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Pupil Dilation Response to Nicotine-Related Visual Stimuli in Smokers and Non-Smokers

Supervisor
Professor Marco Zorzi

Co-supervisor
Dr. Elvio Blini

Candidate: **Dilara Aladağ**
Student ID number: **2015704**

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Abstract

Visual-spatial attention is the process through which we direct our attention to a certain object or scene. We can process visual information more quickly and recall the specifics of what we are seeing when we pay close attention. Biases in attention appear to be a critical part of addiction with an impact on craving levels because drug-dependent people are more prone to have their attention grabbed by drug-related environmental stimuli. Making use of the previously established connection between eye movements and spatial attention, we used eye-tracking techniques to investigate the indicators of attentional priority in smokers. We found in cross-validated logistic regression, that the pattern of pupil dilatation and constriction in response to visual stimuli related to nicotine could successfully predict the smoking status of both young adults contrast, standard proxy metrics based on reaction times or eye location were less accurate. Lower nicotine dependence levels resulted in more pronounced pupil constriction, corroborating earlier asser tions that the incentive value of conditioned stimuli gradually declines and makes room for a more automated, habit-driven processing mode. Additionally, pupil size became more sensitive with longer periods of abstinence, indicating that it might reflect the intensity of craving. We conclude that pupillometry can serve as a reliable marker for the computation of attentional priorities and offer helpful cues about motivational conditions and individual attitudes toward conditioned stimuli.

CHAPTER 1. INTRODUCTION

1.1 Visual-spatial attention

We are surrounded by excessive visual information the instant our eyes open. Despite this flood of colours, shapes, motion, and figures, our ability to make sense of what we see is quick and appears to be effortless. This depends on our ability to separate crucial visual information from unimportant visual noise (Kounte& Sujatha, 2013). One of the basic cognitive processes is visual attention. The visual system encounters an excessive amount of information while navigating our environment, which is too much to process all at once. By prioritising and picking out particular pieces of information for more in-depth investigation, visual attention enables us to make sense of our surroundings (Carrasco, 2011).

Moving our eyes back and forth between points of interest and changing our covert spatial attention are two complementary ways of orienting throughout the visual field that helps us choose and prioritize what to focus on. What information is selected for additional processing and, ultimately, what is viewed, depends on how these two types of orienting are combined. Visual attention will choose information related to the target object (such as the colour green) while suppressing unnecessary information (such as red colour), if the observer wants to find a specific target object, such as a green ball (Gaspelin& Luck, 2018). But the prominence of the stimuli also affects selection. Bright light is a salient stimulus that attracts attention more successfully than dim light, which is a less salient stimulus. The ability to pay attention to a pertinent spot in the environment is one of the main functions of visual attention. This process is called spatial attention. Visual-spatial attention is the process through which we direct our attention to a certain object or scene. (Liu& Jigo, 2017). This kind of attention allows us to process visual information more efficiently, and to better remember the details of what we are seeing. We consider here theories of attention which assume that information is filtered to limit the flow to a level that is cognitively manageable (Anderson et al., 2002). Broadbent's filter theory states that there is an attentional mechanism that filters out certain stimuli for an individual to focus on a particular task (Treisman, 1969). This theory suggests that the attentional mechanism functions like a filter, allowing certain information to pass through while blocking out other information (Treisman, 1969).

Selection based on location is referred to as "spatial attention." Most of the time, a perceptual system cannot fully analyze all the information that enters consciousness, hence processing is restricted to only data from a certain region. Visual-spatial attention has a long history that dates back to the beginning of psychology. William James established one of the first hypotheses about attention in 1890 (Johnston & Dark, 1986). James made the analogy that attention is like a spotlight that may be focused on many elements of the surroundings. Later, many researchers built on this notion, suggesting that attention behaves more like a searchlight that wanders through the surroundings and selects various features. Numerous studies have been done to examine visual-spatial attention over the years. Simons and Chabris (1999) carried out one of the most well-known experiments that demonstrates the consequences of “inattention” to stimuli that are presented outside the participants’ focus of attention. In this study, participants were shown a video of two teams passing a basketball back and counting the number of passes one group made was given to the participants as the task. The participants were engaged in this activity when a person wearing a gorilla suit entered the movie scene (Simons& Chabris, 1999). The viewers were questioned about what they observed once the video had finished. Even though the gorilla was visible in the video, many of the participants claimed not to have seen it.

Spatial attention is the ability to direct attention to specific locations in space and there are two ways that attention can be focused in space: voluntarily (endogenous) and reflexively (exogenous), with each type of attention having a different latency period (Carrasco, 2011). Theoretically, voluntary attention can be kept at the cued area for a considerable amount of time and deploys rather slowly (300ms). Conversely, reflexive attention is deployed quickly (80 ms), is grabbed by sharp onset/offset peripheral signals, but degrades swiftly (Nakayama

&Mackeben, 1989). It has been discovered that properly focused spatial attention can enhance performance on a variety of tasks, such as contrast detection, visual word recognition, and orientation discrimination (Carrasco, 2011). Effectively monitor the surroundings, covert shifts in spatial attention are necessary to effectively monitor the surroundings, because central vision only occupies a tiny portion of the visual field. For many daily activities, including driving and participating in sports, subtle attention shifts are necessary.

1.2. Priority maps

A priority map is a representation of the world that encodes the relative importance of different stimulus features (Bisley& Mirpour, 2019). Several attentional effects, such as the capacity to process relevant information selectively while disregarding irrelevant information, are assumed to be mediated by this map. In a map of the visual scene that is usually referred to as a priority map, objects and locations are represented by their attentional priority, which is a combination of low-level salience and top-down control (Bisley& Mirpour, 2019). The idea of a priority map originates from the saliency map models developed by Itti and Koch (2000), which sought to simulate changes in visual attention. With some top-down inputs, these models were predominantly driven by low-level salience. The highest spot on the map received attention in a winner-take-all fashion before being inhibited to make room for the next highest point. However, a wide range of variables affect how attention is distributed, thus they prefer to refer to the map that ultimately directs eye movements and covert visual attention as a priority map (Itti, Koch 2000).

The saliency map models of Itti and Koch which were intended to describe shifts in visual attention are where the idea of a priority map derives (Bisley, Mirpour, 2019). The priority map is constantly changing as the observer's goals and the properties of the stimulus environment change. For example, if the observer is looking for a specific object, the top-down process associated with that goal will have a high priority on the map. However, if the object is not currently visible, the bottom-up process associated with its last known location will have a higher priority. The priority map is a useful framework for understanding how spatial attention is directed in different situations. Two main types of processes can guide spatial attention: bottom-up and top-down (Treisman, 1991; Wolfe et al., 1989; Yantis, 1993). Bottom-up processes are driven by the properties of the stimulus itself, such as its saliency, contrast, or movement; top-down processes are driven by the goals and expectations of the observer, such as where they are looking for a specific object (Ipata et al., 2009; Ptak and Fellrath, 2013). These two types of processes can interact with each other to influence the final direction of attention.

A priority map is a mapping system that represents the relative importance of different parts of the environment in the context of a particular task. The concept of priority maps moves beyond the traditional dichotomy between endogenous (self-generated) and exogenous (environmental) spatial attention. By doing so, it helps to explain how people can attend to the environment while still focusing on their own goals. Priority maps are based on the idea that the environment can be divided into regions of importance. These areas may be influenced by both endogenous and external elements, including the work at hand, the person's objectives, and the environment itself. For example, if a person is trying to navigate a crowded city, their priority map may focus on the streets and landmarks that are important for getting to their destination. The priority map would also take into account the attentional demands of the environment, such as the presence of obstacles, traffic, and other distractions. Priority maps are useful for understanding how people attend to their environment and make decisions. They provide a means of mapping the environment in terms of relative importance, allowing people to focus on the most important areas while still attending to their own goals. This helps to explain why people can attend to their environment while still focusing on their own goals. In addition, priority maps can help to explain how people can quickly and efficiently attend to their environment, as they can quickly identify the most important areas and focus their attention there.

