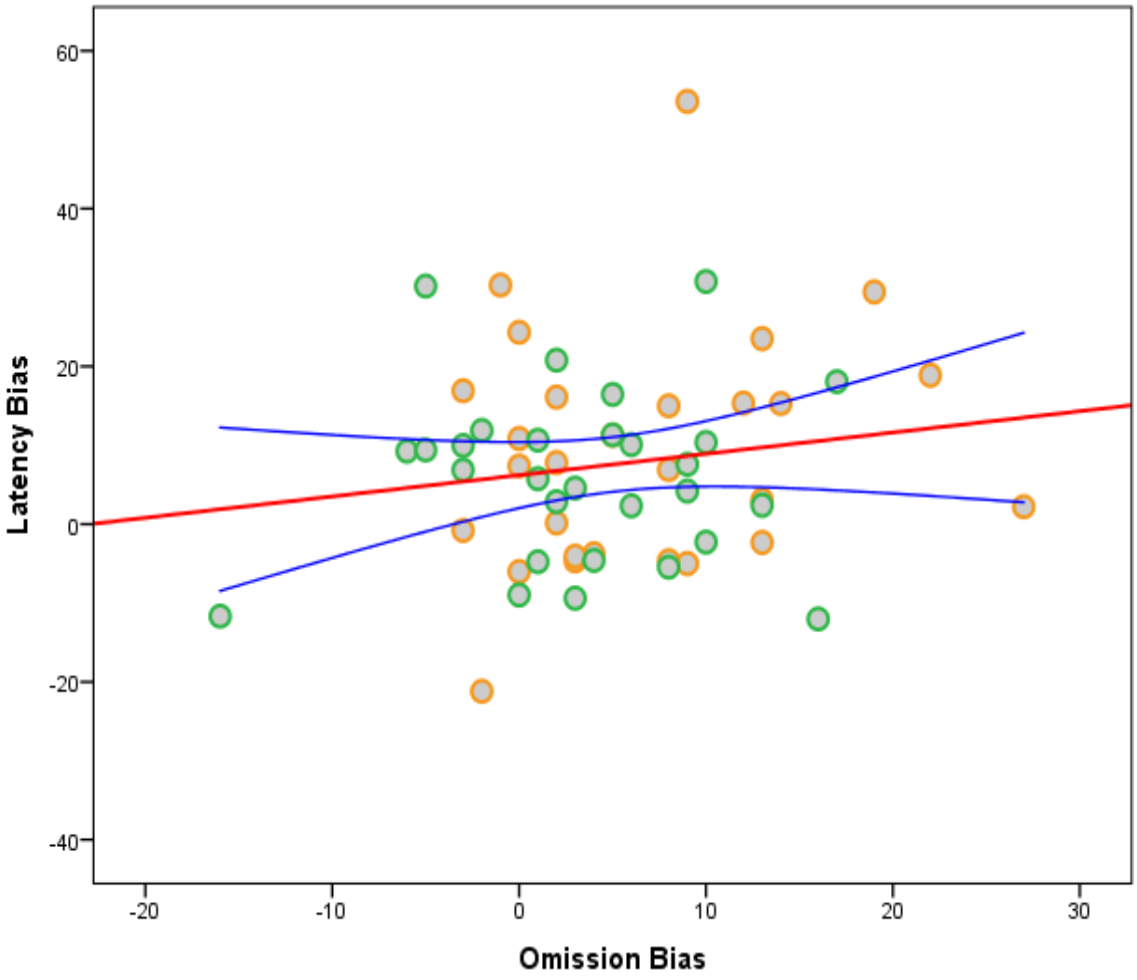
Blue lines depict mean confidence intervals (95%).

9.5 Studies 2 & 3

The samples from Studies 2 and 3 were combined in a results synthesis. The amalgamated samples are used here to only test whether any significant correlation exists between bias scores in order to test if the null findings in Studies 2 and 3 (above) were due to failures of power.

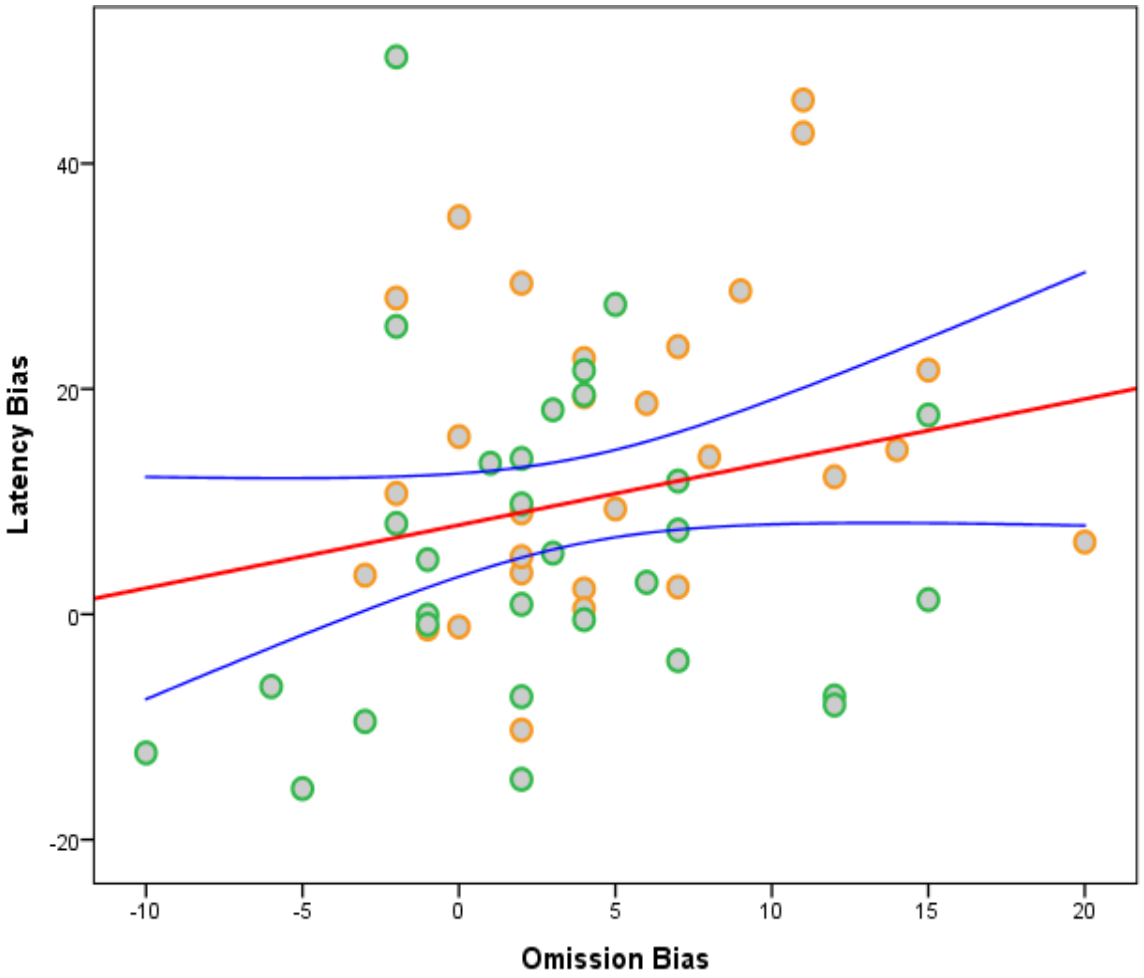
Reaction Time & Omission Biases: Following control consumption, bias scores did not show a statistically significant correlation, $r = .16$, $p = .25$ (see Figure 9.7). Similarly, there was no significant correlation in the alcohol condition, $r = .22$, $p = .09$ (see Figure 9.8). This suggests that the lack of statistically significant associations found earlier may not be due to a lack of power.

Figure 9.7 Scatterplot showing a nonsignificant correlation between bias scores (control condition)



Blue lines depict mean confidence intervals (95%). Orange border = Study 2 sample; Green border = Study 3 sample.

Figure 9.8 Scatterplot showing a nonsignificant correlation between bias scores (alcohol condition)



Blue lines depict mean confidence intervals (95%). Orange border = Study 2 sample; Green border = Study 3 sample.

9.6 Study 4 (Chapter Five)

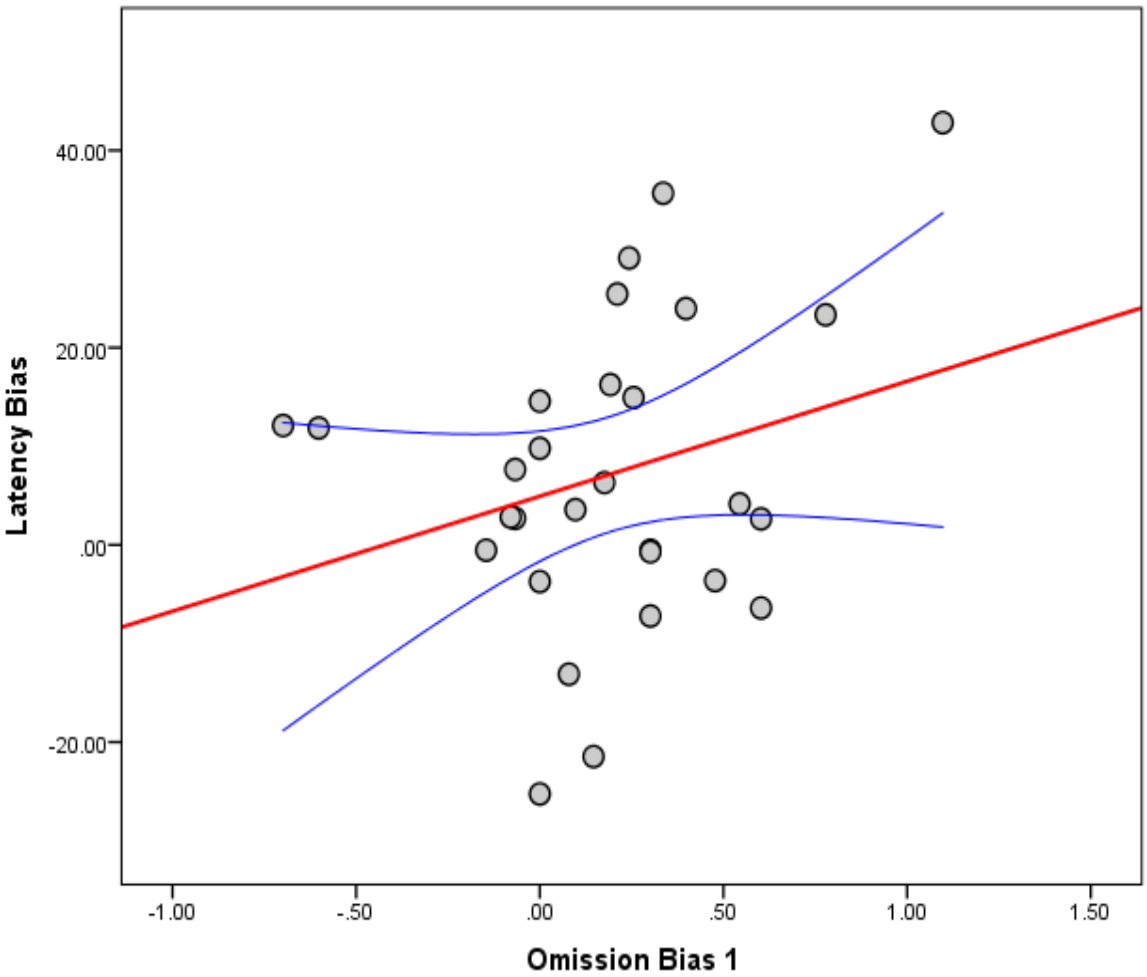
This experiment assessed responses on a variant of the ASTT – the ASTT+ – which employs three CSs rather than two.

CS vs. OT: A Wilcoxon Signed-Rank test revealed that RTs to CSs (*Mdn* = 298.65, *range* = 225.69 – 565.17) were quicker than RTs to the OT (*Mdn* = 366.93, *range* = 311.55 – 413.18), $T = 32.00$, $p < .0001$, $r = 0.53$.

High-value CS vs. Medium-value CS vs. Low-value CS: Given that these analyses were the primary investigation of Study 4 (Chapter Five), these analyses are contained in Chapter Five (p. 11).

