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CHANGES OF OLFACTORY PROCESSING IN CHILDHOOD AND ADOLESCENCE

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Abstract—*Objectives:* Olfactory event-related potentials (OERPs) are widely used to study central odor processing. Only a few studies used this method in children and adolescents. Aim of the current study therefore was to measure OERP and the possible influences of age and sex on central odor processing in this age group.

***Methods:* A total of 81 children between 6 and 17 years of age were included in this study. OERP in response to a rose-like odor were measured from three recording positions (Fz, Cz, Pz) according to the 10–20 system. Stimuli were presented by means of a computer-controlled olfactometer.**

***Results:* Age had a significant influence on the amplitudes of the late positivity with younger children showing larger amplitudes. Although age did not significantly affect the latencies of OERP, interactions of recording positions and latencies between younger and older children and between girls and boys were found.**

***Conclusions:* OERP can be used to study central odor processing in children older than 6 years of age. Central odor processing changes from childhood to adolescents possibly reflecting maturation of the brain.**

Key words: children, olfaction, event-related potentials, olfactory testing, olfactory processing.

INTRODUCTION

Children, as young as newborns, have a well-developed sense of smell. They are able, for example, to discriminate between familiar and unfamiliar odors (Romantshik et al., 2007). In addition previous studies have shown that the sense of smell is already functional *in utero*, exposing the fetus to odorous substances within the amniotic fluid (Schaal et al., 2000). The importance of the sense of smell changes with the development of the child (Schaal, 1988). During the newborn and infant period it is crucial for feeding and bonding with parents (Marlier et al., 1997; Winberg and Porter, 1998). Therefore the sense of smell is of great importance for the newborn, especially because the other senses are not fully developed at this age. It has been suggested that the sense of smell becomes less important as the visual and auditory senses develop (Gilad et al., 2004). This is – at least partly – opposed by studies showing that the sense of smell is of great importance for quality of life in adults (Croy et al., 2014). So far no systemic evaluation of quality of life in children with olfactory impairment has been undertaken. Possible reasons for a reduced olfactory function are many – ranging from congenital anosmia over infections to head trauma (Temmel et al., 2002). Although the prevalence of olfactory dysfunction is by far not as frequent as in older adults, several studies reported an impaired olfactory function in children due to, for example, head trauma (Bakker et al., 2014; Schriever et al., 2014c), psychiatric disorders (Roessner et al., 2005; Schecklmann et al., 2013), obesity (Obrebowski et al., 2000) or rhinological problems (Konstantinidis et al., 2005). Psychophysical smell tests such as the UPSIT (Doty et al., 1984) and the ''Sniffin' Sticks'' battery (Hummel et al., 1997; Kobal et al., 2000) are used to quantify olfactory impairment. Modified olfactory tests, for example, the ''Smell Wheel'' (Cameron and Doty, 2013) and the ''Sniffin' Kids'' test (Schriever et al., 2014b) have been developed to meet the requirements for testing children. In addition to psychophysical measurements, which require the compliance of the patients/subjects a less biased method – measurement of olfactory event-related potentials (OERPs) – has been established, especially in clinical settings (Kobal, 1981; Hummel and Kobal, 2001; Rombaux et al., 2009, 2012). This method is widely used in evaluating the olfactory function in adults. Due to its good temporal resolution the method of measuring OERPs is additionally used to study central odor processing. Factors such as age (Murphy et al., 2000), sex (Stuck et al., 2006) or odor valence (Lundstrom et al., 2006) have been identified to influence the central odor processing in adults by means of OERPs. To our knowledge only a few studies have used this method for evaluating the sense of smell in children and adolescents (Sandford et al., 2006; Hummel et al., 2007; Chopra

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Abbreviations: EEG, electroencephalography; LP, late positivity; OERPs, olfactory event-related potentials; PEA, phenylethylalcohol.

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et al., 2008; Qu et al., 2010; Schriever et al., 2014a). Most of these studies included small numbers of children and adolescents or did not give a detailed report about the obtained OERPs. The aim of the current study therefore was to measure the central odor processing by means of OERPs in children and explore possible effects of age and sex on the detection and components of the OERPs.

