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Preconscious attentional bias in cigarette smokers: a probe into awareness modulation on attentional bias

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ABSTRACT

It has been frequently reported that smokers showed attentional bias toward smoking-related stimuli. The current study aimed to examine whether such bias was also present when subjects were unaware of the presented stimuli and the possible role of awareness modulation on attentional bias. With a psychophysical approach (interocular suppression), we suppressed subjects' awareness to the cigarette pictures presented to one of their eyes. The visual dot probe task was modified to increase the perceptual load and to control the physical features between two rivaling images. Twenty-eight male smokers and 25 male non-smokers participated in the experiment. We found a significant interaction between experiment conditions and subject groups, with only the smoker group showed attentional bias toward cigarette pictures in unaware condition. Moreover, smokers' attentional bias in unaware condition was negatively correlated with their scores on Cigarette Dependence Scale while their attentional bias in aware condition was positively correlated with scores on Questionnaires of Smoking Urges. Such dissociation indicates the possibility of awareness modulation on attentional bias: it is possible that in aware condition, the attentional bias was modulated by smoking urge in awareness, thus concealed the effect of dependence degree. Further studies indicated that awareness modulated attentional bias through many factors, such as craving, quit attempt, attitude and disgust. Interestingly, non-smokers also showed attentional bias in aware condition, which further suggested that due to awareness modulation, attentional bias could even be addiction-unrelated.

Keywords Addiction, awareness, CDS, QSU-brief, tobacco, WISMD-68.

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INTRODUCTION

Attentional bias has been intensively investigated on drug users within the framework of incentive sensitization theory (Robinson & Berridge 1993, 2001, 2008), which proposes that repeated exposure to addictive drugs can sensitize the brain circuits for regulating incentive salience attribution, therefore drug cues can become salient stimuli for drug users to grab their attention. Many experimental reports have confirmed such attentional bias on cigarette smokers (e.g. Mogg & Bradley 2002a; Ehrman *et al.* 2002; Hogarth *et al.* 2003; Mogg *et al.* 2003; Mogg, Field & Bradley 2005; Waters *et al.* 2003; for review see Field & Cox 2008); however, very few study addressed the possible affect of awareness on the spatial allocation of attention in their experiments. Yaxley & Zwaan (2005) reported that when non-smokers were aware of the experiment's smoking focus, they displayed the same attentional bias as smokers did pointed to the possibility of awareness modulation on attentional bias, which could have affected the detected attention bias in previous studies.

For example, previous studies on smokers' attentional bias frequently reported significant correlation with craving level (e.g. Mogg & Bradley 2002; Hogarth *et al.* 2003; Mogg *et al.* 2003, 2005; Waters *et al.* 2003), rather than drug dependence level (Hogarth *et al.* 2003; Mogg *et al.* 2005 are the only two reports); however, a recent meta-analysis showed that the relationship between attentional bias and craving is moderated by various factors (Field, Munafo & Franken, 2009). Therefore, due to the reciprocal relationship

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between attentional bias and craving, and instant changing of craving level, clinical application of attentional bias in predicting relapse is not well established (for review see Field & Cox 2008, section 3.5 and 4). Theoretically speaking, if attentional bias can reliably reflect drug-users' dependence level, it can serve as an implicit assessment of addiction degree, which is a potentially more reliable predictor of subsequent use. We suspect that awareness modulation may be an important factor in the craving-related attentional bias; when subjects consciously perceived drug-related stimuli, their motivation system would be dominated by craving, which affected their attentional bias. If we can exclude awareness from the experiments, we should be able to reveal an attentional bias associated with drug dependence level.

Two previous studies probed into the preconscious attentional bias with backward masking paradigm based on visual dot probe task, but they reported null results (Mogg & Bradley 2002b; Bradley *et al.* 2004). Considering the possible affect of the experimental paradigm as they pointed out, in the current study we adapted a psychophysical paradigm, which differs from the common visual dot probe task in three ways:

Firstly, we suppressed subjects' awareness of the cuing pictures with an approach based on binocular rivalry. If two different images are dichoptically presented to the two eyes, the observers' awareness of what they perceive will alternate between one image and the other; this is known as binocular rivalry. By making one of the two competing stimuli much stronger than the other (high contrast, dynamic, and colorful etc.), the stronger stimulus can dominate subjects' awareness stably for seconds (Fang & He 2005; Tsuchiya & Koch 2005; Jiang & He 2006; Tsuchiya *et al.* 2006). This approach (we will call it interocular suppression in the following context of this article) is very effective in suppressing subjects' awareness to test stimuli while preserving a certain level of cortical processing (Blake 1989; Polonsky *et al.* 2000). Our previous study with this paradigm has successfully demonstrated a gender- and sexual orientation-dependent spatial attention effect of unaware erotic images (Jiang *et al.* 2006). In the study, heterosexual men and women were separately attracted to female and male erotic images that they were unaware of, but such attention effects were concealed when they could consciously perceive the images. Previously, we also applied this paradigm to study the unaware processing of upright face and familiar words (Jiang, Costello & He 2007), emotional faces (Jiang & He 2006; Jiang *et al.* 2009), especially the cortical response to stimuli that subjects were unaware of (Fang & He 2005; Jiang & He 2006; Jiang *et al.* 2009).