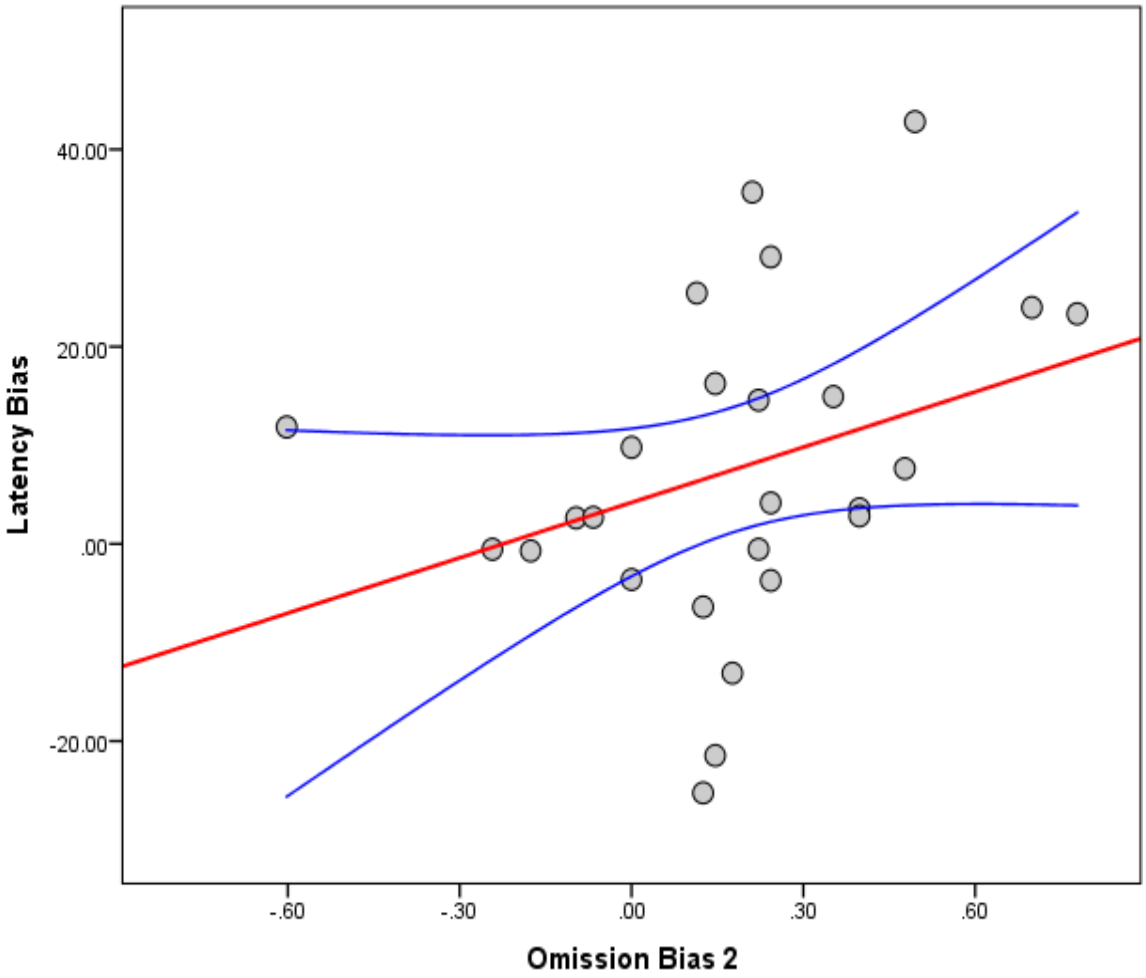
Reaction Time & Omission Biases: RT Bias was analysed with two kinds of Omission Bias, one calculated as the difference score between high and medium omissions ('Omission Bias 1'), the other as the difference between high and low omissions ('Omission Bias 2') (see Appendix F). RT Bias showed no correlation with Omission Bias 1, $r = .27$, $p = .15$ (see Figure 9.9). Likewise, RT Bias showed no correlation with Omission Bias 2, $r = .33$, $p = .09$ (see Figure 9.10). These data suggest that RT and omissions are disparate measures of sign-tracking. Finally, the association between Omission Bias 1 and Omission Bias 2 was investigated. A medium-large positive correlation was found between omission biases, $r = .43$, $p = .03$ (see Figure 9.11). This shows that Omission Biases, though calculated differently, were linked.

Figure 9.9 Scatterplot showing no association between RT Bias and Omission Bias 1 for the ASTT+



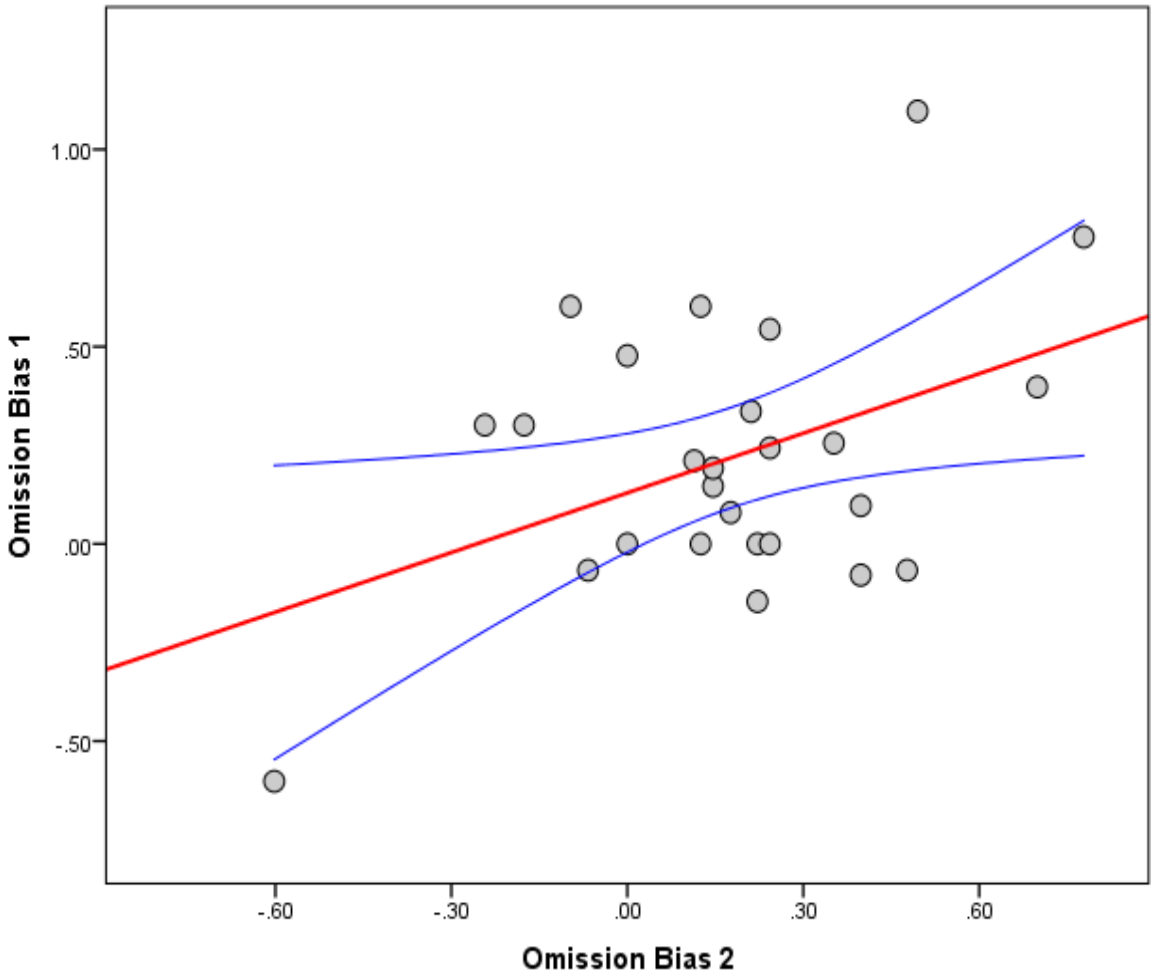
Blue lines depict mean confidence intervals (95%).

Figure 9.10 Scatterplot showing no association between RT Bias and Omission Bias 2 for the ASTT+



Blue lines depict mean confidence intervals (95%).

Figure 9.11 Scatterplot showing no association between Omission Bias 1 and Omission Bias 2 for the ASTT+



Blue lines depict mean confidence intervals (95%).

9.7 Study 5 (Chapter Six)

This experiment investigated potential comparisons between the ASTT (eye-tracker versus button-box) and a PIT task. None of the three tasks elicited sign-tracking. As a result, analyses were not conducted for this study.

9.8 Study 6 (Chapter Seven)

This experiment retested participants who had participated in one of this thesis's previous studies (Studies 1, 2, 3 or 5), this time on the ASTT (BB) whilst undergoing an fMRI scan. There were exceptionally few omissions in this study and thus no high-value CS vs. low-value CS analyses or correlations were performed.

CS vs. OT: A Paired-Samples *t*-test revealed that RTs to CSs (M = 493.83, SD ± 90.06) were quicker than RTs to the OT (M = 578.43, SD ± 73.71), $t(7) = 4.05$, $p = .003$, $r = .84$. This result replicates the findings of the ASTT (EE) attained in studies 1-4.

9.9 Conclusions

Overall conclusions for each analysis type are given below.

CS vs. OT: Analyses from Studies 1, 2, 3, 4, and 6 from every individual ASTT completed (including alcohol/control and ASTT [EE]/ASTT [BB]: nine in total) gave the same result: RTs towards CSs were significantly quicker than RTs towards the OT. This replicates previous research (Failing et al., 2015; Le Pelley et al., 2015; Pearson et al., 2015) and suggests that reward affects early selection processes. Specifically, saccades to the target are wilful/controlled, while saccades towards distractors are involuntary/automatic.

High-value CS vs. Low-value CS: Across most completions of the ASTT (seven in total) CSs of different value (including the ASTT+ which included a medium-value distractor) attracted attention with the same 'force'. That is, RTs for omission responses did not differ, regardless of the value of the distractor on display. Overall, these data replicate previous results (Le Pelley et al., 2015) and suggest that, while CSs of different value slow target RTs at different rates, they do not pull attention *towards* them at different rates.

Reaction Time & Omission Biases: The largest single study conducted (Study 1) showed a moderately strong correlation between bias scores, and a subsample analysis containing only sign-trackers and goal-trackers showed a stronger association. However, all other completions of the ASTT (including a results synthesis combining samples from Studies 2 and 3) (six in total) showed no statistically significant correlation between RT Bias and Omission Bias. Overall, the evidence that the biases are related is weak. It should be noted that standard correlation coefficients are not an ideal way to investigate this question; studies specifically exploring this problem are necessary.

Chapter Ten

General Discussion

10.1 Abstract

Background: Preclinical findings show that sign-tracking (ST; and goal-tracking [GT] in some experimental setups) is associated with cue-evoked drug-seeking, drug consumption, risk-taking, novelty-seeking, and impulsivity. Human research shows a link between ST, impulsivity, deficits in working memory, and substance abuse history. *Aims:* The primary aim of this thesis was to explore human ST using a variation of the additional singleton task (AST), the additional singleton tracking task (ASTT). Specifically, the research investigated whether any link between ST and individual differences (such as alcohol consumption, impulsivity, and childhood trauma) existed, whether ST is influenced by acute alcohol consumption, and whether ST is influenced by the number of response-irrelevant, reward-associated cues present. The neural correlates of ST were also investigated. *Methods:* Across six experiments, sign-tracking was measured in samples of social drinkers and potential links to individual differences were assessed. Methods also included the use of typical alcohol priming paradigms and functional magnetic resonance imaging (fMRI) techniques. *Results:* ST effects were found consistently across all but one study. ST was influenced by a 0.3 g/kg, but not a 0.6 g/kg, dose of alcohol, as well as by the number of reward-associated stimuli present. Neural correlates of ST were those identified in previous research. *Conclusions*: ST may aid our understanding of motivational processing in substance use.

10.2 Summary of Findings

10.2.1 Human Sign-Tracking: Evidence, Mechanisms, and Measurement

10.2.1.1 Evidence

Study 1 (Chapter Three) tested 98 social drinkers on the ASTT[29] and found sign-tracking effects as measured by both reaction time (RT) and omissions (errors). Estimated effect sizes revealed medium effect sizes (RTs: r = .31; omissions: r = .40); these compare to estimated effect sizes of dz = .82, dz = .20 (RTs) and dz = .58 (omissions) in the most closely related experimental setups (Le Pelley et al., 2015; Pearson et al., 2015). Focussing on the more robust RT measure, even after conversion Study 1 produced a much more modest effect size (dz = .33) than Le Pelley et al. (2015), though larger than Pearson et al. (2015). Given that the calculation of Cohen's dz rests partially on sample size (with smaller samples inflating effects), it is unsurprising that the effect is smaller than in Le Pelley et al., although interesting that it is larger than Pearson et al., who used a similarly small sample. Gathering evidence from all other relevant AST studies which have reported effect size information, effect sizes range from dz = .20 to dz = 1.12 (B. A. Anderson, 2016d; B. A. Anderson & Yantis, 2013; Laurent et al., 2014; Le Pelley et al., 2015). All of these studies employed samples ~4 times smaller than the sample size of Study 1, with Study 1's estimate falling within this range though smaller than the average effect size estimate across this body of work (dz = .52)[30]. Thus, Study 1's effect size estimate may arguably be the most realistic estimate of the human sign-tracking effect. Using a common language effect size, this

[29] Participants were also tested on the Multi-Target Tracking Task (MTTT); however, since it was a novel task and no aspect of it worked, it will not be discussed until section 10.3 (Limitations). See Appendix B for an analysis of the failures of the MTTT.

[30] It is also worth noting that the majority of AST studies calculate sign-tracking scores as OT RTs on high-value trials minus OT RTs on distractor-absent trials (rather than low-value trials). This difference may also contribute to the smaller effects found across the studies of this thesis.

suggests that the likelihood a person will produce slower OT RTs on high-value trials compared to low-value trials is 63%.

10.2.1.2 Mechanisms

Maladaptation and Pavlovian vs. Instrumental Conditioning

The ASTT used in Study 1 and throughout this thesis is just one variant of the AST (B. A. Anderson, 2015a; Le Pelley et al., 2016; Theeuwes, 1991, 1992, 2010). The AST variant used by Le Pelley et al. (2015) (Experiment 3) and Pearson et al. (2015) is almost identical to the ASTT, and this variant was used in order to better investigate the mechanisms which lead to a sign-tracking response. In Le Pelley et al. (2015), there was no contingency training phase and, as a result, reward-associated distractors had *never* been response-relevant; however, a sign-tracking effect was still observed. Pearson et al. (2015) followed this up and investigated whether the same AST variant produced sign-tracking even when participants were aware of the omission contingency (participants in the Le Pelley study were not given explicit instructions and they reported no awareness that looking at the distractor caused an omission of reward). Across two experiments Pearson et al. (2015) found sign-tracking effects regardless of whether participants were aware of omission contingencies[31].

Though both of the above studies made significant progress in investigating the conditions under which sign-tracking may be extinguished (total response-irrelevance and participants' omission contingency awareness), both failed to fully control for which learning

[31] Note that sign-tracking as measured by OT RT on high- versus low-value trials was not statistically significant (p = .07) in Experiment 1, though this may have been due to power. In fact, evidence presented in Experiment 2 suggests that while omission contingency awareness may attenuate sign-tracking, it does not extinguish it.

mechanism (pavlovian or instrumental) was driving the effect. Study 1 therefore altered the procedure slightly to better identify which learning mechanism may underlie tracking behaviour. In contrast to Le Pelley et al. (2015) and Pearson et al. (2015), Study 1's ASTT actively punished omissions (rather than simply omitting reward), and rewarded correct responses on a continuous scale based on RT (rather than categorically). These changes in the ASTT had two effects: I) omissions were more costly and thus even more maladaptive, and II) 'covert distractor shifts' (Le Pelley et al., 2015) – wherein initial attentional orienting towards the distractor is followed by overt attention to the OT (which is rewarded) – are, in the ASTT, punished via a loss of points (due to reduced OT RT). Both of these effects serve to reduce both overt and covert attentional capture by the response-irrelevant, reward-associated distractors (i.e., to reduce sign-tracking). However, despite there being no positive effect of attributing salience to distractors (especially not to attribute more salience to distractors of higher value), sign-tracking effects were still observed. This study therefore provided the most convincing evidence yet that human sign-tracking is automatic, persistent in the face of negative consequences, and is driven by pavlovian (and not instrumental) conditioning.

