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J Psychopharmacol published online 17 August 2010
DOI: 10.1177/0269881110379284

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J Psychopharmacol OnlineFirst, published on August 17, 2010 as doi:10.1177/0269881110379284

Research Paper

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Journal of Psychopharmacology
0(0) 1–11
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Implicit and explicit selective attention to smoking cues in smokers indexed by brain potentials

Marianne Littel and Ingmar HA Franken

Abstract

Substance use disorders are characterized by cognitive processing biases, such as automatically detecting and orienting attention towards drug-related stimuli. However, it is unclear how, when and what kind of attention (i.e. implicit, explicit) interacts with the processing of these stimuli. In addition, it is unclear whether smokers are hypersensitive to emotionally significant cues in general or to smoking-related cues in particular. The present event-related potential study aimed to enhance insight in drug-related processing biases by manipulating attention for smoking and other motivationally relevant (emotional) cues in smokers and non-smokers using a visual oddball task. Each of the stimulus categories served as a target (explicit attention; counting) or as a non-target (implicit attention; oddball) category. Compared with non-smokers, smokers' P300 (350–600 ms) was enhanced to smoking pictures under both attentional conditions. P300 amplitude did not differ between groups in response to positive, negative, and neutral cues. It can be concluded from this study that attention manipulation affects the P300 differently in smokers and non-smokers. Smokers display a specific bias to smoking-related cues, and this bias is present during both explicit and implicit attentional processing. Overall, it can be concluded that both explicit and implicit attentional processes appear to play an important role in drug-related processing bias.

Keywords

Processing bias, smoking, ERP, P300, selective attention

Introduction

Drug use disorders are characterized by cognitive processing biases for drug-related stimuli (for reviews see Field and Cox, 2008; Field et al., 2006; Franken, 2003). It is hypothesized that drug users automatically detect and orient their attention toward drug-related stimuli, which in turn diminishes attentional resources left for alternative cues, enhances drug-related cognitions, and causes subjective craving (Franken, 2003). These processes are thought to have mutual excitatory relationships with each other. Consequently the drug user gets caught in a vicious circle of increasing attention and craving. Both craving and attentional bias have been associated with drug use and relapse (e.g. Killen and Fortmann, 1997; Marissen et al., 2006).

The emergence of these processing biases can be explained by the incentive-sensitization theory (Robinson and Berridge, 1993), which posits that repeated administration of a drug causes a sensitization of dopaminergic neurotransmission in the brain. Subsequently, both the drug itself and the drug-related stimuli acquire incentive-motivational properties. In other words, the sensitized dopaminergic system causes the drug and drug-related stimuli to be perceived as particularly salient, reinforcing, and 'wanted', which in turn leads to a greater allocation of attentional resources to them. This hypothesis is confirmed in studies among humans. Heroin users, for example, show less attention for drug-related stimuli after a single dose of the dopamine antagonist haloperidol (Franken et al., 2004).

Research confirms that drug users exhibit an excessive attentional focusing on drug-related cues. Utilizing attention tasks such as the emotional Stroop, dual-task procedures, the flicker-induced change blindness paradigm, and visual probe and attentional cuing tasks, attentional bias has been demonstrated in various drug use disorders, including smoking addiction (see Ehrman et al., 2002; Field and Cox, 2008; Mogg et al., 2003). For example, smokers are slower than non-smokers to colour-name smoking-related words on the smoking Stroop task (Munafo et al., 2003). Furthermore, smokers maintain their gaze on smoking stimuli longer than on neutral stimuli (Mogg et al., 2003).

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Event-related potential studies of addiction and craving

A relatively new approach to assess the processing of drug-related stimuli, and associated biases, is the measurement of event-related potentials (ERP) using electroencephalography (EEG) techniques. Two components of the ERP are of particular interest in drug use research: the P300 and the related slow positive wave. These components have been associated with attention allocation, intensity of processing, the closure of perceptual events and activation of immediate memory (Kok, 2001; Polich and Kok, 1995). Furthermore, it is assumed that enhancement of these late ERP components reflects motivational (emotional) engagement, motivated attention, and the activation of arousal systems in the brain (Cuthbert et al., 2000; Lang et al., 1997; Schupp et al., 2000).

ERP studies of visual processing in addiction show that these later ERP components are more enhanced in drug users than in controls in response drug-related stimuli. This result has been obtained in alcoholics (Herrmann et al., 2000; Herrmann et al., 2001; Namkoong et al., 2004), heroin users (Franken et al., 2003; Lubman et al., 2007, 2008), cocaine users (Franken et al., 2008; Van de Laar et al., 2004), cannabis users (Wölfling et al., 2008), and smokers (Littel and Franken, 2007; McDonough and Warren, 2001; Warren and McDonough, 1999). In all smoking cue-reactivity studies, a centro-frontally distributed enhancement of P300 amplitude has been found in response to smoking cues relative to neutral cues in smokers compared with non-smokers (Littel and Franken, 2007; McDonough and Warren, 2001; Warren and McDonough, 1999). Littel and Franken (2007) found an additional frontally distributed interaction effect on the slow positive wave (400–750 ms), which is in accordance with results from studies among patients addicted to other drugs (e.g. Franken et al., 2004; Van de Laar et al., 2004).

These ERP indices of processing biases are associated with subjective craving (for a review see Field et al., 2006; Franken, 2003). Research repeatedly shows that ERP waves, i.e. enhanced P300 and slow positive wave amplitudes, correlate significantly with subjective drug craving (Franken et al., 2004, 2003; Namkoong et al., 2004). A recent meta-analysis over all drugs of abuse found an overall correlation of $r = 0.37$ between late positive waves (including the P300 and slow positive wave) in passive viewing paradigms and self-reported craving (Field et al., 2009). However, it must be noted that not all ERP studies of addiction find correlations between processing bias and craving (Van de Laar et al., 2004).

Focusing on smoking studies only, a correlation between ERP amplitudes and craving for cigarettes is not unambiguously established. Warren and McDonough (1999) failed to find such a correlation, and Littel and Franken (2007) only found a correlation between P300 amplitude at the Fz electrode and the first subscale of the QSU-brief, 'desire and intention to smoke'.