Secondly, instead of simultaneously presenting two types of stimuli (smoking-related vs. smoking-unrelated) as in common visual dot probe task, we simultaneously presented one intact picture and its corresponding scrambled image in order to control the basic physical features between the two pictures competing for spatial attention (such as color, contrast, brightness, etc). We also randomly presented cigarette pictures (together with its scrambled control) and smoking-unrelated common object pictures (together with its scrambled control) across the 128 trials each subject went through. Therefore, the attentional bias was calculated as '(respond accuracy when targets replace intact cigarettes—respond accuracy when targets replace scrambled cigarettes)—(respond accuracy when targets replace intact common objects—respond accuracy when targets replace scrambled common objects)', so that positive values indicate that subjects had their attention attracted to cigarette pictures.

Thirdly, instead of having subjects to report on which side a 'dot' appears, we used a sinusoidal grating [known as Gabor patch, commonly used in psychophysical experiments (e.g. Fredericksen, Bex & Verstraten 1997; Polat & Tyler 1999)] as the target, and asked subjects to report its orientation (tilted one degree clockwise or counterclockwise). This task is more difficult than responding to a dot, so that the perceptual load is greatly increased. It has been shown that selective processing of task-irrelevant information is determined by the perceptual load of task relevant information (Lavie 1995). In emotional process, when very demanding tasks were employed, attention modulation on the processing of emotional stimuli would be revealed; on the contrary, with low demanding tasks, little or no effect of attention was observed (e.g. Pessoa *et al.* 2002 vs. Vuilleumier *et al.* 2001; for a review see Pessoa 2005). Perceptual load should have more influence when subjects could not consciously perceive the cuing pictures; since subjects could only perceive masks or noises, they would make little effort to maintain their attention throughout the trial if they perform very simple tasks. Therefore adjustment on perceptual load seems necessary.

We also administered to smokers several questionnaires in order to reveal possible correlations with attentional bias, including the Cigarette Dependence Scale (Etter, Houezec & Perneger 2003) which reflects the degree of addiction on smoking, the Questionnaire on Smoking Urges-Brief (QSU-Brief) (Tiffany & Drobes 1991; Cox, Tiffany & Christen 2001) which evaluates the instant craving level, as well as the Wisconsin Inventory of Smoking Dependence Motives (WISDM-68) which provides a multidimensional measurement on motives for drug use and also reflects underlying mechanisms of dependence (Piper *et al.* 2004).

METHODS

Participants

In view of the disproportion of smoking rate among female (< 10%) and male (> 60%) in China (Mackay & Eriksen 2002), only male smokers were recruited in the current study. Twenty-eight male smokers (mean age = 23.6 years) and 25 male non-smokers (mean age = 24.9 years), who were mainly graduate or undergraduate students, were recruited. They all had normal or corrected-to-normal vision, with no psychiatric or physical illness, and no history of drug use (other than nicotine) or alcohol addiction. Smokers smoked 8.04 cigarettes per day on average (SD = 6.34, range 1~20). They were asked during initial contact to abstain from smoking for 24 hours prior to the experiment. Informed consent was obtained from all participants. The Human Subjects Review Committee of the Institute of Psychology, the Chinese Academy of Sciences approved the study. Participants were paid 20 Chinese Yuan (approximately equivalent to 3 US Dollars or 2 Euros) after the experiment.

Stimuli and apparatus

The stimuli were 16 color images including eight photographs of evident cigarettes (e.g. a cigarette or a pack of cigarettes) and eight photographs of common neutral objects (e.g. a comb or a pair of scissors) that were neither smoking-related nor similar to cigarettes or smoking paraphernalia. All of the objects depicted in the photographs were familiar to subjects and were small objects that could be held by one hand. Pictures were scrambled to serve as controls presented simultaneously with test pictures. Stimuli were generated with MATLAB (The MathWorks, Inc., Natick, MA, USA) using the Psychophysics Toolbox extensions (Brainard 1997; Pelli 1997) and presented on a HP ®17-inch CRT monitor (1024 × 768 at 85 Hz).

During experiments, subjects were seated with their head rested on a chinrest and looked at the monitor through a set of mirror stereoscope 40 cm from the monitor (see Figure 1a for illustration and Supporting Information Fig. S1 for a photograph of the apparatus). Each of their eyes viewed a square with a central cross; mirrors were adjusted until perception of the two eyes reached complete convergence, i.e. perception of two eyes were exactly the same as perception of each eye (the subject could perceive one intact square with both eyes open and could also perceive one such square with only one eye open). The pictures were presented within the square frame on the left and right side of the central cross (Fig. 1a). Visual angle of the central cross was $0.86° \times 0.86°$, of the frame was $11° \times 11°$, of each picture was $4.8° \times 6.5°$, and the horizontal distance between the centers of the two images was 6.1°.