Automaticity, Force, Perceptual Salience, and Outcome Measures

Several other important (within-subject) findings were investigated via the ASTT (I, II, and IV, Chapter Nine; III, Chapter Eight): I) *Automaticity:* Investigating the claim that sign-tracking is automatic, II) *Force:* Investigating whether distractors of differing value attract attention with the same 'force', III) *Perceptual Salience:* Investigating whether physical salience, rather than value, was the driver of the sign-tracking effect, and IV) *Outcome Measures:* Investigating whether the two primary ASTT measures – RT Bias and Omission

Bias – correlate. (*Note:* supplementary analyses for Study 5 were not conducted due to null results.)

Across five studies, analyses revealed that RTs towards CSs were quicker than RTs towards the OT, suggesting that sign-tracking omissions are reflexive. Regarding whether CSs of different value pull with similar force, Studies 1-4 found no evidence of high-value CSs eliciting quicker attentional capture than CSs of low value (CS RTs for Study 6 could not be calculated). Regarding perceptual salience, across five studies regardless of the specific task used, there were no differences in OT RTs on trials hosting either a red or a blue (or green) distractor, regardless of value. However, more omissions were made towards blue stimuli compared to red in Studies 1 and 3 (alcohol condition). This may suggest that sign-tracking as measured by omissions may be influenced by a stimulus's perceptual properties. Finally, the link between RT and Omission Biases was found only in Study 1, showing a moderate-large correlation. All other studies showed no significant relationship.

Overall, there is robust evidence – with the same pattern of results spanning all studies – that sign-tracking is automatic, a finding already well-established in the literature (B. A. Anderson, 2014, 2015a, 2016a; Le Pelley et al., 2016). Further, the perceptual salience of cues in the absence of value did not influence sign-tracking as measured by RTs, although it did influence omissions in two conditions. The latter result has precedence in the literature, with some evidence indicating that perceptual salience interacts with value-modulated attentional capture (VMAC) (Wang et al., 2013). Evidence for CSs of differing value attracting attention with the same vigour was found across all analyses, which replicates the results of previous research (Le Pelley et al., 2015) and suggests that reward-associated cues attract attention with the same 'force'. Finally, there was weak evidence of a link between sign-tracking measures, a finding which has not been previously explored in the literature.

Gender and Belief in Reward

Finally, two (between-subject) mechanisms related to categories of different people were explored: I) *Belief in Reward:* Investigating whether sign-tracking differed between those who believed they would win extra rewards based on their performance and those who did not, and II) *Gender:* Investigating whether men and women differed in their propensity to sign-track.

No differences in either RT or Omission Biases were found between participants who believed the deception and those who did not believe. This is, to my knowledge, the first time explicit belief in the availability of reward has been investigated in the sign-tracking literature. However, the result is in line with a previous AST study which showed that participants who knew that they would not receive monetary rewards based on their performance, still showed VMAC towards images of money (Roper & Vecera, 2016). For gender, Studies 1, 2, 4 and 6 showed no gender differences in either RT Bias or Omission Bias. However, Study 3 found that women showed higher RT Bias in the alcohol session compared to men, fitting with one preclinical study that female rats exhibited elevated sign-tracking in an alcohol autoshaping procedure (Madayag et al., 2017). Overall, there appears to be no difference in sign-tracking between people who believed they would receive extra rewards based on performance and those who did not, and the majority of studies showed no gender differences.

10.2.1.3 Measurement

ASTT+

In the fourth study of this thesis (Chapter Five), the ASTT was adapted to include not two, but three discrete, response-irrelevant, reward-associated distractors of differing value (high, medium and low). The ASTT+ was designed in response to Study 1's finding that STs' and GTs' CS RTs did not differ, a finding contradictory to the preclinical literature which consistently finds that STs approach the CS quicker than GTs (on the relatively rare occasions that GTs approach the CS) (Flagel, Robinson, et al., 2010; Flagel et al., 2007; Meyer, Lovic, et al., 2012). The ASTT+ aimed to increase CS RT response variability in order to provide a broader measure on which to better gauge STs' and GTs' CS RT responses. Employing a task with more than two CSs of value was also suggested by others as a promising area of investigation (B. A. Anderson & Yantis, 2012).

Results revealed that the ASTT+ did not elicit any RT response differences towards CSs of differing value, either between STs and GTs or in the sample as a whole. This contrasts with the aforementioned preclinical results, though it replicates previous human studies (Le Pelley et al., 2015). In secondary analyses, typical OT RTs across different trial types were explored. Contrary to all other studies, an RT sign-tracking effect was found as a differential response between high- and medium-value trials, in contrast to the typical sign-tracking effect between high- and low-value trials. An omission sign-tracking effect was found between high- and medium-value trials, as well as between high- and low-value trials (no effect was found between medium- and low-value trials).

The OT RT result – the first ever with >2 CSs – suggests that in more complex stimulus displays incentive value is attributed only to the two CSs of highest value, with other CSs being effectively ignored (as indicated by low-value responses falling in between high- and medium-value responses for both RTs and omissions). This may indicate that some rewards

could be relegated down the chain of attentional priority if more attractive rewards become available, and/or the original reward is devalued, a finding which has basis in the alcohol priming and AB literatures (Field et al., 2016; Rose et al., 2013).

Comparison of Measures

Study 5 (Chapter Six) aimed to compare three different sign-tracking tasks within the same sample to assess how consistent effects were, as well as to replicate the findings of a novel sign-tracking task designed by another research group (Garofalo & di Pellegrino, 2015). The tasks being compared were: I) the ASTT (EE), II) the ASTT (BB), and III) a novel Pavlovian-to-Instrumental Transfer (PIT) task. None of the tasks captured the predicted sign-tracking effects, and so the results of this study are not discussed. The limitations of Study 5 will be detailed in section 10.3.

10.2.2 Human Sign-Tracking: Influence of Acute Alcohol Administration

There is now a large literature detailing the effects of various drugs on sign-tracking behaviours, including the effects of amphetamine, cocaine, ethanol, nicotine, ketamine, antipsychotics and opioids. Typically, amphetamine (M. J. F. Robinson, Anselme, et al., 2015; Wan & Peoples, 2008), cocaine (Saddoris et al., 2016; Saunders & Robinson, 2011), and nicotine (Versaggi et al., 2016) enhance sign-tracking, ketamine (C. J. Fitzpatrick & Morrow, 2016) and antipsychotics (Saunders & Robinson, 2012; Yager et al., 2015) impair it, and opioids appear to enhance both sign-tracking and goal-tracking (DiFeliceantonio & Berridge, 2012; Mahler & Berridge, 2009). For alcohol the results are mixed, with some

suggesting alcohol magnifies sign-tracking (Tomie, Cunha, et al., 1998; Tomie, Festa, et al., 2003), while more recent evidence suggests alcohol may reduce sign-tracking (Versaggi et al., 2016).

No human study to date has investigated the acute effects of drugs on human sign-tracking. The only relevant human studies have so far shown that I) sign-tracking is magnified in opioid-dependent patients (B. A. Anderson et al., 2013), and II) sign-tracking is related to a history of drug abuse (B. A. Anderson, Kronemer, et al., 2016). However, neither of these answer the question of causality in the long-term, nor do they assess how acute consumption of drugs affects sign-tracking.

Studies 2 and 3 (Chapter Four) investigated, for the first time, the influence of acute alcohol administration on human sign-tracking in a group of social drinkers. Following typical alcohol priming attentional bias studies (Rose, 2013; Rose & Duka, 2006, 2007), Study 2 administered a low (0.3 g/kg) dose of alcohol, while Study 3 administered a moderate (0.6 g/kg) dose, and both were compared to a control (lemonade) drink. Sign-tracking was observed in all conditions (alcohol and control) across both studies, suggesting that alcohol consumption at either dose did not attenuate sign-tracking. In Study 2, the magnitude of sign-tracking was enhanced by the low dose (relative to control), though no effect of the moderate dose was found in Study 3. Further, in a results synthesis wherein datasets from both studies were combined, sign-tracking was found to be significantly higher in the 0.3 g/kg alcohol group compared to the 0.6 g/kg alcohol group, even though no difference was found between samples in their respective control sessions. Furthermore, RT Bias after alcohol consumption of the 0.3 g/kg dose was positively correlated with negative reinforcement as measured by the desire for alcohol questionnaire (DAQ). In the second study (0.6 g/kg dose), desire after control consumption was negatively correlated with RT

Bias in the control session. These results suggest that the 0.3 g/kg dose increased alcohol craving (via negative reinforcement, e.g., "drinking would make me feel less tense") and sign-tracking, while the 0.6 g/kg dose did not.

The evidence suggests that low, but not moderate, doses of acute alcohol consumption magnify sign-tracking in social drinkers. This indicates that small amounts of alcohol may cause people to increase the extent to which they attribute motivational salience to reward-associated cues. Results may also suggest that the propensity to make such attributions after small amounts of alcohol may be associated with increased desire to drink to remove negative feelings. These results also support non-sign-tracking studies showing that small doses of alcohol consumption can bias attention towards reward cues (Adams et al., 2012; Duka & Townshend, 2004; Fernie et al., 2012; Schoenmakers & Wiers, 2010; Schoenmakers et al., 2008) and/or arbitrary features of a cue previously associated with alcohol (Field & Duka, 2002).

10.2.3 Human Sign-Tracking: Longevity and Neural Correlates

The primary aim of Study 6 was to assess whether the brain regions identified in previous human AST studies could be identified again in a sample of participants who had previously been classified as STs or GTs, and to investigate whether the activation in these regions was significantly different between tracking groups. A secondary aim was to simultaneously assess the longevity of human sign-tracking; thus, participants who had been classified as STs or GTs in a previous study of this thesis were recruited and retested on the ASTT (albeit the ASTT [BB] rather than the ASTT [EE]).

There is now a vast preclinical literature on the neurobiology of tracking phenotypes. The research has shown that the neurotransmitters and receptors of dopamine (Chow et al., 2016), glutamate (Yau et al., 2016), serotonin (Campus et al., 2016), mu opioid (Peciña & Berridge, 2013), cholinergic (Maddux & Chaudhri, 2017), and DREADDs (Chang et al., 2015) are all involved in sign-tracking, goal-tracking, or both. Further, the brain regions of interest have been consistently identified as the striatum (caudate, putamen and NAcc) (Aitken et al., 2016; Tomie et al., 2000), VTA (Flagel et al., 2007), thalamus (Haight et al., 2017), amygdala (Sciascia et al., 2015), hippocampus (Christopher J. Fitzpatrick, Creeden, et al., 2016) and ventral pallidum (Chang et al., 2015). Work in humans has also revealed that the caudate tail, intraparietal sulcus, inferior and middle frontal gyri, lateral occipital complex, visual cortex, putamen and striatum are activated during fMRI AST procedures (B. A. Anderson, 2016b; B. A. Anderson, Laurent, et al., 2014). A recent PET study also found that dopamine activity in the putamen and striatum generally positively correlated with VMAC on the AST (B. A. Anderson, Kuwabara, et al., 2016). Finally, to my knowledge there is no preclinical or human studies which have directly tested sign-tracking and goal-tracking on separate occasions over time and compared changes in propensity (without direct manipulation or other changes being introduced).

First, it should be noted that a 50/50 split of STs/GTs could not be obtained, and so STs, GTs and members of an intermediate group (ITs) were recruited to Study 6 (see section 10.3). Regarding the behavioural results, a typical sign-tracking effect was observed; however, a very poor test-retest reliability score was found. Most participants originally categorised as GTs would have been reclassified, based on their new ASTT score, and the same was true for half of STs and ITs. These data are the first of their kind obtained, and they suggest that sign-tracking behaviours may have little stability across time. This result indicates that sign-tracking likely fluctuates over time and could therefore be viewed similarly to other

(potential) measures of subjective value and appetitive motivational processes such as attentional bias and craving (Field et al., 2016). This is contrary to the findings of the preclinical literature in which sign-tracking is found to be a stable phenotype (see Meyer et al., 2012 for a meta-analysis and discussion of the findings).

The neuroimaging results revealed a variety of activations across two contrasts in the general linear model (GLM), both contrasting high-value and low-value trials. The first revealed activations in the right lateral superior occipital cortex and bilateral putamen. The second (with RT Bias entered as a correlate in the regression) revealed activation in the right putamen, pallidum, amygdala and superior temporal gyrus. The putamen, amygdala, and lateral occipital cortex have all been implicated in sign-tracking in both the preclinical and human literatures (as reviewed above), with dopamine activity in the putamen and general striatum being directly correlated with sign-tracking on the AST (B. A. Anderson, Kuwabara, et al., 2016). Further, in non-sign-tracking paradigms the pallidum has been associated with reward-seeking, reward processing, pleasure perception, and motivation (Perry et al., 2014; Smith et al., 2009; Tindell et al., 2006), and the right superior temporal gyrus has been associated with salience detection and shifting attention in tasks which involve encoding relative value (Lim et al., 2013; Rapuano et al., 2016). Overall, Study 6 replicated the neurological findings of both human and animal studies, though little to no evidence of the stability of human sign-tracking was found.

10.2.4 Human Sign-Tracking: Individual Differences

Preclinical research shows that sign-tracking is associated with high impulsivity, disinhibition, early life stress and vulnerability to cue-induced stress responses and drug

seeking (King et al., 2016; Lomanowska et al., 2011; Lovic et al., 2012; Morrow et al., 2014; Saunders & Robinson, 2010), and human studies show an association to high impulsivity, poor working memory and a history of drug abuse (B. A. Anderson et al., 2013; B. A. Anderson, Kronemer, et al., 2016). Therefore, this thesis explored these associations in social drinkers via a questionnaire battery measuring alcohol consumption, alcohol-related harm/consequences, subjective alcohol value, impulsivity, and early life stress (e.g., childhood trauma).

