International Journal of Psychophysiology 96 (2015) 201–209

Contents lists available at ScienceDirect

International Journal of Psychophysiology

journal homepage: www.elsevier.com/locate/ijpsycho

An odor identification approach based on event-related pupil dilation and gaze focus

Nadia Aguillon-Hernandez [a,*], Marine Naudin [b], Laëtitia Roché [a], Frédérique Bonnet-Brilhault [a,c], Catherine Belzung [b], Joëlle Martineau [a], Boriana Atanasova [b]

[a] Team 1 "Autism," UMR INSERM U 930, Université François Rabelais de Tours, Tours, France
[b] Team 4 "Affective Disorders," UMR INSERM U 930, Université François Rabelais de Tours, Tours, France
[c] CHRU de Tours, Centre Universitaire de Pédopsychiatrie, France

ARTICLE INFO

Article history:
Received 19 November 2014
Received in revised form 23 March 2015
Accepted 24 March 2015
Available online 31 March 2015

Keywords:
Olfaction
Odor identification
Eye tracking
Pupillary response
Visual attention
Gaze focus
Event-related pupil dilation

ABSTRACT

Olfactory disorders constitute a potential marker of many diseases and are considered valuable clues to the diagnosis and evaluation of progression for many disorders. The most commonly used test for the evaluation of impairments of olfactory identification requires the active participation of the subject, who must select the correct name of the perceived odor from a list. An alternative method is required because speech may be impaired or not yet learned in many patients. As odor identification is known to be facilitated by searching for visual clues, we aimed to develop an objective, vision-based approach for the evaluation of odor identification. We used an eye tracking method to quantify pupillary and ocular responses during the simultaneous presentation of olfactory and visual stimuli, in 39 healthy participants aged from 19 to 77 years. Odor presentation triggered an increase in pupil dilation and gaze focus on the picture corresponding to the odor presented. These results suggest that odorant stimuli increase recruitment of the sympathetic system (as demonstrated by the reactivity of the pupil) and draw attention to the visual clue. These results validate the objectivity of this method.

1. Introduction

Alterations to olfaction have been described in various human neurodegenerative disorders (Atanasova et al., 2011), such as Alzheimer's disease (Warner et al., 1986) and Parkinson's disease (Ansari and Johnson, 1975; Doty et al., 1988b; Hawkes et al., 1997; Hawkes and Shephard, 1993; Ward et al., 1983), neurodevelopmental disorders, such as autism (Baranek et al., 2006; Kientz and Dunn, 1997; Rogers et al., 2003), and neuropsychiatric disorders, such as major depression (Pause et al., 2001; Croy et al., 2014) and schizophrenia (Moberg et al., 1997). In neurodegenerative diseases, both the peripheral and central components of the olfactory system are affected (Braak et al., 2002; Del Tredici et al., 2002; Mesholam et al., 1998; Price et al., 1991). At the very early stages, these neurodegenerative diseases can be difficult to diagnose. In particular, differential diagnosis between Alzheimer disease (AD) and depression in elderly cannot be easy to establish (McLean, 1987) and may impede early therapeutic care. However, these two categories of patients differ in the nature of the olfactory disorder, studies comparing odor identification performance between patients AD and patients with depression have reported most important alterations in AD compared to patients with depression (McCaffrey et al., 2000; Pentzek et al., 2007; Solomon et al., 1998). Recent studies have shown the potential interest of olfactory tests to aid in early diagnosis of these diseases (Naudin et al., 2014). Concerning, autistic spectrum disorder, subjects have also been shown to be significantly less accurate than controls in olfactory identification tests (Bennetto et al., 2007). These findings may have implications for our understanding of these disorders, with the inclusion of sensorial disorders in the clinical profiles of patients, potentially facilitating diagnosis and improving patient care.