Procedure

Upon arrival, smokers were required to fill in the CDS, QSU-Brief, and the WISDM-68. In order to measure the instant pretest urge, QSU-Brief was filled twice prior to the unaware and aware conditions.

The experiment began with a practice session, in which subjects had their dominant eyes identified and became familiar with the Gabor patch orientation discrimination task by responding to Gabor patches rivaling between two eyes; e.g. in the 30 trials, if a subject reported mainly the orientation of the Gabor patch presented to the left eye, then the left eye was the dominant eye and in the experiment session the suppression noise patches would be displayed in the left eye. In order to help subjects perceive the one degree orientation in the main experiment, Gabor patches tilted for one, two and three degrees clockwise and counterclockwise were presented randomly in the practice session. Subjects also practiced the experimental procedure (with pictures irrelevant to the experiment) to make sure they understood the experiment protocol (see below).

The experiment session began with the unaware condition. Each trial began with fixation on a central cross presented to both eyes, then the dominant eye was presented with a pair of identical high contrast dynamic noise patches on both sides of the fixation and the non-dominant eye was presented with a test image and its scrambled control on both sides of the fixation (in spatial locations corresponding to the noise patches so that they could be completely suppressed). Due to strong interocular suppression, observers perceived identical noise patches on both sides of the fixation and were unaware of the cues presented to the non-dominant eye (Fig. 1b). The suppression lasted for 800 ms. Then there was a 100-ms inter-stimulus interval (ISI) in which only the fixation was displayed. After the ISI, a small Gabor patch ($1.8° \times 1.8°$) was presented for 100 ms in the position previously occupied by the intact or scrambled image. The Gabor patch was tilted one degree clockwise or counterclockwise, and participants were required to press one of two keys to indicate their perceived orientation of the Gabor patch [regardless on which side of the fixation it appeared (Fig. 1c)]. Targets (Gabor patches) were presented to both eyes simultaneously with converged perception (Fig. 1b). Observers were required to press a certain key to abort a trial if they perceived any difference between the two sides (they were supposed to perceive identical colorful noise patches on both sides of the fixation), and those trials were excluded from further analysis. Positions of Gabor patches and cuing images