In general, ERP measures of processing bias are moderately associated with self-reported craving. This association appears to be larger for illicit drugs compared with alcohol and tobacco (Field et al., 2009).

To recapitulate, it has become clear from these studies that smokers and non-smokers process smoking-related pictures differently. Because enhancement of late ERP components is associated with the allocation of attentional resources to motivational relevant stimuli (Cuthbert et al., 2000; Lang et al., 1997; Schupp et al., 2000), and is moderately correlated with subjective craving (Field et al., 2009), the enlarged P300 in the smoking studies is believed to be induced by the smokers' allocation of attentional resources toward information relevant to their tobacco-addicted, incentive-motivational states (Warren and McDonough, 1999). This would be in accordance with the aforementioned theories of addiction (Franken, 2003; Robinson and Berridge, 1993) and results from the majority of behavioural studies employing paradigms like the Stroop and visual cuing tasks (Field and Cox, 2008).

Role of attention in ERP processing bias

However, all ERP smoking cue-reactivity studies used passive viewing paradigms in which attention was not manipulated. Moreover, it is still unclear how, when and what kind of attention (i.e. implicit, explicit) interacts with the electrophysiological processing of drug-related stimuli in drug dependent patients. As far as we know, there have only been two studies that used ERP methodology outside a passive viewing paradigm (Fehr et al., 2006, 2007). Fehr and colleagues presented smokers and non-smokers with a smoking-related Stroop task and a smoking-related picture–colour matching task while measuring ERP. On both tasks, smokers displayed a right-frontal relative positivity in the P300 time frame that appeared to be associated with cue interference, indicating a possible association between P300 amplitude and attentional processing. Furthermore, Fehr et al. (2006) showed a P100 modulation for verbal smoking-related stimuli, which might indicate that smokers are affected by smoking-related stimuli during very early stages of information processing. However, in addition to the smoking words and pictures, Fehr et al. (2006, 2007) used 'secondary smoking words and pictures', such as bus stop and kiosk, for which it is unknown to what extent they affect cue reactivity, task interference and/or craving in smokers. Moreover, non-smokers also showed some interference effects – although at different electrode sites – and these effects were not exclusively elicited by smoking-related words and pictures. To conclude, because the present focus and methodology fairly differs from the focus and methodology used in the aforementioned smoking cue-reactivity studies, it is difficult to make comparisons and draw conclusions regarding the issue at hand, i.e. the exact role of attention in ERP processing bias.

Specificity of processing bias

Apart from this issue, it is also unclear whether drug users' enhanced ERP response is uniquely triggered by drug-related cues, i.e. whether there is a selective bias for drug cues, or whether drug users are hyperresponsive to motivational relevant stimuli in general, such as to positively or negatively valenced pictures with certain arousing properties. For example, Stormark et al. (2000) found a greater Stroop interference for negatively valenced words in alcohol-dependent patients

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compared with healthy controls. In line with this, Bauer and Cox (1998) showed that differences between alcoholics and controls in Stroop interference for alcohol-related words disappeared when making use of affective control stimuli. Furthermore, cocaine abusers with high craving levels displayed a more enlarged slow positive wave in response to emotional valenced stimuli than low-level cocaine cravers (Franken et al., 2004). In contrast, Lubman et al. (2008) demonstrated that heroin abusers only displayed P300 processing biases for heroin-related cues. However, no differences were found between P300 amplitudes in response to affective cues and neutral cues, whilst the control group did show significant differences between these. Instead of a hyperreactivity, these results would support a hyporeactivity to emotionally significant stimuli. Recently, Lubman et al. (2009) replicated these findings. Using a variety of psychophysiological measures, they convincingly showed that heroin users demonstrated reduced responsiveness to natural reinforcers, i.e. pleasant stimuli. A plausible explanation for these enhanced and decreased responses to emotional cues might be impaired affect regulation, which is often linked to drug abuse (e.g. Thorberg and Lyvers, 2006).

Unfortunately, research on the processing of general emotional stimuli among smokers is limited. It has been shown that nicotine administration (nicotine patches) directly affects emotional processing in that amplitudes evoked by emotionally negative pictures are enhanced compared with amplitudes evoked by emotionally neutral and positive pictures (Gilbert et al., 2004). When employing a difficult information processing task, nicotine decreases distraction by negative and smoking-related stimuli and promotes attention to task-related stimuli (Gilbert et al., 2007). Nevertheless, these results reflect the direct pharmacological effects of nicotine intake, and cannot be generalized to cue-reactivity due to smoking status.

Present study

Attention is thought to play a major role in smoking-related processing biases, but it is not fully understood whether this role is implicit, explicit or both. In addition, it is unclear whether smokers are hypersensitive to emotionally significant cues in general or to smoking-related cues in particular. Therefore, the main goal of the present study was to enhance insight into smoking-related processing bias by manipulating attention (explicit or implicit) for smoking cues and other motivationally relevant cues, i.e. positive and negative cues, in smokers and non-smokers.

The relationship between attention and motivational significance was recently studied by Schupp et al. (2007) utilizing a rapid and continuous stream of positive, negative and neutral pictures, with each picture category serving as target and non-target in separate series (oddball paradigm). Targets were explicitly attended (silently counted); non-targets were assumed to be implicitly attended, since it is widely believed that emotional stimuli are intrinsically significant and command priority processing (Vuilleumier, 2005). It was demonstrated that explicit attention and emotional significance effects operated additively on earlier processing stages (early posterior negativity (EPN); 200–350 ms), but synergistically on later ERP components (P300; 400–600 ms). In other words, the interaction of emotion and attention appears to be merely present at later information processing stages.

