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Odor Distinctiveness between Enantiomers of Linalool: Difference in Perception and Responses Elicited by Sensory Test and Forehead Surface Potential Wave Measurement

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Abstract

The effects on humans of inhalation of optically active linalools were examined in terms of sensory tests and portable forehead surface electroencephalographic (IBVA-EEG) measurements in order to assess their odor distinctiveness by chiral isomers. (*R*)-(–)-Linalools with specific rotation of $[\alpha]_D = -15.1°$ were isolated by repeated flash column chromatography from lavender oil, while (*S*)-(+)-linalools with $[\alpha]_D = +17.4°$ and (*RS*)-(±)-linalools with $[\alpha]_D = 0°$ and content of (*R*)-form 50.9% and (*S*)-form 49.1% were obtained from coriander oil and commercial linalool, respectively, by using the same method. With the use of an inhalator, each was administered to subjects both before and after 10 min of work. It was found that administration after work evoked different subjective impressions when compared with that before work depending on the configuration of the isomers and the type of work employed. For instance, inhalation of (*R*)-(–)-linalool after hearing environmental sounds not only produced a much more favorable impression in the sensory test but was also accompanied by a greater decrease in beta waves after work in comparison with that before work. This is in contrast to the case of mental work, which resulted in a tendency for agitation accompanied by an increase in beta waves. These findings led us to conclude that enantiomeric stereospecificity of linalool evoked different odor perception and responses not only with chiral dependence but also with task dependence. In addition, in comparing these sensory profiling features and IBVA-EEG tendencies between hearing environmental sound and mental work, a tendency was observed for (*R*)-(–)-linalool to coincide with (*RS*)-(±)-linalool but not with (*S*)-(+)-linalool.

Introduction

As people generally believe that odors may alter mood, alertness and sexual arousal (Billot and Wells, 1975; Valnet, 1982; Morris, 1984), perfumes, room odorizers and incenses have been used for self-adornment and modification of the living environment from ancient times. In spite of these naturalistic uses of odors and anecdotal accounts of their effects, little is known of the scientific grounds for odors and olfaction (Lorig, 1989).

As for enantiomeric stereospecificity on olfaction, the degree to which odor perception and responses depend on structure has remained unresolved inasmuch as most life processes are chiral-dependent and various observations have shown that odor distinctiveness is attributable to difference in configuration of chiral isomers. With use of highly purified compounds by gas–liquid chromatography (GLC), for example, it has been shown that (+)-carvone is characterized as caraway-like, while (–)-carvone is spearmint-like (Friedman and Miller, 1971; Leitereg *et al.*, 1971). The enantiomers of carvotanacetone and *trans*-dehydrocarvone, both synthesized from (+)-carvone, are caraway-like and those from (–)-carvone are spearmint-like (Russell and Hills, 1971); further, (+)- and (–)-linalool are petitgrain-like and lavender-like respectively (Ohloff and Klein, 1962). In spite of these unequivocal studies, however, the close association between the olfactory system and the limbic system, which is also related to mood alteration, memory and sexual activity, should be an obstruction not only in the understanding of odor incongruity and chirality but also in the study of olfaction.

As odor responses are intimately concerned not only with emotional expression but also with genesis of emotions as well, the sensory evaluation method, being a measure of consciousness developed by experimental and mathematical psychology (Stevens, 1951; Guilford, 1954; Torgerson, 1958; Coombs, 1964; Kling and Riggs, 1972), would therefore serve as a basis not only for evaluating olfactory response to a given aroma but also for assessing changes in perception of fragrance of essential oil, both from the standpoint of semantics. In addition, physiological measurement as a complementary method to sensory evaluation would be beneficial in order to elucidate actual physiological changes in humans together with the method of semantics.

In view of this, we developed and formulated a comprehensive sensory test for odors and applied it to essential oils, including lavender, rosemary, linalool, peppermint, marjoram, cardamom, sandalwood, basil and lime (Sugawara *et al.*, 1998b). We have observed that inhalation of essential oil causes a different subjective perception of fragrance depending on the type of work, when the Kraepelin mental performance test (mental work), exercise of stepping up and down (physical exercise) and hearing environmental (natural) sounds were employed as contents of work.