The brain's cortical and subcortical regions have priority maps. These include the superior colliculus (SC), the frontal eye field (FEF) of the prefrontal cortex, the lateral intraparietal area (LIP) of the posterior parietal cortex, and several visual cortical regions (Sprague& Serences, 2013). The concept of a priority map refers to what we have coined as a map that integrates top-down and bottom-up inputs to direct attention and eye movements. The brain areas that either represent a priority map or are engaged in selective attention and reward processing are described by Chelazzi et al. (2014). Priority maps appear to be produced by a dispersed network that includes the midbrain, hippocampus, frontal, and parietal cortices. Different brain areas may be the starting point for priority signals with various origins. The early visual cortex and subcortical structures like the superior colliculus (Itti and Koch, 2001), for example, may be the source of stimulus-driven salience, but evolutionary-old systems like the hippocampus, amygdala, and striatum may be the source of subconscious value sets. The different priority messages that come from various parts of the brain do not preclude the possibility of measuring their effects elsewhere, but interactions between various priority signals will significantly impact brain activity (Kennerley et al., 2011). Some value sets might take longer to compute than others, which would cause the system's overall priority map to change when new value-set contributions were made available (Krauzlis et al., 2014). The priority maps discovered in the intraparietal cortex and frontal eye fields can be viewed as behavioural planning maps produced as a result of distributed value signals and direct covert attention shifts and eye movements (Bisley and Goldberg, 2010).

1.3. Nicotine Addiction

The principal pharmacologically active ingredient in tobacco products is nicotine, which is only responsible for the short-term pharmacological effects of smoking. The harmful long-term cardiovascular, pulmonary, and carcinogenic consequences of tobacco are caused by

its additional components. In addition to having a significant impact on heart rate, blood pressure, the electroencephalogram, and deep tendon reflexes like the patellar and Hoffmann reflexes, nicotine is a nonselective cholinergic nicotinic agonist (Benowitz, 2009).
The stimulatory alkaloid nicotine is what gives tobacco products their addictive qualities (Benowitz, 2010). Nicotine is derived from burning tobacco and transported on tar droplets once tobacco smoke has been produced (Benowitz et al., 2009). When breathed, these droplets travel to the lungs where they are quickly absorbed into the pulmonary venous circulation (Benowitz et al., 2009). Nicotine can pass the blood-brain barrier after 10 to 20 seconds of inhalation thanks to its high lipophilicity.

The autonomic nervous system is composed of the sympathetic and parasympathetic nervous systems. Adrenergic receptors can be found at the preganglionic and postganglionic terminals of the sympathetic nervous system. The somatic motor and preganglionic terminals of the parasympathetic nervous system have cholinergic nicotinic receptors, and the postganglionic terminals have cholinergic muscarinic receptors. The sphincter iris muscle and the dilatator iris muscle are under the control of sympathetic and parasympathetic nerves, respectively, indicating that the iris gets dual innervation from both the sympathetic and the parasympathetic nervous systems.

Nicotine is known to stimulate brain nicotinic acetylcholinergic receptors (nAChRs), which have been implicated in a wide variety of behavioural and cognitive functions (Griesar& Zajdel& Oken, 2002). In nicotine-dependent cigarette smokers, the physiological effects of smoking are thought to be a motivating factor for maintaining their smoking practice. As observed in psychomotor, vigilance, and memory tasks, smoking has been proven to improve task performance. Animal and human studies have provided evidence that it is connected to nicotine's central effects, the primary psychoactive component of tobacco that promotes smoking (Levin, 2002). The key driving force for smoking, according to the majority of smoking cessation theories, is nicotine dependence and the associated urge to keep nicotine levels above a certain point. These theories do acknowledge the significance of specific environments or cues in triggering need and cueing smoking, though.

Conditioning plays a critical part in the development of tobacco addiction. Variations of positive rewards, such as mood-lifting effects and the avoidance of withdrawal symptoms, are the basis of nicotine addiction (Benowitz, 2009). When a nicotine addict stops smoking, the impulse to pick up again is persistent even after the withdrawal symptoms subside. Regular smoking causes the smoker to develop an association between particular emotions, circumstances, or environmental elements — smoking-related cues — and the pleasurable effects of nicotine (Le Houezec, 2003). These cues frequently cause a relapse. The impulse to consume nicotine that results from the link between these cues and the expected effects of nicotine is a sort of conditioning. Such conditioning helps to retain the desire to smoke. Smokers typically light up after eating, with a cup of coffee or an alcoholic beverage, or with other smokers. Such circumstances can trigger the desire to smoke when they occur frequently.

The manipulation of smoking materials, or the flavour, smell, or sensation of smoke in the throat, are all aspects of smoking that come to be connected to its enjoyable benefits (Cohn& Ganz et al, 2020). Even unpleasant emotions can develop into conditioned cues for smoking. For example, a smoker may learn that going without a cigarette makes them irritable and that having one calms them down (Rösler et al., 2005). Smokers with insula damage are more likely to quit smoking quickly after the injury, maintain their abstinence, and experience less conscious cravings to smoke than smokers with insula-unaffected brain injuries (Benowitz, 2009). Since nicotine was discovered to be the main psychoactive substance in tobacco smoke, extensive study has been done to understand the neuropharmacological, anatomical, and behavioural bases of nicotine's psychoactive effects (Benowitz, 2009).

1.4. Attentional Bias

According to Tiffany's (1990) cognitive model of drug use, the bias in selective attention is a result of a substance's repeated use, which strengthens the action schemata that support drug-using behaviours and makes drug use an automatic process that can happen quickly without effort or conscious awareness. The "action schemata," which are unitized sequences of related connections, are kept in memory and contain all the necessary information to commence and plan drug usage (Tiffany, 1990). For example, alcohol abusers' action schemata are engaged by signals linked with drinking, which in turn activates other cognitive processes related to urges. As a result, urges can be felt in the presence of prominent alcohol cues (Johnsen et al., 1994). A bias in selective processing takes place at the cognitive level of a person who abuses substances when a substance-related trigger is present. Additionally, Tiffany (1990) found that when a person is abstinent, they pay more attention to these stimuli that are associated with substances, creating an attentional bias.

Craving is among the most fundamental characteristics in the subject of addiction. It generally refers to the cravings or desires to feel the effects of a psychoactive substance that has already been used (Mogg et.al.,2003). It also exemplifies the basic problem of an addiction fixation. Both the persistence of substance usage and the onset of relapse after drug abstinence are influenced by drug cravings. "Craving is the compulsive, unreasonable, pathologically severe drug "wanting" or no apparent cause," according to the definition of addiction (Robinson & Berridge, 1993). Because it gradually alters the brain substrate that controls drug cravings and because it gives drug-related stimuli incentive salience, which makes them more noticeable, repeated, intermittent drug use is a necessary component (Robinson & Berridge, 1993). As drug-related cues become more prominent, users interpret this attribution, which is an unconscious process, as craving and wanting (Robinson & Berridge, 1993). Therefore, continued, intermittent drug use is a necessary component because it gradually alters the brain substrate that controls drug cravings and because it gives drug-related stimuli incentive salience, which makes them stand out more (Robinson & Berridge, 1993). As drug-related stimuli become more prominent, this attribution is an unconscious process that users interpret as craving and wanting (Robinson & Berridge, 1993). By claiming that attentional bias and appetites have a mutually stimulating relationship, Franken (2003) expanded the idea. Cravings are induced and amplified when attention is focused on the cue, and this increase strengthens the cue's attention-grabbing qualities. Until drug delivery, these two components—attention and craving—enter a mutually cyclical excitatory interaction (Field& Cox, 2008).

As drug-dependent people are more likely to have their attention drawn to drug-related environmental stimuli, biases in attention seem to be a key component of addiction. For instance, Sayette and Hufford (1994) discovered that in the presence of stimuli connected to smoking, smokers responded to an auditory probing stimulus more slowly than non-smokers. The modified Stroop test, in which words are given in various colours and participants name the colour of the terms while ignoring their meaning, has been used to explore the distraction-causing effects of smoking cues. According to incentive theories of drug dependence, stimuli linked to drug use become extremely alluring, “desired”, and "grab attention" because they have increased motivational salience for the individual. This suggests that there may be an attentional bias for drug-related cues in addiction. The incentive-salience mechanism that drives this process, according to Robinson & Berridge (2001), is governed by dopamine levels in the mesolimbic dopamine system and is crucial in sustaining drug-taking behaviour. As a result, the degree to which drug cues draw in and maintain attention may precisely correspond to the degree to which the mechanism of incentive salience is being triggered by those signals. Numerous nicotine addiction studies have revealed increased attentional biases for both drug-related phrases and visual stimuli. For instance, using the modified Stroop colour-word interference task and the Serial Probe Task, attentional bias has been inferred from an increase in the time required to identify the ink colour of smoking-related words and as a speeding-up in the time required to detect a probe when it replaces a smoking-related cue (Waters& Feyerabend, 2000). Even while these studies have been effective at identifying smokers' attentional biases, they have a shallow level of analysis. The modified Stroop task, according to

Mogg et al. (2003), does not distinguish between biases arising from attention to the relevant stimuli (such as the smoking image) or from potential biases arising from the intrinsic thoughts that may be generated from the presented cues, even though it gives insight into the cognitive processes involved in bias.

