SHORT COMMUNICATION

Failure to Demonstrate Systematic Changes in Olfactory Perception in the Course of Pregnancy: a Longitudinal Study

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Abstract

Olfactory function was assessed in 20 women during each trimester of pregnancy and post partum, and compared with that of 20 non-pregnant women tested in parallel. In contrast to earlier reports, no consistent differences in olfactory sensitivity or odor evaluation were found between the two groups. **Chem. Senses 21: 567–571, 1996.**

Introduction

Investigators have long been interested in the possible influence of hormonal state on olfactory function (Le Magnen, 1982; Doty, 1986). Not surprisingly, this has led to a number of studies of changes in olfactory perception during pregnancy, the results of which have been somewhat contradictory. Whereas several investigators have reported a general increase in sensitivity, the time of maximum effect varies between studies from the first trimester (Zwaardemaker, 1895; Steiner, 1922; Henssge, 1930; Le Magnen, 1952; Luvara and Murizi, 1961) to the second and third trimesters (Good et al., 1976). Furthermore, other investigators report decreased sensitivity in late pregnancy (Hansen and Glass, 1936; Noferi and Giudizi, 1946; Luvara and Murizi, 1961) or even cases of anosmia during the first trimester (Schmidt, 1925), while results of the National Geographic Smell Survey indicate considerable heterogeneity in odor perception during pregnancy (Gilbert and Wysocki, 1991).

However, all studies to date have been either cross-sectional or only partially longitudinal, most have been based on a very small sample or even single cases, most have failed to include a non-pregnant control group tested in parallel so as to control for possible changes in responding due to experience with the odorants or to seasonal variations, and most have failed to check subjective reports of altered sensitivity using more objective psychophysical procedures. It was therefore the purpose of the present study to overcome these methodological limitations by employing a full longitudinal design, and by including an age-matched, non-pregnant control group tested in parallel with pregnant subjects.

Methods, results and conclusions

Twenty pregnant, unpaid volunteers (mean age 27.5 ± 3.6 years) were recruited from a gynecological clinic in southern Germany. All were non-smokers and had uncomplicated pregnancies and deliveries. Each subject was informed as to the purpose of the study and then given the same test during each trimester of pregnancy (gestation weeks 8–11, 20–23 and 32–36) and 2–3 months after delivery. A control group of 20 non-pregnant female volunteers (mean age 26.2 ± 4.5 years) was tested in parallel.

Twelve odorants (Table 1), diluted in diethyl phthalate (Merck) and intensity matched to a 2% *n*-butanol standard (ASTM, 1975), were presented in squeeze bottles as described previously (Laska and Hudson, 1991, 1992; Hudson *et al.*, 1994). Four odorants corresponded to substances in the National Geographic Smell Survey (3, 4, 9, 10 in Table 1; Gilbert and Wysocki, 1991) and nine to substances used in our earlier studies.

Subjects were tested for detection threshold, intensity perception, hedonic evaluation and odor identification as follows: the absolute threshold for *n*-butanol was determined in a triangular test procedure using an ascending staircase method in which concentrations increased by a factor of 5 (cf. Laska and Hudson, 1991). Intensity discrimination was assessed by presenting subjects with four bottles containing either 0.9 g/l linalool or 5-, 25- and 125-fold dilutions, and asking them to rank the bottles according to intensity. They were then informed of the correct sequence and asked to judge the intensity of each stimulus using the highest concentration as a 100% standard. For hedonic evaluation and odor identification subjects were successively presented with the first 10 odorants of Table 1 and asked to rate them according to familiarity (11-point scale), pleasantness (11-point scale), intensity (6-point scale) and edibility (yes or no). In addition, they were asked to assign a verbal label to each odorant, or to attempt to describe it.

Within-group comparisons across sessions were performed using the Friedman two-way analysis of variance by ranks followed by post hoc Wilcoxon signed-rank tests. Between-group comparisons within a given session were performed using the Mann–Whitney *U* test, and frequencies in discrete categories were compared using the χ^2 test. All tests were two-tailed and the alpha level was set at 0.05.

Table 1 Substances and concentrations [g/l] used for the stock solutions

1	phenyl ethanol[a]	(rose)	18.75
2	citronellyl nitrile[b]	(lemon)	12.50
3	isoamyl acetate[c]	(banana)	25.00
4	galaxolide[e]	(musk)	25.00
5	peanut aroma[f]	(peanut)	25.00
6	Chanel No. 5	(perfume)	pure
7	anethole[c]	(aniseed)	12.50
8	12-component mixture*	(chemical)	see below
9	eugenol[c]	(clove)	25.00
10	androstenone[d]	(urine, sweat)	2.50
11	linalool[c]	(lavender)	22.50
12	*n*-butanol[a]	(oily, alcoholic)	22.50

Obtained from [a]Aldrich, [a]BASF, [b]Merck, [d]Sigma, [e]IFF, [f]Dragoco.

