Chem. Senses 31: 699–704, 2006

doi:10.1093/chemse/bjl011
Advance Access publication July 18, 2006

Laterality of the Olfactory Event-Related Potential Response

Jonas K. Olofsson[1], Daniel A. Broman[1], Paul E. Gilbert[2,3], Pamela Dean[3], Steven Nordin[1,3] and Claire Murphy[2,3,4]

[1]Department of Psychology, Umeå University, Umeå, Sweden, [2]Department of Head and Neck Surgery, University of California San Diego, San Diego, CA, USA, [3]Department of Psychology, San Diego State University, San Diego, CA, USA and [4]San Diego State University–University of California San Diego Joint Doctoral Program in Clinical Psychology, San Diego, CA, USA

Correspondence to be sent to: Claire Murphy, San Diego State University–University of California Joint Doctoral Program in Clinical Psychology, 6363 Alvarado Ct, Suite 101, San Diego, CA 92120-4913, USA. e-mail: cmurphy@sciences.sdsu.edu

Abstract

In experimental practice, odors are commonly applied to only one nostril for recordings of olfactory event-related potentials (OERPs), but the lateralization aspect of the OERP response is unclear regarding both stimulated nostril and cortical topography. The purpose of the present study was to investigate whether stimulated-nostril side affects OERP amplitudes and latencies and whether these potentials indicate lateralization of brain response in healthy, right-handed, young adults. OERPs were recorded from nine electrode sites in response to monorhinal stimulation with amyl acetate in 28 participants. The results showed a general increase in amplitude from frontal to parietal electrode sites (in particular for N1/P3) and generally larger amplitudes on the left hemisphere and midline than on the right hemisphere. There was no main effect of stimulated-nostril side on amplitude. Interactions indicated that N1/P2 amplitude was larger for left- than right-nostril stimulation and larger on the left hemisphere and midline than on the right hemisphere in left-nostril stimulation. No main effect or interactions of stimulated-nostril side over latencies were found and no effects on latencies of sagittal or coronal sites. These findings suggest a general parietal, left-hemisphere predominance in response amplitude to odorous stimulation and imply that either the left or the right nostril may be sufficient for accurate assessment of OERP latency in right-handed, young adults.

Key words: ERP, hemisphere, laterality, OERP, olfaction, smell

Introduction

Recordings of event-related potentials (ERPs) involving the auditory, visual, and somatosensory systems have provided useful, noninvasive assessment of neurophysiological function of sensory and cognitive character over the past four decades (Sutton *et al.*, 1965). These electroencephalographic (EEG) recordings are analyzed by assessing the amplitude and latency of brain activity waves. The amplitude has traditionally been regarded as reflecting the amount of neural resources allocated to the stimulus and the latency reflecting the speed of stimulus processing (e.g., Polich, 1986). However, recent findings indicate that the amplitudes result primarily from dipole orientations and the latencies from combinations of different simultaneously active dipoles and their strength and orientation (e.g., Jing *et al.*, 2006). Although developed much later (Kobal, 1981), the technique for recording olfactory event-related potentials (OERPs) has proven to be fruitful for investigating olfaction in various conditions (Lorig, 2000), including normal aging (e.g., Murphy *et al.*, 2000), dementia (Morgan and Murphy, 2002), gender (Olofsson and Nordin, 2004), brain tumors (Daniels *et al.*, 2001), head trauma (Geisler *et al.*, 1999), and epilepsy (Hummel *et al.*, 1995).

It is well demonstrated that several aspects of the stimulus presentation must be considered for accurate assessment and interpretation of OERPs, such as intensity, quality, and duration of the stimulus as well as interstimulus interval (ISI) and airflow rate (Kobal, 1981, 2003; Morgan *et al.*, 1997; Tateyama *et al.*, 1998; Covington *et al.*, 1999; Lorig, 2000; see also Evans *et al.*, 1993). A potentially important stimulation parameter that has received very limited attention in this respect is whether the left or the right nostril is stimulated.