Among these samples, linalool produced very interesting results after hearing environmental sounds in sensory tests and by portable forehead surface electroencephalography (IBVA-EEG, Psychic Lab. System). Accordingly the linalool effect in relation to hearing environmental sounds was studied using optically active linalools, that is (*R*)-(–)-, (*S*)-(+)- and (*RS*)-(±)-forms, which were isolated from lavender oil, coriander oil and commercial linalool respectively, with use of repeated flash column chromatography (Sugawara *et al.*, 1998a). It was demonstrated that the favorable impression of the (*RS*)-(±)-form after hearing environmental sounds accompanied by a tendency for the beta wave to decrease was due to (*R*)-(–)-linalool rather than (*S*)-(+)-linalool, in which an unfavorable impression tended to be accompanied by an increase of the beta wave. In this connection, linalool was also of great interest in that its sensory profiling after hearing environmental sounds was the reverse of linalool inhalation after mental work (Sugawara *et al.*, 1998b).

The objective of this investigation was to examine whether odor perception and responses depend on enantiometric structure of linalool or not. This was accomplished by comparing the data derived from sensory profiling study and IBVA-EEG measurement when enantiomers of linalool were administered to subjects under different tasks.

Materials and methods

Materials

Linalool and diethyl phthalate were purchased from Kanto Kagaku Co. Ltd (Tokyo, Japan), activated charcoal of column chromatography grade from Wako Pure Chemical Ind. Ltd (Osaka, Japan) and silica gel 60 (230–400 mesh) for flash column chromatography from Merck (Rahway, NJ).

(R)-(–)-, (S)-(+)- and (RS)-(±)-linalools were prepared by repeated flash column chromatography on silica gel (solvent:hexane/ethyl acetate, 9:1 v/v) from lavender oil (a generous gift from Takasago-Koryo, Osaka, Japan), coriander oil (by courtesy of Shiono-Koryo, Osaka, Japan) and commercial linalool respectively, and each product was identified by spectral (EI-MS, IR and ^{1}H-NMR) and chromatographic (analytical thin-layer chromatography, TLC and GLC) behaviors with those of authentic specimens (kindly supplied by Dr Y. Hiraga of Hiroshima University, Hiroshima, Japan), as described elsewhere (Sugawara *et al.*, 1998a). (*R*)-(–)-Linalool used had a 21.95% total yield, a 97.0% purity on GLC (CP-cyclodextrine-β-236M-19) and a specific rotation $[\alpha]_D = -15.1°$ (c 0.88, ethanol), while (S)-(+)-linalool with a 32.9% total yield, a purity of (*S*)-form 88.3% and (*R*)-form 11.7% on GLC and a specific rotation $[\alpha]_D = +17.4°$ (c 3.19, ethanol) and (*RS*)-(±)-linalool with a 74.5% total yield, a purity of (*S*)-form 49.1% and (*R*)-form 50.9% on GLC and a specific rotation $[\alpha]_D = 0°$ (c 3.19, ethanol) were obtained and used in the following study.

Sensory test

The subjects were healthy 20- to 26-year-old adults. Sensory test was carried out before and after work with the inhaler according to the specifications of Sugawara *et al.* (Sugawara *et al.*, 1998b), when the Kraepelin mental performance test (mental work), exercise by stepping up and down (physical work) and hearing environmental sounds were employed as types of work.

To identify the best concentration of optically active linalools for the following experiments, a preliminary sensory test was performed with serially diluted solutions of 50, 20, 10, 1 and 0.1 mg/ml for linalools with deodorized diethyl phthalate which was loaded in an inhaler (300 ml) and moistened by applying 20 μl of solution on a tiny strip of filter paper. Usual procedures of deodorization were employed by soaking activated charcoal in diethyl phthalate (1/10 v/v). A volume of 20 mg/ml for the concentration of each isomer was selected for each optically active linalool evaluated as being ‘comfortable’ by several judges. This was used in the subsequent study. The 1/10 diluted solution was also used in the experiments of commercial linalool, as described previously (Sugawara *et al.*, 1998a).

As mental work we used the Uchida–Kraepelin mental work test consisting of numbers as a line in a row (100 numbers per row) and addition of neighboring numbers was repeated side by side. Each row was worked on for 40 s before changing to the next row, for a total of 5 min, which was followed by a 1 min rest and then another 5 min of work. Assigned to subjects was physical work of stepping up and down a 20 cm step at a rate of 30 times per min for 5 min with a break of 1 min, followed by an additional 5 min of exercise. Listening activity was performed while sitting on a chair and listening to natural sounds such as bird songs or the murmuring of a small stream from a compact disc player for a total of 10 min with a 1 min break.

