Attentional bias and treatment adherence in substitute-prescribed opiate users

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Abstract

Background: Attentional bias (AB) is implicated in the development and maintenance of substance dependence and in treatment outcome. We assessed the effects of attentional bias modification (ABM), and the relationship between AB and treatment adherence in opiate dependent patients. **Method:** An independent groups design was used to compare 23 opiate dependent patients with 21 healthy controls. Participants completed an AB task before either a control or an ABM task designed to train attention *away* from substance-related stimuli. Pre- and post-ABM AB and craving were assessed to determine any changes. Relationships between treatment adherence ('using on top' of prescribed opiates or not) and AB, craving and psychopathology were also examined. **Results:** There was no baseline difference in AB between patients and controls, and no significant effect of ABM on AB or substance craving. However, treatment adherent patients who did not use illicit opiates on top of their prescribed opiates had statistically significantly greater AB *away* from substance-related stimuli than *both* participants using on top and controls, and reported significantly *lower* levels of craving than non-treatment adherent patients. **Conclusion:** While we did not find any significant effects of ABM on AB or craving, patients who were treatment adherent differed from both those who were not and to controls in their attentional functioning and substance craving. These findings are the first to suggest that AB may be a within-treatment factor predictive of adherence to pharmacological treatment and potentially to recovery in opiate users.

1.1 Introduction

Attentional bias (AB) – where disorder-related stimuli become the focus of one's attention – has been consistently demonstrated for substance-related stimuli in substance users relative to non-users (Wiers and Stacy, 2006; Field and Cox, 2008). Furthermore, AB is associated with craving in addiction (Field et al., 2006), is positively correlated with frequency of substance use (Townsend and Duka, 2001; Morgan et al., 2008; 2010) and has been linked to relapse in individuals abstaining from substance use (Cox et al., 2002; Marissen et al., 2006).

Consequently, AB features as a key component of many recent theoretical models of addiction (Ryan, 2002; Franken, 2003; Wiers and Stacy, 2006), where it is awarded a central role in the development and maintenance of substance use. These models suggest a reciprocal causal relationship between craving and AB. It follows, therefore, that direct manipulation of AB should produce meaningful changes in clinically relevant variables such as substance craving and frequency of substance use.

One approach to addressing this question has used the modified visual probe task, which aims to experimentally manipulate AB (MacLeod et al., 2002). Here, the task is modified by adjusting task contingencies, so that probes replace neutral images more often than substance-related images thereby *training* participants' attention towards neutral stimuli.

To date, the modified visual probe paradigm has been applied to tobacco smokers (e.g. Attwood et al., 2008) and to alcohol users both in the community and the clinic (Schoenmakers et al., 2007; 2010). These studies typically suggest that AB can be readily modified. However, mixed findings have been reported for the broader effects of ABM on craving and substance use behaviour (e.g. Field et al., 2007; Attwood et al., 2008). For example, in studies with healthy controls, rather than clinically relevant benefits (when training *away* from substance cues), it appears more common to induce 'adverse' effects

(when training *towards* substance cues) such as increased subjective craving (Field et al., 2007, for participants aware of experimental contingencies only; Attwood et al., 2008, in men only).

There has been only one ABM study to date examining a treatment-seeking, clinical sample (alcohol dependent patients; Schoenmakers et al., 2010). Importantly, this study did report broader beneficial effects of ABM away from substance-related stimuli: training effects generalised to novel substance-related stimuli (i.e. to stimuli other than those used during ABM) and participants were also discharged from treatment significantly earlier than the control group. However, while successful generalisation to novel stimuli was reported here, other studies have failed to demonstrate this effect (Schoenmakers et al., 2007).

Although only a preliminary study, Schoenmakers et al. (2010) provide some tentative yet important evidence of clinically-relevant benefits of ABM. Given that AB is positively correlated with frequency of substance use, it may be that AB is more modifiable in clinical samples, and as Field et al. (2013) have pointed out, the inconsistent findings regarding ABM in substance use to date is possibly because almost all studies have used non-clinical, student samples.

The present study had a primary and secondary aim. Primarily, we set out to investigate the effects of a single session of ABM on AB, craving, and frequency of substance use using a modified visual probe task in opiate dependent participants receiving opiate substitute treatment. No study to date has investigated ABM in this population. The secondary aim was based on our previous finding in a similar patient population that AB away from substance-related stimuli was positively correlated with length of abstinence in ex-opiate users (Constantinou et al., 2010). This suggestion of a link between AB and treatment progress therefore led us to also explore in the present study the relationship

between AB and a key aspect of treatment adherence: whether participants were using illicit opiates on top of their prescribed opiates.