Behavioral studies comparing effects of stimulated nostril on odor detection, discrimination, and recognition memory have demonstrated discrepant findings pertaining to hemispheric superiority and that handedness may interact (for review, see Broman *et al.*, 2001). Neuroimaging studies of

olfactory processing have also resulted in discrepant findings, with the suggestion that activation may be not only task dependent but also dependent on stimulus characteristics (Zald and Pardo, 1997; Royet *et al.*, 1999; O'Doherty *et al.*, 2000; Cerf-Ducastel and Murphy, 2001, 2003).

There is to date only one report of lateralization of brain response in normal individuals during odor information processing using the ERP technique (Kobal *et al.*, 1992). These authors noted that the pleasantly perceived nontrigeminal odorant vanillin tended to elicit higher amplitudes presented to the left compared to the right nostril. An interaction effect between stimulated nostril and odorant on latencies was also reported, in that vanillin elicited longer latencies in left- compared to right-nostril stimulation, whereas hydrogen sulfide (typically perceived as pleasant) elicited shorter latencies in left-nostril stimulation. However, the study did not investigate effects on the P3 response. Daniels *et al.* (2001) studied effects of ipsilateral and contralateral olfactory stimulation in patients with unilateral supratentorial brain tumors. They showed a significant effect of stimulated side on P3 amplitude in patients with left-sided tumors and no such effect in patients with right-sided lesions. Lateralization of response in control participants was not a focus of that study. Thus, lateralization of the P3 response during processing of information following odorant stimulation of the left and right nostril in normal individuals is yet unknown.

The objective of the present study was to investigate hemispheric differences in odor information processing, reflected in N1/P2 and N1/P3 OERP amplitudes and N1, P2, and P3 latencies, in response to monorhinal odorant stimulation of the left or right nostril in healthy, right-handed, young adults. Amyl acetate is an odorous substance that is the most commonly used for OERP recordings and was therefore used also in the present study. The N1, P2, and P3 components were chosen for evaluation since these are typically the most stable components and therefore also the most commonly studied components. In olfaction, the N1 and P2 components, obtained about 300–700 ms after stimulus onset, are considered to reflect predominantly sensory processing, whereas the later P3 component, as in the visual and auditory modalities, is thought to be related to the cognitive features of attention allocation and working memory (Polich, 1986; Pause *et al.*, 1996; Morgan *et al.*, 1999).

Materials and methods

Participants

Participants were 28 young, healthy adults, ranging in age from 18 to 30 years [M = 23.2, standard deviation (SD) = 3.2], with equal numbers of men (M = 23.1, SD = 2.6) and women (M = 23.4, SD = 4.1). They were recruited primarily from the local San Diego community and included undergraduate students from the psychology department at San Diego State University. All participants were screened for impairment, assessing each nostril separately in odor-detection sensitivity using a modified version of the CCCRC threshold test (Cain, 1989; Murphy *et al.*, 1990), the alcohol sniff test (Davidson and Murphy, 1997), and for impairment in odor identification ability using the San Diego Odor Identification Test (Murphy *et al.*, 2002). According to self-reports, all participants were right-handed (Edinburgh Inventory; Oldfield, 1971) nonsmokers and free from colds, allergies, or breathing problems at the time of testing. The study was approved by the Institutional Review Board at San Diego State University and carried out in accordance with the Helsinki Declaration. A signed informed consent form was obtained from each participant.

OERP apparatus and stimuli

Monorhinal olfactory stimuli were delivered via an olfactometer developed for ERP recordings (Murphy *et al.*, 1994). Heated breathing air at a temperature of 36.5°C and humidified to 80% relative humidity was delivered to the participant's nostril at a constant flow rate (8.88 l/min) and adjusted by a flowmeter. A small section of Teflon tubing (1.6 mm inner diameter) was placed inside the tip of the nostril during stimulation and in periods between stimuli. The flow rate into the nostril was kept constant by a pair of electromagnetic valves which opened for 230 ms, during which time the main airflow was replaced by an equal portion of odor flow (2.0 l/min; Murphy *et al.*, 1994). A concentration of 1493 ppm amyl acetate was delivered, which is below the threshold for trigeminal stimulation (Cometto-Muniz and Cain, 1991) and has been demonstrated to elicit robust OERP waveforms (Morgan *et al.*, 1997). An ISI of 45 s was applied to allow for neuronal recovery in the olfactory system (Morgan *et al.*, 1997).