The present study utilizes an adapted version of the abovementioned design of Schupp et al. (2007). In order to investigate drug-related processing biases, we added a third oddball category, i.e. a category of smoking-related pictures, and a second group of participants, i.e. smokers. No passive viewing condition was employed. Since in previous addiction research results have only been obtained on later components of the ERP, and because we are mainly interested in the abovementioned emotion–attention interaction, the focus of the present study will be on the P300. As Fehr et al. (2006) showed a P100 modulation for verbal smoking-related stimuli, the early ERP components (P100 and N100) will be exploratively investigated.

Hypotheses

The main hypothesis of the current study is that smokers will display a processing bias similar to the biases found in previous studies (Littel and Franken, 2007; McDonough and Warren, 2001; Warren and McDonough, 1999). This bias will be stronger for smoking cues than for general emotional cues and will be present under both implicit and explicit attention conditions. The P300 will be larger for smokers than non-smokers in response to smoking cues compared with positive, negative and neutral cues. P300 amplitude will be larger for explicitly attended stimuli. Yet, since it is hypothesized that attentional bias is at least partly implicit in nature (e.g. Mogg et al., 2003), we also expect to find group differences and differences between the stimulus types in the implicit attention condition.

Since there is evidence that attentional bias is associated with craving levels (Field et al., 2006, 2009; Franken, 2003), we assessed smokers' subjective craving scores before and after the task. It is hypothesized that craving levels will increase between pre- and post-test, and that this increase will be correlated with P300 magnitude. Furthermore, the present study investigated the differences between smokers and non-smokers on arousal and valence judgments of the positive, negative and smoking-related pictures. Previous studies show that smokers evaluate smoking-related pictures more positively than neutral stimuli (Geier et al., 2000; Hogarth and Duka, 2006; Mogg et al., 2003), whereas non-smokers evaluate them more negatively than neutral stimuli (Mogg et al., 2003). As positive, negative, and smoking pictures were matched on arousal levels, we expect all pictures to be equally arousing for smokers. For non-smokers, we expect the emotional stimuli to be more arousing. Correlations between arousal and valence, carbon monoxide (CO) level, nicotine dependence and P300 amplitude will be investigated in order to receive more information on the factors that modulate the P300.

Method

Participants

A total of 27 smokers and 27 non-smokers were recruited at the Erasmus University Rotterdam (the Netherlands).

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They were all students and received either course credit or financial compensation for participation. Smokers were included if they smoked >10 cigarettes a day. Smokers (mean age 23.3 years, SD = 3.1 years) had a smoking duration of 7.1 years (SD = 3.0), smoked 15.1 cigarettes a day on average (SD = 5.3), had a mean score of 3.8 (SD = 1.9) on the Fagerström Test for Nicotine Dependence (FTND) (Vink et al., 2005), and had a mean CO level of 12.5 parts per million (Ppm) (SD = 7.5) at the time of testing. Non-smokers (mean age 21.7 years, SD = 2.3) had smoked 2.6 (SD = 7.8) cigarettes in their lifetime. They had a mean CO level of 1.0 Ppm (SD = 1.2) and differed significantly from smokers on this last measure, $t(52) = 7.85$, $p < 0.001$. Smokers (33.3% male) and non-smokers (29.6% male) did not differ on sex ratio, χ^2 (1) = 0.09, $p = 1$, and the number of ambidextrous, right- and left-handed participants was equal in both groups χ^2 (2) = 0.86, $p = 0.65$. The participants provided written informed consent for the protocol approved by the institutional ethical board.

Experimental stimuli

Stimuli consisted of 150 neutral pictures, 22 positive pictures (animals), 22 negative pictures (garbage), and 22 smoking-related pictures (smoking-related attributes, e.g. cigarettes and lighters, and people smoking). Oddball pictures were selected from one category to prevent category effects. All of the neutral pictures, all of the positive pictures, and six of negative pictures were selected from the International Affective Picture System (IAPS) (Lang, 1995). The other 16 negative pictures were selected via internet search. The 22 smoking pictures were selected from a database and were the same as those used in a previous study (Littel and Franken, 2007).

Previous studies indicate that smoking-related pictures are only moderately arousing for smokers (e.g. Littel and Franken, 2007), so the positive and negative pictures in this study could not be too arousing either. Instead of the erotic and mutilation pictures that are usually adopted in studies of emotion, we chose to present subjects with somewhat less arousing animal and garbage pictures. This way we were able to match the arousal levels of the positive, negative and smoking stimuli (4.5, 4.5 and 4.6, respectively), and thus to control for the effects of non-specific arousal on ERP amplitude.

To make sure that our positive pictures were more positively valenced than our negative pictures, the most positively valenced positive ($M = 7.3$) and most negatively valenced negative pictures ($M = 3.2$) were selected from the IAPS. Participants rated all pictures on arousal and valence properties.

Procedure

Smokers were instructed to abstain from smoking for at least 1 h in order to avoid direct effects of nicotine on task performance and ERP signals. They were told that this would be checked with a smoke analyser. Subjects were tested alone in a light and sound-attenuated room. After obtaining written informed consent, subjects proceeded to a non-invasive CO Ppm estimate using the EC50 Micro III Smokerlyzer® (Bedfont Scientific, Medford, NJ, USA), a portable device which measures breath CO levels. In addition, subjects filled out questionnaires about demographics, smoking history, cigarette craving (smokers) and smoking dependence (smokers). After completion, participants were seated in a comfortable chair and electrodes were attached. Then the task was explained and instructions were given.

The experiment consisted of three separate stimulus conditions. In each condition, subjects were asked to silently count the (1) animal, (2) garbage, or (3) smoking pictures. The order of the three stimulus conditions was counterbalanced across subjects. Within each condition, pictures from every category, including the neutral category, were repeated three times, resulting in 66 animal, 66 garbage and 66 smoking pictures (132 not counted/implicitly attended; 66 counted/explicitly attended) per condition. Pictures were presented for 333 ms in a continuous stream without perceivable inter-stimulus intervals. This fast-stimulus presentation procedure was adopted from Schupp et al. (2007) and served to enhance attention for the stimuli by increasing perceptual demands and making the identification of target stimuli more challenging. The pictures were presented in a perceptually random order. However, there were no successions of two or more targets or non-targets (Figure 1).