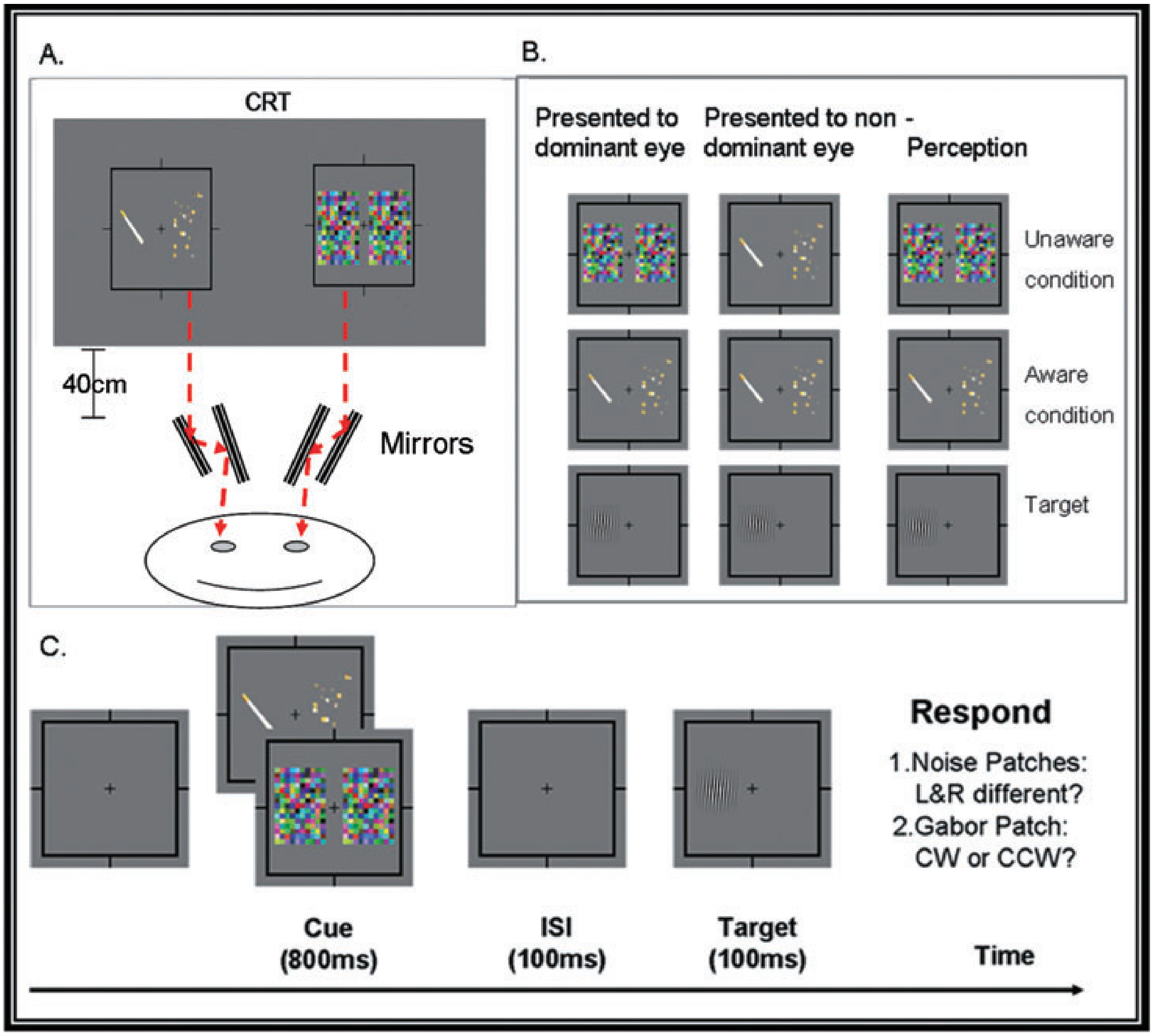

Figure 1 Illustration of experimental methodology*
(a) Schematic illustration of the light path (red dotted line) during experiment. The gray region shows what is displayed on the CRT-screen; note that the two squares and fixations are crucial markers when adjusting the facility to reach binocular convergence. (b) Illustration of the stimuli presented to each eye and subjects' perception. In the unaware condition, awareness of the cuing pictures were suppressed by the dynamic colorful noise patches presented to the dominant eye so that subjects could only perceive the noise patches; while in the aware condition, subjects could perceive the test images and its scrambled control presented identically to both eyes. In both conditions, targets were always presented identically to both eyes to guarantee subjects' perception. (c) Schematic illustration of the experimental paradigm for the unaware condition (for the aware condition, the cue was presented for 200 ms and the noise patches were replaced with identical cuing pictures presented to the other eye). Each trial began with central fixation, followed by a pair of cuing pictures presented for 800 ms at the left and right side of the fixation, and then came an inter-stimuli-interval (ISI) of 100 ms followed by the target (Gabor patch) presented for 100 ms. At the end of each trial, observers pressed one of two buttons to indicate the perceived orientation (Clockwise or Counterclockwise) of a Gabor patch briefly presented on either side of fixation. In the unaware condition, if observers detected any difference between the two sides of the fixation, they pressed another button to abort that trial.

*Note: Gabor patches in this figure were tilted to 3 degree instead of 1 degree and adjusted to a higher contrast to facilitate readers' perception.

were balanced and randomized across the 128 trials. Subjects were required to respond 'as accurately as possible' to the Gabor patches.

Immediately after the unaware condition, all participants completed a two-alternative forced choice (2AFC) experiment to check whether their awareness to test images was really suppressed. The stimuli and procedure in this 2AFC experiment were exactly the same as those in the preceding experiment except for the response at the end of each trial: in the 2AFC test participants were asked to make a forced guess on which side the intact picture was presented instead of discriminating the Gabor patch orientation. We applied a very strict inclusion criteria when analyzing the data to ensure the data we included in unaware condition were obtained when subjects were really unaware of the test pictures: only data from participants who performed at chance level in the 2AFC test [verified with a bimodal statistical test on correct ratio against 50%, data showed $P < 0.01$ were excluded (indicating significantly different from 50%, thus not at chance level)] and had less than 5% of trials abandoned in the preceding main test were included in further analyses. The 2AFC test was followed by the aware condition, in which the dominate eye was presented with identical cuing pictures presented to the non-dominant eye so that subjects had converged perception on the cuing pictures (Fig. 1b). The cuing pictures were presented for 200 ms. The ISI, targets and required response were exactly the same as that of the unaware condition. There were also 128 trials in the aware condition.

RESULTS

Questionnaire results of smokers

Range of scores on CDS was 21~52 with a mean of 34.75 (SD = 8.75). For reference, the 12-item version of CDS applied in the current study has a middle value of 36 with range of 6~60, with 6 indicating not addicted at all while 60 indicating heavily addicted to cigarettes, therefore our study covered a sufficiently wide range of subjects for correlation analysis. Mean scores of QSU were 43.25 (SD = 17.43) before aware condition and 41.47 (SD = 14.93) before unaware condition, with no significant difference [t (19) = –0.24, $P = 0.82$]. For reference, the 10-item version of QSU applied in the current study has a middle value of 50 with a range of 0~100, where 0 indicates no smoking urge and 100 indicates greatest smoking urge. Mean scores of WISMD-68 subscales were 'Affiliative Attachment' 19.11 (SD = 5.78), 'Automaticity' 21.82 (SD = 5.98), 'Loss of Control' 12.25 (SD = 5.54), 'Behavioral Choice/Melioration' 24.21 (SD = 7.54), 'Cognitive Enhancement' 19.07 (SD = 7.54), 'Craving' 17.04 (SD = 4.83), 'Cue Exposure/Associative Processes' 31.50 (SD = 5.48), 'Negative Reinforcement' 29.64 (SD = 5.82), 'Positive Reinforcement' 22.54 (SD = 4.69), 'Social/Environmental Goads' 18.71 (SD = 5.13), 'Taste/Sensory Processes' 29.61 (SD = 4.11), 'Tolerance' 20.32 (SD = 7.98) and 'Weight Control' 10.79 (SD = 5.59) (refer to Piper *et al.* 2004 for detailed explanation of subscales). It is worth noting that the highest score is on 'Cue Exposure/Associative Process', indicating that the highly smoking-exposed environment was the main reason for smoking among the subjects of the current study.