OERP recording

Multichannel neuroelectrical activity was recorded by affixing electrodes to the participant's scalp. Using the 10/20 international system of electrode placement, EEG activity was recorded from the midline (Fz, Cz, and Pz) and lateral sites over each hemisphere (F3, C3, and P3 at the left hemisphere and F4, C4, and P4 at the right hemisphere). Electrodes were placed on the forehead (ground) and both earlobes (reference), as well as on the lateral canthus of the left eye and supraocularly to measure electro-ocular (EOG) activity. Trials containing electro-ocular activity of ±50 μV resulting from eye movement were rejected. Neuroelectrical activity was recorded for 2000 ms (500 ms prestimulus and 1500 ms poststimulus) and amplified 20,000 times (Astro-Med Grass Instrument Company, Model 12 Neuro-Data Acquisition System, Quincy, MA) through a 0.1–30 band-pass filter (6 dB per octave). The participants were seated in a reclining chair with armrest to reduce muscle tension. A minimum of 20 trials without artifacts were recorded and averaged with a low band-pass of 10 Hz. Amplitudes were identified as the

maximum size of the peak compared to prestimulus baseline. Latencies were measured from stimulus onset to the point of maximum amplitude of the peak of interest.

Procedure

Participants were instructed to breathe through the mouth throughout the testing session using the velopharyngeal closure technique in order to maintain a constant rate of airflow through the nasal cavity (Murphy *et al.*, 1994; Thesen and Murphy, 2001; Kobal, 2003). After the presentation of each stimulus, the participant acknowledged the perception of that stimulus by lifting the right index finger. Both nostrils were tested within the same session, and the nostril order was randomized.

Data analysis

The ERP data were analyzed with SPSS software and submitted to a four-way repeated measures analysis of variance (ANOVA) with Greenhouse–Geisser correction separate for amplitude and latency, with sagittal site (frontal, central, parietal), coronal site (left, midline, right), peak (N1/P2, N1/P3 for amplitude; N1, P2, P3 for latency), and stimulated-nostril side (left, right) as within-group factors. Significant main effects and interactions were analyzed with *post hoc* Newman–Keuls Multiple Range Tests (alpha level set at 0.05).

Results

Table 1 presents mean peak-to-peak OERP amplitudes for N1/P2 and N1/P3. Results from repeated measures ANOVAs are given in Table 2. Significant main effects on amplitudes were found for sagittal site, coronal site, and peak but not for stimulated-nostril side. The *post hoc* analyses showed that amplitudes at parietal sites were larger than those at central sites and amplitudes at central sites were larger than those at frontal sites. Amplitudes were larger at left-hemisphere sites and at midline than at right-hemisphere sites. Regarding the main effect of peak, N1/P3 amplitudes were generally larger than N1/P2 amplitudes.

The four-way ANOVA did also yield significant sagittal site × peak, peak × stimulated-nostril side, and coronal site × peak × stimulated-nostril side interactions (Table 2). *Post hoc* analyses show that the sagittal site × peak interaction can be referred to larger N1/P3 amplitudes at parietal sites than at central and frontal sites. The interaction for peak × stimulated-nostril side is due to left-nostril stimulation generating larger N1/P2 amplitudes than right-nostril stimulation. Finally, the coronal site × peak × stimulated-nostril side interaction can be referred to larger N1/P2 amplitudes at the left-hemisphere and midline sites than at the right-hemisphere sites when the left nostril was stimulated.

Mean N1, P2, and P3 latencies are given in Table 1, and results from the repeated measures ANOVA are shown in Table 2. The ANOVA showed an expected main effect of peak but no other main effects on latency. The only significant interaction was sagittal site × peak, which according to a *post hoc* analysis can be referred to P2 latencies being longer at parietal sites than at central and frontal sites.