At irregular intervals, the stream of pictures was stopped and subjects were asked to report the number of target pictures they had identified. They had to make a choice between four on-screen options by pressing a corresponding button. Participants immediately received feedback (correct or incorrect). All answers were recorded. The tests and test intervals were the same for all participants.

After the picture viewing, electrodes were removed and smokers filled out the craving questionnaire for the second time. Subsequently, all participants rated the pictures on their valence and arousal properties. Both for stimulus presentation and valence and arousal judgments e-prime® software (Psychology Software Tools, Pittsburgh, PA, USA) was used.

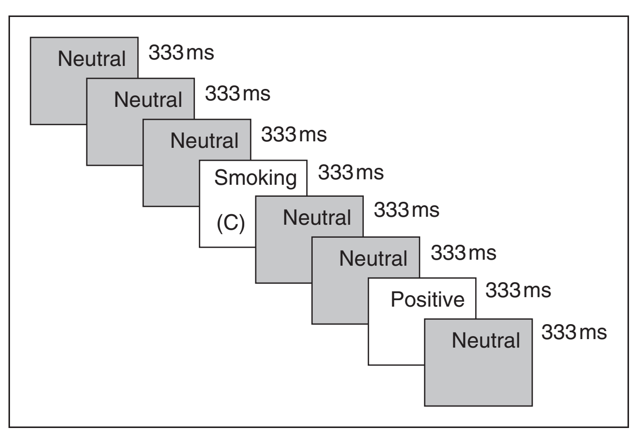

Figure 1. Study design. Participants were presented with three blocks of frequent neutral pictures and infrequent (oddball) smoking, animal and garbage pictures, all presented for 333 ms. In each block they had to count pictures from one of the three categories (C).

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Self-report measures

Smoking history and demographic data were self-reported (sex, age, smoking duration, number of cigarettes a day). Handedness was measured with a 10-item Dutch handedness questionnaire, the 'Vragenlijst voor handvoorkeur' (Van Strien, 1992), which has been shown to have excellent reliability.

Smoking dependence was measured by the Dutch version of the FTND (Vink et al., 2005), which has good reliability and holds a significant correlation with number of cigarettes smoked per day. The FTND is composed of six items, which are scored according to the scoring system described in Heatherton et al. (1991).

Subjective craving was assessed by means of the QSU-brief (Cox et al., 2001; Littel et al., in press). This questionnaire was adapted from the Questionnaire on Smoking Urges (QSU) (Tiffany and Drobes, 1991) and consists of two subscales: 'desire and intention to smoke' (reward-craving) and 'the relief from nicotine withdrawal or negative affect' (withdrawal-craving). The QSU-brief and its subscales have adequate psychometric properties (Cox et al., 2001).

Arousal and valence properties of the positive, negative, and smoking-related pictures were assessed by a computerized Self Assessment Manikin (Bradley and Lang, 1994), which is a non-verbal pictorial assessment technique that directly measures the pleasure and arousal associated with a person's affective reaction to stimuli. The arousal scale ranged from a relaxed, sleepy figure to an excited, wide-eyed figure; the valence scale ranged from a frowning, unhappy figure to a smiling, happy figure.

EEG recording and signal processing

The EEG was recorded with a digital Active-Two system (BioSemi, Amsterdam, the Netherlands), using active Ag/AgCl electrodes at 34 scalp sites according to the International 10/10 system (Dien and Santuzzi, 2005; 32 standard channels mounted in an elastic cap and two mastoid locations, which were used for off-line re-referencing). The vertical electro-oculogram (VEOG) was recorded with two active Ag/AgCl electrodes located above and underneath the left eye. The horizontal electro-oculogram (HEOG) was recorded with two Ag/AgCl electrodes located at the outer canthus of each eye. An additional active electrode (common mode sense) and a passive electrode (driven right leg) were used to comprise a feedback loop for amplifier reference. All signals were digitized with a sampling rate of 512 Hz, a 24-bit A/D conversion, and a low-pass filter of 134 Hz. Off-line, data were processed with BrainVision Analyzer 2 (Brain products GmbH, Munich, Germany).

First of all, the EEG signals were referenced to the mathematically linked mastoids and EEG and EOG were phase-shift-free filtered using a 0.1–30 Hz (24 dB/Octave roll off) band-pass filter. EEG and EOG recordings were segmented in 800 ms epochs, including 100 ms pre-stimulus baseline. For correction of vertical and horizontal eye movements and eye blinks we applied automatic processing algorithms, i.e. Gratton and Coles algorithm (Gratton et al., 1983). After ocular correction, the ERPs were baseline corrected. Artifact rejection criteria were minimum and maximum baseline-to-peak -75 to $+75\,\mu V$, and a maximum allowed voltage skip (gradient) of $50\,\mu V$. Epochs were averaged across trials. Number of artifact-free epochs did not differ between groups and stimulus conditions (smoking-explicit: smokers $M = 63$, non-smokers $M = 64$; positive-explicit: smokers $M = 64$, non-smokers $M = 65$; negative-explicit: smokers $M = 63$, non-smokers $M = 64$; smoking-implicit: smokers $M = 127$, non-smokers $M = 129$; positive-implicit: smokers $M = 127$, non-smokers $M = 129$; negative-implicit: smokers $M = 127$, non-smokers $M = 129$; all p-values ns).

Overall grand averages were obtained for each attention condition and picture category in the two groups, yielding six conditions per group (smoking explicitly attended; smoking implicitly attended/oddball; positive-explicit; positive-implicit; negative-explicit; negative-implicit).

Analyses

Resulting ERP waves were visually inspected and both a N100 (maximum negative peak in the time window from 50–80 ms) and a P100 (maximum negative peak in the time window from 110–150 ms) were identified. In contrast to Schupp et al. (2007), no clear EPN could be observed. Most important, in the 350–600 ms time window a clear P300 was identified. For each component, mean activities (average amplitude in the time window) were computed per group, attention and stimulus category.