*Linalool (20.50) + cineole (22.50) + (–)-carvone (25.00) + isoamyl acetate (25.00) + α-pinene (22.50) + methyl propyl ketone (3.75) + cyclohexanone (22.50) + 2-methyl-4-phenyl-2-butanol (25.00) + *t*-butylcyclohexyl acetate (25.00) + amyl propionate (12.50) + decyl acetate (25.00) + *n*-butanol (22.50); (Laska and Hudson, 1992).

In general, the findings failed to provide support for the existence of a systematic shift in olfactory function during pregnancy. On the various measures of sensitivity, and of familiarity, identification, hedonic evaluation and palatability, differences between pregnant and control subjects were typically small or non-existent, and when present, the direction and pattern of their expression varied considerably.

Sensitivity

In the threshold test for *n*-butanol, scores for the control subjects remained stable across the four sessions (Friedman, $P > 0.20$) whereas a significant increase in sensitivity was recorded for the pregnant women in the third session compared with the first and second sessions or with the fourth, post-partum session (Friedman, $P < 0.0001$; Wilcoxon, $P < 0.01$ for all comparisons). Compared with controls, thresholds were significantly higher for pregnant women in the first and significantly lower in the third session (Mann–Whitney, $P < 0.004$ and 0.03 respectively). However, in the task requiring subjects to rank the four bottles of linalool, no significant difference was found between groups for any of the four sessions (χ^2, $P > 0.10$ for all comparisons). In both groups correlations between odor concentration and judgement of intensity were very consistent across sessions (Friedman, $P > 0.10$ for all concentrations) and no significant differences were found between the groups for any session (Mann–Whitney, $P > 0.10$ for all concentrations).

Of the 10 odorants used in the test of hedonic evaluation, six were perceived by all subjects in all sessions. Isolated instances of failure to perceive the odor of clove, aniseed, musk or androstenone varied randomly across sessions and to a similar extent in the two groups. Intensity ratings for both groups were rather stable across sessions, with significant fluctuations only found in the control group for androstenone, which was rated significantly less intense in the first session (Friedman, $P < 0.01$; Wilcoxon, $P < 0.05$). Ratings were also similar between groups with the exception of musk, which pregnant women rated as significantly more intense in sessions 2, 3 and 4 (Mann–Whitney, $P < 0.01$), and androstenone, which they rated as significantly more intense in sessions 1 and 3 (Mann–Whitney, $P < 0.01$).

Odor evaluation

Except for androstenone, all odorants used in the test of hedonic evaluation were rated as moderately to highly familiar by both groups. Familiarity ratings remained rather stable across sessions, with significant fluctuations found only for the pregnant women, who rated clove as significantly less familiar in the third session and aniseed as less familiar in the third and fourth sessions (Friedman, $P < 0.01$; Wilcoxon, $P < 0.05$). Although significant differences between groups in one or more sessions were found for peanut, banana, aniseed, 12-component mixture and musk (Mann–Whitney, $P < 0.05$), the pattern of difference was quite variable. Thus, peanut was judged less familiar by pregnant women in the first session, banana in the second, third and fourth sessions, aniseed in the third and fourth sessions, the 12-component mixture in the second and fourth sessions (but rose as more familiar in the third session) and musk in the fourth session (Mann–Whitney, $P < 0.05$).

Again, with the exception of androstenone, >60%, and in most cases >90%, of subjects in both groups assigned some form of label to each of the odorants. However, the pregnant women were significantly less often able to provide any verbal description for the food-associated odorants peanut, aniseed and lemon (χ^2, $P < 0.01$ for each odorant across the four sessions). They also performed significantly less well in providing appropriate descriptions or exact conventional labels for peanut, banana, aniseed and lemon, although they out-performed controls on clove (χ^2, $P < 0.01$ for each odorant across the four sessions).

Most substances were rated as slightly to moderately pleasant, and in both groups only the 12-component mixture and androstenone consistently yielded negative ratings. Ratings were rather stable across sessions, with significant fluctuations only recorded in the control group for musk and aniseed in the third and fourth sessions respectively (Friedman, $P < 0.01$; Wilcoxon, $P < 0.05$). Peanut was judged less pleasant by pregnant women and clove as more pleasant in all four sessions, although only in the first, second and third sessions for peanut and in the third session for clove was the difference significant (Mann–Whitney, $P < 0.05$). Aniseed was judged less pleasant by pregnant women in the fourth session, and banana in the second and fourth sessions, whereas perfume was judged more pleasant in the fourth session, and musk in the second and fourth sessions (Mann–Whitney, $P < 0.05$).