Discussion

The objective of the present study was to investigate hemispheric differences in N1/P2 and N1/P3 OERP amplitudes and N1, P2, and P3 latencies in response to amyl acetate presented to the left or right nostril in healthy, young, right-handed adults. The results suggest increasingly larger amplitudes as the recording site moves from frontal to central to parietal, in particular for the more cognitive component (N1/P3) and larger amplitudes on the left hemisphere and midline than on the right hemisphere. The smaller N1/P2 amplitude

Table 1 Mean (SD) peak-to-peak OERP amplitudes (μV) and latencies (ms) recorded at various electrode sites in response to stimulation of the left and right nostrils

	Amplitude				Latency					
	N1/P2		N1/P3		N1		P2		P3	
	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right
F3	8.5 (5.4)	7.3 (4.0)	8.7 (6.8)	9.0 (3.9)	508 (62)	518 (58)	670 (70)	682 (50)	879 (77)	888 (82)
Fz	8.0 (5.1)	7.7 (4.3)	8.0 (7.3)	8.2 (4.6)	512 (64)	517 (62)	666 (58)	690 (62)	880 (84)	887 (81)
F4	7.2 (4.8)	6.2 (3.4)	7.0 (7.0)	8.4 (5.1)	512 (65)	524 (61)	662 (57)	678 (45)	873 (78)	880 (80)
C3	10.2 (5.4)	9.2 (4.8)	12.2 (6.0)	11.1 (4.4)	513 (57)	517 (56)	683 (64)	683 (54)	886 (81)	890 (79)
Cz	10.3 (6.1)	10.3 (5.1)	11.1 (7.6)	11.5 (5.9)	515 (61)	510 (66)	665 (65)	678 (60)	874 (78)	885 (89)
C4	8.0 (5.8)	8.1 (4.4)	10.0 (7.0)	10.2 (4.6)	523 (55)	512 (55)	677 (62)	684 (49)	875 (81)	889 (79)
P3	10.8 (5.6)	10.2 (5.3)	14.0 (7.3)	14.4 (6.1)	514 (63)	516 (58)	682 (67)	693 (50)	890 (73)	889 (74)
Pz	11.3 (6.9)	11.5 (6.4)	14.4 (7.1)	14.0 (6.7)	510 (62)	510 (60)	681 (57)	692 (64)	876 (79)	888 (82)
P4	10.6 (6.1)	9.8 (6.0)	13.7 (7.1)	14.3 (8.0)	506 (64)	511 (62)	686 (65)	686 (46)	887 (75)	891 (75)

Table 2 Results of repeated measures ANOVAs with Greenhouse–Geisser correction for amplitude and latency, with sagittal site (frontal, central, parietal), coronal site (left, midline, right), peak (N1/P2, N1/P3 for amplitude; N1, P2, P3 for latency), and nostril stimulated (left, right)

	Amplitude	Latency
Sagittal site (S)	$F(2,54) = 40.49^{***}$	$F(2,54) = 1.24^{NS}$
Coronal site (C)	$F(2,54) = 5.07^{**}$	$F(2,54) = 0.86^{NS}$
Peak (P)	$F(1,27) = 5.28^{*}$	$F(2,54) = 474.72^{***}$
Nostril (N)	$F(1,27) = 0.03^{NS}$	$F(1,27) = 0.71^{NS}$
S × C	$F(4,108) = 1.41^{NS}$	$F(4,108) = 0.64^{NS}$
S × P	$F(2,54) = 12.25^{***}$	$F(4,108) = 2.72^{*}$
S × N	$F(2,54) = 0.07^{NS}$	$F(2,54) = 2.76^{NS}$
C × P	$F(2,54) = 1.87^{NS}$	$F(4,108) = 0.44^{NS}$
C × N	$F(2,54) = 1.12^{NS}$	$F(2,54) = 0.36^{NS}$
P × N	$F(1,27) = 4.25^{*}$	$F(2,54) = 0.29^{NS}$
S × C × P	$F(4,108) = 2.29^{NS}$	$F(8,216) = 0.95^{NS}$
S × C × N	$F(4,108) = 0.42^{NS}$	$F(4,108) = 0.15^{NS}$
S × P × N	$F(2,54) = 0.57^{NS}$	$F(4,108) = 1.12^{NS}$
C × P × N	$F(2,54) = 5.03^{**}$	$F(4,108) = 0.96^{NS}$
S × C × N × P	$F(4,108) = 1.83^{NS}$	$F(8,216) = 1.21^{NS}$