Statistics

As aroma perception was evaluated by 13 impression descriptors consisting of contrasting pairs of adjectives and scored on an 11-point scale (–5 to +5), the difference in score of impression descriptors recorded before and after work was obtained and the statistical significance of the difference for each descriptor was evaluated by Student's *t*-test. All data were analyzed statistically with a Power Macintosh 8100/100AV personal computer. The statistical significance of each impression descriptor was then scored as follows: (1) significance score = 1, if the impression difference is regarded to be significant with $P < 0.05$; (2) significance score = 0.5, if regarded to be significant with $0.05 \le P < 0.1$; and (3) significance score = 0, if regarded to be insignificant with $P \ge 0.1$, where P is the level of significance.

The addition of these scores provided the following score for total significance:

$$\text{Total significance score} = \Sigma_{(i=1-13)}(\text{significance score of descriptor})i$$

The value of this total significance score was then statistically evaluated by a sign test with $n = 13$, since 13 pairs of impression descriptors were used in our sensory test. Accordingly, by using the total significance score defined above, we could statistically evaluate the change in perception of fragrance before and after each type of work.

IBVA-EEG measurements

As a physiological measurement, an IBVA-EEG was used, which is composed of three-point wave sensors on the headband equipped with a telegraph system and a Macintosh personal computer for recording and analyzing IBVA-EEG data with receiving equipment. After fast Fourier transformation (FFT) analysis, intensities (per min) of 8–13 Hz for the alpha rhythm and of 14–30 Hz for the beta rhythm were depicted according to the protocol for IBVA-EEG measurement described as follows: (1) non-smell blank as control (3 min, including presence of non-smell blank for 30 s), (2) inhalation of essential oil before work (5 min, including presence of fragrance for 1 min), (3) work—5 min of work followed by 1 min of rest, and an additional 5 min of work (total = 11 min); (4) inhalation of essential oil after work (5 min, including presence of fragrance for 1 min); and (5) non-smell blank as control after work (3 min, including presence of non-smell blank for 30 s).

Results

The present inhalation experiments were carried out with a constant concentration of 20 mg/ml of linalool enantiomers each loaded and moistened in 300 ml of the inhaler by applying 20 µl of solution on a tiny strip of filter paper. In screening sensory experiments, in which change in perception of fragrance was assessed and depicted as a bar graph in terms of the mean of the difference in impression score recorded before and after work on an 11-point scale (–5 to +5) for 13 impression descriptors against the descriptors, commercial linalool was found to have total significance scores of 5.5 for mental work (Figure 1a), 1 for physical work (Figure 1b) and 5 for hearing environmental sounds (Figure 1c) respectively.

In Figure 1, the statistical significance by determined by *t*-test for each descriptor was marked by ** and * as follows: score = 1 for **, 0.5 for * and 0 for unmarked. The total significance score for each test was then calculated by addition of the respective scores of the marks. This corresponds to the number of impression items regarded to be significant by *t*-test with the level of $P < 0.05$ among the 13 descriptors, as detailed under Statistics.

It is evident from our statistical arguments (Sugawara *et al.*, 1998b, 1999) that the total significance score is regarded as follows on the basis of the sign test with $n = 13$, since 13 pairs of adjective words are used in our sensory test: (1) if >10, the perception difference in fragrance between before and after work can be regarded as significant; and (2) if <3, the null hypothesis can be rejected. Accordingly, the case of total significance score = 1 for linalool with physical work was then ruled out, while the other cases with a total significance score of 5.5 for mental work and of 5 with that for hearing environmental sounds remained to be examined, so that the null hypothesis could not be rejected. Even with these samples, none could be deemed as being significant statistically because the values were not more than 10.

It should be noted, however, that there was no sample with a total significance score of >10 among 48 cases (Sugawara *et al.*, 1999), in which 16 essential oils in relation to the three types of work were examined, including lavender, rosemary, linalool, peppermint, marjoram, cardamom, ylang ylang, lime, basil, sandalwood, orange, geranium, cypress, bergamot, spearmint and juniper, while there were 30 samples with a value of <3 so that null hypothesis could be rejected. This implies that there should be no sample with a total significance score >10 because of the extraordinary scatter of both impression scores before and after work.