Specifically, we hypothesised that: 1) Opiate dependent participants would show a significant baseline AB toward substance-related stimuli relative to non-substance using controls. 2) Participants receiving ABM *away* from substance-related stimuli would show decreased AB and substance craving following ABM compared with those receiving the control visual probe task. In addition, we explored the differences between treatment adherent and non-treatment adherent participants in the opiate using group and controls on AB, substance craving and other clinically relevant measures.

2.1 Method

2.2 Design and Participants

An independent groups design was used to compare 23 current opiate users (patient group) with 21 participants (control group) who did not use illicit substances.

Patient group participants were required to be opiate users prescribed a substitute medication as part of their treatment within National Health Service (NHS) drug services. In the NHS treatment typically includes substitute opiate prescription and regular meetings with a key worker who provides advice and support. Patients were recruited via their key workers and advertisements. Exclusion criteria were a current diagnosis of a psychotic disorder or alcohol dependence; use of illicit substances and alcohol on testing days.

To control for the relatively high levels of depression and anxiety in opiate users (Regier et al., 1998), control participants were recruited from an NHS primary care mental health service (Improving Access to Psychological Therapies; IAPT). However, to address the gender imbalance of patients comprising substance misuse (majority male) and IAPT (majority female) services, we also recruited healthy male participants from the local

community. The final control group consisted of 10 participants recruited from IAPT, and 11 healthy control participants. IAPT participants were recruited via poster advertisements or a database of the service's patients who expressed interest in research. Healthy participants were recruited via University College London's online community participant recruitment service. Exclusion criteria for controls were a history of or current illicit substance use, alcohol dependence or psychotic disorder.

The study was approved by the NHS National Research Ethics Committee, Surrey, and the UCL Psychology Ethics Committee. Written, informed consent was obtained from all participants. Patients were paid £20 and controls £10 for participation.

2.3 Materials and Measures

2.3.1 Stimuli

Stimuli were 44 picture pairs (Figure 1). Forty pairs, each matched for visual complexity and composition, contained one opiate-related (e.g. spoons, needles, lighters, heroin-like substance) and one non-opiate related (neutral; e.g. forks, pencils) image. The remaining four pairs contained neutral images only. The 40 opiate-neutral pairs were divided into five sets of eight.

[*Figure 1* about here]

2.3.2 Substance use

The Timeline Followback method (Sobell & Sobell, 1996) was used to gather substance use (including alcohol and tobacco) over the past 28 days.

2.3.3 Questionnaire measures

Baseline measures comprised the Patient Health Questionnaire (PHQ-9; Kroenke et al., 2001), Beck Depression Inventory-II (BDI-II; Beck et al., 1996, Generalized Anxiety Disorder-7 (GAD-7; Spitzer et al., 2006), and the Barratt Impulsiveness Scale-11 (BIS-11; Patton et al., 1995); on each of these, higher scores reflect greater symptomology. Subjective craving was assessed by a three 10 cm Visual Analogue Scales (VAS; Bond & Lader, 1972): "I would like to use drugs," "I want to use drugs," and "I have an urge to use drugs," each anchored "Not at all" and "Extremely".

2.4 Procedure

There were 3 separate testing sessions for the patient group: Session 1 (day 0), Session 2 (day 8) and Session 3 (day 28). For controls, only session 1 was attended as they would not be expected to derive any clinical benefit from ABM. Sessions 1, 2 and 3 took approximately 90, 15 and 20 minutes to complete, respectively.

On Session 1, eligible participants were randomly assigned to receive either ABM away from substance-related stimuli (ABM-away) or a standard visual probe control task (ABM-control). The day before each test sessions, all participants were reminded not to consume illicit substances or alcohol on the test day. On each test day, they were asked if they had consumed any, and appointments rearranged accordingly (one participant); no participant was visibly intoxicated. Participants next completed questionnaires and a 28-day substance use history.