$^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.05$, NS, nonsignificant.

at frontal sites compared to central and parietal sites is consistent with prior work on OERPs (e.g., Hummel and Kobal, 1992; Olofsson and Nordin, 2004). The result for the olfactory P3 (N1/P3) amplitude being largest at parietal sites agrees with that of the auditory and visual P3 amplitudes (Polich and Heine, 1996).

The present findings on hemispheric differences evoke the question whether these electrophysiological data can be related to prior neuroimaging data and whether these two types of studies mirror similar processes? Imaging data of this kind have made clear that laterality effects are highly dependent on the subject's task, although lateralization of different olfactory functions has continued to present an inconsistent set of findings derived from different methodological approaches (see Royet and Plailly, 2004). Some imaging studies have shown preferential activation in the right hemisphere in response to odorants. Tendencies to show bilateral activation in the primary olfactory cortex and greater activation in the right than in the left orbitofrontal cortex prompted Zatorre and Jones-Gotman (2000) to postulate that the primary sensory response appears to be bilateral, while higher processing preferentially involves the right orbitofrontal cortex. In the case of magnetoencephalographic studies, Kettenmann *et al.* (1997) have reported greater activation in the right hemisphere than in the left during a passive smelling task. Using positron emission tomography (PET), Savic and Gulyas (2000) observed greater activation in the right hemisphere during passive smelling, irrespective of the stimulated nostril. Other imaging studies suggest a left-hemisphere dominance. In functional magnetic resonance imaging (fMRI) studies, greater activation in left than in right cortex has been observed when subjects evaluated the stimulus (O'Doherty *et al.*, 2000; Cerf-Ducastel and Murphy, 2001, 2003). Activation appears to be stronger in the left compared to right amygdala and orbitofrontal cortex for emotionally valenced olfactory stimuli (Zald and Pardo, 1997; Royet *et al.*, 2001). Yet other studies have noted hemispheric specialization based on the familiarity of odors (Royet *et al.*, 1999). Using PET, they demonstrated activation in the right orbital frontal area, the left inferior frontal gyrus, the left superior frontal gyrus, and the anterior cingulate while subjects evaluated odor familiarity. Our conclusion is that to date it is difficult to make direct comparison between existing electrophysiological and imaging data and that multimodal recordings (e.g., ERP and fMRI) are needed within the same subjects and stimulus conditions for direct comparisons.

Although the data suggest no general effect of stimulated-nostril side on OERP amplitudes, the analyses showed interesting interaction effects. Thus, the relatively sensory N1/P2 amplitude was found to be larger for left- compared to right-nostril stimulation. Considering that the olfactory projections are predominantly ipsilateral to the side of stimulation (Price, 1990), it is not surprising that the N1/P2 amplitude also was larger over the left hemisphere and midline than over the right hemisphere when the left nostril was stimulated. These results for the left side, using the pleasantly perceived odorant amyl acetate at a nontrigeminal concentration, are consonant with prior data for a pleasant odorant (vanillin) and contrast data for a trigeminal stimulant (CO_2) and an unpleasant odorant (hydrogen sulfide) that suggest larger amplitude from right-nostril stimulation (Kobal *et al.*, 1992). Whereas many odorants stimulate both the olfactory (CN I) and the trigeminal (CN V) systems, the neural projections differ in that the trigeminal system projects contralaterally to the side of stimulation (Doty *et al.*, 1997). The different results for amyl acetate and hydrogen sulfide imply that the present findings for amyl acetate can perhaps only be generalized to odorants perceived as pleasant. The absence of an effect of stimulated-nostril side on N1/P3 amplitude suggests that the higher order cognitive function involved in stimulus evaluation and updating is a more bilateral task and rather independent of stimulated nostril.