Attentional bias

Based on the strict inclusion criteria described above, data from 20 of the 28 smokers and 16 of the 25 non-smokers were included for attentional bias analysis. Overall, the smoker and non-smoker groups did not show a significant difference in their overall performance on the Gabor patch orientation discrimination task in either the aware [66.2% vs. 66.4%, t (34) = –0.05, $P > 0.9$] or unaware conditions [68.7% vs. 64.0%; t (34) = 1.28, $P > 0.2$].

We calculated the attentional bias with the following formula: attentional bias = (respond accuracy when targets replace intact cigarettes—respond accuracy when targets replace scrambled cigarettes)—(respond accuracy when targets replace intact common objects—respond accuracy when targets replace scrambled common objects). A split-half test was conducted to evaluate the reliability of this index. There were no significant differences between randomly divided two subgroups within each experimental group as well as between each subgroup and the grand mean ($P = 0.3$~1, NS) on their attentional bias scores in both aware and unaware conditions. One sample t-test against zero was conducted on each experimental group to see if they showed attentional bias in each condition. Figure 2 showed the group means (Fig. 2a) and individual data (Fig. 2b). Figure 2a shows the mean scores of attentional bias in unaware and aware conditions of each group, as well as the interaction of the two factors (group and experiment condition). In Fig. 2b, the attentional bias score of each participant is represented by one point (x, y) in the coordinate system, in which the horizontal (x) axis shows the attentional bias in aware condition, and the vertical axis (y) shows the attentional bias in unaware condition. The more strongly observers' attention was attracted by cigarette pictures, the further away from the central zero (dashed line) are the individual data, either rightward along the horizontal axis (x) (aware condition) or upward along the vertical axis (y) (unaware condition).

We discovered a significant interaction between subject group (smokers vs. non-smokers) and experiment condition (unaware vs. aware) (F (1, 34) = 13.6, $P < 0.001$) (Fig. 2a). In unaware condition only smokers showed attentional bias toward cigarette pictures (t (19) = 4.79, $P < 0.001$), while non-smokers showed no such bias (t (15) = 0.36, $P > 0.7$), with a significant between-group difference (t (34) = –2.29, $P < 0.05$). Thus in Fig. 2b, the smokers (small orange triangles) are mostly on the upper half the coordinate system while the non-smokers (small cyan circles) spread evenly in the upper and lower part. However, in aware condition, both smokers and non-smokers showed a significant attentional bias toward cigarette pictures [smokers: t (19) = 2.47, $P < 0.02$ and non-smokers: t (15) = 5.66, $P < 0.001$]. Thus in Fig. 2 both smokers (small orange triangles) and non-smokers (small cyan circles) fall mostly on the right part of the coordinate system. The

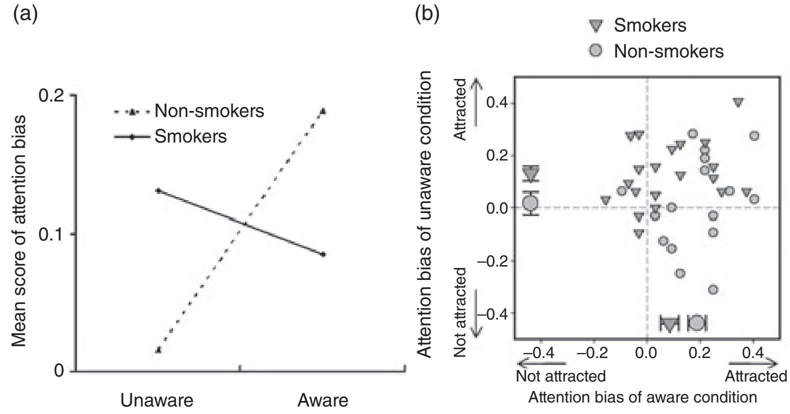

Figure 2 (a) Schematic plot of the interaction between experiment conditions and subject groups with group mean scores of attentional bias of each experimental condition. (b) Individual data of attentional bias scores. Attentional bias was calculated as '(respond accuracy when targets replace intact cigarettes—respond accuracy when targets replace scrambled cigarettes)—(respond accuracy when targets replace intact common objects—respond accuracy when targets replace scrambled common objects)'. The horizontal (x) axes shows attentional bias score in the aware condition and the vertical (y) axes shows attentional bias score in the unaware condition, with positive values indicating subjects were attracted to cigarette pictures. Individual data (individual bias scores at both aware and unaware conditions) are shown with symbols (smokers: triangles; non-smokers: circles). Group means (large symbols) are plotted along each axis with error bars indicating SEM Data of smokers are clustered at the upper right quadrant, indicating that they were attracted to cigarettes in both unaware and aware conditions; while data of non-smokers scattered around the two quadrants on the right side, indicating that they were attracted to cigarettes in aware condition only

mean bias score of non-smokers was even larger than smokers [t (34) = 2.13, $P < 0.05$].