Users of alcohol and drugs should not only show a bias for their respective substances but also show that the focus on such stimuli will make them more likely to seek out and use that substance. According to Franken (2003), attentional biases associated with substances may have three different effects on how addictive behaviours emerge, are maintained, and relapse. First of all, due to the increased likelihood of detecting and subsequently becoming aware of the substance-related stimuli in the environment, addictive behaviours may continue. Second, it might be challenging for users to divert their attention from substance-related stimuli after they have been identified, which may lead to increased subjective yearning. Lastly, because of the attentional capacity limitations, stimuli connected to substances will be processed more favourably than ones related to competition.

1.4.1. Attentional bias and smoking

Nicotine is the unconditioned stimulus that causes physiological reactions when tobacco is smoked. The nicotine delivery method, cigarettes become the conditioned stimulus after prolonged use. Then, cigarettes have the power to draw in experienced drug users who show attentional bias for cues connected to smoking and cause cue-responsive cravings in smokers. Attentional bias can trigger cravings that are potent enough to lead people to smoke. Yaxley and Zwann (2005) focused on smoking behaviours while abstaining from drugs and employed Tiffany's addiction hypothesis (1990), which states that when drug-seeking plans are thwarted, the attentional bias for the specific drug is displayed. The presentation of attentional bias may exhaust attentional resources that could otherwise be utilised for other tasks. As a result, attentional bias can be seen in smokers who are exposed to smoking-related stimuli but are unable to respond to them by smoking (Yaxley & Zwann, 2005). Additionally, it has been discovered that quitting smoking causes attentional bias to increase (Gross et al., 1993). Smokers, regardless of their abstinence status, exhibit a bias in their attention to the smoking-associated cue when they are presented with two stimuli, with one of the pair being related to smoking, in an experimental paradigm. Smokers would discover that they were more drawn to one cue than another, and since the substance-related cue is connected to the enjoyable and rewarding aspects of smoking, there would be a bias in favour of that cue.

When a certain category of stimuli has more of an effect on attentional processes than competing stimuli, it is argued that attentional bias, a manifestation of selective attention, is present. If seasoned users of a substance exhibit a propensity to selectively attend to substance-related information at the expense of other categories of information, this would be indicative of a substance-related attentional bias in the setting of addiction. Attentional biases play a role in drug use and relapse, according to Franken's (2003) drug relapse model. Regular drug usage will be linked to attentional biases for drug-related signals following these traits of drug craving.

An attentional bias is a propensity to selectively pay to specific cues while ignoring other inputs. Particular attentional biases for smoking-related stimuli among smokers are connected with differences in subjective craving. On word-Stroop and dot-probe tasks, there is evidence that smokers, but not non-smokers, exhibit an attentional bias for words related to nicotine (Johnsen et al., 1997; Ehrman et al., 2002). Additionally, smoking cessation has been shown to increase attentional bias in smokers performing the card word-Stroop task.

There are many approaches to measuring attentional bias. These include verbal reporting, watching for obvious behaviour, and taking physiological readings. Because eye movements are often automatic and closely followed and are led by changes in covert selective attention, measuring eye movements is a sensitive method (Kwak et, al, 2007). Initial fixation and gaze duration can be indicators of attentional bias, even if there is an ongoing debate over the precise measurement of attentional bias in eye movement. There is evidence to suggest that smokers first focus on smoking-related images more than neutral images and linger on these images longer than non-smokers. As a result of nicotine withdrawal, smokers experience higher levels of yearning and anxiety and exhibit an attentional bias toward certain cues (Mogg et al, 2005).

An image of smoking is known as a smoking cue. A pack of cigarettes, a smoker smoking, a cigarette, and so forth are examples of these. Smokers exhibit a larger attentional bias toward smoking cues than other items; specifically, they spend more time looking at information containing smoking signals in still images (Ehrman et al., 2002) than other information and become aware of them more quickly than other objects (Yaxley & Zwaan, 2005). Differences between individuals can reduce the impact of smoking cues on urge (e.g., Doran, Cook, McChargue, Myers, & Spring, 2008; Waters, Shiffman, Bradley, & Mogg, 2003).

1.5. Dot-probe task

The dot-probe task is a type of reaction time task used to measure attention bias towards or away from certain stimuli. It is a computer-based task in which two stimuli, such as pictures or words, are presented on the computer screen. One of the stimuli is then replaced with a dot, and participants must press a button to indicate which side the dot was on. The time it takes for the participant to respond is measured and used to infer whether they are paying more attention to one stimulus over the other. The dot-probe task is also used in research on the automatic activation of mental content. In this case, researchers may present participants with a stimulus that is related to a certain mental content (e.g. a picture of a snake for those with a fear of snakes) and a neutral stimulus. Behavioural, electrophysiological, and hemodynamic neuroimaging indices mostly show that unpleasant or threatening stimuli given away from an observer's fixation catch and hold spatial attention.

The dot-probe task was established for the first time by MacLeod et al. (1986) to assess how attention is allocated in emotional disorders. On a computer screen, two images (text or pictures) are presented to the side of the subject by side. A target stimulus (the dot probe) replaces one of the two pictures after they both vanish. Subjects are instructed to strike a key as rapidly and precisely as they can to identify the target's location. Faster reaction times (RTs) when a certain class of events is replaced by the target suggest a skewed focus on those events. The dot-probe task has been effectively used to show that people with mood disorders like anxiety or depression turn their attention to situations that are connected to those moods (MacLeod et al., 1986). It was first used in addiction research by Lubman, Peters, Mogg, and Bradley (2001) to assess attentional bias to stimuli associated with substances. The task entails the simultaneous presentation of two stimuli—one neutral image and one substance-related image—on opposing sides of a computer screen, followed by an immediate dot-probe, such as an arrow or "X," which swaps out one of the stimuli. The dot-probe must be responded to as rapidly as possible by participants by clicking a button to indicate whether it appeared on the left or right side of the screen.

One could argue that the dot-probe task circumvents some of the Stroop task's shortcomings. Since the extent and functions of various attentional components can be examined by varying the image display time, it has been argued that the dot-probe task is more effective than the modified Stroop task. This, as was mentioned above, will be a significant advancement in research to understand which particular attentional processes are involved in substance use (Mogg et al., 2003).

A modified version of the original visual dot-probe task using visual representations rather than words was used in all the studies that were found. Images connected to smoking (such as a person holding a cigarette) were exhibited for 500 or 2000 ms on either side of the screen, along with images that were similar in content but unrelated to smoking (such as a person holding a pen). By pressing one of two keys, participants were told to swiftly reply to whether the probe substituted the right or left picture or which of the pair of dots they saw. Then either one of the picture's locations at the offset of the images was immediately replaced with a dot-probe or a pair of dots (: or..). Because the cue-induced need is known to be a significant factor in smoking, paying biased visual attention to cues connected to cigarettes may make smokers more motivated. Smokers may notice an ashtray or pack of cigarettes more frequently than non-smokers, which could increase their susceptibility to cue-induced cravings (Ehrman et al., 2002). Early conceptual criticism of this approach was based on results from cued spatial attention tests using explicit cues like arrows telling observers to "attend left" rather than "implicit" cues like threat or emotion (Posner, 1980). When the stimuli are offered at 500 ms and 2000 ms but not at 200 ms, Field et al. (2004) showed that heavy social drinkers as compared to light social drinkers display a stronger alcohol-related attentional bias, with subjective desire being positively connected with attentional bias at 2000 ms. These findings have also been confirmed regarding attentional biases caused by smoking, with smokers showing a larger smoking-related attentional bias than non-smokers when the stimuli are given for 500 ms and 2000 ms (Erhman et al., 2002; Bradley, Field., Healy, & Mogg, 2008). When stimuli were exhibited for 500ms, Bradley et al. (2004) were unable to show a difference in smoking-related attentional bias between smokers and non-smokers. Nonetheless, they did demonstrate that, at 2000 ms, smokers were faster to identify probes replacing smoking-related stimuli than neutral stimuli, although this was not observed in non-smokers. The authors argued that the results above demonstrate that an alcohol-related attentional bias in social drinkers and a smoking-related attentional bias in smokers operate about maintained attention and are unrelated to the initial orienting of attention because the longer stimulus exposure times (500 ms and 2000 ms) are thought to measure maintained attention while the shorter durations (200 ms) are thought to represent initial orienting of attention (Field et al., 2004). Yet, as the results show, there were mixed findings in terms of what caused such a bias at 500 ms (Bradley et al., 2004).