It is also important to appreciate that lateralization of OERP responses is expected to depend not only on the character of the stimulus but also critically on the subject's task, the cortical regions involved in performing the task, and the extent to which those regions are intact. For example, in patients with unilateral supratentorial brain tumors, Daniels *et al.* (2001) investigated the effects of ipsilateral and contralateral stimulation and showed a significant effect of side of stimulation on P3 amplitude in patients with left-sided

tumors but no effect of side of stimulation in patients with right-sided lesions.

In contrast to the results for amplitudes, the OERP latencies were consistent between sagittal sites and between coronal sites, as well as between stimulated-nostril sides. It may be difficult to generalize any of the results in this study to individuals who are not right handed and not healthy, young adults. Nevertheless, with these restrictions, an implication of the findings for latencies and stimulated-nostril side is that monorhinal stimulation of either the left or the right nostril may be sufficient for accurate assessment and interpretation of OERP latencies in the single-stimulus paradigm with amyl acetate, which is one of the most commonly used stimuli in OERP research. This is of particular value in settings where latency measures are sensitive indicators of brain function and assessment with time-efficient procedures is required.

The effects seen in young, healthy individuals motivate further research of this kind on other populations. For example, in olfaction as well as in other modalities, aging dramatically affects cortical activation in fMRI studies (Cerf-Ducastel and Murphy, 2003; Ferdon and Murphy, 2003; Murphy *et al.*, 2005). Interestingly, tasks that evoke unilateral activity in young subjects evoke bilateral activity in older adults, prompting a compensation hypothesis (Cabeza, 2002). Thus, because of significant impairment in olfaction in older adults (Murphy *et al.*, 2000, 2002, 2003), they may recruit more brain areas and different neural networks than would young adults to accomplish a given task. Thus, it is important to appreciate the limitation that the results of the present OERP study apply to healthy, right-handed, young adults.

Acknowledgements

This study was supported by National Institutes of Health (NIH) grant numbers DC02064 and AG04085 to C.M. and by grants from the Swedish Research Council to S.N. NIH training grant DC00032 to Dr Terence M. Davidson also supported P.E.G. We gratefully acknowledge Eva Bringlöv for valuable assistance.

References

Broman, D.A., Olsson, M.J. and **Nordin, S.** (2001) *Lateralization of olfactory cognitive functions: effects of rhinal side of stimulation*. Chem. Senses, 26, 1187–1192.

Cabeza, R. (2002) *Hemispheric asymmetry reduction in older adults: the HAROLD model*. Psychol. Aging, 17, 85–100.

Cain, W.S. (1989) *Testing olfaction in a clinical setting*. Ear Nose Throat J., 68, 78–86.

Cerf-Ducastel, B. and **Murphy, C.** (2001) *FMRI activation in response to odorants orally delivered in aqueous solutions*. Chem. Senses, 26, 625–637.

Cerf-Ducastel, B. and **Murphy, C.** (2003) *FMRI brain activation in response to odors is reduced in primary olfactory areas of elderly subjects*. Brain Res., 986, 39–53.

Cometto-Muniz, J.E. and **Cain, W.S.** (1991) *Nasal pungency, odor, and eye irritation thresholds for homologous acetates*. Pharmacol. Biochem. Behav., 39, 983–989.

Covington, J.W., Geisler, M.W., Polich, J. and **Murphy, C.** (1999) *Normal aging and odor intensity effects on the olfactory event-related potential*. Int. J. Psychophysiol., 32, 205–214.

Daniels, C., Gottwald, B., Pause, B.M., Sojka, B., Mehdorn, H.M. and **Ferstl, R.** (2001) *Olfactory event-related potentials in patients with brain tumours*. Clin. Neurophysiol., 112, 1523–1530.

Davidson, T.M. and **Murphy, C.** (1997) *Rapid clinical evaluation of anosmia*. Arch. Otolaryngol. Head Neck Surg., 123, 591–594.