Correlations between attentional biases and questionnaire scores

We further examined the relationship between attentional bias and questionnaire scores. The attentional bias in the unaware condition was negatively correlated with CDS scores ($r = -0.6$, $P < 0.01$), but not significantly correlated with scores of QSU ($r = 0.01$, $P = 0.96$, NS). Attentional bias in the aware condition was positively correlated with scores of QSU ($r = 0.36$, $P = 0.06$), but not significantly correlated with CDS scores ($r = 0.2$, $P = 0.93$, NS).

Attentional bias scores in the unaware condition were also significantly correlated with 'Loss of Control' ($r = -0.51$, $P < 0.05$) and 'Tolerance' ($r = -0.49$, $P < 0.05$) of WISMD-68 which reflect compulsion and the ability to smoke large amounts without acute toxicity according to Piper *et al.* (2004). These measures were also positively correlated with CDS ($r = 0.75$, $P < 0.001$; $r = 0.78$, $P < 0.001$), as well as 'Taste/Sensory Processes' ($r = 0.45$, $P < 0.05$) of the WISMD-68, indicating smokers' attentional bias in unaware condition mainly reflected their dependence on cigarettes. Attentional bias in the aware condition was significantly correlated with 'Behavioral Choice-Melioration' ($r = 0.55$, $P < 0.01$) which was positively correlated with QSU ($r = 0.48$, $P < 0.01$) and marginally significantly correlated with 'Cue Exposure/Associative Processes' of the WISMD-68 ($r = 0.33$, $P = 0.086$), indicating that the attentional bias in aware condition mainly reflected the influence of factors in their awareness such as their subjective choice or influence of environment.

DISCUSSION

The objective of the current study was to examine the presence of preconscious attentional bias on smokers and possible awareness modulation on attentional bias toward drug stimuli. We applied a psychophysical approach to reveal the preconscious attentional bias on smokers and contrasted the bias with that of aware condition and that on non-smokers. We found out that smokers, rather than non-smokers, showed attentional bias toward subliminal cigarette pictures; and there was a significant interaction between subject group (smokers vs. non-smokers) and experiment condition (unaware vs. aware). Presence of preconscious attentional bias and the interaction highlighted the independence between attention and awareness.

Generally speaking, the relationship between visual attention and awareness is very intricate; although in everyday observation visual attention and awareness are almost equivalent, the independence between them is considerable. Neuroscience evidences show that they are subserved by independent neural networks despite of some overlapping brain regions (for a review see Lamme 2003), psychophysical evidences also show that they are 'distinct phenomena that need not occur together and that can be manipulated using distinct paradigms' (cited from the abstract of the review by Koch & Tsuchiya 2007). Early in 1990s, researchers have addressed the possibility of perception in unawareness (Jacoby, Lindsay & Toth 1992; LaBerge 1997) and developed experimental paradigms to explore such processes (Debner & Jacoby 1994; McCormick 1997). Up to now, many approaches have been invented to suppress observers' awareness to experimental stimuli, such as disrupting visual awareness via masking or crowding, or by distracting observers' attention as in change blindness and attentional blink, or by presenting strong noise to one eye to suppress subjects' awareness to stimuli presented in the other eye (interocular suppression) (for review see Kim & Blake 2005). The interocular suppression approach is outstanding compared to other approaches in that it can provide reliable and sustainable suppression (table 1 in Kim & Blake 2005). Previously, Bradley *et al.* probed into smokers' preconscious attentional bias with backward masking technique, but they obtained null results (Mogg & Bradley 2002b; Bradley *et al.* 2004). Before making a conclusion that 'processing biases for smoking cues only occur when the stimuli are available to awareness', they also pointed out the possibility that the masking conditions they applied were 'too effective to allow subthreshold effects to emerge' (Mogg & Bradley 2002b, p. 391; Bradley *et al.* 2004, p. 35). Considering the independent relationship between attention and awareness discussed above, as well as the large body of literature on preconscious attentional bias toward emotional stimuli (Mogg, Bradley & Hallowell 1994; Mogg, Bradley & Williams 1995; Mogg & Bradley 1999, 2002a; Fox 2002; Schultheiss & Hale 2007), especially considering the amazing overlap of emotion-related and addiction-related brain regions (for reviews see Goldstein & Volkow 2002; Panksepp, Knutson & Burgdorf 2002), possible presence of preconscious attentional bias on drug users cannot be excluded, and they may be revealed by proper approaches such as the interocular suppression in the present study.