Due to the short stimulus presentations and the absence of inter-stimulus intervals, P300 waveforms overlapped with waveforms of the following stimuli, resulting in somewhat deviant amplitude values. Nevertheless, it is unlikely that this has confounded the results. First of all, positive, negative, and smoking pictures never appeared in succession, but were always followed by neutral pictures with low arousal and moderate valence levels. Accordingly, neither the attention nor the stimulus effect is likely to be contaminated by systematic differences in emotional valence of the subsequent stimuli. Second, the P300 appeared with similar polarity, topography and latency as in previous studies (see Schupp et al., 2007; Figures 2–6).

For the P300, ERP effects were assessed by performing repeated measurement analyses of variance (ANOVA) on crossed lateral and caudal sites, including 15 electrodes (F7, F3, Fz, F4, F8, T7, C3, Cz, C4, T8, P7, P3, Pz, P4, P8), resulting in a 5 (laterality) $\times$ 3 (caudality) $\times$ 2 (attention) $\times$ 3 (stimulus) $\times$ 2 (group) repeated measures ANOVA. Since N100 and P100 components are predominantly present at posterior electrodes (PO3, O1, Oz, O2, and PO4), two 5 (electrode site) $\times$ 2 (attention) $\times$ 3 (stimulus) $\times$ 2 (group) repeated measures ANOVAs were conducted for these components.

Arousal and valence ratings of the pictures and results of the counting task were analysed using three 3 (stimulus) $\times$ 2 (group) repeated measurement ANOVAs. To examine exact differences for the significant group, stimuli, and attention condition interactions, pairwise post-hoc follow-up analyses with Bonferroni correction were applied to all ANOVAs. Greenhouse–Geisser correction was applied to all ANOVAs (uncorrected degrees of freedom (df) are reported).

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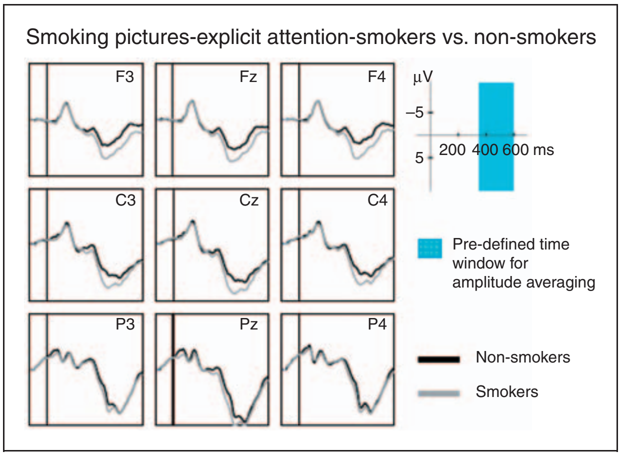

Figure 2. Average event-related potentials at nine electrode sites for smokers (grey) and non-smokers (black) in response to explicitly attended smoking stimuli.

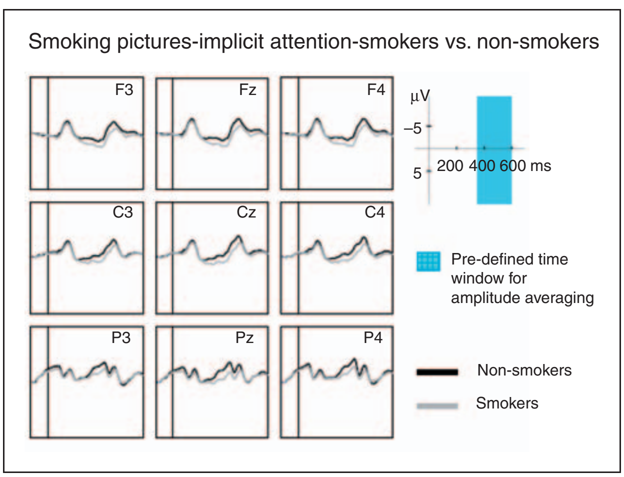

Figure 3. Average event-related potentials at nine electrode sites for smokers (grey) and non-smokers (black) in response to implicitly attended smoking stimuli.

To determine whether craving was significantly increased after picture viewing, a paired *t*-test was performed (pre-versus post-test craving). To assess relationships between cue-evoked ERP amplitudes, self-reported craving, CO level, nicotine dependence level, and valence/arousal assessments, Spearman correlation coefficients were calculated between significant ERP amplitudes, increases in craving between pre- and post-measure, CO measures, FTND score, and valence/arousal judgments. An alpha-level of 0.05 was used for all statistical tests.

Results

Behavioural and self-reported data

Counting task. On the counting task, no Stimulus (S) × Group (G) interactions were found, $F_{2,104} = 0.14$,

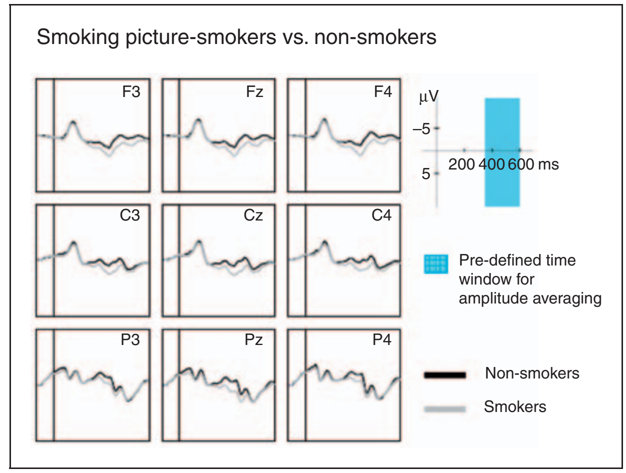

Figure 4. Average event-related potentials at nine electrode sites for smokers (grey) and non-smokers (black) in response to smoking stimuli.