1.6. Eye tracking

Acuity in the peripheral region declines rapidly due to the anatomy of the eye (Curcio, et al., 1990). For tasks requiring fine spatial resolution, such as contrast discrimination (Virsu & Rovamo, 1979), colour recognition (Hansen, Pracejus, & Gegenfurtner, 2009), and reading (Battista, Koalloniatis, & Metha, 2005), foveal vision is specialized. On the other hand, peripheral vision is particularly sensitive to movement, dim lighting, and keeping an eye on the environment (McKee & Nakayama, 1984). Because of this division of labour, the eye must move numerous times each second for stimuli to hit the fovea in the centre (Rayner, 1998). Quick saccades, and ballistic eye movements, are what allow for this repositioning. Saccades can be planned consciously, reflexively, or spontaneously, with each form of eye movement having a unique latency between preparation and execution.

Eye tracking continually records eye movements in response to stimuli displayed on a mobile head-centred video device or a computer screen. "fixations" and "saccades" are derived using predefined spatial (e.g., displacement) and temporal (e.g., velocity and acceleration) eye movement characteristics. (Conklin et al.,2018). The benefit of shifting gaze is noticeable even before the eyes start to move, and these frequent and abrupt changes in fixation are crucial factors in the selection and priority of visual information. Indeed, it is discovered that at least 100 ms before the start of a saccade, discrimination performance at the target of a future eye movement improves (Born, Ansorge,& Kerzel, 2012). Typically, it is believed that spatial attention is either directed with overt eye movements or without them (covert). One of the most well-known tasks used to research the use of spatial attention is the Posner (1980) cueing paradigm. In this exercise, a cue draws the user's spatial attention to a spot on the outskirts. In general, discriminating against a target that appears at the cued place (valid) is preferable to discriminating against a target that appears elsewhere (invalid). The "cueing effect" is a difference in performance between valid and invalid cue circumstances that is attributed to the shifting of spatial attention. Participants are typically instructed to maintain fixation by researchers who are specifically interested in covert shifts in spatial attention, and researchers will then set a time limit between the cue and target that is shorter than what is necessary to execute an explicit eye movement (Hallett, 1978).

To directly measure biases in visuospatial attention in substance use, researchers monitored participants' eye movements while they completed the visual probe task. This has helped to overcome the interpretation issues associated with inferring the roles of initial orienting and maintained attention. Researchers can thus directly separate the initial orienting of attention and attention maintenance by the observation of eye movements. For instance, the timing and location of the first fixations indicate the initial orienting of attention, and the proportion of fixations on stimuli associated with substances compared to neutral stimuli as well as the length of fixations on such stimuli can be used to suggest sustained attention.

Monitoring eye movements allows for directly visible measures of attentional allocation, which is an improvement over earlier measures of attentional bias that depended on indirect measures of attention (Field et al., 2004). Researchers can thus directly separate the initial orienting of attention and attention maintenance by the observation of eye movements. For instance, the timing and location of the first fixations indicate the initial orienting of attention, and the percentage of fixations on stimuli related to substances compared to neutral stimuli as well as the length of fixations on such stimuli can be used to determine the maintenance of attention.

Eye tracking was originally used by Mogg, Bradley, Field, and De Houwer (2003) to study the role of attentional biases in addictive behaviours while utilising the visual probe task. Based on reaction time data, it was discovered that during the 2000ms presentation of the stimuli, smokers responded to probes replacing the smoking images noticeably faster than non-smokers did to neutral images. Additionally, eye movement analysis that looked only at the direction and length of initial fixations revealed that smokers had a bias toward orienting towards and fixating on smoking-related stimuli for longer than neutral stimuli and that quicker initial orienting and longer fixation times were associated with higher levels of subjective craving. Non-smokers, however, did not exhibit any such biases. Only the first fixation within trials was analysed by Mogg et al. (2003), who found that smokers exhibit biassed attentional orienting to smoking-related stimuli that is proportional to the intensity of subjective craving and compatible with IST models of addictive behaviours (Franken, 2003; Robinson & Berridge, 1993).

Following this research, Mogg, Field, and Bradley (2005) used eye tracking in a visual probe task with a 2000ms stimulus exposure length to assess early orienting and sustained attention. The study did not include a non-smoking control group, and it only included low- and moderate-dependent smokers. Although both moderately dependent and low-dependent smokers displayed a smoking-related attentional bias, the authors proved that there was no difference between the groups using response time data. However, eye movement data showed a bias for low-dependent smokers to initially concentrate on smoking-related cues as opposed to neutral stimuli, but not moderately dependent smokers. Additionally, the authors examined the length of fixations on smoking and neutral stimuli throughout each trial, showing that both moderate and low-dependent smokers focused on smoking for longer than they did on neutral stimuli, but those low-dependent smokers focused on smoking for noticeably longer periods than moderately dependent smokers did.

1.6.1. Pupil dilation

We can monitor pupil dilation, fixation duration and locations using an eye tracker. Therefore, utilising the eye tracker, we may examine how information on the screen and behavioural decisions made during experiments related to fixations (seeing at the same location for a time), saccades (rapid eye movements), and pupil dilation responses (changes in pupil diameters). The duration of fixations indicates attention, whereas pupil dilation responses reveal emotion, arousal, tension, pain, or cognitive load. Fixations and saccades explain how humans process information and what they perceive when matched with information on the screen. Care must be made to identify the trigger signal of the response because a variety of factors might produce pupillary responses. Human pupils can enlarge for a variety of causes, including mental strain, difficulties with cognitive tasks, valence, arousal, pain, and more (Beatty, 1982). According to Hess (1972), such dilation would take place for single answers 2–7 seconds after emotional stimuli were delivered, with a faster dilation predicted for stronger stimuli. When performing a cognitively demanding task, pupils enlarge in response to the mental strain of the task, peaking at about 1-2 seconds after the demand begins (Beatty, 1982), and then constrict either gradually (Kahneman and Beatty, 1966; Hess, 1972) or instantly (Beatty, 1982) after the task is complete.

Hess and Plott (1960) reported pupillary dilation reactions to what they refer to as "emotionally toned or appealing visual stimuli" in terms of pupil dilation as an emotional response. According to research by Chapman et al. (1999), pupil dilation in reaction to pain peaked at 1.25 seconds after the stimulus started and started at 0.33 seconds. Peak dilation considerably increased as pain level increased. When individuals heard affect noises, including both positive (baby laughing) and negative (baby crying), their mean pupil width increased (0.2mm vs. 0.14mm) in comparison to neutral sounds (office noise). Positive and negative noises elicited equivalent pupillary responses, while females responded more strongly to the former and males to the latter.

To investigate the effects of smoking on human pupils, Lie and Domino (1999) carried out a significant investigation. Smokers and non-smokers who had avoided caffeine-containing goods for at least eight hours before the experiment had their pupils measured. Both participant groups were exposed to nicotine-containing tobacco and placebo (fake) cigarette circumstances. The diameter of the pupil was measured under a mesopic, or medium illumination, environment. First, their findings showed that before engaging in sham- or tobacco smoking, there were no baseline differences between smokers and non-smokers.

Second, both smokers and non-smokers experienced pupillary constriction following tobacco and sham use. But the tobacco smoker's condition was more pronounced in terms of this restriction.