Across all studies and hundreds of correlations, only one correlation remained statistically significant after corrections: Omission Bias 2 (*high−low*) on the ASTT+ strongly positively correlated with CATS: Sexual Abuse in Study 4. This link is likely spurious. It should be noted that when further correlations were conducted using only key variables and scale total scores (and thus no familywise error correction), RT Bias in Study 1 was correlated with TLFB (average alcohol unit consumption; r_s = .20), and RT Bias in Study 4 was associated with both B-YAACQ: Total (alcohol consequences; r_s = .31) and ImpSS (impulsivity; r_s = .33). Although these results do not show consistency (RT Bias did not correlate with the same measure across studies), they might indicate which measures should be included in future studies using larger and/or clinical samples. Furthermore, the inconsistency in associations may simply be due to the fluctuating nature of sign-tracking in humans. See section 10.3 below for a discussion of the problems with the current use of individual difference measures.

10.3 Limitations

Sample Size

Excluding Study 1 (Chapter Three), all studies possessed relatively small sample sizes ($N \approx$ 20-30). Studies 2 and 3 possessed greater power than Studies 4-6, given both raw numbers and their within-subject, multi-testing procedures. The sample sizes used within the thesis were based on typical sample sizes within this field of research (e.g., *Ns* = 15-25) and ST was observed in five of the six studies. However it is still possible that power was insufficient. Study 6, in particular (fMRI; $N = 20$), possessed a very small sample, especially given the initial aim of comparing tracking groups (group comparisons were made even worse by the compelled recruitment of three groups rather than two). This appears to be a widespread problem in both psychology and neuroscience, in particular (Button et al., 2013). Given the interest in sign-tracking as a potentially useful phenotype in the study of addiction and other disorders (Belin et al., 2016), if future research wishes to tease out related effects (such as sign-tracking's potential relation to impulsivity, risk-taking, alcohol consumption etc.) then larger samples – determined via power calculations – are needed.

Procedure and Task Failures

There were a number of aspects of this thesis which did not work; primarily, such failures can be attributed to specific tasks or procedural setups. Regarding task failures, the multi-target tracking task (MTTT) employed in Study 1 (Chapter Three) and solely created for use in this study, simply failed to detect a sign-tracking effect, or any general attentional effect. Even when *post-hoc* analyses were conducted to ascertain why null results were obtained (see Appendix B), few answers were forthcoming. Therefore, this task was not used again.

An additional (partial) task issue was observed in Study 4 (Chapter Five). Although sign-tracking effects were found, the ASTT+ was constructed to increase variability in CS RT responses which, while technically obtained, CS RT responses on the ASTT+ were not statistically significantly different from CS RTs on the ASTT. Thus, failure to find any difference in STs' and GTs' RT responses towards the CS may still be a product of constrained variability in the possible range of speeded responses.

Regarding procedural concerns, none of the tasks employed in Study 5 (Chapter Six) detected sign-tracking effects. However, unlike the MTTT in Study 1, all three tasks in Study 5 had been previously validated and the ASTT (EE) had detected sign-tracking effects in every other study of this thesis. Thus, the problem here was likely procedural, rather than task-specific. In particular, the use of three tasks which all ran for approximately 20 minutes each (60 minutes in total), and which require constant attention likely induced boredom and/or fatigue. Compounding this problem was a small sample size (N = 25) and a large number (k = 12) of conditions, meaning that *post-hoc* analyses could not be reliably conducted to ascertain if sign-tracking effects were found in the first task participants completed (in order to rule out boredom/fatigue).

A final procedural limitation is noted in Study 6 (Chapter Seven). Participants were recruited from previous studies and their sign-tracking scores were again assessed to establish whether sign-tracking was stable over time. However, participants were initially tested on the ASTT (EE) and later tested in Study 6 on the ASTT (BB). Given the different method of response – as well as the crucial timing differences on the fMRI ASTT (BB) – these scores cannot be interpreted as being obtained from strictly the same task. Unfortunately, no study has compared scores on eye-tracking versus button-box responding on an AST variant within

the same sample, and my attempt to do so in Study 5 failed to work. Thus, we do not know how reliably we can translate the scores from each task.

Alcohol Priming

In Studies 2 and 3, there were two primary limitations: I) limited doses, and II) lack of a placebo. Given limited time and funds, only two doses (0.3 g/kg and 0.6 g/kg) were tested. A much more detailed and insightful study could employ a range of doses in order to assess how sign-tracking is affected at each dosing level, and explore if the effects match those found in general attentional bias priming research (Rose, 2013). In both studies a control drink rather than a placebo was used and, as such, the pharmacological effects of alcohol cannot be disentangled from its anticipated effects. Although this design was chosen tom maximise application to real-world situations, an ideal experimental setup would contrast alcohol dose, placebo and control drinks (Christiansen et al., 2013).

Limitations of the ASTT

As expressed throughout this thesis, although robust sign-tracking effects have been found (RT effects consistently, omission effects less so), the two measures of sign-tracking do not correlate. Only in Study 1 (Chapter Three) was a statistically significant association between RTs and omissions found (ignoring the results of the ASTT [BB] in Study 5), which may suggest that omissions are a less reliable measure and should be given less evidential weight in AST paradigms. The use of correlations to test the agreement between these two measures is also unsuitable, but was the only tool at hand (see Chapter Nine). Another

potential limitation of the ASTT as employed throughout this thesis is that rewards were always monetary. Given social drinking populations were always tested, alcohol rewards could have been tested to assess if they too elicited sign-tracking CRs, as has been done with a variety of other rewards on the AST (B. A. Anderson, 2016c; Camara et al., 2013; Roper & Vecera, 2016).

Limitations of Individual Difference Measures

Throughout the six studies of this thesis only one association between sign-tracking and an individual difference measure was found between Omission Bias 2 (*high−low*) on the ASTT+ and the CATS: Sexual Abuse subscale measure. There are several problems with this specific correlation: I) as stated earlier (*Limitations of the ASTT*), omission measures are inherently less reliable than RT measures, II) the ASTT+ has been used only once, and thus requires further validation with larger samples, and III) CATS questions received very few responses which indicated moderate or high levels of abuse of any kind, with the vast majority of responses indicating little to no childhood trauma or abuse. Thus, given the unreliability and infrequency of both omissions and CATS measures (in terms of producing reliable and/or consistent responses) and the novelty of the ASTT+, this link is likely specious.

Regarding the lack of association between sign-tracking and individual differences more generally, perhaps the biggest issue of this thesis was its overly exploratory and ambitious attempt to find important links between human traits, behaviours and sign-tracking. Excluding the Alcohol Purchase Task (which was only used in Study 1; see footnote 15 in General Methods, Chapter Two) and the craving and intoxication measures used in Studies 2

and 3, every study employed eight questionnaires – this adds up to thirty-two individual measures of individual differences in each sample. Even employing the less restrictive sequentially-rejective Bonferroni correction (Holm, 1979), the statistical restraints were likely too great to overcome. However, it should be noted that using only scale total scores (thus reducing the number of tests and excluding the need for error correction) produced only three statistically significant correlations across five studies (excluding Study 5). This perhaps suggests that statistical constraints made by error correction was not the primary cause of a lack of association between sign-tracking and individual differences.

Another aspect to take into consideration is the method through which other human AST studies have calculated sign-tracking. Most AST studies create bias scores by subtracting RTs on distractor absent trials from RTs on high-value distractor trials, whereas all studies in this thesis calculate bias as high-value RTs−low-value RTs. This likely reduces the size of the effect, and may possibly have implications for studying sign-tracking's potentially related traits and behaviours.

10.4 Future Research and Applications

How future research can build on the work in this thesis will be described across each chapter, so that simple additions and/or alterations may be made. Potential applications will be discussed last.

Chapter Three: The ASTT could be employed across abstinent, social, heavy and dependent drug and alcohol samples to assess if sign-tracking differs between samples, as has been found in previous sign-tracking studies (B. A. Anderson et al., 2013) and is partially supported (users vs non-users) by general drug-related AB research (Field et al., 2016).

Further, future research could investigate how quickly the sign-tracking effect can be obtained using the ASTT; such research may produce methodical advantages, such as enabling a reduction in task time.

Chapter Four: Future alcohol priming studies as employed in a sign-tracking procedure could be improved in several ways: I) increase sample size, II) increase the range of doses tested, III) investigate whether acute alcohol administration not only enhances sign-tracking, but also whether it increases (possibly cue-evoked) *ad lib* alcohol consumption.

Chapter Five: The ASTT+ needs to be validated with a larger sample and, once validated, future work could employ more than 3 CSs of value to assess the effect of increased contingencies and, possibly, increased complexity on sign-tracking (e.g., do only the two highest value CSs attract attention?). Working memory could be assessed to investigate if those with better WM perform better with ever-increasing reward contingencies.

Chapter Six: In addition to again using a larger sample, a study comparing several different sign-tracking tasks could be improved either by I) if possible, using shorter tasks to reduce fatigue/boredom effects (see '*Chapter Three*', above), II) only comparing two tasks in a single session, or III) testing participants on each task across multiple, consecutive days.

Chapter Seven: Perhaps more than any other, future fMRI studies would benefit from the use of larger samples. Additionally, if a similar method of testing sign-tracking longevity is to be used, it would be beneficial to keep the methods of measurement identical across time (e.g., if participants were previously tested on the ASTT [EE], they should be tested on the ASTT [EE] again). Even in situations such as Study 6 where the ASTT (EE) could not be

used in the fMRI scanner, ideally participants would have first been tested in the eye-tracking lab on the ASTT (EE), before their fMRI session on the ASTT (BB).

Discrete vs. Contextual cues: Given that goal-tracking has also been linked to similar maladaptive associations as sign-tracking (T. E. Robinson et al., 2014), that 'goal-tracking paradigms' can induce goal-tracking CRs almost exclusively (Saunders et al., 2014), and that it can be argued that contexts are more important to humans than discrete cues, future work on human sign-tracking may build on previous work (B. A. Anderson, 2014): assessing discrete versus contextual cues on human sign-tracking, and how each relates to individual differences and *ad lib* consumption.

Associations to individual differences: Future studies may benefit from the use of fewer outcome measures. Specifically, using only total scores (rather than second- or even third-order factors) would reduce the need for such extensive Type I error correction.

Applications: There is now a wealth of preclinical studies showing that both tracking phenotypes can be motivated to seek and consume drugs by reward-associated cues or contexts (Tomie et al., 2008), human studies showing elevated sign-tracking in opioid-dependent patients and associations with a history of drug abuse (B. A. Anderson et al., 2013; B. A. Anderson, Kronemer, et al., 2016), and reviews suggesting that these phenotypes are important in the study and understanding of addiction and other disorders (Belin et al., 2016; Flagel, Akil, et al., 2009, 2010; T. E. Robinson et al., 2014). Though human sign-tracking research is still in its early stages, it is possible that in the future it may be added to the roster of dependence-related and drug abuse predictors such as impulsivity, disinhibition, cue reactivity, inattention, sensation-seeking, and conduct disorder/oppositional behaviours, each of which accounts for a relatively small amount of the variance explained in the development of substance dependence (Dalsgaard, Bo, Frydenberg, & Hove, 2014; Ersche et al., 2012;

Fleury, Grenier, Bamvita, Perreault, & Caron, 2014; Meier et al., 2016; Pingault et al., 2014). This may be especially true as sign-tracking is related to a reward's subjective value, which is thought to underlie drug-related behaviours (Field et al., 2016). Thus, if the two are connected and it can be determined that the two fluctuate (somewhat) in sync, then we could have an important measure of value which may potentially contribute to the phenotypical profile of substance dependence and perhaps aid cognitive and behavioural treatments.

10.5 Conclusions

This thesis set out to contribute to and extend the literature on human sign-tracking. More specifically, it sought to investigate I) the possible role of instrumental learning, II) the effect of acute alcohol administration, III) the influence of employing more than two CSs of value, IV) comparisons between three different sign-tracking tasks, V) the neural correlates of sign-tracking on the ASTT, and VI) sign-tracking's relation to individual differences. The studies of this thesis have shown I) that instrumental learning likely plays no role in the development of sign-tracking, II) that low (0.3 g/kg), but not moderate (0.6 g/kg), doses of alcohol enhance sign-tracking, III) that employing a medium-value distractor causes the low-value distractor to be virtually ignored, with sign-tracking effects being shown only between high- and medium-value CSs, IV) that comparison of tasks could not be effectively evaluated due to boredom and fatigue effects, V) that the striatum, ventral pallidum and lateral occipital cortex are activated during the ASTT, replicating previous human and animal findings, and VI) that there is no evidence sign-tracking relates to individual risks factors for harmful drinking (although note limitations discussed above). Overall, the results of this thesis suggest that human sign-tracking can be reliably measured via the ASTT, that sign-tracking possesses neural correlates in the so-called 'reward circuits' of the brain, and that acute, low-level

consumption of alcohol can exacerbate people's propensity to attribute incentive salience to discrete, response-irrelevant, reward-associated stimuli. Finally, if tracking behaviour is a continuous variable associated with substance value, future research should identify the factors that influence tracking across different drinking populations. This could contribute to our understanding of the motivational processes involved in substance use and may help inform treatment for hazardous drinking.

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Appendices

The following appendices contain information (descriptive and analytic) which was deemed too cumbersome for inclusion in the experimental chapters, but which are presented here for clarity and completeness.

Appendix A

This appendix presents information from Study 1 (Chapter Three) regarding the calculation of task outcome variables for the MTTT[32] *(Table A1) and ASTT (Table A2).*

[32] It should be noted that there were originally 52 outcomes measures in Table 1, with the now-absent variables all consisting of "Reward" variables – the mean of chocolate and alcohol responses. The reason these were dropped is because many of them were simply the inverse of the "Neutral" variables, due to the way they are calculated. For example, Reward dwell time bias was calculated *as (Alcohol OT GDT bias + Chocolate OT GDT bias) ÷ 2 – Neutral OT GDT bias*, while Neutral bias was calculated as *Neutral OT GDT bias – (Alcohol OT GDT bias + Chocolate OT GDT bias) ÷ 2*. It was also decided that the remaining Reward variables should be removed as such variables would be unlikely to add any substance to the analyses if neither reward variables (chocolate or alcohol) produced significant results; likewise, if one (alcohol) did and the other (chocolate) didn't, a generic reward variable – an average of the two – would not provide any new information (i.e., alcohol may have been "pulled down" by chocolate, or chocolate "pulled up" to significance by alcohol – either way, nothing new is learned).