The tests most widely used to investigate olfactory identification disorders in clinical research are the University of Pennsylvania Smell Identification Test (UPSIT) (Doty et al., 1984) and the "Sniffin' Sticks" test (Hummel et al., 1997). In these tests, the participants are asked to identify the perceived odor, in a four-alternative forced-choice procedure. These tests are currently the best tools available for the diagnosis of olfactory disorders. However, they are subject to certain limitations because they require the active participation of the subject and good language acquisition. Speech may be impaired or not yet learned in some patients, so an alternative approach is required. We propose here an alternative method for evaluating odor identification that does not involve speech or active cognitive participation and is therefore suitable for use with a large number of patients. This alternative objective method is based on the principle of the multimodal

* Corresponding author at: Inserm U 930, Bâtiment B1A, CHRU Bretonneau, 37044 Tours Cedex 9, France. Tel.: +33 2 47 47 97 47; fax: +33 2 47 47 67 47.
E-mail address: nadia.aguillon@univ-tours.fr (N. Aguillon-Hernandez).

http://dx.doi.org/10.1016/j.ijpsycho.2015.03.009
0167-8760/

convergence of primary sensory inputs. Studies in mammals (rat and monkey) suggest that primary sensory information converges on common structures, such as the hippocampus (Deadwyler et al., 1987) and orbitofrontal cortex (Carmichael and Price, 1995). The orbitofrontal cortex has been shown to receive afferent input from both the primary olfactory (piriform) cortex and visual association areas (Carmichael and Price, 1995), and as has been shown in humans by an fMRI study, it participates in the orientation of visual attention in the presence of a salient visual stimulus (Armony and Dolan, 2002). In our study, we call this orientation of the eyes guided by exogenous events: the event-related gaze focus (ERGF). Multimodal integration of this type has been described in studies combining auditory and visual stimuli. For example, subjects hearing a word spontaneously oriented their gaze to the picture corresponding to this word in an eye tracking study (Huettig and Altmann, 2005). A similar phenomenon has been demonstrated in studies of the multimodal integration of visual and olfactory stimuli, in which odors were found to draw the attention of test subjects to visual objects corresponding to the odors concerned (Chen et al., 2013; Seigneuric et al., 2010; Seo et al., 2010).

The orbitofrontal cortex is involved in the orientation of visual attention in the presence of a stimulus, and odor identification is facilitated by searches for visual clues (Chen et al., 2013; Gottfried and Dolan, 2003; Seigneuric et al., 2010; Seo et al., 2010). We therefore used this principle to develop a method based on perceptual processes without the need for active cognitive processes, for tests of odor identification in patients unable to participate in conventional tests. We also assessed subjective perceptions of the intensity and hedonism of the odor, as such factors have been shown to influence odor identification (Kare, 2012). In addition to the ERGF, we also considered a physiological response to olfactory stimulation—pupil dilation (Winneke, 1992)—which reflects the physiological mobilization of the body. Various autonomic parameters, including heart rate (Alaoui-Ismaïli et al., 1997; Bensafi et al., 2002a; Brauchli et al., 1995), electrodermal activity (Bensafi et al., 2002b; Borsanyi and Blanchard, 1962; Møller and Dijksterhuis, 2003; Shock and Coombs, 1973), respiratory frequency (Doty et al., 1988a; Eccles et al., 1989; Laing, 1983) and pupil size (Schneider et al., 2009; Winneke, 1992), react to olfactory stimuli. Pupillary response is known to be modulated by two major reflexes: the photomotor reflex (inducing constriction of the pupil in response to light stimulation under the influence of the parasympathetic nervous system) (Beatty and Lucero-Wagoner, 2000) and the psychosensory reflex (inducing dilation of the pupil in response to a cognitive load, under the influence of the sympathetic nervous system) (Andreassi, 2000; Granholm et al., 1996). Pupillary dilation is a useful parameter for two key reasons: (1) changes in pupillary dilation are more sensitive than many other physiological parameters (Bradley et al., 2008; Kahneman and Peavler, 1969), and (2) this parameter can be recorded simultaneously with gaze position with a non-contact method (Martineau et al., 2011). In our study, we call this pupil dilation in response to stimulation: the event-related pupil dilation (ERPD).