Baseline assessment of AB (AB-0) was then completed. This comprised a standard visual probe task. Each trial began with a fixation point (500ms). A pair of images then appeared on the left and right of the screen. Images appeared for either a short (200ms) or long (500ms) duration to assess automatic orienting and controlled attention processing respectively. Image pairs were then replaced by a probe (an arrow pointing upwards or

downwards) in the location of either the neutral or opiate-related image. The probe remained on screen until the participant responded to identify the probe type (upwards or downwards) by pressing one of two appropriate response keys as quickly and accurately as possible. Probes replaced the opiate-related and neutral images equally often. The right/left position of image type, probe location, and stimulus duration were all counterbalanced and inter-trial interval (250-500ms) was randomly determined. Trials were displayed in a single block, with each pair presented eight times, producing 64 critical trials and 16 neutral trials. Trials were displayed in a new random order for each participant.

Immediately afterwards participants completed either ABM-away or ABM-control. Stimuli consisted of Sets 1-4 of the opiate-neutral pairs. Each pair was presented 16 times, producing 512 critical trials. Stimuli were presented in two equal blocks of 256 trials, with participants having the opportunity for a 5 minute break between blocks. For ABM-away and ABM-control, probes replaced neutral images on 100% and 50% of trials, respectively, and ABM-control was counterbalanced in the same manner as AB-away. Thus, the sole difference between the ABM-away and ABM-control tasks was the probe's position.

Following a 30-minute break, a further assessment of attentional bias (AB-1) and a VAS were then administered to re-assess AB and craving. AB-1 featured Sets 1 and 5, plus all four neutral-neutral image pairs, thus allowing the assessment of the effects of ABM on both familiar (Set 1 and two neutral pairs from AB-0) and novel (Set 5 and two unseen neutral pairs) stimuli. Each pair was presented eight times, giving 128 critical (64 familiar, and 64 novel) and 32 neutral (16 familiar, 16 novel) trials. The task was counterbalanced in the same way as AB-0. Stimuli were presented in a single block and displayed in a new random order for each participant.

Control participants' awareness of the experimental contingencies was assessed at the end of Session 1 by asking them (a) their views about the aim of the study; (b) whether they

detected any patterns in the probe location during the ABM task. ‘Aware’ participants correctly answered either question. Control participants were then debriefed and paid. Debriefing outlined the study aims in detail and the intended effects of the ABM task. They were told which group they had been randomised to, and those in the ABM-control group could complete the ABM-away task if they wished. Their wellbeing was enquired about, and provision was in place for further support if required from the experimenters (MC, CW and CM) or from service staff.

In Sessions 2 and 3 (patient participants only) further assessments of attentional bias (AB-2 and AB-3, both having the exact stimuli, specifications and counterbalancing as AB-1) were administered together with questionnaires In Session 3 an additional 28-day substance use history was taken, participants’ awareness was assessed and they were debriefed and paid.

2.5 Statistical Analysis

For the visual probe data, trials were excluded i) with neutral-neutral stimulus pairs, ii) where a response error was made (3.3% of baseline trials, 3.5% over post-ABM assessments), or where reaction time (RT) was <200ms or >2000ms (2% baseline, 0.2% over post-ABM assessments). Within opiate-neutral stimulus pairs, *attentional bias scores* were calculated by subtracting mean RTs to probes that replaced opiate-related stimuli from mean RTs to probes that replaced neutral stimuli. A positive AB score therefore indicates AB towards opiate-related stimuli.

Data from one patient participant were missing at Day 2 due to non-attendance (99% overall retention). Administrative error meant one patient’s (ABM-control) VAS data were unavailable following the Session 1break.

Four groups (patient ABM-away and ABM-control; control ABM-away and ABM-control) were compared with one way or repeated measures ANOVAs. *Post-hoc* comparisons were Bonferroni corrected *t*-tests. Investigation of treatment adherence (3 groups: treatment adherent patients, non-treatment adherent patients, controls) used Dunnett's *post-hoc* comparisons with treatment adherent patients as the reference group.