Table A1 MTTT outcome measures

Outcome Measure Type	*Outcome Measure*	*Outcome Measure Description*
Omissions		
OM(1)	**Error alcohol OT frequency**	Total number of fixations towards the alcohol OT when the alcohol CS is *not* present
OM(2)	**Error chocolate OT frequency**	Total number of fixations towards the chocolate OT when the chocolate CS is *not* present
OM(3)	**Error neutral OT frequency**	Total number of fixations towards the neutral OT when the neutral CS is *not* present
Frequencies		
	Correct alcohol OT frequency	Total number of fixations towards the alcohol OT when the alcohol CS is present
	Correct chocolate OT frequency	Total number of fixations towards the chocolate OT when the chocolate CS is present
	Correct neutral OT frequency	Total number of fixations towards the neutral OT when the neutral CS is present
OM(4)	**Overall alcohol OT frequency**	*(Correct alcohol OT frequency + Error alcohol OT frequency) ÷ 2*
OM(5)	**Overall chocolate OT frequency**	*(Correct chocolate OT frequency + Error chocolate OT frequency) ÷ 2*
OM(6)	**Overall neutral OT frequency**	*(Correct neutral OT frequency + Error neutral OT frequency) ÷ 2*
OM(7)	**Total alcohol CS frequency**	Total number of fixations towards alcohol CS
OM(8)	**Total chocolate CS frequency**	Total number of fixations towards chocolate CS
OM(9)	**Total neutral CS frequency**	Total number of fixations towards neutral CS
RT		

	Mean alcohol OT RT	Mean RT towards alcohol OT when the alcohol CS *is* present
	Mean chocolate OT RT	Mean RT towards chocolate OT when the chocolate CS *is* present
	Mean neutral OT RT	Mean RT towards neutral OT when the neutral CS *is* present
RT: Bias		
OM(10)	**Alcohol RT bias**	*(Mean chocolate OT RT + Mean neutral OT RT) – Mean alcohol OT RT*
OM(11)	**Chocolate RT bias**	*(Mean alcohol OT RT + Mean neutral OT RT) – Mean chocolate OT RT*
OM(12)	**Neutral RT bias**	*(Mean alcohol OT RT + Mean chocolate OT RT) – Mean neutral OT RT*
Gaze Dwell Time		
	Correct alcohol OT GDT	Fixation duration within the alcohol OT when the alcohol CS *is* present
	Correct chocolate OT GDT	Fixation duration within the chocolate OT when the chocolate CS *is* present
	Correct neutral OT GDT	Fixation duration within the neutral OT when the neutral CS *is* present
	Error alcohol OT GDT	Fixation duration within the alcohol OT when the alcohol CS is *not* present
	Error chocolate OT GDT	Fixation duration within the chocolate OT when the chocolate CS is *not* present
	Error neutral OT GDT	Fixation duration within the neutral OT when the neutral CS is *not* present
	Overall alcohol OT GDT	*(Correct alcohol OT GDT + Error alcohol OT GDT) ÷ 2*
	Overall chocolate OT GDT	*(Correct chocolate OT GDT + Error chocolate OT GDT) ÷ 2*
	Overall neutral OT GDT	*(Correct neutral OT GDT + Error neutral OT GDT) ÷ 2*

	Alcohol CS GDT	Fixation duration within the alcohol CS
	Chocolate CS GDT	Fixation duration within the chocolate CS
	Neutral CS GDT	Fixation duration within the neutral CS
Gaze Dwell Time: Bias		
	Alcohol OT bias control	*(Overall chocolate OT GDT + Overall neutral OT GDT) ÷ 2*
	Chocolate OT Bias control	*(Overall alcohol OT GDT + Overall neutral OT GDT) ÷ 2*
	Neutral OT bias control	*(Overall alcohol OT GDT + Overall chocolate OT GDT) ÷ 2*
OM(13)	**Alcohol OT bias**	*Overall alcohol OT GDT – Alcohol OT bias control*
OM(14)	**Chocolate OT bias**	*Overall chocolate OT GDT – Chocolate OT bias control*
OM(15)	**Neutral OT bias**	*Overall neutral OT GDT – Neutral OT bias control*
	Alcohol CS bias control	*(Chocolate CS GDT + Neutral CS GDT) ÷ 2*
	Chocolate CS bias control	*(Alcohol CS GDT + Neutral CS GDT) ÷ 2*
	Neutral CS bias control	*(Alcohol CS GDT + Chocolate CS GDT) ÷ 2*
OM(16)	**Alcohol CS bias**	*Alcohol CS GDT – Alcohol CS bias control*
OM(17)	**Chocolate CS bias**	*Chocolate CS GDT – Chocolate CS bias control*
OM(18)	**Neutral CS bias**	*Neutral CS GDT – Neutral CS bias control*

A tabulation of the 42 potential outcome measures of the MTTT. Not all measures were utilised for analysis; their inclusion here is simply necessitated by the need to clarify what calculations were performed, with which already existing outcome measures, to produce the variables central to statistical analysis (n = 18). All variables directly used in analyses are highlighted in bold. CS = Conditioned Stimulus; OT = Outcome Target; OM = Outcome Measure; GDT = Gaze Dwell Time.

Table A2 ASTT outcome measures

Outcome Measure Type	Outcome Measure	Outcome Measure Description
Omissions		
OM(1)	**High distractor omission frequency**	Total number of error fixations made towards the high-value distractor
OM(2)	**Low distractor omission frequency**	Total number of error fixations made towards the low-value distractor
Omissions: Bias		
OM(3)	**Omission bias**	*High distractor omission frequency – Low distractor omission frequency*
RT		
OM(4)	**Mean high-distraction RT**	Mean RT towards the diamond on high-value distractor trials
OM(5)	**Mean low-distraction RT**	Mean RT towards the diamond on low-value distractor trials
RT: Bias		
OM(6)	**RT bias**	*Mean high-value CS RT – Mean low-value CS RT*

A tabulation of the outcome measures of the ASTT (n = 6). Unlike in Table A1, all measures presented here were used for statistical analysis (for consistency, all variables have been highlighted in bold). OM = Outcome Measure; RT = Reaction Time.

Appendix B

This appendix again refers to Study 1 (Chapter Three), this time concerning supplementary analyses conducted to ascertain why the MTTT failed to capture tracking behaviour. Hypotheses and analyses are presented below.

A major drawback of the MTTT could have been that the OTs themselves became conditioned over time, diluting sign-tracking behaviours as participants become conditioned to not one, but two CSs for each reward (the original CS and, eventually, the OT). This would make it difficult to distinguish between tracking behaviours. It was thus hypothesised that I) CS fixation frequencies in the second half of the task would be significantly *lower* than in the first half, II) OT fixation frequencies in the second half would be significantly *higher* than in the first half (as attention with the CS becomes more equally shared), III) CS GDT would be significantly *lower* in the second half compared to the first, and IV) OT GDT would be significantly *higher* in the second half of the task compared with the first half. For the analyses below all three CSs were combined, as were all three OTs. As data were non-normally distributed, Wilcoxon Signed-Ranks tests were performed (all analyses were 2-tailed).

Hypothesis I) was supported as CS fixation frequencies were lower in the second half (*Mdn* = 15.50, *range* = 0.00-273.00) of the task compared to the first (*Mdn* = 18.50, *range* = 0.00-264.00), $T = 111$, $z = -2.46$, $p = .01$, $r = -0.25$. However, II) was not; no difference in fixation frequencies towards the OTs was found between the first half and second half of the task, $T = 128$, $z = -1.15$, $p = .25$. Hypothesis III) was supported as CS dwell times for the second half of the task (*Mdn* = 2871.00, *range* = 0.00-102127.00) were significantly lower than for the first half (*Mdn* = 3165.50, *range* = 0.00-99391.00), $T = 107$, $z = -3.86$, $p = .0003$,

r = -0.39. However, IV) was not; for OT dwell times an opposing pattern to that predicted was found: dwell times for the second half (*Mdn* = 69220.00, *range* = 0.00-104524.00) of the task were significantly lower than for the first half (*Mdn* = 73751.00, *range* = 0.00-103682.00), *T* = 106, *z* = -5.08, *p* < .001, *r* = -0.51.

Since hypotheses I) and III) were supported and showed that attention to CSs diminished over time, but attention to OTs did not increase (dwell times actually *decreased* over time), GDT and frequency data were analysed to see if participants were simply looking more in the irrelevant portions of the screen, outside of any areas of interest (AOIs). It was therefore hypothesised V) that GDTs and fixation frequencies must have increased over time in non-AOI areas of the screen. However, neither GDTs, *T* = 40, *z* = -1.06, *p* = .29, nor fixation frequencies, *T* = 46, *z* = -0.83, *p* = .41, showed such a pattern.

Although the reasons for this are uncertain, it cannot be explained by the OTs becoming conditioned and diluting CS sign-tracking effects. One possibility however, may be that the longer the task went on, the more participants looked off-screen and/or closed their eyes for longer periods on each trial as fatigue set in.

Appendix C

This appendix concerns the correlation matrix for Study 1 (Chapter Three) between task and self-report measures (Table C1) as well as Welch's t-test contrasts for trait and state measures between sign-trackers and goal-trackers (Table C2).

Whether task performance was associated with alcohol use and personality factors was investigated. In the correlations shown below (Table C1), Holm's (1979) sequentially-rejective Bonferroni correction has been applied to control the familywise Type 1 error rate (but not the experimentwise error rate), with each 'family' being chosen due to the measures' relation to each other. For example, all measures of impulsivity constitute a family, as we predict that sign-tracking will be broadly related to impulsivity (without any specific predictions regarding impulsivity subcomponents). This method of correction can be shown as

$$\frac{\alpha}{n - \text{number of corrections already applied}}$$

where *n* is the number of 'family' components. The first correction (the most stringent) is applied to the correlation possessing the highest level of significance; thus, the familywise corrected alphas for impulsivity measures are .05/4 = .01, .05/3 = .02, .05/2 = .02 and .05/1 = .05. Testing ceases when the first non-significant interaction is encountered in each family, after which all remaining (untested) null hypotheses are accepted (Sankoh, Huque, & Dubey, 1997). All correlations are 2-tailed.

Table C1 Spearman (r_s) correlations between MTTT and ASTT bias scores and individual differences

	MTTT									ASTT	
	Alcohol bias (RT)	Chocolate bias (RT)	Neutral bias (RT)	Alcohol OT bias (GDT)	Chocolate OT bias (GDT)	Neutral OT bias (GDT)	Alcohol CS bias (GDT)	Chocolate CS bias (GDT)	Neutral CS bias (GDT)	RT Bias	Omission Bias
Drinking measures											
TLFB	.15	-.03	.05	-.16	.01	.14	.06	.02	-.10	.19	-.03
Units per hour	.07	.06	.10	.02	-.06	-.001	-.03	.10	-.05	-.07	-.08
Drunk frequency	.07	-.05	-.08	.05	-.07	.01	-.08	-.10	.04	.03	.04
Drunk percentage	-.04	-.01	-.01	.06	-.05	-.04	-.06	-.12	.06	-.11	-.05
First drink	.04	.09	**.24**†	.02	-.05	.001	-.05	-.02	.11	-.17	.03
Drink regularly	.07	.12	**.22**†	-.05	-.05	.08	-.02	-.02	.05	.01	.06
Binge frequency	.18	-.04	-.05	-.09	.01	.09	.03	-.12	.02	.14	-.08
AUDIT	.01	-.15	-.19	-.03	-.05	.11	-.03	-.09	.03	-.06	-.001
Drinking motives											
M DMQ-R: Social	-.04	.02	-.01	.06	.03	-.01	-.19	-.01	.03	-.13	-.06
M DMQ-R: CwA	.08	.07	.13	.03	.08	-.07	**-.20**†	.03	.07	-.08	-.13
M DMQ-R: CwD	.13	**.25**†	.17	-.01	.10	-.11	-.09	.03	.03	-.07	-.14

M DMQ-R: Enhancement	.14	.10	.07	.12	.04	-.07	**-.25**†	-.10	.14	-.12	.05
M DMQ-R: Conformity	-.05	.14	.16	-.05	-.03	.09	-.04	.09	-.02	**-.21**†	-.08
Drinking Consequences											
B-YAACQ: Social	-.03	.04	-.12	-.12	-.07	.11	.07	.11	-.02	-.01	.01
B-YAACQ: Impaired control	.12	.07	-.03	-.02	-.10	.15	-.10	.04	-.01	-.10	.02
B-YAACQ: Self-perception	.04	-.12	**-.26**†	.03	.02	-.05	-.06	-.08	**.25**†	-.06	.17
B-YAACQ: Self-care	.07	.03	.06	-.05	-.06	**.21**†	.07	-.05	-.11	-.20	-.20
B-YAACQ: Risk	.10	.01	-.07	-.11	-.04	**.22**†	.15	-.03	-.07	-.11	-.03
B-YAACQ: Ac/Occ	.13	.15	.10	-.14	.12	.10	.16	-.13	-.03	-.08	.03
B-YAACQ: Dependence	.18	.03	.06	-.05	-.11	.18	-.02	.05	-.10	-.07	-.09
B-YAACQ: Blackout	-.04	-.07	-.11	.07	-.08	.09	-.09	.11	-.05	-.09	-.13
B-YAACQ: Total	.10	.02	-.03	-.07	-.09	**.23**†	.04	.04	-.10	-.16	-.11

Perceived Alcohol Value											
APT: Breakpoint	.18	.08	.17	.04	.08	-.17	-.07	-.07	.12	-.04	-.02
APT: Intensity of Demand	.11	-.10	-.02	-.01	.08	-.09	-.04	-.03	.04	.01	.01
APT: P_{max}	.19	.10	.10	.01	.0004	-.12	.03	-.06	.10	.02	.06
APT: O_{max}	.18	-.01	.06	-.02	.11	-.12	.001	-.07	.05	-.01	.01
APT: Elasticity of Demand	-.07	.02	.02	-.02	-.04	.12	.04	.06	-.08	.02	.03
Impulsivity											
BIS: Attentional	.10	.15	.02	-.15	.01	.17	.06	.02	-.13	-.16	-.01
BIS: Motor	.17	.20	.13	-.09	.09	.05	.07	-.02	-.14	-.05	-.09
BIS: Non-planning	.16	**.22**†	.11	-.17	.08	.06	.13	.02	-.17	.07	.05
BIS: Total	.17	.21	.10	-.16	.07	.12	.11	.04	**-.22**†	-.02	-.01