However, it is still unclear how nicotine from smoking affects pupillary constriction. The impact of persistent smoking on pupillary responses in smokers and non-smokers was examined by Sobaci and colleagues (2013). Before the experiment, smokers abstained from smoking and caffeine for at least 12 hours. Both photopic and scotopic measurements were made of the individuals' pupils' sizes. They discovered that under the scotopic condition, there was no variation in pupil size between smokers and non-smokers. Smokers' pupils were bigger than non-smokers' pupils under the photopic conditions. However, there were several ambiguities in Sobaci and colleagues' (2013) study. The subjects were not informed of the nicotine dose or the procedure used to induce it.

1.7 Our Research

In light of all the evaluations mentioned above, the present study aims to: I. whether a pupil can accurately assess attentional biases toward NRS in a quick event-related design; II. how this measure compares to more popular ones (like those obtained from a DPT task); III. whether it can be used to accurately categorise smokers; and IV. whether it correlates with either smoking intensity or craving urges. To test this, making use of the previously established connection between eye movements and spatial attention, we used eye-tracking techniques to research the indicators of attentional priority in smokers.

CHAPTER 2. METHOD

All materials, raw data, and analysis scripts for this study are available at the following link (referred to as Supplementary materials): https://osf.io/6r5ch/

2.1.Participants

In this study, we aimed to compare smokers and controls using a variety of measures of attentional and autonomic involvement with nicotine-related stimuli (NRS). We thought that trying to classify the recruitment plan group according to these criteria, that is a multivariate approach would be more appropriate and powerful rather than calibrating it on each measure. Therefore idea was to use a multivariate classifier as the primary inferential approach. For this reason, we calculate a priori power analysis for a one-sided binomial test (i.e. a test that classification performance is superior to chance level). We establish a range of potential proportion and sample size values and we predicated the minimum effect size of interest to be a 70% classification probability. About 40 people will be able to identify these highlighting these effect sizes statistically about 80% of the time with a type 1 error rate set to alpha= 0.05 (Fig.1).

Simulations were used to conduct the power analysis, and the corresponding scripts are accessible in the Supplementary Materials. It should be noted that, at N=40, a classification accuracy of 65% would be significantly better than chance (p=0.04) according to this test; however, this should be viewed as the underlying, "true" effect size, which does not always result in the same classification accuracy due to random fluctuations, hence the concept of statistical power of a test. As a result, we had a minimum enrollment goal of 20 smokers and 20 matched controls. Our optional multivariate had the assumption that every participant had every pre-identified behavioural predictor, without any missing data. This resulted in the recruitment of a total of 51 participants based on the quality of our set of data (described below). All participants were chosen from among University of Padova (Italy) students. The sample was composed of two groups: 28 smokers (age: 24.04 2.69 years; 18 women; 4 left-handed) group and 23 non-smokers (age: 23.13 2.75 years; 16 women; 1 left-handed) group. Inclusion requirements were normal (or corrected-to-normal) vision and a lack of a history of neurological or psychiatric illnesses. All smokers in the final sample smoked a self-reported mean of 8.1 cigarettes a day for an average duration of 5 years after occasional (i.e., non-daily) smokers were excluded.

However, as seen by their low average scores (1.96 ± 2.1) on the Fagerström test for Nicotine Dependence, the majority of them were light smokers (FTND; Heatherton et al., 1991). They were all instructed to abstain from smoking for at least 90 minutes before the experiment (mean: 7.5 hours; indeed, half of them last smoked the evening before the experiment) since nicotine can significantly diminish pupil size (Wardhani et al., 2020) and because we wanted to assess the tasks under relative craving settings. Smokers were also asked to complete the FTND and two questionnaires to measure self-reported craving: the Questionnaire of Smoking Urges (QSU-brief; Cox et al., 2001) and the Severity of Dependence Scale (SDS; Gossop et al., 1992). The University of Padova's Ethics Committee gave the study their approval (protocol number 3568). Due to the covid-19 pandemic, was conducted during a time of constraints, and all essential hygienic precautions were performed.

2.2. Materials and Methods

Participants were tested in the university laboratory room. They filled out consent forms before the experiment. Subjects performed testing while their heads were firmly secured by chinrests in a calm, dimly lighted space, while positioned in front of a remote, infrared-based eye-tracker (TOBIITM Spectrum) with a built-in, 24-inch monitor at a distance of around 57 cm.

The eye-tracker was calibrated with a 9-point procedure before the session and configured to constantly track participants' gazes at a sampling rate of 600 Hz. To display experimental stimuli on the screen and record the subjects' reactions, OpenSesame (Mathôt et al., 2012) was utilized. Each participant's dominant hand's index and middle fingers were used to press keys on a normal QWERTY keyboard to respond. Each participant completed two tasks in a specific order: Dot-Probe Task (DPT) and Passive Viewing (PV) (Fig. 1).

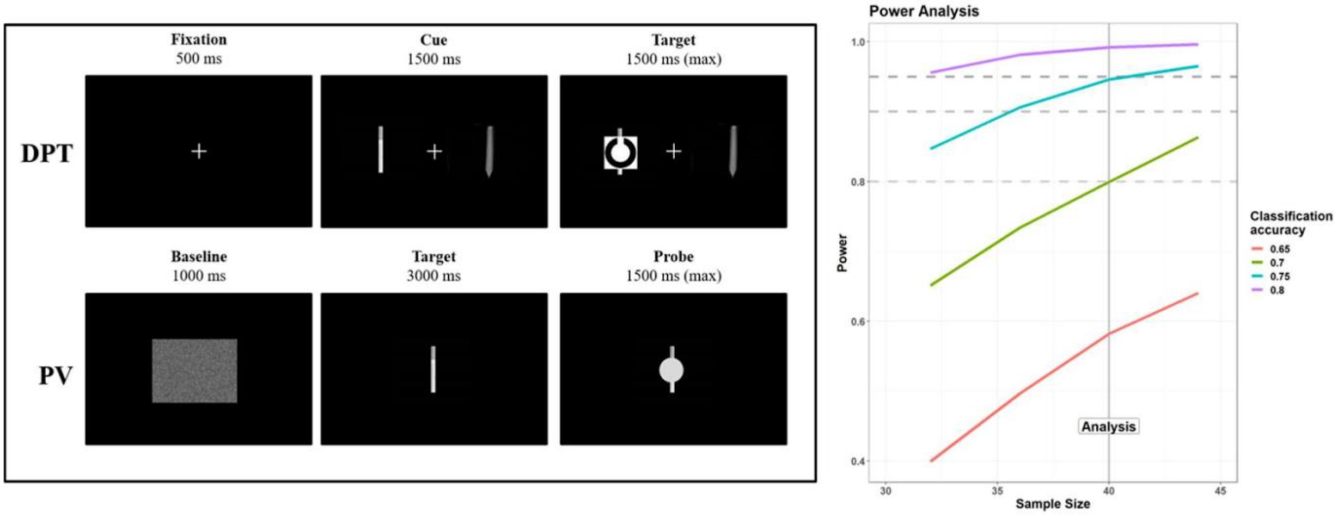

Fig. 1. Dot-Probe task (DPT, upper row) and Passive Viewings are two experimental tasks that differ in their structure and time course (PV, bottom row). Note that the image's stimuli are merely examples; both tasks entailed seeing images of people smoking (see main text). The nominal power for our design is shown in the right panel as a function of sample size and various a priori effect sizes (i.e., classification accuracy to a binomial test).

2.2.1. DPT

It was the first step and the purpose of this was to evaluate whether and how quickly nicotine-related stimuli captured spontaneous (spatial) attention (NRS). A 500-ms fixation cross emerged in the centre of the screen to start each trial. Then, on the left and right sides of the screen, two images (6° x 4.5°) were always shown side by side, around 2° from fixation. A nicotine-related stimulus (NRS, such as a smoker) was shown in one image, while a perceptually identical control stimulus was shown in the other (e.g., a person with otherwise similar features, see the paragraph below). The left and right sides of the NRS's appearance were equal. For these images, we selected a lengthy on-screen duration (i.e., SOA, 1.5s). Previous research has demonstrated how attentional capture effects can manifest differently at various temporal windows, for example, differently at 200 ms than 800 ms (Della Libera et al., 2019). This fine-grained dissociation will be missed if you use a single, extra-long SOA. Nevertheless, our decision was driven by pilot testing, which led us to emphasize overt attentional measures (such as eye movements) over response times, which have been demonstrated to be more responsive to desire (Field et al., 2009), despite needing a longer time range (Field et al., 2004; Mogg et al., 2003). The target eventually appeared after this prolonged SOA, either above the NRS or the control image (balanced). Participants had to use the corresponding arrow keys to indicate where the target, a circle with a gap in either its upper or below part and a 1.5° diameter, was located. The target was displayed on the screen for a maximum of 1.5 seconds before the participants responded. Before the 240 experimental trials, participants underwent 12 practice trials that were subsequently removed from the analysis. Halfway through the activity, a break was planned to give participants a chance to rest.