In the present study, smokers' preconscious attentional bias was negatively correlated with their cigarette dependence level but not significantly correlated with their craving level, whereas their attentional bias in aware condition was significantly correlated with their craving level but not with their dependence level. The dissociation indicated that the positive correlation between attentional bias and craving level frequently reported in previous literature (e.g. Mogg & Bradley 2002b; Hogarth *et al.* 2003; Mogg *et al.* 2003, 2005; Waters *et al.* 2003; for review see Field & Cox 2008; for a meta-analysis see Field *et al.* 2009) may be affected by awareness modulation. According to the incentive sensitization theory, sensitized dopamine system mediates attention allocation to drug cues that are salient to drug users; therefore when smokers 'saw' (perceived consciously) the cigarette pictures, they allocated attention to such stimuli out of their 'wanting' for cigarettes (Robinson & Berridge 1993, 2001, 2008); on the other hand, attentional bias and craving have a mutual excitatory relationship (Field & Cox 2008), so attentional bias toward drug stimuli can also induce craving. Our results suggest that in the above process, subjects' awareness on stimuli is very necessary, because smokers' attentional bias was associated with their smoking urge only in the aware condition. On the other hand, the negative correlation between cigarette dependence level and attentional bias, although seems to be counter-intuitive, was also reported previously in a few studies. Hogarth *et al.* (2003) found that heavy smokers showed smaller attentional bias than light smokers, and they interpreted the result with the dual-process theories of Tiffany (1990), Dickinson *et al.* (1995), Holland (1998) and Baxter & Hinson (2001), which contend that drug-taking behavior in heavy smokers has become an automatic habit, thus the role of conditioned attentional orientation has been diminished (Hogarth *et al.* 2003, p. 158). Mogg *et al.* (2005) also reported longer gaze dwell time (of eye movement) on smoking cues was associated with lower levels of nicotine dependence and fewer cigarettes smoked per day. Such results were considered as 'consistent with integrated "incentive-habit" theories of addiction (e.g. Tiffany 1990; Di Chiara 2000), which suggest that the effect of incentive motivational processes on behavior diminishes in strength as addiction progresses, due to a switch from "incentive responding" to "habit responding" ' (Mogg *et al.* 2005, p. 340) Loeber *et al.* (2009) reported a negative correlation between attentional bias score and duration of alcohol dependence, besides interpreting the results with the 'incentive-habit' theory, they pointed out the possible effect of cognitive impairment on working memory and attention concentration. In comparison, the negative correlation in the present study can also be explained with the dual-process theory and the 'incentive-habit' theory, but the possible role of cognitive impairment is much more complicated. Unlike alcohol, acute nicotine use has been confirmed as enhancing attention concentration (Henningfield & Goldberg 1983; Kassel 1997; Kassel & Unrod 2000; Lawrence, Ross & Stein 2002), although nicotine may have long term impairment on the cognition of elders (Zhou *et al.* 2003) and offspring (Milberger *et al.* 1996; Thapar *et al.* 2003). Pharmacological studies on rats showed that chronic nicotine administration also enhanced accuracy on an attention task (5-choice serial reaction time) (Semenova, Stolerman & Markou 2007), but nicotine withdraw caused performance deficits in the same task (Shoaib & Bizarro 2005; Semenova *et al.* 2007). Therefore we still need direct evidence to make a conclusion whether the lower attentional bias on heavy smokers was a result of cognition impairment caused by nicotine.

It seems intuitively reasonable that preconscious processing is automatic processing; therefore the preconscious attentional bias should be considered as reflecting smokers' automaticity on drug seeking, which should be positively correlated with cigarette dependence level. Such intuitive reasoning mistook attention as equaling to automaticity and also neglected the independent relationship between attention and awareness. Attention, by nature, is a kind of cognitive processing resources (Wickens 1991; Norman & Shallice 2000); allocation of attention can be affected by subjects' inner states such as addiction and emotion, considering the independence between attention and awareness, such affect should be consistent across awareness states. For example, in studies on emotional attentional bias, Mogg *et al.* repeatedly found high anxiety trait subjects showed greater attentional bias than low anxiety trait subjects, either in restricted aware condition (Mogg & Bradley 1999) or in aware condition (Mogg *et al.* 2000). It is worth further study why emotion and addiction has different effect on attentional bias (attentional bias is positively correlated with anxiety trait but negatively correlated with drug dependence level); the complex comparison between emotion and addiction is beyond discussion of this article. Nonetheless, it is reasonable to predict a negative correlation between preconscious attentional bias and cigarette dependence level rather than a positive one, considering the theoretical background and previous experimental reports in the above paragraph.