Both groups judged the five food-associated odorants peanut, banana, clove, aniseed and lemon to be edible more frequently than the non-food substances. However, as can be seen from Table 2, the pregnant women consistently rated peanut, banana, aniseed and lemon as less and clove as more palatable, although these differences were only significant for peanut (χ^2, $P < 0.03$). Differences between groups were greatest during the first three sessions, corresponding to the trimesters of pregnancy, and were reduced or absent in the post-partum session (χ^2, $P > 0.8$ for all odorants).

This pattern was clearest for the peanut aroma. As shown in Table 3, ratings by pregnant subjects on the four measures of palatability, pleasantness, familiarity and intensity were more labile than for controls, and the percentage of pregnant women reversing their judgement from one test session to the next was significantly higher for all parameters except palatability (χ^2, $P < 0.03$).

Thus, previous suggestions of early pregnancy- or trimester-specific changes in olfactory function (Zwaardemaker, 1895; Steiner, 1922; Henssge, 1930; Hansen and Glass, 1936; Noferi and Giudizi, 1946; Le Magnen, 1952; Luvara and Murizi, 1961) were not borne out by the present study, since differences between pregnant women and controls on the various measures were few and scattered across sessions. One reason for the inconsistency between this and previous reports is suggested by the behavior of the control subjects. Their performance suggests that the inherent variability in responding to odorants may be

Table 2 Judgement of food-associated odorants as edible

Odorant	Tests 1–3 (%)	Test 4 (%)	
Peanut	25	55	pregnant
	63	65	controls
Banana	45	70	pregnant
	60	60	controls
Clove	68	55	pregnant
	47	50	controls
Aniseed	44	50	pregnant
	47	60	controls
Lemon	15	20	pregnant
	37	25	controls

Table 3 Individuals reversing judgement for peanut aroma across the four test sessions

	Pregnant (%)	Controls (%)	Criteria
Palatability	50	20	+ versus –
Pleasantness	65	25	<0 versus ≥0
Familiarity	65	25	≤0 versus >0
Intensity	90	50	<mean versus ≥mean

considerable, and underlines the importance of a longitudinal design and of including a control group.

A second reason for such inconsistency might lie in the timing and frequency of testing. Little is known about fluctuations in physiological or psychological factors during pregnancy which might affect sensory performance, and it is possible that in the present study tests were too widely spaced to detect subtle but relevant changes in olfactory function.

Despite this, there seems little reason to doubt the adequacy of the test procedures themselves. Using the same sniff-bottles, similar tasks and several of the same stimuli, reliable estimates of detection threshold and odor discrimination have been obtained for normosmics (Laska and Hudson, 1991, 1992), and clear distinctions made between the olfactory performance of patients with hypogonadotropic hypogonadism (Hudson *et al.*, 1994). Nevertheless, a potentially important methodological issue concerns the nature of the odor stimuli used in this and previous studies. These have been typically artificial, monomolecular substances and—compared with natural stimuli—of low chemical complexity and limited behavioral relevance. Thus, the use of everyday foods such as egg, cabbage and sardines as odor stimuli might reveal clearer changes in response and help in understanding the underlying mechanisms.

Tentative support for the importance of such considerations is provided by the pattern of response to peanut aroma in the present study. Composed of >50 substances, it was the most complex stimulus used, and, having the greatest similarity to a real food product, it probably had the greatest everyday relevance. Furthermore, it is an odorant to which subjects typically respond with a wider and more ambiguous range of labels and associations than, for example, to the unambiguous 'lemon' or 'detergent' odor of citronellyl nitrile (cf. Hudson *et al.*, 1994). Together, these characteristics might help explain the clearer differences between pregnant and control subjects in responding to this particular stimulus.

In conclusion, although the present study provides little firm evidence of a systematic shift in olfactory function during pregnancy, or support for the attractive hypothesis that changed odor perception might be adaptive in terms of fetal survival (cf. Hook, 1976; Profet, 1992), this could have been due to the sub-optimal nature of the stimuli used in this and indeed most previous studies. Thus, it is expected that efforts to identify and employ stimulus material of greater biological and psychological relevance may yet reveal robust and instructive changes in olfactory function with changes in physiological state such as occur during pregnancy.

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