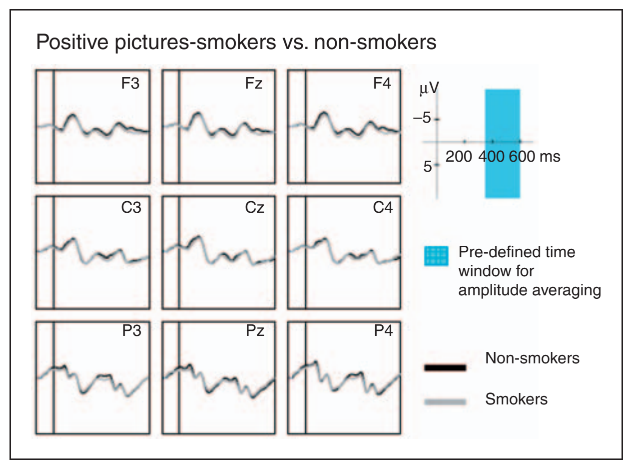

Figure 5. Average event-related potentials at nine electrode sites for smokers (grey) and non-smokers (black) in response to positive stimuli.

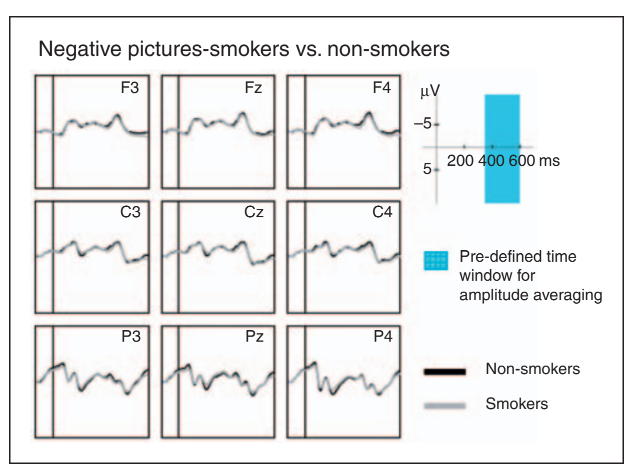

Figure 6. Average event-related potentials at nine electrode sites for smokers (grey) and non-smokers (black) in response to negative stimuli.

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$p = 0.87$, indicating that smokers and non-smokers counted stimuli from the positive, negative, and smoking-related stimulus conditions equally well.

Craving. QSU score increased significantly between the first measure (before the task; $M = 18.19$, $SD = 13.70$) and the second measure (after the task; $M = 40.44$, $SD = 13.73$), $t(26) = 2.71$, $p < 0.05$. This effect appeared to be driven by the increase in scores on the first subscale, 'desire and intention to smoke', $t(26) = 2.78$, $p < 0.05$. There was no increase in scores on the second subscale, 'the relief from nicotine withdrawal or negative affect with an urgent and overwhelming desire to smoke', although there was a trend to significance, $t(26) = 1.91$, $p = 0.07$.

Arousal and valence. On both arousal and valence judgments significant S × G interactions were found, respectively $F_{2,104} = 10.48$, $p < 0.001$ and $F_{2,104} = 21.49$, $p < 0.001$. Smokers rated smoking pictures as significantly more arousing than non-smokers, $t(52) = 3.01$, $p < 0.01$. They also found smoking pictures more positive than non-smokers, $t(52) = 6.42$, $p < 0.001$. Groups did not differ on valence and arousal judgments of the positive and negative pictures (all p-values > 0.25). As intended, there was no difference within the smokers group between arousal of smoking, negative, and positive cues (all p-values > 0.22). Non-smokers also found positive pictures as arousing as negative pictures, $t(26) = 1.19$, $p < 0.001$. However, smoking pictures were rated by non-smokers as less arousing than positive and negative cues, respectively $t(26) = 4.25$, $p < 0.001$ and $t(26) = 6.19$, $p < 0.001$.

Smokers rated positive pictures more positively than smoking cues and negative cues, respectively $t(26) = 2.51$, $p < 0.05$ and $t(26) = 14.21$, $p < 0.001$. Negative pictures were rated more negatively than smoking pictures, $t(26) = 8.92$, $p < 0.001$. The same pattern was observed in non-smokers: smoking pictures were more positive than negative pictures, $t(26) = 4.63$, $p < 0.001$, but more negative than positive pictures, $t(26) = 12.78$, $p < 0.001$, and positive cues were rated as more positively than negative cues, $t(26) = 15.13$, $p < 0.001$. See Table 1 for all mean arousal and valence ratings.

Table 1. Mean self-reported arousal and valence ratings (SD) of the smokers and non-smokers

		Smokers	Non-smokers
Arousal	Positive	3.6 (1.5)	3.6 (1.7)
	Negative	3.4 (1.3)	4.0 (2.0)
	Smoking	3.8 (2.2)	2.3 (1.3)
Valence	Positive	6.8 (0.9)	6.8 (0.9)
	Negative	2.4 (1.1)	2.6 (1.1)
	Smoking	5.9 (1.4)	3.6 (1.2)

Electrophysiological data

P300. On the P300 wave, a significant S × G interaction effect was found, $F_{2,104} = 3.36$, $p < 0.05$. Post-hoc comparisons revealed that smokers and non-smokers did not differ on P300 amplitude in response to positive stimuli ($p = 0.15$) and negative stimuli ($p = 0.54$). However, smokers' P300 response to smoking-related pictures was significantly larger than that of non-smokers ($p < 0.01$). See Figures 4–6 for P300 amplitudes in response to smoking, positive, and negative cues.

Furthermore, a significant S × G × Attention (A) interaction was observed, $F_{2,104} = 3.04$, $p = 0.05$. Post-hoc analyses showed that the aforementioned significant interaction between smokers and non-smokers of P300 amplitude to smoking-related pictures was present in both the implicit and the explicit attention condition ($p = 0.035$ and 0.003, respectively). See Figures 2 and 3 for P300 amplitudes to implicitly and explicitly attended smoking cues. In neither of the attention conditions smokers and non-smokers differed in their P300 response to negative and positive stimuli (all p-values ns).