2.2.2. PV

The goal of the second task, a passive watching task of NRS or control images given in the middle of the screen (4.8° x 3.6°), was to measure autonomic activity through pupil dilation and constriction patterns. The target image was first presented in the fovea for 1 second in each trial, followed by a 3-second display of each image. In both of these periods, the diameter of the pupil was continually measured. A visual cue (a grey dot, 1° in diameter) was presented after the target image in 30% of the trials. In the absence of an otherwise active behavioural task, the goal was to promote persistent attention to the images. The cue was visible on the screen for a maximum of 1.5 seconds until the participants detected it (responded with the spacebar). To maintain a steady luminance across all luminance sources, we also displayed scrambled images on the screen during the inter-trial period. 200 experimental trials were given to participants after 8 practice trials that were later eliminated from analyses. Halfway through the activity, a break was planned to give participants a chance to relax.

2.2.3. Images selection

Images were taken from the validated and comprehensive collection of smoking-related images known as the SmoCuDa database (Manoliu et al., 2020). Pilot testing led to the final selection of 10 smoking-related images (i.e., social stimuli). To the best of our ability, each stimulus was matched with a control image that was similar to it but for the information connected to smoking. Each stimulus was converted to a grayscale image and then processed to equalize its mean luminance. All of the images were scaled down from their original sizes of 800 × 600 pixels to meet the requirements of each job.

2.3. Data processing

2.3.1. DPT

Practice trials and anticipations were disregarded (responses less than 100 ms, 0.005%). There were no exclusions linked to poor task accuracy because all individuals performed well on this task (minimum accuracy: 80.4%). Furthermore, this measure was not considered further in the analysis because accuracy was on average quite high (M= 98.4%, SD= 2.95%), with little variability. Instead, we looked at the average Response Times (RTs) for correct answers. To get positive results that indicate increased attentional engagement with NRS, we computed RTs for each Condition (NRS, control), and then subtracted the former from the latter (i.e., faster responses when probes appear over NRS).

The next step was to measure eye movements. When data were available for both eyes, we only kept the X and Y positions of the gaze and averaged them. We also decided, before testing, to eliminate from the sample any participant who had less than 50% of valid trials. As a precaution, we discarded the trials in which more than 40% of the data were missing (this includes blinks, artefacts, lost connection with the eye-tracker, etc.). Due to this, 6 subjects were discarded from the primary analysis (note: other participants, for a total of 11, were discarded for the same reason applied to the PV task). There were very few missing trials for the remaining subjects (2.5% - 5.2% for smokers and 5.2% - 8.2% for controls). The remaining recordings were then linearly interpolated for the X and Y axes to fill in the gaps. Before the target probe, the cue was shown for 1500 ms during which time we concentrated on the analyses. Through an automated, velocity-based technique, we were able to recreate the pattern of eye fixations during this window. Only fixation events lasting at least 40 ms were taken into account. As a starting point, we calculated for each participant the percentage of initial fixations that occurred in the NRS region as opposed to the control region. This variable was created to measure how quickly and automatically NRS was able to capture attention and eye movement data. The total duration of fixations for each image Condition was then used to calculate the dwell time for each trial. This variable, which was intended to index a more or less thorough visual scanning of the various image classes, is also consistent with earlier research. Both of these factors were subtracted to create bias scores, with negative values reflecting a bias toward control pictures and positive ones reflecting a bias toward NRS.

2.3.2. PV part

We initially eliminated practice trials. Missed responses to the infrequent probe were extremely uncommon (0.002%), indicating some interaction with the visuals that were displayed. The RTs to the probe for NRS vs. control images were calculated as a preliminary indicator, and the former was subtracted from the latter so that positive values indicated increased attentional involvement with NRS. Next, we evaluated the time course of pupil dilation, mostly utilizing preprocessing techniques used in earlier studies (Dureux et al., 2021). The average pupil size of the left and right eyes was measured first, but only when both signals were reliable as indicated by the eye tracker's flanking signals. The baseline period (1s scrambled images) and the 3s window during which the images were displayed were the main subjects of our analyses. Although rare (0.0002%), unrealistic values for pupil diameter (2 mm and > 7 mm) were left out. We employed an interpolation method similar to the DPT for missing samples within each trial, excluding trials with more than 40% missing data (this includes blinks, artefacts, lost connection with the eye tracker, etc.), and linearly interpolating gaps in the remaining trials. The primary analysis excluded participants (N=11) with fewer than 50% of valid trials. There were not many missing trials for the remaining participants (controls: 10% ± 13% and smokers: 8.4% ± 13.6%). By obtaining the median pupil diameter for each time bin, we down-sampled the data to 25ms epochs after applying a low-pass filter to the raw traces. The two groups' average pupil sizes were comparable (4.7mm for smokers vs. 4.56mm for controls, t(37.66)= 0.462, p= 0.647). It should be noted that all individuals were advised to abstain from smoking before the experiment, even though the acute effects of nicotine intake are known to broadly constrict the pupils (Wardhani et al., 2020). For each participant, we independently z-transformed pupil diameter values to better account for individual (and group) differences (Dureux et al., 2021). In this method, scores represent dilatation (positive values) or constriction (negative values) expressed as a fraction of the overall participant's variability and, regardless of baseline values, a value of 0 represents the subject-specific mean pupil diameter. By subtracting the first sample from this epoch, all series were finally realigned to the start of the target image phase (either NRS or control). When analyses were limited to the PV task, we fully evaluated the traces. But instead of focusing on the extraordinarily high dimensionality of these data, which leads to overfitting, for the major analysis using a multivariate classifier, we chose to concentrate on a time window determined via a cluster-based permutation test. The multiple comparisons in autocorrelated data problems can be handled very elegantly by the cluster-based permutation test, but this may result in a less accurate estimation of the temporal features of the reported effects (for example, latency; Sassenhagen & Draschkow, 2019); however, since pupil dilation is a physiological signal that is much slower than, say, the electric or magnetic signals captured by EEG or MEG, we did not anticipate this to be problematic. Positive values denoted greater pupil dilatation to NRS and negative values a relative constriction; traces from NRS versus control pictures were subtracted in this manner (see Fig. 2); the values employed as predictors were therefore the mean, cluster-wide differences in these curves for each participant.

2.4. Analyses

R 4.1.2 was used to perform the analyses (The R Core Team, 2018). First, individual two-sample t-tests were used to evaluate each measure of interest with Welch's correction for uneven variances (two-tailed). The primary focus of this research was to test the generalizability of these indicators and their capacity to foretell smoking status in brand-new, untested individuals. This was done to test if autonomic measurements and eye tracking may serve as reliable biomarkers for smoking behaviour on a global level. We started by using a Best Subset Regression method to compute general (logistic) linear models. The issue of numerous comparisons was addressed by testing all potential predictor combinations in glms and only choosing the model with the lowest Bayesian and Akaike Information Criteria as the overall best model.

The best features were then investigated in subsequent cross-validated logistic regressions using this method, which was also employed for the initial features selection stage. Using a Leave-One-(Subject)-Out (LOO) cross-validation design, we only included one participant in the test set circularly. After that, we calculated the classifier's sensitivity, specificity, and area under the curve along with a measure of overall classification accuracy, which was put into a one-tailed binomial test.

Finally, we conducted correlation analyses between the relevant variables derived from the two tasks, the individual measures of smoking intensity (e.g., daily cigarette consumption) or subjective craving (e.g., QSU-brief, abstinence duration), and the predictions of the classifier for each participant (i.e., the estimated probability to belong to one group or another). The tiny sample size should be taken into consideration when using correlation analysis.

CHAPTER 3. RESULTS

3.1. Individual results

Table 1 presents descriptive findings.