3.1 Results

3.2 Participant Characteristics (see Table 1)

One-way ANOVAs which showed significant group differences in years of education [$F(3, 40) = 6.68$, $p = .001$], VAS 'like' [$F(3, 40) = 4.83$, $p = .006$], VAS 'want' [$F(3, 40) = 5.26$, $p = .004$], VAS 'urge' [$F(3, 40) = 6.09$, $p = .002$], BDI-II [$F(3, 40) = 4.56$, $p = .008$], and PHQ-9 [$F(3, 40) = 5.52$, $p = .003$]. *Post-hoc* comparisons (Bonferroni) revealed that control participants allocated to ABM-control had significantly more years of education than patient participants allocated to ABM-away ($p = .001$) and to ABM-control ($p = .014$)[VAS 'like', VAS 'want' and VAS 'urge' were significantly greater in patient participants allocated to ABM-control than controls allocated to ABM-away (like: $p = .015$; want: $p = .006$; urge: $p = .003$) and to ABM-control (like: $p = .019$; want: $p = .022$; urge: $p = .006$). The group difference in BDI-II was driven by patient participants allocated to ABM-away scoring significantly higher than controls allocated to ABM-control ($p = .040$); the difference in PHQ-9 reflected higher scores in patient participants allocated to ABM-control than controls allocated to ABM-control ($p = .004$).

[Table 1 about here]

3.3 Attentional Bias and ABM (Table 2)

At baseline, patient participants did not differ from controls on stimuli displayed for 200ms [$t(42) = -0.11$, $p = .912$] or 500ms [$t(42) = -1.92$, $p = .066$].

To assess the effects of ABM on AB, only AB scores for familiar stimuli were used from AB-1. AB scores of the 4 groups were compared using a mixed-design 4x2x2 ANOVA, with group as a between-subjects factor and within subjects factors of stimulus duration (200ms, 500ms) and time (AB-0, AB-1). The predicted interaction between group and time was non-significant [$F(3, 40) = 0.82$, $p = .491$, $\eta_p^2 = .058$, observed power = .211], and no other significant effects emerged.

[Table 2 about here]

3.4 Effects of ABM on AB and craving over Time for Patient Participants

AB scores were analysed using the same 2x2x4 ANOVA; no significant main effects or interactions emerged.

VAS 'like', 'want' and 'urge' data were analysed separately using 2x3 ANOVAs, with a of ABM condition (2 levels: ABM-away, ABM-control) as between-subjects factor and a within-subjects factor of time (pre-ABM, post-ABM, after 30-minute delay). No significant main effects or interactions emerged.

3.5 Contingency Awareness

Only one control participant (allocated to ABM-away), and no patients, correctly identified the task contingency.

3.6 Substance Misuse Treatment Adherence

At baseline, 12 patient participants reported that they used illicit opiates on top of their prescribed substitute, while 11 reported that they did not use on top.

[Table 3 about here]

These three groups (patients not using on top, patients using on top, controls) were compared on each variable in Table 3 using one-way ANOVAs. There were significant group differences in BDI-II [$F(2, 41) = 7.01$, $p = .002$], PHQ-9 [$F(2, 41) = 8.59$, $p = .001$], and BIS-11 scores [$F(2, 41) = 5.59$, $p = .007$]. *Post-hoc* comparisons (Bonferroni) indicated that participants using on top had significantly greater BIS-11 ($p = .005$) and PHQ-9 ($p = .001$) scores than controls. BDI-II scores were higher than controls for participants using on top ($p = .005$) and not using on top ($p = .028$).

There were significant baseline differences in VAS 'like' [$F(2, 41) = 15.53$, $p < .001$], 'want' [$F(2, 41) = 13.39$, $p < .001$] and 'urge' [$F(2, 41) = 14.71$, $p < .001$]. In all cases participants using on top reported higher cravings than those who did not use on top (like: $p = .001$; want: $p = .006$; urge: $p = .001$) and controls (all subscales: $p < .001$). Methadone dose did not differ between participants who did and did not use on top [$t(15) = 1.27$, $p = .222$].

Table 4 displays the baseline AB scores for patient participants using on top, not using on top and control participants. A 3x2 ANOVA, with a between-subjects factor of group (patients not using on top, patients using on top, controls), and a within subjects factors of stimulus duration (200ms, 500ms) revealed a significant main effect of group [$F(2, 41) = 3.80$, $p = .031$, $\eta_p^2 = 0.156$, observed power = .659; *Figure 2]* *Post-hoc* tests (Dunnett's) showed that participants not using on top had significant bias *away* from opiate-related stimuli and *towards* neutral stimuli to a greater extent than those using on top ($p = .043$) and controls ($p = .027$). No other significant effects emerged.

[Table 4 & *Figure 2* about here]

Table 5 displays the number of patient participants using other illicit and licit psychoactive substances. Small numbers precluded statistical analyses but 7/12 of those using illicit opiates on top also used crack cocaine but this was not the case with those not using on top.