ImpSS: Total	**.23**[†]	.16	.04	-.13	.01	.20	.07	-.04	-.13	.07	.08
Trauma and Abuse											
CATS: Sexual abuse	.09	-.04	-.06	-.05	-.001	-.01	.07	.08	.03	-.02	-.06
CATS: Punishment	.01	.11	.02	-.01	-.01	.01	-.02	.05	-.02	-.03	.14
CATS: Neglect/Negativity	.10	-.03	-.19	-.09	.01	.12	.13	-.04	-.03	-.01	.12
CATS: Emotional abuse	-.03	-.08	-.21	-.10	.05	.11	.17	-.08	-.03	-.06	-.02
CATS: Total	.04	-.04	-.14	-.12	.07	.09	.14	-.07	-.01	-.04	.06

[†]Significant only without corrected alpha ($p < 0.05$), *Significant at the level of the corrected alpha. All 2-tailed. OT = Outcome Target; CS = Conditioned Stimulus; TLFB = Timeline FollowBack; AUDIT = Alcohol Use Disorders Identification Test; M DMQ-R = Modified Drinking Motives Questionnaire – Revised; CwA = Coping with Anxiety; CwD = Coping with Depression; *B-YAACQ* = Brief Young Adult Alcohol Consequences Questionnaire; Ac/Occ = Academic/Occupational; APT = Alcohol Purchase Task; *BIS* = Barratt's Impulsivity Scale; *ImpSS* = Impulsive Sensation Seeking; *CATS* = Child Abuse and Trauma Scale

Table C2 Participant characteristics: goal- versus sign-trackers (Means ± SD)

Participant Characteristics	Goal-Trackers	Sign-Trackers	*p*-value	Effect Size (Cohen's d_s)
Age	23.96 (± 4.70)	24.20 (± 4.16)	.85	-
Gender[†]	11 male, 14 female	14 male, 11 female	1.00	-
TLFB	18.34 (± 12.35)	24.16 (± 13.38)	.12	-
Binge frequency	1.17 (± 0.73)	1.38 (± 0.82)	.34	-
Units consumed per hour	4.29 (± 2.65)	3.99 (± 1.31)	.62	-
Age at first drink	14.88 (± 2.73)	13.60 (± 3.02)	.12	-
Age at regular drinking	17.32 (± 1.73)	17.40 (± 1.90)	.88	-
Drunk frequency	24.48 (± 18.64)	26.92 (± 16.75)	.63	-
Drunk percentage	58.06 (± 31.92)	52.14 (± 32.04)	.52	-
AUDIT	12.28 (± 4.78)	12.32 (± 5.19)	.98	-
BIS: Attentional	17.00 (± 3.97)	15.40 (± 3.40)	.14	-
BIS: Motor	22.26 (± 4.96)	23.16 (± 4.92)	.53	-
BIS: Non-planning	23.25 (± 5.83)	24.92 (± 5.69)	.32	-
BIS: Total	61.71 (± 12.43)	63.50 (± 12.39)	.63	-
ImpSS	8.43 (± 4.32)	9.12 (± 4.94)	.61	-
M DMQ-R: Social	13.42 (± 2.52)	13.18 (± 1.79)	.69	-
M DMQ-R: CwA	7.74(± 2.42)	7.08 (± 1.95)	.29	-
M DMQ-R: CwD	12.82 (± 6.25)	10.56 (± 2.73)	.11	-
M DMQ-R: Enhancement	11.42 (± 2.57)	10.80 (± 2.19)	.37	-
M DMQ-R: Conformity	5.91 (± 2.07)	5.20 (± 2.20)	.25	-
B-YAACQ: Social	0.76 (± 0.88)	0.68 (± 0.69)	.72	-
B-YAACQ: Impaired Control	0.48 (± 0.82)	0.32 (± 0.63)	.44	-

B-YAACQ: Self-perception	0.16 (± 0.37)	0.08 (± 0.28)	.40	-
B-YAACQ: Self-care	0.72 (± 0.89)	0.28 (± 0.46)	.03	**0.62**
B-YAACQ: Risk	0.64 (± 0.91)	0.40 (± 0.76)	.32	-
B-YAACQ: Ac/Occ	0.32 (± 0.69)	0.12 (± 0.33)	.20	-
B-YAACQ: Dependence	0.32 (± 0.56)	0.20 (± 0.41)	.39	-
B-YAACQ: Blackout	1.24 (± 1.27)	0.692 (± 1.04)	.33	-
B-YAACQ: Total	4.64 (± 4.43)	3.00 (± 3.12)	.14	-
APT: Breakpoint	4.54 (± 3.77)	4.27 (± 3.13)	.78	-
APT: Intensity of Demand	4.82 (± 5.85)	5.82 (± 5.78)	.55	-
APT: P_{max}	2.85 (± 3.00)	2.85 (± 3.05)	1.00	-
APT: O_{max}	7.53 (± 8.49)	8.67 (± 10.15)	.67	-
APT: Elasticity of Demand	-0.28 (± 0.73)	-0.17 (± 1.25)	.70	-
CATS: Sexual abuse	0.24 (± 0.72)	0.85 (± 1.92)	.15	-
CATS: Punishment	8.58 (± 3.35)	7.74 (± 3.40)	.38	-
CATS: Neglect/Negativity	15.03 (± 13.38)	9.55 (± 8.98)	.10	-
CATS: Emotional abuse	9.30 (± 6.84)	6.58 (± 3.38)	.08	-
CATS: Total	38.32 (± 26.50)	28.36 (± 16.76)	.12	-

[†]All values are means except gender, which is a total count. All analyses are 2-tailed. *Consumption* = UK units (1 UK unit = 10 ml or 8 g of pure alcohol); *TLFB* = Timeline FollowBack, based on prior/typical week's alcohol consumption; *Age at regular drinking* = age at which regular drinking was undertaken; *Drunk frequency* = number of times individuals have been drunk in the previous 6 months; *Drunk percentage* = percentage of drinking occasions in which individuals become drunk; *AUDIT* = Alcohol Use Disorders Identification Test; *BIS* = Barratt's Impulsivity Scale; *M DMQ-R* = Modified Drinking Motives Questionnaire – Revised; *B-YAACQ* = Brief Young Adult Alcohol Consequences Questionnaire; *ImpSS* = Impulsive Sensation Seeking; *APT* = Alcohol Purchase Task; *CATS* = Child Abuse and Trauma Scale. *Note.* Unlike for the correlation matrices, these p-values have not been adjusted for familywise error.

Appendix D

This appendix concerns Study 2 (Chapter Four). It presents ANOVA analyses for the Subjective Intoxication Scale (SIS), assessing whether potential changes in SIS scores were being driven by drink type (alcohol/control) or time (pre/post consumption) and whether interaction effects existed. This appendix also presents correlation matrices between ASTT bias scores (across alcohol and control conditions) and individual differences (Table D1), bias scores and craving change scores (Table D2), bias scores and subjective intoxication change scores (Table D3), and bias scores and breath alcohol for Study 2, which used a 0.3 g/kg alcohol priming dose.

Subjective Intoxication Scale (SIS)

Two (drink) × two (time) Repeated-Measures ANOVA were also conducted to assess changes in SIS measures. For 'light-headedness', both main effects of drink and time, as well as their interaction, were statistically significant. For the main effect of drink, reports of 'light-headedness' were higher in the alcohol condition (M = 24.34, SD ± 21.93) compared to control (M = 9.95, SD ± 20.31), $F(1, 27) = 42.94$, $p < .0001$, $\eta_p^2 = .61$. For the main effect of time, reports of 'light-headedness' were higher after consumption (M = 25.57, SD ± 22.27) compared to before (M = 8.71, SD ± 20.62), $F(1, 27) = 41.93$, $p < .0001$, $\eta_p^2 = .61$. The interaction produced an effect of similar magnitude, $F(1, 27) = 38.83$, $p < .0001$, $\eta_p^2 = .59$.

Post-hoc Paired-Samples *t*-tests were conducted for these effects (all 2-tailed). The main effect of drink was not found at baseline (before control vs. before alcohol), $t(27) = -0.13$, $p = .90$, $r = .03$. However, 'light-headedness' was found to be higher after the alcohol drink (M = 38.89, SD ± 29.01) compared to after control (M = 11.25, SD ± 20.34), $t(27) = -6.59$, $p <$

.0001, r = .79. The main effect of time was present across drink conditions, both before (M = 8.64, SD ± 20.57) and after (M = 11.25, SD ± 20.34) the control drink, $t(27) = -2.89$, p = .008, r = .49, as well as before (M = 8.79, SD ± 21.10) and after (M = 39.89, SD ± 29.01) the alcohol drink, $t(27) = -6.46$, $p < .0001$, r = .79. The interaction effect indicates that while consumption of either beverage increased reports of 'light-headedness', participants reported higher levels after alcohol compared to after control.

For the 'irritable' measure, a 2 (drink) × 2 (time) Repeated-Measures ANOVA found no main effect of either drink, $F(1, 27) = 3.29$, p = .08, η_p^2 = .11, or time, $F(1, 27) = 0.93$, p = .34, η_p^2 = .03, and no interaction, $F(1, 27) = 0.22$, p = .64, η_p^2 = .01.

For the 'stimulated' measure, a 2 (drink) × 2 (time) Repeated-Measures ANOVA found a main effect of drink, with the alcohol group showing higher levels (M = 39.59, SD ± 22.34) of being 'stimulated' than the control group (M = 30.79, SD ± 23.24), $F(1, 27) = 4.65$, p = .04, η_p^2 = .15. There was also a main effect of time, with post-consumption reports showing higher (M = 38.75, SD ± 19.59) levels of stimulation than pre-consumption (M = 31.63, SD ± 22.00), $F(1, 27) = 11.53$, p = .002, η_p^2 = .03. There was no significant interaction effect, $F(1, 27)$ = 1.89, p = .18, η_p^2 = .07.

Post-hoc Paired-Samples t-tests were conducted to assess these main effects (all 2-tailed). The main effect of drink was not found at baseline (before control vs. before alcohol), $t(27)$ = 1.29, p = .21, r = .24. However, 'stimulation' was found to be higher after the alcohol drink (M = 44.50, SD ± 22.73) compared to after control (M = 33.00, SD ± 22.61), $t(27) = 2.67$, p = .01, r = .46. The main effect of time was driven by the alcohol group, with no pre-post difference being found in the control group, $t(27) = -1.90$, p = .07, r = .34. Conversely, 'stimulation' was significantly higher post alcohol (M = 44.50, SD ± 22.73) compared to pre alcohol (M = 34.68, SD ± 25.22), $t(27) = -2.96$, p = .006, r = .49. Thus, these results suggest

that participants felt significantly more stimulated after alcohol consumption compared to after control consumption, as well as displaying a significant increase in reported stimulation after alcohol consumption compared to before consumption, while no such increase was noted after control consumption.

For the 'alert' measure, a 2 (drink) × 2 (time) Repeated-Measures ANOVA found main effects for both drink and time, though no interaction effect. For drink, feeling 'alert' was higher in the control group (M = 53.85, SD ± 22.40) compared to the alcohol group (M = 45.37, SD ± 20.84), $F(1, 26) = 9.02$, $p = .006$, $\eta_p^2 = .26$. For time, feeling 'alert' was higher before consumption (M = 53.44, SD ± 21.49) compared to after (M = 45.78, SD ± 21.43), $F(1, 26) = 8.49$, $p = .007$, $\eta_p^2 = .25$. The interaction was nonsignificant, $F(1, 26) = 2.18$, $p = .15$, $\eta_p^2 = .08$.

Post-hoc Paired-Samples *t*-tests were conducted to assess these main effects (all 2-tailed). The main effect of drink was not found at baseline (before control vs. before alcohol), $t(26) = 1.70$, $p = .10$, $r = .32$. However, feeling 'alert' was found to be lower after the alcohol drink (M = 39.46, SD ± 22.68) compared to after control (M = 51.46, SD ± 25.44), $t(27) = 2.88$, $p = .008$, $r = .48$. For the main effect of time, there was no pre-post difference found in the control group, $t(26) = 1.19$, $p = .25$, $r = .23$. The difference is driven by alcohol consumption, with 'alertness' being reported as lower after alcohol consumption (M = 39.46, SD ± 22.68) compared to before (M = 50.86, SD ± 22.87), $t(27) = 3.28$, $p = .003$, $r = .53$. Thus, reported 'alertness' was lower after alcohol consumption compared to after the control drink, with the same pattern emerging after alcohol consumption compared to before, with this effect being absent in the control condition.

For the 'relaxed' measure, a 2 (drink) × 2 (time) Repeated-Measures ANOVA found a main effect of time, though no effect of drink, $F(1, 27) = 0.78$, $p = .39$, $\eta_p^2 = .03$, and no

interaction effect, $F(1, 27) = 3.88$, $p = .06$, $\eta_p^2 = .13$. For the main effect of time, feeling 'relaxed' was higher after consumption ($M = 67.23$, $SD \pm 16.09$) compared to before ($M = 61.50$, $SD \pm 15.01$), $F(1, 27) = 5.17$, $p = .03$, $\eta_p^2 = .16$.

Post-hoc Paired-Samples *t*-tests were conducted to assess the main effect of time (2-tailed). There was no significant difference in reported 'relaxation' scores between pre and post consumption of the control drink, $t(27) = 0.15$, $p = .88$, $r = .03$. In the alcohol condition, 'relaxation' was higher after consumption ($M = 68.79$, $SD \pm 20.39$) compared to before ($M = 56.89$, $SD \pm 24.39$), $t(27) = -2.44$, $p = .02$, $r = .41$. Thus, self-reported 'relaxation' is driven by alcohol consumption, with 'relaxation' reported as being higher after alcohol than before.

For the 'contented' measure, a 2 (drink) × 2 (time) Repeated-Measures ANOVA found no main effect of drink, $F(1, 27) = 0.31$, $p = .58$, $\eta_p^2 = .01$, no main effect of time, $F(1, 27) = 0.33$, $p = .57$, $\eta_p^2 = .01$, and no interaction effect, $F(1, 27) = 0.20$, $p = .66$, $\eta_p^2 = .007$. No post-hoc tests were conducted.