EXPERIMENTAL PROCEDURES

All parts of the study were conducted according to the declaration of Helsinki and were approved by the local Ethics Committee of the Medical Faculty of the Technical University of Dresden (number EK121042013). The study was verbally explained to the parents and participating children in great detail involving the study design, procedure and possible risks. In addition written study information was provided to the parents and children separately, according to the age of the children. Children younger than 8 years of age only received verbal information. Thus, informed consent/assent was obtained from all parents and children participating in the study.

Participants

A total of 94 children between 2 and 17 years of age were recruited by flyers distributed on the University Campus of the Technical University of Dresden. None of the children exhibited any neurological disease or diseases, which are known to influence the sense of smell (e.g. diabetes mellitus, epilepsy). All children ($n = 11$) below the age of 6 years were excluded from the final analysis because we were not able to finish the study in all children of this age group as planned so that the number of children in this particular age group was much smaller than in other age groups, which made comparisons difficult. In addition 2 children (7 and 8 years) were excluded because they tested hyposmic by means of the ''Sniffin' Kids'' odor identification test. Therefore 81 children (45 girls, 36 boys) between 6 and 17 years (mean 11.8 ± 3.4 years), were included in the final analysis. The mean age did not differ between girls (mean 12.2 ± 3.5 years) and boys (mean 11.2 ± 3.3 years) ($t = 1.25$, $p = 0.22$). To observe possible age differences regarding OERPs the study population was divided into two age groups – 6–11 years and 12–17 years. These age groups were chosen according to a previous study of OERPs in children and adolescents, which used similar age groups (Chopra et al., 2008).

Psychophysical testing

All children were tested with the modified version of the ''Sniffin' Sticks'' odor identification test, the ''Sniffin' Kids'' test (Schriever et al., 2014b), in order to ascertain normosmia. The ''Sniffin' Sticks'' are odor-filled felt-tip pens. The odor is released upon removing the cap of the pen. Each odor is presented for approximately 2 cm under the nostrils for 3 s. The children were asked to identify the presented odor with the help of four descriptors, which were given in pictures, written and read to the children.

Procedure

The study was conducted in one session, which lasted approximately one hour. At the beginning a medical history was obtained regarding possible factors that could influence the sense of smell or alter electroencephalography (EEG) recordings. Then children received the 14-item odor identification test (''Sniffin' Kids'' test).

After this the children were seated in a comfortable chair for measuring OERPs. The EEG electrodes were placed in the appropriate locations and the task was explained to the children. During the measurements the children were asked to play a computer game, in which they had to keep the cursor of the computer mouse in a moving square. This ensured their attention and prevented fast eye movements and blinking. In addition children were sheltered from surrounding sounds by applying white noise, approximately 50 dB, with headphones.

Olfactory stimuli

To elicit OERP phenylethylalcohol (PEA, rose-like smell, Sigma, Deisenhofen, Germany) was used. PEA is used to specifically activate the olfactory system with little or no trigeminal activation. For odor presentation a computer-controlled olfactometer was used (type: OM2s; Burghart, Wedel, Germany). The olfactometer provided a continuous airflow of 6 l/min with heated and humidified air (36.5 °C, 80% relative humidity). The stimulus concentration was set to 50% (v/v) with a duration of 200 ms and an average inter-stimulus interval of 15 s. The odor was monorhinally presented 20 times to each nostril so that subjects received a total of 40 stimuli. The side of the presentation was changed every 10th stimulus.

Data acquisition

Data were recorded using a 16-channel amplifier (SIR: Röttenbach, Germany). Recordings were made from three positions, Fz, Cz and Pz, which were placed according to the international 10–20 system (Jasper, 1958). All electrodes are being located at the vertex of the scalp with Cz in the middle, Fz in the front and Pz parietal to Cz. Linked earlobes were used as reference and grounding electrodes were placed on the mastoids. EEG-segments of 2048 ms, starting 500 ms before stimulus onset, were recorded at a frequency of 250 Hz using a band-pass filter of 0.2–30 Hz.

Data analysis

EEG data were processed using the Matlab (MathWorks, Natick, MA, USA) toolbox Letswave 5 (Mouraux, Brussels, Belgium, http://nocions.webnode.com/letswave). Data were additionally filtered off-line using a band-pass filter (FFT) of 0.3–15 Hz. A baseline correction was applied with a reference interval of 500 ms before stimulus onset. EEG