Table 1 Mean (standard deviation) descriptive values for the five variables of interest, separately for group and image condition

		Non-smokers		Smokers	
Task	Variable	Control	NRS	Control	NRS
DPT	RTs (ms)	540(69)	537(71)	547(88)	538(87)
	Dwell time (ms)	463(118)	468(116)	502(85)	513(84)
	First Fixation (%)	51(3.2)	49(3.2)	50(2.9)	50(2.9)
PV	RTs (ms)	416(68)	420(70)	448(106)	448(105)
	Pupil size (z scores)	0.175(0.148)	0.211(0.137)	0.140(0.104)	0.116(0.083)

NRS nicotine-related stimuli, *DPT* dot-probe task, *RT* response time, *PV* passive viewing

3.1.1. DPT

None of the three factors that were taken into account for this task varied between groups. RTs: t(36.59) = 1.51, p = 0.139, two-tailed. Dwell time: t(28.89) = 0.485, p = 0.631, two-tailed. Proportion of first fixations: t(37.88) = 0.169, p = 0.867, two-tailed.

3.1.2. PV

When the probe was displayed over images of the NRS versus the control (t(37.82) = 0.55, p = 0.58, two-tailed), RTs did not differ between the two groups. However, the measurement of pupil size showed considerable group variations. A consistent, steep pattern of pupil dilation predominated the changes in pupil diameter overall. However, there was also a relationship between Group and Condition (Fig. 2). Pupil size to NRS versus control pictures significantly differed between groups ($p < 0.001$, 5,000 permutations) in a large temporal cluster (800-2,850 ms), according to a cluster-based permutation test. Thus, for each participant between 800 and 2,850 ms, we estimated the mean, cluster-wide difference between pupil diameter to NRS versus control images. Smokers showed an overall pattern of pupil constriction (M = -0.025, SD = 0.075) in this window, which result was significantly different (M = 0.036, SD = 0.067) (t(37.58) = 2.7, p = 0.01, two-tailed) from the overall pattern of pupil dilation seen in non-smokers. This variable was then used for classification. We also performed the cluster-based permutation test once again for each group to find any significant time points for dilatation or constriction (instead of a difference compared with the other group). Smokers showed considerable pupil constriction for NRS images during a temporal cluster (925–1,175 ms) (t(19) = –2.83, p = 0.01). Later, however, a significant dilatation was seen in non-smokers (1,475-2,375 ms, t(19) = 2.75, p = 0.013). No more notable departures from the norm were found.

3.2. Multivariate classification

The best model linked pupil size to NRS pictures and RTs, and it had an AUC of 0.745, cross-validation accuracy of 75%, and extremely good sensitivity and specificity (both 75%). A one-tailed binomial test (p = 0.001, CI 95% [58.8- 87.3]) revealed that the performance was significantly better than chance. Only pupil size was used as a predictor of smoking status in the second-best model. In this instance, the classifier performed well, achieving an accuracy of 65% (its sensitivity and specificity were both 65%, and its AUC was 0.723).

A one-tailed binomial test revealed that this performance was likewise considerably better than chance (p = 0.04, CI 95% [48.3-79.4]). The model with both predictors was not noticeably superior when measured against a chance level of 65% (p = 0.12). In contrast, the model that just included RTs fared quite poorly, with a cross-validation accuracy of 52.5% (Sensitivity: 55%; Specificity: 50%; AUC: 0.535). Overall, these findings imply that measures of attentional bias, particularly the autonomic response communicated by pupils, which is required and sufficient for the classification of the smoking state, have extremely excellent classification capabilities.

3.3. Explorative analyses and correlations

In the next PV task, two DPT task measurements were associated with pupil size. This implies that the pattern of pupil constriction seen in smokers may be somewhat correlated with behavioural variables more traditionally linked to attentional bias.

First, there was a negative correlation with dwell time (r = -0.42, CI95% [-0.65, -0.12], t(38) = 2.83, p = 0.0073), which was of similar magnitude in the two groups. An intensified constriction of the pupils during the PV task was connected with a more comprehensive visual investigation of the NRS images. In the DPT task, there was a second positive association between pupil size to NRS and the percentage of initial fixations toward NRS stimuli (r = 0.29, CI95% [-0.02, 0.55], t(38) = 1.89, p = 0.066). Only smokers (smokers: r = 0.54, CI95% [0.12, 0.79], t(18) = 2.69, p = 0.015; non-smokers: r = 0.07, p = 0.76, n.s.) showed a significant correlation when it was evaluated within each group though the difference between the correlations did not show a significant correlation (Fisher's z = 1.533, p = 0.125). Smokers who displayed a more significant pupil constriction in the PV tended to move their initial attention away from NRS. Overall, non-smokers showed a positive correlation between dwell time and the initial fixation's direction (r = 0.46, CI95% [0.02-0.75], t(18) = 2.186, p = 0.042), while smokers did not (r = -0.02, p = 0.95, n.s.).

Then we turned our attention to the group of smokers. First, we saw that there was a correlation between all three questionnaires, but not with the behavioural measures derived from the tasks. For each smoker, we evaluated the classifier's predictions, i.e., the likelihood of being in the smokers' group as opposed to the non-smokers' group (values 0.5, i.e., classification errors). Surprisingly, for those who smoked less (r = -0.48, CI 95% [-0.76, -0.05], t(18) = 2.33, p = 0.03), the classifier worked best (and the pupil contracted more forcefully). We also observe a relationship between classifier performance and abstinence duration, or the number of hours since the previous smoke. The classification is more accurate the longer the abstinence has been maintained (r = 0.55, CI95% [0.15-0.8], t(18) = 2.82, p = 0.01). In other words, those who had smoked more recently had a higher rate of false negatives (Fig. 3).

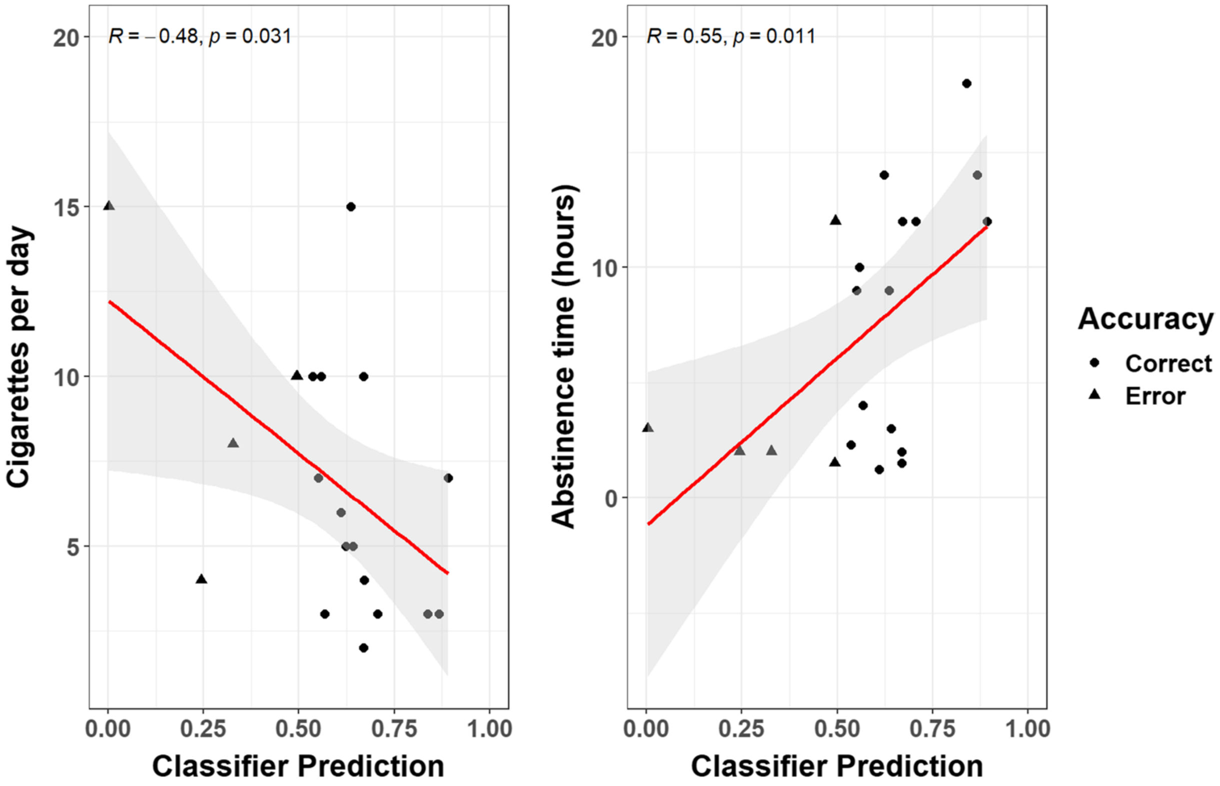

Fig 3. *Measures of smoking intensity (self-reported cigarettes per day) and abstinence duration and the performance of the classifier (data points are either circles or triangles, indicating the classification was right or incorrect) (hours). Data depictions are limited to smokers, therefore all errors are false negatives. Although RTs played a small influence in the DPT task, pupil dilation was mostly responsible for the classifier's results. Light smokers and those who abstained from smoking for longer lengths of time before the experiment had the best results from the classifier, with the pupil contracting more forcefully (which are partly the same subgroup of participants).*