[Table 5 about here]

4.1 Discussion

Our hypotheses related to our primary aim in this study were not supported. Specifically, there was no baseline difference in attentional bias between opiate dependent patients and controls, nor was there any significant effect of ABM on AB or substance craving. Therefore, the present findings do not lend support to the use of ABM as a possible adjunct to treatment. However, the weaknesses of the present study, discussed below, should be borne in mind and improvements in future studies' design may provide more hopeful results, as did Schoenmakers et al. (2010).

However, analyses related to our secondary aim revealed a significant relationship between attentional bias away from substance-related stimuli and adherence to substance misuse treatment (using additional illicit opiates, as well as prescribed methadone or buprenorphine). Participants not using illicit opiates showed an attentional bias *away* from substance-related stimuli and *towards* neutral stimuli, relative to *both* participants using on top and control participants. This resonates with Constantinou et al.'s (2010) finding that ex-opiate users in rehabilitation showed a bias away from substance-related stimuli that

correlated positively with their length of abstinence. It is also in keeping with a recent finding reported by Peuker and Bizarro (2014) who found attentional avoidance of smoking-related stimuli in former smokers, and with Schoenmakers et al.'s (2010) findings where AB *away* from alcohol-related stimuli induced by ABM was associated with earlier discharge from treatment for alcohol dependent inpatients. Our results may also extend these findings to specify within treatment differences (i.e. simultaneous use of illicit opiates) that may be predictive of "recovery" (i.e. ex-opiate user status). However, this would require further investigation. For example, although self-reported drug use, which our study relied upon, has respectable reliability and validity in similar populations to those from which we recruited (e.g. Darke, 1998), urinary drug screens could be used to objectively verify treatment adherence to provide better support to this idea.

In addition, participants using on top had significantly greater craving for substances (as indexed by substance liking, wanting and urge to use) at baseline than participants not using on top, as well as controls. Further, those using on top scored significantly higher at baseline than controls on depressive symptomatology (PHQ-9; BDI-II) and impulsivity (BIS). Those not using on top only differed from controls on depression as indexed by BDI-II scores and showed similar scores on all other self-rated measures including substance craving. Given that there was no difference in self-reported levels of depression, anxiety or impulsivity between the two patient (treatment adherent, and non-treatment adherent) groups, and the only differences found were with respect to AB and self-reported craving, a possible clinical implication arises in that AB could potentially be used as a psychological measure of treatment engagement. However, this would require closer examination in future studies, for example through a more comprehensive assessment of anxiety (Cisler & Koster, 2010).

The lack of significant results in relation to our primary hypotheses may have arisen for a number of reasons. The most significant of these is the major limitation of our study,

namely low statistical power. This is largely a product of the fact that we investigated a clinical sample of opiate dependent patients, of which recruitment is challenging. However, we did achieve our required sample size based on our *a priori* power calculation, although this was based on effect size estimates also generated from a relatively small clinical sample (Schoenmakers et al., 2010) and thus was also likely affected by a similar issue. As small samples can bias estimates of effect size, it is possible that there was a true effect of ABM in our sample, except our study was not adequately powered to detect it. It is also important to highlight, of course, that the implications of our findings outlined above need to be considered in light of this limitation. Whilst acknowledging the limitation of power, the treatment-seeking, opiate dependent group we recruited is a key strength of this study, and an important criterion for assessing the clinical relevance of AB and its modification.

Given that we recruited opiate using participants, we specifically designed our ABM task to be brief (e.g. compared to Schoenmakers et al., 2010), taking approximately 20-25 minutes to complete including a short break half-way through the task. Advantages of this approach include minimisation of possible boredom and errors, although fewer trials might have limited the efficacy of the intervention.

The fact that we found no baseline difference in AB between opiate users and controls is also interesting. This may partly be due the relative novelty of opiate-related stimuli compared to neutral stimuli for control participants. Although visual attributes of the two types of stimuli were matched, novelty of substance-related images to a non-substance using population is hard to control. It is also noteworthy that the opiate-related stimuli used in the AB tasks consisted of heroin and its paraphernalia, but *not* of methadone or buprenorphine.

Our findings would benefit from replication in future studies with greater statistical power. Future studies may also wish to examine the association between AB and craving and methadone or buprenorphine dose at baseline, and the differences in licit and illicit substance

use between patients who do and do not use illicit opiates on top. It may also be useful to include images of methadone and buprenorphine as stimuli in all AB tasks.