Doty, R.L., Bromley, S.M., Moberg, P.J. and **Hummel, T.** (1997). *Laterality in human nasal chemoreception*. In Christman, S. (ed.), Cerebral Asymmetries in Sensory and Perceptual Processing. North Holland, Amsterdam, pp. 497–542.

Evans, W.J., Kobal, G., Lorig, T.S. and **Prah, J.** (1993) *Suggestions for collection and reporting of chemosensory (olfactory) event-related potentials*. Chem. Senses, 18, 751–756.

Ferdon, S. and **Murphy, C.** (2003) *The cerebellum and olfaction in the aging brain: an fMRI study.* Neuroimage, 20, 12–21.

Geisler, M.W., Schlotfeldt, C.R., Middleton, C.B., Dulay, M.F. and **Murphy, C.** (1999) *Traumatic brain injury assessed with olfactory event-related potentials*. J. Clin. Neurophysiol., 16, 77–86.

Hummel, T. and **Kobal, G.** (1992) *Differences in human evoked potentials related to olfactory or trigeminal activation*. Electroencephalogr. Clin. Neurophysiol., 84, 84–89.

Hummel, T., Pauli, E., Schuler, P., Kettenmann, B., Stefan, H. and **Kobal, G.** (1995) *Chemosensory event-related potentials in patients with temporal lobe epilepsy.* Epilepsia, 36, 79–85.

Jing, H., Pivik, R.T. and **Dykman, R.A.** (2006) *A new scaling method for topographical comparisons of event-related potentials*. J. Neurosci. Methods, 151, 239–249.

Kettenmann, B., Stefan, H. and **Kobal, G.** (1997) *Differences in magnetoencephalographically identified sources of cortical olfactory activity after stimulation with different odorants*. Chem. Senses, 22, 347–361.

Kobal, G. (1981) Electrophysiologishe Untersuchungen des Menschlichen Geruchssinns. Thieme Verlag, Stuttgart, Germany.

Kobal, G. (2003) *Electrophysiological measurement of olfactory function*. In Doty, R.L. (ed.), Handbook of Olfaction and Gustation. Marcel Dekker, New York, pp. 229–249.

Kobal, G., Hummel, T. and **Van Toller, S.** (1992) *Differences in human chemosensory evoked potentials to olfactory and somatosensory chemical stimuli presented to left and right nostrils*. Chem. Senses, 17, 233–244.

Lorig, T.S. (2000) *The application of electroencephalographic techniques to the study of human olfaction: a review and tutorial*. Int. J. Psychophysiol., 36, 91–104.

Morgan, C.D., Covington, J.W., Geisler, M.W., Polich, J. and **Murphy, C.** (1997) *Olfactory event-related potentials: older males demonstrated the greatest deficits*. Electroencephalogr. Clin. Neurophysiol., 104, 351–358.

Morgan, C.D., Geisler, M.W., Covington, J., Polich, J. and **Murphy, C.** (1999) *The olfactory P3 in young and older adults*. Psychophysiology, 36, 281–287.

Morgan, C.D. and **Murphy, C.** (2002) *Olfactory event related potentials in Alzheimers disease*. J. Int. Neuropsychol. Soc., 8, 753–763.

Murphy, C., Cerf-Ducastel, B., Calhoun-Haney, R., Gilbert, P.E. and **Ferdon, S.** (2005). *ERP, fMRI, and functional connectivity studies of brain response to odor in normal aging and Alzheimer's disease*. Chem. Senses, 30, 170–171.

Murphy, C., Doty, R.L. and **Duncan, H.J.** (2003) *Clinical disorders of olfaction*. In Doty, R.L. (ed.), Handbook of Olfaction and Taste. Marcel Dekker, New York, pp. 461–478.

Murphy, C., Gilmore, M.M., Seery, C.S., Salmon, D.P. and **Lasker, B.R.** (1990) *Olfactory thresholds are associated with degree of dementia in Alzheimer's disease*. Neurobiol. Aging, 11, 465–469.

Murphy, C., Morgan, C., Geisler, M.W., Wetter, C., Covington, J.W., Madowitz, M.D., Nordin, S. and **Polich, J.** (2000) *Olfactory event-related potentials and aging: normative data*. Int. J. Psychophysiol., 36, 133–145.