It is worth noting that when subjects were aware of the cigarette pictures, non-smokers also showed such bias. Experiment 2 with a common visual dot probe task (in supplementary material) further verified that such effect was paradigm independent (Supporting Information Figs S2 & S3). Although it appears counter-intuitive, it is not reported for the first time. A previous study also found non-smokers showed similar attentional bias as smokers when they were aware of the smoking focus of the experiment (Yaxley & Zwaan 2005). Considering that non-smokers in the current study lived in a highly smoking-exposed and smoking-encouraged environment, such bias was not unexpected because cigarette pictures were no longer neutral to them [studies showed that over 60% Chinese males smoke, compared to the 20%~30% ratio in North America and West Europe (Niu *et al.* 1998; Mackay & Eriksen, 2002; Yang *et al.* 2005; The Associated Press 2007)]. It is worth noting that non-smokers paid special attention on cigarette pictures out of completely different reasons as smokers; we preliminarily explored possible reasons such as disgust avoidance (see section 3 in supplementary material, non-smokers showed significantly higher disgust level to cigarette pictures than to object pictures, and their disgust levels were correlated with their attentional bias scores in aware condition but not in unaware condition), but the exact reason (s) for such bias were still unclear. Nonetheless, it is certain that all of the possible factors induced non-smokers' attentional bias through the modulation of awareness, because non-smokers showed no attentional bias in unaware condition. On the other hand, the comparatively lower mean attentional bias score of the smoker group was due to the negative scores of eight smokers (Fig. 2b, the eight orange triangles on the right of the dashed vertical line), which counteracted the group mean score. It is possible that some smokers consciously diverted their attention away from cigarette pictures, as indicated by the correlation between attentional bias scores in aware condition and scores of the 'Behavioral Choice-Melioration' subscale of WISMD-68 as well as our preliminary results that smokers with a negative attitude toward smoking had a significantly lower attentional bias than smokers with a positive attitude and more times of quit attempt (see section 4 in supplementary material). Previous studies also reported negative attentional bias on patients undergoing detoxification treatment out of active avoidance strategies (Noël *et al.* 2006; Townshend & Duka 2007) or inconclusive reason (Loeber *et al.* 2009).

Another important issue is the presentation duration of cuing stimuli. In the unaware condition of the present study, the cuing stimuli were presented for 800 ms with stable suppression of awareness. Previous studies showed that attention can be orientated without awareness (McCormick 1997; Mogg & Bradley 1999; Ivanoff & Klein 2003); in the current study, attentional bias in unaware condition was not correlated with any other evaluated factor (craving, attitude) except for the dependence level, indicating that volitional attention shift did not happen after initial orientation. In the aware condition, cuing pictures were presented for 200 ms, previously considered as reflecting attention orientation (Bradley *et al.* 2004; Field & Cox 2008). However, since the attentional bias was found to be affected by many factors in awareness, especially some smokers showed negative attentional bias, we cannot exclude the possibility that strategic attention shifting also happened in the 200 ms as a result of awareness modulation.

It is important to consider the limitations of the present study. For example, a CO assessment device such as a smokerlyzer was not applied in the current study, thus lacking an objective measurement for their smoking situation. Secondly, only male subjects were recruited considering the significant imbalance in the smoking ratio among males and females in China. Female smokers in a society that associates smoking with male characteristics may smoke out of very different motivations such as weight control or rebel against social norm (Chollat-Traquet 1992), therefore their attentional bias are worth a special study. It is also worth intensive study about the numerous potential factors contributing to the non-smokers' attentional bias, such as cross-culture comparison, investigation into their microenvironment, survey about their conceptions of the association between smoking and male characteristics, etc. Different cue exposure time can also be adopted in the current paradigm to reveal the different components in attentional bias and their different relationships with addiction characteristics (dependence level, craving, affective attribute to cigarettes, etc). It is also important to evaluate the possible cognitive impairment on heavy smokers, as well as its contribution to attentional bias. Beyond the visual probe paradigm and psychophysical technique, other paradigms and indexes can also be considered to evaluate the subliminal attentional bias, as did in previous studies on other kinds of stimuli (e.g. heroin, alcohol, cocaine, sex, etc.), such as Stroop task (Franken *et al.* 2000), heart rate (Ingjaldsson, Thayer & Laberg 2003), pictorial subliminal repetition priming task (Leventhal *et al.* 2008) and backward masking in functional neuroimaging (fMRI) (Childress *et al.* 2008).

Taken together, the current study provided evidence for the presence of preconscious attentional bias on cigarette smokers as well as the possibility of awareness modulation on attentional bias. Discovery of preconscious attentional bias on smokers can be attributed to the psychophysical approach we adopted. Several phenomenon in the aware condition of the experiment, such as non-smokers' attentional bias, and the influence of craving, attitude, and motives on smokers' attentional bias collectively indicated the strong influence of awareness modulation on attentional bias.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Figure S1 Photograph of the experimental apparatus.
Figure S2 Mean scores of RT (in s) when subjects responded to targets appearing at the location of smoking related and smoking unrelated cuing pictures.
Figure S3 The mean scores of attention bias (in ms with standard error bars) of non-smokers and smokers in Experiment 2 with visual dot probe task. Non-smokers rather than smokers had a mean bias score significantly different from zero ($P < 0.01$); but the two groups had no significant difference.

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