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#### Full length article

# Neural correlates of cigarette health warning avoidance among smokers

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#### ABSTRACT

*Background:* Eye-tracking technology has indicated that daily smokers actively avoid pictorial cigarette package health warnings. Avoidance may be due to a pre-cognitive perceptual bias or a higher order cognitive bias, such as reduced emotional processing. Using electroencephalography (EEG), this study aimed to identify the temporal point at which smokers' responses to health warnings begin to differ. *Method:* Non-smokers (n = 20) and daily smokers (n = 20) viewed pictorial cigarette package health warnings and neutral control stimuli. These elicited Event Related Potentials reflecting early perceptual processing (visual P1), pre-attentive change detection (visual Mismatch Negativity), selective attentional orientation (P3) and a measure of emotional processing, the Late Positive Potential (LPP).

*Results*: There was no evidence for a difference in P1 responses between smokers and non-smokers. There was no difference in vMMN and P3 amplitude but some evidence for a delay in vMMN latency amongst smokers. There was strong evidence for delayed and reduced LPP to health warning stimuli amongst smokers compared to non-smokers.

*Conclusion:* We find no evidence for an early perceptual bias in smokers' visual perception of health warnings but strong evidence that smokers are less sensitive to the emotional content of cigarette health warnings. Future health warning development should focus on increasing the emotional salience of pictorial health warning content amongst smokers.

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#### 1. Introduction

Cigarette package health warnings increase awareness of the health risks of smoking, and attention to health warnings has been shown to lead to meaningful changes in behaviour, such as forgoing cigarettes and contemplating quitting smoking (Hammond, 2011). However, interviews with regular smokers have found that 36% reported making some attempt at avoiding the warnings, such as hiding them, using a cigarette case, or requesting a specific package to avoid a particular warning (Hammond et al., 2004). Using eyetracking technology, we have previously measured health warning avoidance at a more implicit level and found that daily smokers also actively avoid pictorial health warnings by directing visual attention away from them within the first seconds of viewing (Maynard et al., 2014).

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Recent neuroimaging research has highlighted some of the possible neural mechanisms involved in the processing of health warnings amongst smokers. Smokers show less activation in, and connectivity between, the medial pre-frontal cortices and the insula when viewing aversive smoking related stimuli compared to aversive non-smoking related stimuli, i.e., they are less responsive to drug-specific aversive stimuli (Dinh-Williams et al., 2014a, 2014b). The level of brain activity whilst viewing aversive smoking related images has also been correlated with intentions to quit and reductions in subsequent smoking behaviour (Wang et al., 2013). Interestingly these changes occur in the context of an increase in brain activity amongst substance users when presented with substance related images (see Littel et al., 2012 for a meta-analysis and review), suggestive of a specific adaptation of neural responses to health warnings that dissociates them from other smoking related cues.

What remains unclear from the current neuroimaging research is the cognitive locus of this reduction in neural activity, i.e., where in the perceptual/attentional/cognitive processing stream does the consequence of being a smoker impact on the process-

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ing of health warnings? One possible explanation is that through repeated exposure to warnings, a pre-cognitive perceptual bias may develop, leading to the reduced attentional salience of the warnings. Previous research has shown early perceptual biases *towards* smoking-related stimuli among smokers (Versace et al., 2011). It is therefore possible that a stimulus presenting an antismoking message (e.g., a health warning) may be associated with an early perceptual bias *away* from it. Alternatively (or additionally), avoidance behaviours may be a result of higher order cognitive biases, such as reduced emotional processing, that functions to inhibit afferent perceptual information (Loeber et al., 2011).

Using electroencephalography (EEG), the aim of this study was to identify the temporal point at which smokers' responses begin to differ and consequently identify the underlying biases. Four Event Related Potentials (ERPs) were used to address this guestion, the visual P1, visual Mismatch Negativity (vMMN), the P3 and the Late Positive Potential (LPP). The amplitude and latency of these components reflect the integrity and efficiency of the early stages of perception, change detection and attentional orientation through to higher level cognitive emotional processing. The visual P1 response is believed to represent the processing of stimulus characteristics and visuo-spatial selection (Clark et al., 1994; Clark and Hillyard, 1996; Di Russo et al., 2002; Proverbio et al., 2007). It is typically unaffected by complex visual features and often overlooked in favour of later components, however Versace et al. (2011) demonstrated cue-reactivity like increases in P1 amplitude to cigarette stimuli amongst smokers. vMMN provides a measure of pre-attentive visual change detection and discriminative processing of stimuli (see Kimura et al., 2011; Stefanics et al., 2015 for reviews). It is sensitive to changes in simple physical characteristics (e.g., Tales et al., 1999) as well as more complex characteristics of visual images, such as emotional content during face processing (Kecskés-Kovács et al., 2013) and symmetry (Kecskés-Kovács et al., 2012). It is elicited in response to a rare deviant stimulus embedded amongst repeating standard stimuli. Importantly for the current study, the extent to which the deviant oddball stimulus differs from preceding standard stimuli affects the magnitude of the vMMN response. Therefore if the deviant stimulus is of high valence to one group (e.g., smokers) they will show a larger vMMN response compared to a second group (e.g., non-smokers) for whom the deviant stimulus is of a lower valence.