In addition, a significant Lateral (L) × S × G interaction effect was found. Smokers displayed a significantly more enhanced P300 amplitude in response to smoking cues than non-smokers on all five lateral clusters (F7, T7, P7, $p = 0.05$; F3, C3, P3, $p = 0.004$; Fz, Cz, Pz, $p = 0.002$, F4, C4, P4, $p = 0.002$; and F8, T8, P8, $p = 0.036$). On neither of the lateral clusters smokers and non-smokers differed in P300 amplitude elicited by positive and negative cues (all p-values ns).

In addition to the group effects, a significant main effect for Stimulus (S), $F_{2,104} = 69.42$, $p < 0.001$, a significant main effect for Attention (A), $F_{1,52} = 238.90$, $p < 0.001$, and a significant A × S interaction, $F_{2,104} = 55.66$, $p < 0.001$, was found. P300 amplitude in response to negative pictures was smaller than P300 amplitude in response to smoking and positive pictures (both p-values < 0.001). Furthermore, P300 in response to explicitly attended stimuli was more enhanced than in response to implicitly attended stimuli ($p < 0.001$). In the explicit attention condition, P300 responses to all stimuli differed from each other (smoking > positive > negative; all p-values < 0.01), whereas in the implicit attention condition responses to negative and smoking-related pictures did not (positive > negative, smoking; ns).

Early components. In contrast to the P300, neither on the P100 peak nor on the N100 peak were group interaction effects found, all p-values ns.

On the P100, both a significant Stimulus effect, $F_{2,104} = 5.37$, $p < 0.05$, and a significant Attention effect, $F_{1,52} = 10.34$, $p < 0.01$, were found. Post-hoc comparisons revealed that positive stimuli elicited larger P100 amplitudes than smoking stimuli ($p < 0.05$), and that there was a trend for negative stimuli to elicit more positive P100 amplitudes than smoking stimuli ($p = 0.06$). There was no difference between P100 in response to negative cues and P100 in response to positive cues. The P100 amplitude in response to implicitly attended stimuli appeared to be larger than in response to explicitly attended stimuli ($p < 0.01$).

On the N100 peak, both a significant Stimulus effect, $F_{2,104} = 35.97$, $p < 0.001$, and a significant Attention effect were found, $F_{1,52} = 37.67$, $p < 0.001$. Post-hoc tests showed that both negative and smoking stimuli evoked larger N100

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amplitudes than positive stimuli (both p-values < 0.01), but they did not differ from each other. Explicitly attended stimuli elicited larger N100 amplitudes than implicitly attended stimuli ($p < 0.001$). Furthermore, a significant A × S interaction effect, $F_{2,104} = 19.72$, $p < 0.01$ was observed. The enlargement of the N100 evoked by negative stimuli did not differ between the implicit and explicit attention condition, whereas the N100 in response to positive and smoking pictures was more enlarged in the explicit than in the implicit condition (both p-values < 0.001).

Correlations

Nicotine dependence and CO level. In smokers, CO level correlated significantly with P300 amplitude to explicitly attended smoking cues on electrodes F4 ($\rho = 0.40$, $p < 0.05$) and F8 ($\rho = 0.47$, $p < 0.05$), indicating that more enhanced CO levels are related to more enhanced right-frontal P300 amplitudes in response to explicitly attended smoking stimuli. No correlations were found between FTND score and P300 in response to smoking, positive or negative stimuli.

Craving. Increases on the QSU-brief were negatively correlated with the P300 to explicitly attended smoking cues on electrodes Pz ($\rho = -0.38$, $p < 0.05$) and F8 ($\rho = -0.39$, $p < 0.05$), indicating that decreases in subjective craving are related to more enhanced right-central/parietal P300 waves in response to explicitly attended smoking stimuli. No other significant correlations between ERP amplitude and subjective craving were found.

Arousal and valence. In the smokers group analyses revealed no correlations between arousal and valence judgments of the smoking pictures and ERP amplitude in response to the smoking pictures.

Discussion

The main goal of the present study was to examine smoking-related processing bias by manipulating attention (i.e. explicit versus implicit conditions) for smoking cues and other motivationally relevant cues (i.e. positive and negative cues) in smokers and non-smokers. It was hypothesized that in both attention conditions the P300 would be larger for smokers than non-smokers in response to smoking cues compared with positive, negative and neutral cues.

This hypothesis is confirmed by the results of the present study. P300 amplitude in response to smoking-related cues was more enhanced in smokers than in non-smokers, irrespective of attention condition. This implies that smokers display a processing bias that is similar to biases observed in previous smoking studies (Littel and Franken, 2007; McDonough and Warren, 2001; Warren and McDonough, 1999) and other addiction studies (Franken et al., 2003, 2008; Herrmann et al., 2000, 2001; Lubman et al., 2007, 2008; Namkoong et al., 2004; Van de Laar et al., 2004; Wölfling et al., 2008).

Moreover, this processing bias is present during both implicit and explicit attention. The results show that when smoking-related stimuli are presented as oddballs in a continuous stream of neutral stimuli, they automatically attract smokers' attention to a greater extend than non-smokers' attention. So, even when the smokers are instructed to pay attention to non-smoking cues, they automatically and unintentionally pay attention to smoking-related stimuli. In addition, if instructions are to explicitly pay attention to and count the smoking-related stimuli, smokers do this in a more elaborate and/or motivated way than non-smokers.

Moreover, smokers and non-smokers did not differ in P300 amplitude to positive and negative stimuli in general, confirming the hypothesis that smoking-related processing bias is very selective and specific and is not caused by some sort of hyper-responsivity to motivationally relevant stimuli in general. This is partly in line with a study among heroin users (Lubman et al., 2008), showing that heroin users only exhibit ERP processing biases for heroin-related cues. However, in contrast to this study and the Lubman et al. (2009) study, no hyporeactivity to emotional stimuli was found either. Smokers appear to respond normal to general motivationally relevant stimuli.