In summary, our findings suggest that opiate dependent patients are not a homogenous group since, depending on their illicit opiate use, they differed in attentional bias and craving. Our findings are the first to suggest that attentional bias may reflect adherence to pharmacological treatment in opiate users.

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Table 1

Mean (SD) of demographic and baseline variables for each group

	Patient group		**Control group**		
	ABM-away (*n*=11)	ABM-control (*n*=12)	ABM-away (*n*=11)	ABM-control (*n*=10)	p^a
Age	43.91 (6.77)	45.17 (8.89)	41.00 (8.53)	38 (6.68)	
Gender (M:F)	10:1	10: 2	8:3	7:3	
Years of education	11.91 (1.64)	13.33 (2.81)	14.00 (4.02)	17.30 (2.32)	*
Methadone dose	62.75 (25.78)	60.56 (36.70)	-	-	
Buprenorphine dose	9.33 (2.31)	7.33 (7.57)	-	-	
n using illicit opiates	4	8	-	-	
BDI-II	22.7 (13.9)	21.8 (10.3)	10.6 (13.1)	8.4 (7.0)	*
PHQ-9	10.7 (6.3)	13.3 (6.2)	6.4 (7.5)	3.6 (3.7)	*
GAD-7	9.1 (7.4)	7.3 (6.1)	4.6 (5.9)	6.3 (3.9)	
BIS	66.9 (11.4)	72.9 (19.9)	58.6 (13.5)	59.0 (8.3)	
VAS ‘like’	2.1 (2.3)	3.4 (3.5)	0.4 (0.7)	0.4 (0.7)	*
VAS ‘want’	1.8 (2.0)	3.1 (3.1)	0.1 (0.2)	0.5 (1.0)	*
VAS ‘urge’	1.3 (1.7)	3.3 (3.4)	0.1 (0.2)	0.3 (0.7)	*

Note: As is typical of this patient group, most patients were White-British men. ABM-away patient participants: 8 were prescribed methadone, 3 buprenorphine. ABM-control 9 patient participants were prescribed methadone, versus, 3, buprenorphine.

[a] *p<.01

Table 2

Mean (SD) attentional bias pre- and post-ABM (i.e. AB-0 and AB-1) for patient and control participants in each experimental group.

	Patient group		**Control group**	
	ABM-away (*n*=11)	ABM-control (*n*=12)	ABM-away (*n*=11)	ABM-control (*n*=10)
Pre-ABM (200ms)	-7.45 (102.40)	-10.49 (75.25)	4.21 (44.66)	-18.43 (63.52)
Pre-ABM (500ms)	-26.10 (96.06)	-23.10 (74.15)	4.26 (33.93)	18.75 (26.88)
Post-ABM (200ms)	-2.53 (31.74)	-11.76 (56.24)	-3.92 (31.00)	12.91 (34.85)
Post-ABM (500ms)	23.68 (54.24)	-5.70 (52.07)	-16.80 (44.92)	5.32 (29.07)

Table 3

Clinically relevant variables at baseline for patient participants who were using on top, not using on top, and controls.

	Patient group		**Control group (c)**	
	Not using on top **(a)**	Using on top **(b)**		
	(*n*=11)	(*n*=12)	(*n*=21)	*p*[a]
Methadone dose	74.33 (44.14)[b]	54.64 (20.48)[c]	-	
BDI-II	21.1 (7.4)	23.3 (15.1)	9.6 (10.5)	2, 3
PHQ-9	10.1 (3.6)	13.9 (7.6)	5.1 (6.0)	2
GAD-7	7.1 (6.0)	9.1 (7.3)	5.4 (5.0)	
BIS-11	64.4 (14.0)	75.3 (17.1)	58.8 (11.0)	2
VAS 'like'	1.2 (1.6)	4.2 (3.3)	0.4 (0.6)	1, 2
VAS 'want'	1.2 (1.7)	3.7 (2.9)	0.3 (0.7)	1, 2
VAS 'urge'	0.8 (1.47)	3.7 (3.2)	0.2 (0.5)	1, 2

Note: Buprenorphine dose is not reported due to low numbers of participants in the non-adherent group (n=1).
[a] 1 = a vs b, $p < .050$; 2 = b vs c, $p < .050$; 3 = a vs c, $p < .050$
[b] n=6; the 5 other participants in this group were prescribed buprenorphine
[c] n=11; the 1 other participant in this group was prescribed buprenorphine

Table 4

Baseline mean (SD) attentional bias scores for patient participants using on top, not using on top and controls.