Table D1 Spearman (r_s) correlations between ASTT bias scores and individual differences

	RT Bias (Alcohol)	Omission Bias (Alcohol)	RT Bias (Control)	Omission Bias (Control)
Drinking measures				
TLFB	.10	.01	-.06	-.01
Units per hour	-.21	.26	.22	.21
Drunk frequency	-.04	.06	.07	.20
Drunk percentage	.02	.21	.26	-.04
First drink	.13	.01	-.05	**-.40**[†]
Drink regularly	.05	.21	.05	-.07
Binge frequency	.15	.29	.09	.02
AUDIT	.23	.22	.10	-.10
Drinking motives				
M DMQ-R: Social	.20	.17	.22	-.03
M DMQ-R: CwA	-.06	-.19	-.18	-.38
M DMQ-R: CwD	-.09	-.11	-.17	-.09
M DMQ-R: Enhancement	-.10	.21	.15	-.18
M DMQ-R: Conformity	.03	-.06	.15	-.24
Drinking Consequences				
B-YAACQ: Social	.25	.11	.19	.13
B-YAACQ: Impaired control	.01	-.06	-.08	-.03
B-YAACQ: Self-perception	-.19	-.24	-.35	-.23
B-YAACQ: Self-care	.01	-.58	-.28	.09
B-YAACQ: Risk	.18	.08	.23	-.31
B-YAACQ: Ac/Occ	.12	-.28	.13	.05
B-YAACQ: Dependence	-.03	-.02	-.14	.04

B-YAACQ: Blackout	.09	.15	.15	-.14
B-YAACQ: Total	.11	-.15	-.01	-.11
Impulsivity				
BIS: Attentional	-.25	-.54	-.10	.04
BIS: Motor	**.38**†	-.16	.09	.22
BIS: Non-planning	.21	.008	.30	.35
BIS: Total	.28	-.19	.22	.23
ImpSS: Total	.15	-.24	.05	.02
Trauma and Abuse				
CATS: Sexual abuse	-.12	-.14	-.07	.06
CATS: Punishment	-.01	-.14	.16	.13
CATS: Neglect/Negativity	-.13	-.11	.06	.11
CATS: Emotional abuse	.14	-.15	.08	.12
CATS: Total	-.04	-.22	.06	.11

†Significant only without corrected alpha ($p < 0.05$), *Significant at the level of the corrected alpha. All 2-tailed. *TLFB* = Timeline FollowBack (average consumption over previous fortnight); *AUDIT* = Alcohol Use Disorders Identification Test; *M DMQ-R* = Modified Drinking Motives Questionnaire – Revised; *CwA* = Coping with Anxiety; *CwD* = Coping with Depression; *B-YAACQ* = Brief Young Adult Alcohol Consequences Questionnaire; *Ac/Occ* = Academic/Occupational; *BIS* = Barratt's Impulsivity Scale; *ImpSS* = Impulsive Sensation Seeking; *CATS* = Child Abuse and Trauma Scale. *Note.* Omission bias (alcohol and control) have been log-transformed.

Table D2 Spearman (r_s) correlations between DAQ change scores and sign-tracking measures

	RT Bias (Alcohol)	Omission Bias (Alcohol)	RT Bias (Control)	Omission Bias (Control)
Pre-post (Alcohol)				
Desire	.14	-.004	-	-
Pos + Control	-.04	-.20	-	-
Negative	.23	-.04	-	-
Total	.19	-.03	-	-
Pre-post (Control)				
Desire	-	-	.03	-.13
Pos + Control	-	-	-.34	-.17
Negative	-	-	-.29	.04
Total	-	-	-.23	-.20
Pre-drink comparison				
Desire	.32	-.18	.04	.19
Pos + Control	.28	-.003	.12	.19
Negative	.29	-.30	-.21	-.13
Total	**.38**†	-.19	.004	.12
Post-drink comparison				
Desire	.31	.03	.07	.36
Pos + Control	.21	-.11	.15	**.51***
Negative	**.53***	-.18	.11	-.13
Total	**.38**†	-.14	.14	.27

†Significant only without corrected alpha ($p < 0.05$), *Significant at the level of the corrected alpha. All 2-tailed. *Pre-post (Alcohol)* = change scores after alcohol consumption; *Pre-post (Control)* = change scores after lemonade consumption; *Pre-drink comparison* = comparison of alcohol and control groups, before consumption; *Post-drink comparison* = comparison of alcohol and control groups after consumption. *Desire* = desire to drink; *Pos + Control* = positive reinforcement and ability to control drinking; *Negative* = negative reinforcement; *Total* = total DAQ score.

Table D3 Spearman (r_s) correlations between SIS change scores and sign-tracking measures

	RT Bias (Alcohol)	Omission Bias (Alcohol)	RT Bias (Control)	Omission Bias (Control)
Pre-post (Alcohol)				
Lightheaded	.17	.22	-	-
Irritable	-.01	.09	-	-
Stimulated	.03	-.07	-	-
Alert	-.17	-.26	-	-
Relaxed	-.07	.22	-	-
Contented	.16	.24	-	-
Pre-post (Control)				
Lightheaded	-	-	**.40**†	-.01
Irritable	-	-	.22	**-.47**†
Stimulated	-	-	.07	.32
Alert	-	-	-.18	.20
Relaxed	-	-	-.10	.21
Contented	-	-	-.30	.26
Pre-drink comparison				
Lightheaded	0	-.28	-.22	-.08
Irritable	-.20	.30	.22	-.15
Stimulated	.12	.03	.14	.20
Alert	.36	.03	-.02	.23
Relaxed	-.19	-.23	-.15	-.03
Contented	-.26	-.16	-.17	-.06
Post-drink comparison				
Lightheaded	.08	.14	-.13	-.09
Irritable	-.32	.02	-.09	-.03
Stimulated	.33	-.14	.23	-.02
Alert	.25	.03	.08	-.25

Relaxed	-.32	-.13	.03	-.37
Contented	.07	.03	.17	.01

†Significant only without corrected alpha ($p < 0.05$), *Significant at the level of the corrected alpha. All 2-tailed. *Pre-post (Alcohol)* = change scores after alcohol consumption; *Pre-post (Control)* = change scores after lemonade consumption; *Pre-drink comparison* = comparison of alcohol and control groups, before consumption; *Post-drink comparison* = comparison of alcohol and control groups after consumption.

Table D4 Pearson (*r*) correlations between BrAC and sign-tracking measures

	RT Bias (Alcohol)	Omission Bias (Alcohol)	RT Bias (Control)	Omission Bias (Control)
Pre-BrAC	.46	-.25	.38	.14
Post-BrAC	.19	.17	.17	.18

*Significant at $p < .05$ (2-tailed); *Pre-BrAC* = BrAC taken before ASTT; *Post-BrAC* = BrAC taken after ASTT. *Note.* Due to missing data, Pre-BrAC $N = 12$; Post-BrAC $N = 18$.

Appendix E

This appendix concerns Study 3 (Chapter Four). It presents ANOVA analyses for the Subjective Intoxication Scale (SIS), assessing whether potential changes in SIS scores were being driven by drink type (alcohol/control) or time (pre/post consumption) and whether interaction effects existed. This appendix also presents correlation matrices between ASTT bias scores (across alcohol and control conditions) and individual differences (Table E1), bias scores and craving change scores (Table E2), bias score and subjective intoxication change scores (Table E3), and bias scores and breath alcohol (Table E4) for Study 3, which used a 0.6 g/kg alcohol priming dose.

Subjective Intoxication Scale (SIS)

Two (drink) × two (time) Repeated-Measures ANOVA were also conducted to assess changes in SIS measures. For 'light-headedness', both main effects of drink and time, as well as their interaction, were statistically significant. For the main effect of drink, reports of 'light-headedness' were higher in the alcohol condition (M = 23.13, SD ± 14.01) compared to control (M = 3.82, SD ± 10.73), $F(1, 29) = 43.89$, $p < .0001$, $\eta_p^2 = .60$. For the main effect of time, reports of 'light-headedness' were higher after consumption (M = 23.70, SD ± 15.56) compared to before (M = 3.25, SD ± 7.67), $F(1, 29) = 53.58$, $p < .0001$, $\eta_p^2 = .65$. The interaction produced an effect of similar magnitude, $F(1, 29) = 33.57$, $p < .0001$, $\eta_p^2 = .54$.

Post-hoc Paired-Samples *t*-tests were conducted for these effects (all 2-tailed). The main effect of drink was not found at baseline (before control vs. before alcohol), $t(29) = 1.11$, $p = .28$, $r = 20$. However, 'light-headedness' was found to be higher after the alcohol drink (M = 42.07, SD ± 27.13) compared to after control (M = 5.33, SD ± 15.17), $t(29) = 6.48$, $p < .0001$,

r = .77. The main effect of time was driven by the alcohol condition, with 'light-headedness' reported as higher after alcohol (M = 42.07, SD ± 27.13) compared to before (M = 4.20, SD ± 10.48), $t(29) = -6.89$, $p < .0001$, r = .79. There was no pre-post difference in the control condition, $t(29) = -1.64$, p = .11, r = .29. The interaction effect suggests an alcohol priming effect both post-alcohol consumption compared to pre-consumption, as well as post-alcohol consumption compared to post-control consumption.

For the 'irritable' measure, a 2 (drink) × 2 (time) Repeated-Measures ANOVA found no main effect of either drink, $F(1, 29) = 0.64$, p = .43, η_p^2 = .02, or time, $F(1, 29) = 0.14$, p = .71, η_p^2 = .005, and no interaction, $F(1, 29) = 1.93$, p = .18, η_p^2 = .06.

For the 'stimulated' measure, a 2 (drink) × 2 (time) Repeated-Measures ANOVA found a main effect of time, with the post-consumption group showing higher levels (M = 36.42, SD ± 20.01) of being 'stimulated' than the pre-consumption group (M = 26.37, SD ± 20.99), $F(1, 29) = 11.73$, p = .002, η_p^2 = .29. There was no main effect of drink, $F(1, 29) = 4.00$, p = .06, η_p^2 = .12, though there was a significant interaction effect, $F(1, 29) = 7.38$, p = .01, η_p^2 = .20.

Post-hoc Paired-Samples t-tests were conducted to assess these effects (all 2-tailed). The main effect of time was not found in the control condition, $t(29) = -0.62$, p = .54, r = .11. However, 'stimulation' was found to be higher post alcohol (M = 44.57, SD ± 28.12) compared to pre alcohol (M = 26.47, SD ± 23.75), $t(29) = -3.66$, p = .001, r = .56. The interaction effect is driven by consumption of alcohol, with no difference found between pre-alcohol and pre-control consumption, $t(29) = 0.04$, p = .97, r = .008, though post-alcohol consumption showed higher 'stimulation' (M = 44.57, SD ± 28.12) than post-control consumption (M = 28.27, SD ± 21.41), $t(29) = 2.98$, p = .006, r = .48. Thus, these results suggest that 'stimulation' is primed by alcohol consumption, both compared to pre-alcohol consumption and post-control consumption.

For the ‘alert’ measure, a 2 (drink) × 2 (time) Repeated-Measures ANOVA found main effects for both drink and time, though no interaction effect, $F(1, 29) = 0.25$, $p = .62$, $\eta_p^2 = .008$. For drink, feeling ‘alert’ was higher in the control group ($M = 56.63$, $SD \pm 19.55$) compared to the alcohol group ($M = 48.80$, $SD \pm 21.09$), $F(1, 29) = 5.50$, $p = .03$, $\eta_p^2 = .16$. For time, feeling ‘alert’ was higher before consumption ($M = 56.57$, $SD \pm 20.27$) compared to after ($M = 48.87$, $SD \pm 20.14$), $F(1, 29) = 5.66$, $p = .02$, $\eta_p^2 = .16$.

Post-hoc Paired-Samples *t*-tests were conducted to assess these main effects (all 2-tailed). The main effect of drink was not found at baseline (before control vs. before alcohol), $t(26) = -1.90$, $p = .07$, $r = .33$, nor post consumption, $t(29) = -1.81$, $p = .08$, $r = .32$. For the main effect of time, there was no pre-post difference found in the alcohol group, $t(29) = 1.75$, $p = .09$, $r = .31$. The difference is driven by control drink consumption, with ‘alertness’ being reported as lower after control consumption ($M = 53.47$, $SD \pm 20.70$) compared to before ($M = 59.80$, $SD \pm 21.77$), $t(29) = 2.09$, $p = .05$, $r = .36$. The finding of no effect of drink in post-hoc analyses is surprising given the main effect found in the ANOVA – this may be due to small simultaneous increases and decreases in opposing drink conditions, which don’t reach statistical significance. The results also suggest a decrease in ‘alertness’ after control consumption compared to before, though no such effect in the alcohol condition. Both results are contrary to expectation.

For the ‘relaxed’ measure, a 2 (drink) × 2 (time) Repeated-Measures ANOVA found a main effect of drink, though no effect of time, $F(1, 29) = 1.64$, $p = .21$, $\eta_p^2 = .05$. For the main effect of drink, feeling ‘relaxed’ was higher in the alcohol condition ($M = 64.93$, $SD \pm 14.81$) compared to control ($M = 58.58$, $SD \pm 15.20$), $F(1, 29) = 4.30$, $p = .05$, $\eta_p^2 = .13$. There was also an interaction effect, $F(1, 29) = 5.53$, $p = .03$, $\eta_p^2 = .16$.

Post-hoc Paired-Samples *t*-tests were conducted to assess these effects (2-tailed). There was no significant difference in reported 'relaxation' scores between alcohol and control at baseline (before consumption), $t(29) = -0.18$, $p = .86$, $r = .03$. However, 'relaxation' was significantly higher after alcohol ($M = 70.63$, $SD \pm 21.43$) compared to after control ($M = 57.50$, $SD \pm 19.28$), $t(29) = 2.42$, $p = .02$, $r = .41$. The dis-ordinal interaction indicates that 'relaxation' decreased (non-significantly) post-control consumption, $t(29) = 0.53$, $p = .60$, $r = .10$, while significantly increasing from pre- ($M = 59.23$, $SD \pm 19.20$) to post-alcohol consumption ($M = 70.63$, $SD \pm 21.43$), $t(29) = -2.24$, $p = .03$, $r = .38$. Thus, the interaction effect was driven by alcohol consumption, with 'relaxation' higher post consumption compared to both pre consumption and post control consumption.

For the 'contented' measure, a 2 (drink) × 2 (time) Repeated-Measures ANOVA found a main effect of time, but no main effect of drink, $F(1, 29) = 2.41$, $p = .13$, $\eta_p^2 = .08$, and no interaction effect, $F(1, 29) = 3.73$, $p = .06$, $\eta_p^2 = .11$. For time, reports of feeling 'contented' were higher post consumption ($M = 66.02$, $SD \pm 16.00$) compared to pre consumption ($M = 60.85$, $SD \pm 18.49$), $F(1, 29) = 4.82$, $p = .04$, $\eta_p^2 = .14$.