CHAPETER 4. DISCUSSION

With the aid of eye-tracking methods, we set out to look at the markers of attentional priority in smokers. The results demonstrate that behavioural (e.g., RTs) and eye fixation measures were not sensitive enough to indicate attentional capture, much less correctly predicting smoking status, in contrast to earlier results. However, we found variations between smokers and non-smokers in the time course of pupil dilation to NRS, which served as a valid indicator of smoking status. We asked participants to dwell on smoke-related or unrelated images for 3 seconds in a passive viewing task, waiting for an infrequently presented probe. This led to the primary pattern at the level of pupil diameter, which is a very significant, sustained, steep, and dilation across the whole temporal window and conditions. However, the effect of smoking status on pupil dilatation to NRS stimuli as opposed to neutral ones varied. We found an interaction in which, on average, smokers' pupils tended to constrict more than non-smokers' ones. This interaction began at about 800 ms and persisted for up to 2850 ms. Additionally, the one prior study (Chae et al., 2008) that measured pupil size in response to NRS reported pupil dilatation in a sample of 7 smokers (compared to 12 controls), analogous to when viewing highly arousing images (regardless of their valence). However, their task was purely passive gazing, requiring them to watch images on a screen for a very long duration (30 s). In our study, the primary challenge was waiting for and responding rapidly to the infrequent probe. It's probable that attentional resources were slightly diverted from this main objective because the pupil largely reflected this with a strong dilation-relative constriction. Thus, the pupil constriction seen in this context might be task-related. We cannot extrapolate the results beyond 3 s due to our more constrained temporal window, and the risk of dilation at subsequent stages is still present. On the other hand, our study's quick event-related architecture may have allowed for an unheard-before level of precision in the first perceptual phase. We believe that the results could be explained by smokers' early attentional orienting toward NRS, even though this is not the only reason. The pupillary light reflex (PLR), which initiates at 200–250 ms and can extend to 1-2 s (Mathôt, 2020), is the primary cause of pupil constriction. PLR may still happen even when brightness is precisely accounted for, depending on a shift in the visual scene and several variables like awareness, eye movements, or visual attention (Mathôt & van der Stigchel, 2015). We expect that NRS stimuli may cause eye movements or patterns of visual attention in smokers that are more likely to amplify the PLR in particular images. Since smaller pupils result in improved visual acuity, the subsequent pupil responses can be thought of as predictive sensory tuning processes (Mathôt, 2020). Constriction signals a bias in favour of central vision. Another option relates to the particular work requirements of our paradigm. The primary objective in this situation was to respond rapidly to the irregular probing, and the pupil was primarily reflecting that with a strong dilatation. In this situation, relative constriction may indicate that attentional resources were diverted from the primary objective. In other words, the restriction we discuss here could vary depending on the task. Finally, our findings do not completely rule out theories that do not implicate attentional processes. The results could, for instance, be explained by the two groups' distinct affective reactions, with non-smokers subconsciously interpreting NRS stimuli as more aversive, leading to the observed pupil dilation. This pattern, which is absent among smokers, might disappear as a result of more people being familiar with NRS, albeit it would be difficult to explain how it would reverse in a constriction using these terms. Besides dwell times, which are more traditionally linked to spatial attentional biases, showed an association with the outcomes of the DPT task. Although smokers did not exhibit significantly longer stay periods for NRS, or longer visual exploration of NRS images, at least not in our environment, the preference for NRS was associated with a more pronounced pupillary constriction in a subsequent, independent task (PV). The link between pupil dilation and directional bias toward NRS, for which there was a positive correlation, and for smokers exclusively, revealed the contrary to be true. In other words, pupil contraction was more pronounced in those who preferred to first look away from NRS stimuli during the DPT task. It is useful to think about how well these results match up with prior research when interpreting them. Smokers looked at smoking-related images more often than control images, shifted their focus there more frequently, and responded to probes there more quickly (Field, Mogg, Brandley, 2003).

Pupil constriction to NRS in this scenario still had some predictive validity, albeit possibly being task-dependent. In contrast to other conventional proxy measures of attentional capture, pupil size's autonomic signal was a far stronger predictor of smoking status in our study. Although additional proxy measures, such as RTs gains to NRS stimuli, may also help the classifier perform better, increasing its accuracy to 75%, it appears that the information communicated by pupil size is both necessary and sufficient for a successful categorization of smoking status (65% accuracy). Both the modelling approach was chosen and the variety of behavioural indicators to be fed to the classifier have a lot of space for improvement. However, based on our findings, pupil dilation is a particularly strong and sensitive candidate for achieving this goal. Furthermore, we contend that the emphasis on prediction performance -as opposed to traditional inference and significance testing- represents a significant advancement in the effort to describe reliable biomarkers of addiction and their cognitive impacts (Yarkoni & Westfall, 2017). Focusing on the occasions where the classifier fails to accurately predict a person's smoking status is also fascinating (i.e., false negatives). Even though it seems contradictory, those who smoked more cigarettes per day—a proxy measure for smoking intensity—had a higher incidence of this. In other words, for people who smoked less, the classifier worked best and the pupil contracted more forcefully. These findings are consistent with Mogg et al. (2005), smokers with lower degrees of nicotine dependency were able to keep their attention for longer during a visual probe task and approached smoking-related signals more quickly than smokers with higher levels of nicotine dependence. Additionally, the results of this study showed that nicotine dependency increases biases for cues connected to smoking. These findings agree with those of Mogg et al. (2003) and Kwak et al. (2007), who discovered that smokers look at images of smoking for a longer period than they do at images of nonsmoking. As a result, earlier research discovered longer NRS dwell times even at lower nicotine dependence levels. Although our findings extend to the autonomic response communicated by pupil size, they are consistent with previous ground-breaking investigations and theoretical theories (Di Chiara, 2000).

One of the purposes of the current study was to investigate the relationship between the stimulus valence and attentional bias measures, as well as the motivational and emotional valence of smoking-related signals in smokers versus non-smokers using both implicit and explicit measures. Smokers and non-smokers showed significantly different preferences for smoking-related cues on both measures of stimulus valence. This pattern of outcomes is consistent with earlier data from rating activities. Similarly, this may somewhat detract from the concept that treatments to modify attentional bias can be successful. Perhaps not the most significant trait of smokers seeking therapy is attentional bias Attentional bias may not be the most important characteristic of smokers seeking treatment, aside from the challenging significant choice of a paradigm that can significant attention for an extended amount of time in real-world settings (i.e., outside the lab) and yet retains a short administration time. On the other hand, attentional capture may still be effective in identifying the stage of addiction and thus information about alternate management approaches. Additionally, we did discover some inconclusive evidence that attentional bias was stronger for those who abstained from smoking for a longer period before the experiment, which may indicate a connection with craving. Accordingly, a more inclusive conclusion may be that attentional bias is potentially a helpful, objective measure that can be obtained in longitudinal and interventional studies, however, a full picture wouldn't be realized until all the remaining pieces were in place. Eye tracking has been extensively examined and linked to cognitive functions in both health and disease, making it a viable method for future research. It is also a relatively simple, portable, and affordable technology. More particular, pupil dilation appears to be at a position that is more than optimal for achieving this goal since it can simultaneously represent affective, perceptual/attentional, and cognitive processes, providing an appropriately complex picture.

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