	Patient group		**Control group (c)**	
	Not using on top (a) (*n*=11)	Using on top (b) (*n*=12)	(*n*=21)	*p*[a]
AB at 200ms	-31.63 (97.98)	11.68 (74.13)	-6.57 (54.28)	
AB at 500ms	-46.56 (54.88)	-4.34 (101.11)	11.16 (30.91)	
AB (collapsed)	-37.48 (52.98)	3.23 (53.35)	1.82 (26.31)	1, 3

[a] 1 = a vs b, $p < .050$; 2 = b vs c, $p < .050$; 3 = a vs c, $p < .050$

Table 5

Number of patient participants using illicit substances on top of their prescribed substitute, including mean quantity used over the past 28 days.

	Not using on top (*N*=11)		**Using on top (*N*=12)**	
	n using	Mean (*SD*)	*n* using	Mean *(SD)*
Illicit opiates (g/day)	-	-	12	0.09 (0.09)
Crack cocaine (g/day)	0	-	7	0.07 (0.06)
Cannabis (*n* joints/day)	2	1.45 (2.00)	4	1.00 (0.96)
Alcohol (units/week)	4	7.00 (9.42)	3	43.67 (14.15)
Benzodiazepines (mg/day)	5[a, b]	6.46 (7.87)	3[c, d]	19.00 (0.00)

[a] 1 participant was on a reducing prescription for diazepam
[b] Quantity used data missing for 1 participant who reported using
[c] 2 participants were on a reducing prescription for diazepam
[d] Quantity used data missing for 2 participants who reported using

Figure 1: Examples of opiate-neutral picture pair stimuli used in the visual probe tasks.

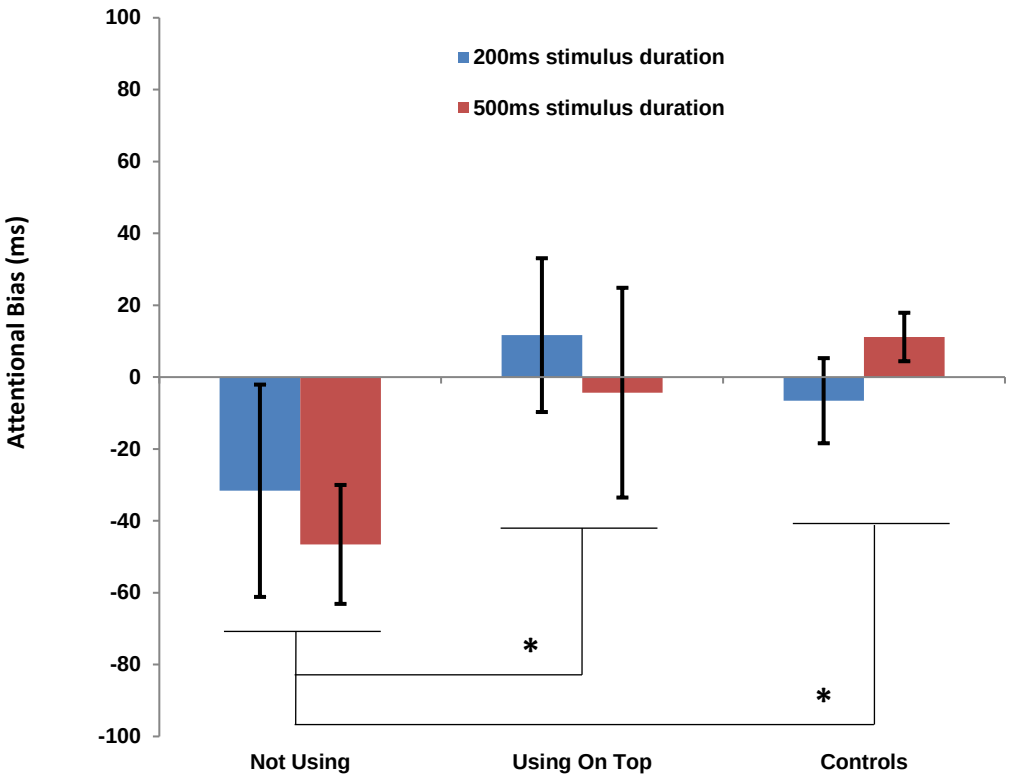

Figure 2: Mean attentional bias (plus standard error) at baseline for patient participants not using on top, using on top and controls.