Post-hoc Paired-Samples *t*-tests were conducted to assess this effect (2-tailed). There was no difference in feeling 'contented' after control consumption compared to before, $t(29) = -0.20$, $p = .84$, $r = .04$. However, there was a pre-post alcohol consumption, with feeling 'contented' higher after consumption ($M = 70.20$, $SD \pm 19.33$) compared to before ($M = 60.40$, $SD \pm 20.26$), $t(29) = -2.49$, $p = .02$, $r = .42$. Thus, the main effect of time was driven by alcohol consumption, with 'contentedness' found to be higher after alcohol consumption compared to before, with no significant differences compared to control.

Table E1 Spearman (r_s) correlations between ASTT bias scores and individual differences

	RT Bias (Alcohol) (Male | Female)	Omission Bias (Alcohol)	RT Bias (Control)	Omission Bias (Control)
Drinking measures				
TLFB	.34 | -.27	-.21	.04	-.14
Units per hour	**.50**† | **-.57**†	-.22	.23	-.29
Drunk frequency	.10 | -.23	**.32**†	-.08	-.05
Drunk percentage	.05 | .28	**.42**†	.16	.20
First drink	-.19 | .15	-.22	.19	.26
Drink regularly	-.40 | .39	**-.40**†	-.14	.24
Binge frequency	.28 | -.40	-.08	-.16	**-.42**†
AUDIT	.48 | -.20	.11	-.23	-.05
Drinking motives				
M DMQ-R: Social	-.03 | .03	.13	.09	-.03
M DMQ-R: CwA	-.02 | -.33	.11	-.11	-.09
M DMQ-R: CwD	.41 | -.33	-.13	-.18	-.28
M DMQ-R: Enhancement	-.33 | -.22	-.02	.04	.007
M DMQ-R: Conformity	-.11 | -.30	.12	-.22	-.10
Drinking Consequences				
B-YAACQ: Social	.38 | -.13	.18	-.30	.22
B-YAACQ: Impaired control	.41 | -.31	.10	**-.48**†	-.10
B-YAACQ: Self-perception	.07 | -.32	.20	-.20	-.06
B-YAACQ: Self-care	-.04 | -.26	-.10	-.29	.05
B-YAACQ: Risk	.02 | -.26	-.19	-.21	-.17
B-YAACQ: Ac/Occ	.45 | -.20	.14	-.30	.01
B-YAACQ: Dependence	**.53**† | .32	.06	-.05	.27

B-YAACQ: Blackout	.25 | -.31	.10	-.11	.10
B-YAACQ: Total	.27 | -.21	.04	-.30	.03
Impulsivity				
BIS: Attentional	.39 | -.16	.22	-.19	-.19
BIS: Motor	.05 | .03	.09	-.30	.02
BIS: Non-planning	.28 | .26	.30	-.10	-.04
BIS: Total	.34 | .07	.22	-.20	-.08
ImpSS: Total	-.01 | -.20	.07	-.19	-.30
Trauma and Abuse				
CATS: Sexual abuse	. | -.38	.09	.0001	-.21
CATS: Punishment	.24 | -.07	-.03	-.26	.01
CATS: Neglect/Negativity	-.36 | **-.52**†	-.06	-.30	**-.41**†
CATS: Emotional abuse	-.56 | **-.52**†	.06	-.33	-.30
CATS: Total	-.42 | -.46	-.04	**-.37**†	-.30

†Significant only without corrected alpha ($p < 0.05$), *Significant at the level of the corrected alpha. *TLFB* = Timeline FollowBack (average consumption over previous fortnight); *AUDIT* = Alcohol Use Disorders Identification Test; *M DMQ-R* = Modified Drinking Motives Questionnaire – Revised; *CwA* = Coping with Anxiety; *CwD* = Coping with Depression; *B-YAACQ* = Brief Young Adult Alcohol Consequences Questionnaire; *Ac/Occ* = Academic/Occupational; *BIS* = Barratt's Impulsivity Scale; *ImpSS* = Impulsive Sensation Seeking; *CATS* = Child Abuse and Trauma Scale. *Note.* Omission bias (alcohol and control) have been log-transformed.

Table E2 Spearman (r_s) correlations between DAQ change scores and sign-tracking measures

	RT Bias (Alcohol)	Omission Bias (Alcohol)	RT Bias (Control)	Omission Bias (Control)
Pre-post (Alcohol)				
Desire	-.24	-.06	-	-
Pos + Control	-.02	-.04	-	-
Negative	-.04	-.11	-	-
Total	-.14	-.07	-	-
Pre-post (Control)			-	-
Desire	-	-	**-.45***	-.05
Pos + Control	-	-	**-.38**†	.07
Negative	-	-	.26	.13
Total	-	-	**-.39**†	.13
Pre-drink comparison				
Desire	-.30	-.03	-.03	-.01
Pos + Control	-.22	-.02	.19	.02
Negative	.22	.03	.23	.20
Total	-.18	-.09	.19	.13
Post-drink comparison				
Desire	**-.43**†	-.24	-.13	-.35
Pos + Control	-.22	.10	.08	-.09
Negative	-.14	-.15	-.01	-.24
Total	-.28	-.15	-.004	-.19

†Significant only without corrected alpha ($p < 0.05$), *Significant at the level of the corrected alpha. All 2-tailed. *Pre-post (Alcohol)* = change scores after alcohol consumption; *Pre-post (Control)* = change scores after lemonade consumption; *Pre-drink comparison* = comparison of alcohol and control groups, before consumption; *Post-drink comparison* = comparison of alcohol and control groups after consumption. *Desire* = desire to drink; *Pos + Control* = positive reinforcement and ability to control drinking; *Negative* = negative reinforcement; *Total* = total DAQ score.

Table E3 Spearman correlations (r_s) between SIS change scores and sign-tracking measures

	RT Bias (Alcohol)	Omission Bias (Alcohol)	RT Bias (Control)	Omission Bias (Control)
Pre-post (Alcohol)				
Lightheaded	-.28	-.35	-	-
Irritable	.21	-.21	-	-
Stimulated	-.27	-.14	-	-
Alert	-.26	.25	-	-
Relaxed	.09	-.02	-	-
Contented	-.19	-.04	-	-
Pre-post (Control)				
Lightheaded	-	-	-.06	-.05
Irritable	-	-	-.26	.09
Stimulated	-	-	-.07	-.05
Alert	-	-	.14	-.14
Relaxed	-	-	-.05	.13
Contented	-	-	.02	-.13
Pre-drink comparison				
Lightheaded	-.34	-.10	-.08	**-.37**†
Irritable	-.22	-.02	.07	**-.42**†
Stimulated	.03	-.13	.07	.16
Alert	.03	.13	.13	-.05
Relaxed	-.26	-.07	-.003	.13
Contented	.03	-.03	.21	-.18
Post-drink comparison				
Lightheaded	-.31	**-.40**†	.15	-.29
Irritable	.11	-.11	.19	**-.43**†
Stimulated	**-.39**†	-.14	.06	.12
Alert	-.20	.24	-.22	-.16

Relaxed	-.12	-.29	-.26	-.15
Contented	-.36	-.08	-.28	.05

†Significant only without corrected alpha ($p < 0.05$), *Significant at the level of the corrected alpha. All 2-tailed. *Pre-post (Alcohol)* = change scores after alcohol consumption; *Pre-post (Control)* = change scores after lemonade consumption; *Pre-drink comparison* = comparison of alcohol and control groups, before consumption; *Post-drink comparison* = comparison of alcohol and control groups after consumption.

Table E4 Pearson (*r*) correlations between BrAC and sign-tracking measures

	RT Bias (Alcohol)	Omission Bias (Alcohol)	RT Bias (Control)	Omission Bias (Control)
Pre-BrAC	-.18	.25	.03	-.07
Post-BrAC	-.24	-.21	-.34	-.23

*Significant at $p < .05$ (2-tailed); *Pre-BrAC* = BrAC taken before ASTT; *Post-BrAC* = BrAC taken after ASTT. *Note.* Due to missing data, Pre-BrAC $N = 12$; Post-BrAC $N = 18$.

Appendix F

This appendix presents correlation matrices between ASTT+ bias scores (Study 4, Chapter Five) and individual differences. This version of the ASTT includes three CSs rather than the typical two used throughout the rest of this thesis. RT Bias was created not by calculating a difference score between high and low RTs (as has been done in the other studies of the thesis), but rather by calculating a difference between high and medium RTs. These measures were chosen as bases for calculating a bias score as only this difference was found to be statistically significant (see Study 4, Chapter Five). For Omission Bias, two bias scores were created, one a difference score between high and medium, and a second between high and low – these differences were again found to be statistically significant in Study 4.

Table F1 Spearman (r_s) correlations between ASTT+ bias scores and individual differences

	RT Bias (High – Medium)	Omission Bias 1 (High – Medium)	Omission Bias 2 (High – Low)
Drinking measures			
TLFB	.11	.07	.16
Units per hour	.05	-.05	-.12
Drunk frequency	.09	-.02	-.16
Drunk percentage	-.002	.10	.02
First drink	-.14	.14	-.05
Drink regularly	-.05	.25	.10
Binge frequency	.04	.22	.27
AUDIT	.09	-.01	.09
Drinking motives			
M DMQ-R: Social	-.03	.12	.37
M DMQ-R: CwA	.06	.14	**.44**[†]
M DMQ-R: CwD	.30	.16	.11

M DMQ-R: Enhancement	.32	.24	.30
M DMQ-R: Conformity	-.23	-.16	-.06
Drinking Consequences			
B-YAACQ: Social	.28	**.41**†	.22
B-YAACQ: Impaired control	.33	.32	-.17
B-YAACQ: Self-perception	.05	-.004	.06
B-YAACQ: Self-care	.21	.27	-.02
B-YAACQ: Risk	.25	.30	-.07
B-YAACQ: Ac/Occ	.22	.14	-.14
B-YAACQ: Dependence	.25	.06	-.09
B-YAACQ: Blackout	**.43**†	.13	.06
B-YAACQ: Total	.31	.25	-.07
Impulsivity			
BIS: Attentional	.27	-.22	.25
BIS: Motor	.29	-.01	.37
BIS: Non-planning	.01	-.24	-.02
BIS: Total	.22	-.20	.27
ImpSS: Total	.33	.04	-.09
Trauma and Abuse			
CATS: Sexual abuse	.31	.22	**.52***
CATS: Punishment	-.20	-.02	.28
CATS: Neglect/Negativity	.17	-.10	.15
CATS: Emotional abuse	-.02	.24	.05
CATS: Total	.02	.04	.27

†Significant only without corrected alpha ($p < 0.05$), *Significant at the level of the corrected alpha. All tests are 2-tailed. *TLFB* = Timeline FollowBack (average consumption over previous fortnight); *AUDIT* = Alcohol Use Disorders Identification Test; *M DMQ-R* = Modified Drinking Motives Questionnaire – Revised; *CwA* = Coping with Anxiety; *CwD* = Coping with Depression; *B-YAACQ* = Brief Young Adult Alcohol Consequences Questionnaire; *Ac/Occ* = Academic/Occupational; *BIS* = Barratt's Impulsivity Scale; *ImpSS* = Impulsive Sensation Seeking; *CATS* = Child Abuse and Trauma Scale. *Note.* Omission bias scores have been log-transformed.

Appendix G

This appendix presents correlation matrices between ASTT (BB; button-box) bias scores and individual differences (Study 6, Chapter Seven). This version of the ASTT was conducted whilst participant underwent brain scanning in a Functional Magnetic Resonance Imaging scanner (fMRI). Due to this, the trial number, sequences and durations differed from previous studies. Additionally, eight stimuli (1 OT, 1 CS and 6 grey, neutral distractors) were presented rather than the usual six. Omission Bias scores were not calculated due to the very low number of overall omissions (e.g., only one participant produced an omission on a low-value trial).

Table G1 Spearman (r_s) correlations between ASTT (BB) bias scores and individual differences

	RT Bias
Perceived task difficulty	
SEQ	-.02
Drinking measures	
TLFB	-.38
Units per hour	-.37
Drunk frequency	-.20
Drunk percentage	.004
First drink	.22
Drink regularly	.11
Binge frequency	.06
AUDIT	-.17
Drinking motives	
M DMQ-R: Social	.23
M DMQ-R: CwA	-.04
M DMQ-R: CwD	-.04

M DMQ-R: Enhancement	-.15
M DMQ-R: Conformity	.13
Drinking Consequences	
B-YAACQ: Social	.09
B-YAACQ: Impaired control	-.10
B-YAACQ: Self-perception	-.06
B-YAACQ: Self-care	-.22
B-YAACQ: Risk	.31
B-YAACQ: Ac/Occ	-.14
B-YAACQ: Dependence	-.28
B-YAACQ: Blackout	.22
B-YAACQ: Total	-.03
Impulsivity	
BIS: Attentional	.17
BIS: Motor	-.09
BIS: Non-planning	-.14
BIS: Total	-.07
ImpSS: Total	.09
Trauma and Abuse	
CATS: Sexual abuse	-.26
CATS: Punishment	.03
CATS: Neglect/Negativity	-.01
CATS: Emotional abuse	-.01
CATS: Total	-.02

†Significant only without corrected alpha ($p < 0.05$), *Significant at the level of the corrected alpha. All tests are 2-tailed. *SEQ* = Single Ease Questionnaire (participants' perception of ASTT task difficulty); *TLFB* = Timeline FollowBack (average consumption over previous fortnight); *AUDIT* = Alcohol Use Disorders Identification Test; *M DMQ-R* = Modified Drinking Motives Questionnaire – Revised; *CwA* = Coping with Anxiety; *CwD* = Coping with Depression; *B-YAACQ* = Brief Young Adult Alcohol Consequences Questionnaire; *Ac/Occ* = Academic/Occupational; *BIS* = Barratt's Impulsivity Scale; *ImpSS* = Impulsive Sensation Seeking; *CATS* = Child Abuse and Trauma Scale. *Note. 'RT Bias'* refers to fMRI ASTT (BB) RT Bias scores and not ASTT (EE) RT Bias scores from previous studies.