Murphy, C., Nordin, S., de Wijk, R.A., Cain, W.S. and **Polich, J.** (1994) *Olfactory-evoked potentials: assessment of young and elderly, and comparison to psychophysical threshold*. Chem. Senses, 19, 47–56.

Murphy, C., Schubert, C.R., Cruickshanks, K.J., Klein, B.E.K., Klein, R. and **Nondahl, D.M.** (2002) *Prevalence of olfactory impairment in older adults*. J. Am. Med. Assoc., 288, 2307–2312.

O'Doherty, J., Rolls, E.T., Francis, S., Bowtell, R., McGlone, F., Kobal, G., Renner, B. and **Ahne, G.** (2000) *Sensory-specific satiety-related olfactory activation of the human orbitofrontal cortex*. Neuroreport, 11, 893–897.

Oldfield, R.C. (1971) *The assessment and analysis of handedness: the Edinburgh Inventory*. Neuropsychologia, 9, 97–113.

Olofsson, J.K. and **Nordin, S.** (2004) *Gender differences in chemosensory perception and event-related potentials*. Chem. Senses, 29, 629–637.

Pause, B.M., Sojka, B., Krauel, K. and **Ferstl, R.** (1996) *The nature of the late positive complex within the olfactory event-related potential (OERP)*. Psychophysiology, 33, 376–384.

Polich, J. (1986) *P300 development from auditory stimuli*. Psychophysiology, 23, 590–597.

Polich, J. and **Heine, M.R.D.** (1996) *P300 topography and modality effects from a single-stimulus paradigm*. Psychophysiology, 33, 747–752.

Price, J.L. (1990). *Olfactory system*. In G. Paxinos (ed.), The Human Nervous System. Academic Press, San Diego, CA, pp. 979–1001.

Royet, J.P., Hudry, J., Zald, D.H., Godinot, D., Gregoire, M.C., Lavenne, F., Costes, N. and **Holley, A.** (2001) *Functional neuroanatomy of different olfactory judgments*. Neuroimage, 13, 506–519.

Royet, J.P., Koenig, O., Gregoire, M.C., Cinotti, L., Lavenne, F., Le Bars, D., Costes, N., Vigouroux, M., Farget, V., Sicard, G., Holley, A., Maugière, F., Comar, D. and **Froment, J.C.** (1999) *Functional anatomy of perceptual and semantic processing for odors*. J. Cogn. Neurosci., 11, 94–109.

Royet, J.P. and **Plailly, J.** (2004) *Lateralization of olfactory processes*. Chem. Senses, 29, 731–745.

Savic, I. and **Gulyas, B.** (2000) *PET shows that odors are processed both ipsilaterally and contralaterally to the stimulated nostril*. Neuroreport, 11, 2861–2866.

Sutton, S., Braren, M., Zubin, J. and **John, E.R.** (1965) *Evoked potential correlates of stimulus uncertainty*. Science, 150, 1187–1188.

Tateyama, T., Hummel, T., Roscher, S., Post, H. and **Kobal, G.** (1998) *Relation of olfactory event-related potentials to changes in stimulus concentration*. Electroencephalogr. Clin. Neurophysiol., 108, 449–455.

Thesen, T. and **Murphy, C.** (2001) *Age-related changes in olfactory processing detected with olfactory event-related brain potentials using velopharyngeal closure and natural breathing*. Int. J. Psychophysiol., 40, 119–127.

Zald, D.H. and **Pardo, J.V.** (1997) *Emotion, olfaction, and the human amygdala: amygdala activation during aversive olfactory stimulation*. Proc. Natl. Acad. Sci. USA, 94, 4119–4124.

Zatorre, R.J. and **Jones-Gotman, M.** (2000) *Functional imaging of the chemical senses*. In Toga, A.W. and Mazziotta, J.C. (eds), Brain Mapping: The Applications. Academic Press, San Diego, CA, pp. 403–424.

Accepted June 19, 2006