The P3 component provides the first index of selective attentional orientation and is proposed to represent the updating of working memory representations of incoming stimuli (Polich et al., 2008). The Late Positive Potential (LPP) provides a measure of higher order cognitive biases and reflects the cortical prioritisation of emotional information during visual processing (Brown et al., 2012; Littel and Franken, 2011). It is typically elicited in passive viewing paradigms, manifests as a midline centroparietal ERP 300–400 ms following stimulus onset, and is larger following the presentation of both pleasant and unpleasant compared to neutral visual stimuli (see Hajcak et al., 2011 for a review).

Two separate EEG paradigms were designed to elicit these specified ERP components. An 'oddball' perceptual paradigm was designed to elicit the P1, vMMN and P3. A separate passive viewing paradigm was designed to elicit a higher order cognitive LPP response, avoiding any contamination of the LPP response with preceding task-associated responses, e.g., P3.

We hypothesised that daily smokers would show reduced neural responses to pictorial health warnings, in particular familiar health warnings. The point in the processing stream at which smokers and non-smokers begin to differ will elucidate the underlying cause of any changes. Long-term habituation of the perceptual/attentional responses would be predicted to manifest as reduced amplitudes/delayed latencies of the earlier ERP components (e.g., P1, vMMN, P3). By contrast, a reduced cognitive emotional response would be predicted to manifest as a reduction in the amplitude/delay in the latency of the LPP.

#### 2. Materials and methods

#### 2.1. Study design

This was an EEG study of visual perception of pictorial health warning labels, with a between-subjects design, using two separate paradigms: an oddball paradigm and a passive viewing paradigm. Testing took place at the University of Bristol (ethics approval code: 12121). The study was conducted according to the revised Declaration of Helsinki 2013 and Good Clinical Practice guidelines, and the study protocol was registered on the Open Science Framework prior to commencing testing (https://osf.io/zea2t/).

#### 2.2. Participants

Daily smokers (n=20) were defined as smoking at least 5 cigarettes a day, smoking their first cigarette of the day within one hour of waking. Non-smokers (n=20) were defined as not having smoked more than 100 cigarettes in their lifetime. Smokers' CO reading was required to be higher than 3 parts per million (ppm). Participants were recruited from the general population, were aged between 18 and 40 years, had English as their first language, and had normal or corrected to normal vision and hearing.

#### 2.3. Materials

Participants completed the Edinburgh Handedness Inventory (EHI; Oldfield, 1971), the Fagerström Test for Nicotine Dependence (FTND; Heatherton et al., 1991), the Questionnaire of Smoking Urges (QSU-brief; Cox et al., 2001) and the Quitting Smoking Contemplation Ladder (QSCL; Biener and Abrams, 1991).

The oddball paradigm used cigarette pack stimuli, comprised of cigarette branding on the top 40% of the pack and either a cigarette pack health warning (n=20), or a control image of an object (n=20), or a landscape (n=20) on the bottom 60% of the pack. Branded cigarette pack images were 10 popular UK tobacco brands (bought in February 2014). Control object and landscape images were sourced from the International Affective Picture System (IAPS; Lang et al., 2008) database. Images were selected based on the following criteria: neutral emotional valence ratings (objects M = 5.03, SD = 0.79; landscapes M = 4.99, SD = 0.48), low arousal ratings (objects M = 2.60, SD = 0.53; landscapes M = 3.63, SD = 0.74), and not containing images of people or faces.<sup>1</sup> All IAPS images had a black border added to match the health warning images. In order to explore the impact of health warning familiarity on EEG responses, health warnings comprised 10 pictorial health warnings taken from the 11 European Union (EU) pictorial warnings currently used in the UK and therefore familiar to smokers (hereafter 'UK warnings'), and 10 EU warnings not used in the UK and therefore unfamiliar to smokers (hereafter 'non-UK warnings'), please see Supplementary material for images of all the health warnings and cigarette packs used. UK and non-UK warnings were matched for health warning effectiveness based on pre-study piloting, (four questions assessing health warning effectiveness) with 40 participants (20 smokers, 20 non-smokers).

Each branded pack image was combined with each of the 20 health warnings as well as 20 control object images and 20

<sup>&</sup>lt;sup>1</sup> Image numbers objects: 5510, 6150, 7000, 7002, 7003, 7004, 7009, 7010, 7012, 7017, 7020, 7034, 7056, 7077, 7170, 7185, 7187, 7233, 7235, 7950. Image numbers landscapes: 5390, 5395, 5471, 5661, 5731, 5900, 6930, 7033, 7036, 7037, 7242, 7491, 7495, 7500, 7546, 7547, 7560, 7590, 7595, 7620.

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