Early components of the ERP

In line with the majority of addiction ERP studies, no differences were found between smokers and non-smokers on the P100 and N100 components of the ERP, indicating that there are no differences between these groups with regard to early oriented attention for implicitly or explicitly attended smoking-related stimuli. This is in contrast with the results of Fehr et al. (2006). Smokers in their study showed increased P100 and N100 amplitudes in response to Stroop interference caused by smoking-related words. The discrepancy between the studies might be explained by the fact that the present study did not comprise any interference, i.e. there was no information to be consciously ignored during neither attention conditions. Furthermore, our study did not comprise any reading, because our experiment consisted of pictures instead of (primary and secondary) words.

Behavioural measures

Although it has been demonstrated that ERP processing biases are related to subjective craving (e.g. Field et al., 2009), in smokers no clear-cut relation has yet been found. In the present study craving increased between pre- and post-task measures, but this increase correlated negatively with P300 amplitude on two right-central/parietal electrode sites. Although this is difficult to explain from a theoretical point of view, it might be that attending to the smoking cues in this paradigm is quite difficult and associated with increased cognitive efforts and therefore reduced craving.

Perhaps craving for cigarettes cannot be compared with craving for other, illicit drugs, for which the correlation with ERP amplitude is clearer and always positive (Field et al., 2009). The period of abstinence is considerably shorter (1–2 h compared with > 2 weeks; e.g. Lubman et al., 2008), cigarettes are evidently more readily available than illicit drugs, and in smoking addiction both the pleasurable effects and withdrawal symptoms are of less relevance.

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Arousal and valence ratings of the smoking-related pictures did not correlate with P300 amplitude to implicitly or explicitly attended stimuli. In contrast, CO level correlated with P300 amplitude to explicitly attended smoking stimuli on several frontal electrode sites. Higher CO levels are related to more enhanced right-frontal P300 amplitudes in response to explicitly attended smoking stimuli.

To summarize, smokers display an increase in craving between the first measure (before the task) and the second measure (after the task). Besides, they find smoking pictures more positive and more arousing than non-smokers. In contrast with several studies on illicit drugs (e.g. Franken et al., 2003; Lubman et al., 2008), but in line with studies in smokers (e.g. Warren and McDonough, 1999), these measures do not have an unequivocal relationship with ERP responses. However, CO level and nicotine dependence level appear to have some relation to frontal ERP responses, but only in the explicit attention condition, indicating that more severe smokers might process smoking-related stimuli in a more elaborate and/or motivated way than lighter smokers, whereas it is possible that they do not differ in their automatic and unintended attention to smoking-related stimuli.

Limitations

In the present study the emotional stimuli had relatively moderate levels of valence. This can be interpreted as both a strength and a weakness. As we were able to match arousal levels, the P300 differences we found could not be ascribed to arousal differences. However, the negative pictures elicited amplitudes substantially smaller than what is commonly seen in ERP studies of emotion. This might have been caused by the fact that some of the pictures in the negative (garbage) category were more difficult to recognize and categorize than pictures in the positive (animal) and smoking categories. After all, garbage is a broadly based concept that includes dirt, trash, rubbish bags, litter bins, etc. It is possible that not all garbage pictures in either the explicit and implicit attention condition actually captured attention. However, garbage pictures elicited enhanced P100 and N100 amplitudes and were rated significantly more negative than positive and smoking pictures, providing support for the suitability of the present research design. Another explanation for the reduced amplitudes to negative pictures is that the negative pictures were inanimate, whereas the positive pictures were animate. However, smoking pictures were both animate and inanimate, but still yielded the largest ERP effects.

The short stimulus presentations in combination with the absence of inter-stimulus intervals caused the P300 waveforms to overlap with the waveforms of subsequent stimuli. This resulted in divergent P300 amplitudes and makes it difficult to directly compare our study with other studies. Nevertheless, it is unlikely that it has confounded the (group) effects. First of all, positive, negative and smoking pictures never appeared in succession, but were always followed by neutral pictures with low arousal and average valence levels. Accordingly, neither the attention nor the stimulus effect is likely to be contaminated by systematic differences in emotional valence of the subsequent stimuli. Moreover, the P300 appeared with similar polarity, topography and latency as in previous studies (see Schupp et al., 2007; Figures 2–6).

Of course it is possible that because of the fast-stimulus presentations and the absence of perceivable inter-stimulus intervals, participants elaborated less on the pictures. However, we had several reasons to present the stimuli this way. First of all, we wanted to enhance attention for the stimuli by increasing perceptual demands and making the counting more challenging. Second, we wanted the implicit stimuli to be as implicit as possible, but still visible and not different from the explicit stimuli. Finally, we did not want the task to last too long, to prevent participants from getting bored and drowsy. In addition, we wanted to adopt the procedure which was published by Schupp et al. (2007), and which turned out to be an adequate method to investigate implicit and explicit attention.

It should be noted that in the present study only the explicit attention condition, and not the implicit condition, calls upon working memory capacity because of the intermediate storage and rehearsal of counted numbers in short-term memory. This might have interacted with category-related picture processing in the counting, but not in the pure oddball task. However, if working memory capacity interacts with picture processing, this would very likely be the case in both smokers and non-smokers and probably does not account for the ERP differences we found between the groups on both the implicit and explicit processing of smoking pictures.

Another point that should be noted in future research is that data on number of cigarettes smoked before testing as well as time to the last cigarette were not questioned, whereas these variables might co-vary with cue reactivity and craving.

Conclusion

The current ERP study is the first to demonstrate that smokers display a processing bias that cannot be attributed to hyperreactivity to motivationally relevant cues in general or to hyporeactivity to emotional cues, but is specific to smoking-related cues. Moreover, this is the first ERP study in which smokers' attention for smoking cues is manipulated, and it can be concluded that processing bias is present in both explicit and implicit attentional processing. Smokers display both an implicit and explicit attentional bias to smoking cues in particular.

Concerning the societal impact, these results emphasize that enlarged P300 amplitudes in response to both implicitly and explicitly presented drug cues may provide an indicator of important psychological mechanisms relevant to addiction. Therefore, future research should also focus on the possibilities to change drug-related implicit and explicit attentional biases.

Funding

This work was supported by a VIDI grant funded by the Netherlands Organization for Scientific Research (NWO).

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