The aim of our study was to validate, in an adult population, the association between odor recognition and the direction of attention to a picture corresponding to the odor and pupillary dilation. Using an eye tracking system to measure the pupil (ERPD) and visual exploratory responses (ERGF) associated with olfactory stimulation, we tested the hypothesis that olfactory stimulation leads to pupil dilation and an increase in exploration of the picture corresponding to the odor.

2. Experimental procedures

2.1. Participants

We recruited 39 non-smokers (23 women and 16 men), aged 19 to 77 years (mean ± SD age = 37.6 ± 15.1 years). At recruitment, the subjects were informed that they would have to smell different compounds that can be found in food products and in the environment (urban or countryside). They were provided with full details about the experimental protocol before the tests began. All participants were informed of their rights before taking part in procedures approved by the local ethics committee, and all gave written informed consent in accordance with the Helsinki Declaration (World, 2004).

The inclusion criteria included normal or corrected vision, no history of an eye disorder, and no self-reported problems relating to sense of smell. The exclusion criteria for all participants included possible brain damage, major medical problems, intake of pharmacological molecules targeting the vegetative system, current substance abuse, allergy, a current cold, or a transient problem with sense of smell. All subjects were selected on the basis of an absence of anosmia to the odorants used.

2.2. Stimuli

2.2.1. Olfactory stimuli

We presented 10 familiar odors, corresponding to plants (mint), foods (orange, mushroom, bread, vanilla, coconut, strawberry, raw potato), industrial materials (oil paint), and agricultural products (wet earth). The olfactory stimuli used, developed by Sentosphere®, were non-toxic and were presented in a solid form, in a cup at suprathreshold concentrations. They were obtained by adding between 10% and 30% (according to the odor) of fragrance ingredient on the "seeds", which allow fixing the odors on a solid support. All olfactory stimuli were presented during 10 s.

2.2.2. Visual stimuli

Olfactory stimuli were presented simultaneously with a visual stimulus consisting of a board bearing four color pictures. The creation of the database of visual stimuli involved three stages of validation. 1)

All the pictures on a given board belonged to the same semantic field (e.g., forest smells). Picture fidelity was validated with a questionnaire completed by 150 people aged from 2 to 80 years (mean age = 37.6 years ± 15.1), and only pictures accepted by over 80% of respondents were used to form the database. (2) On each board, the surface brightness and visual characteristics of each picture were homogenized and a pilot study was carried out with 15 people (mean age = 28.8 ± 12.6 years) to check that each image had a similar influence on visual exploration behavior in the absence of olfactory stimulation. (3) The four pictures on each board included one corresponding to the odor (the target), a picture of an item with a smell very similar to that presented (the competitor. For example, for the smell of orange, the competitor image was a picture of a lemon), a picture of an item with a smell different from that presented (distractor 1; for example, for the smell of orange, the distractor 1 image was that of a kiwi) and a picture of an item with a smell very different from that presented (distractor 2; for example, for the smell of orange, the distractor 2 image was that of a pear). This gradient of correspondence between the items and the odor was established in a pilot study including 10 control participants (mean age = 31.1 years ± 4.9).

Between boards, the participants were presented with an image of a central cross, to refocus the gaze. The pupillary reflex in response to light (photomotor reflex) was prevented by ensuring that the brightness of the cross image was identical to that of the boards. The stimuli were presented on a computer screen (17″), at a distance of about 90 cm from the subjects' eyes. Each board was 47.5 cm × 27 cm in size, with a resolution of 1920 × 1080 px (visual angle = 30°). All visual stimuli were homogenized (brightness (20 lx), color (histogram values for the red, green, and blue components of each board: R = 242, G = 239, B = 234), and size (1920 × 1080 px)).

2.3. Materials

2.3.1. Eye tracking

Visual stimuli were delivered by the head-free mounted FaceLab® eye tracking system, which consists of a computer equipped with two