In order to evaluate the case with a total significance score of ≥3, therefore, we employed the sensory evaluation spectrum illustrated in Figure 1 to assess not only olfactory response to a given aroma but also change in perception. In the graphs, if there is any favorable correlation between fragrance of aroma and type of work, a positive value for each descriptor is given above the horizontal axis, while a negative value is given below the horizontal axis if there is any unfavorable correlation. In view of this, it was apparent that linalool created a favorable impression after hearing environmental sounds when compared with that before work (Figure 1c), while the spectrum after mental work indicates an unfavorable one (Figure 1a). This feature of the

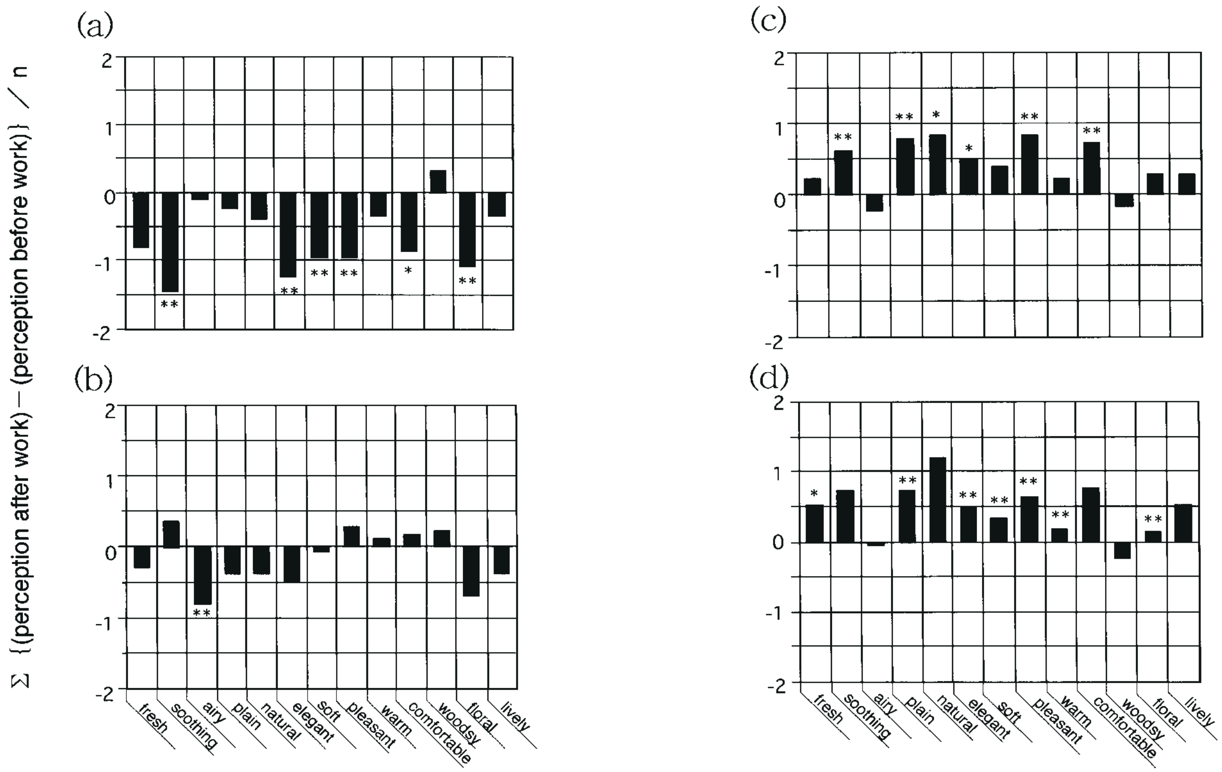

Figure 1 Bar graph (sensory evaluation spectrum) for odor perception of linalool and its purified compound in relation to type of work. **(a)** Linalool versus mental work, **(b)** linalool versus physical work, **(c)** linalool versus hearing environmental sounds and **(d)** purified linalool, (*RS*)-(±)-linalool versus hearing environmental sounds. The difference in score for 13 impression descriptors recorded before and after work was obtained and the statistical significance of the difference of each descriptor was tested by Student's *t*-test. The mean of the difference in score before and after work for each descriptor was then plotted against the 13 descriptors. Statistical significance by *t*-test was scored and marked with ** or * (see text). (*RS*)-(±)-Linalool with $[\alpha]_D = 0°$ and content of (*R*)-form 50.9% and (*S*)-form 49.1% was obtained from commercial linalool by repeated flash column chromatography. Total significance score was calculated to be 5.5 for (a), 1 for (b), 5 for (c) and 6.5 for (d) respectively. The number of subjects was (a) 20, (b) 19, (c) 22 and (d) 21.

spectrum for mental work was thus completely opposite to that for hearing environmental sounds.

The other spectrum (Figure 1d) depicts the profiling for inhalation of (*RS*)-(±)-linalool versus hearing environmental sounds, which was prepared from commercial linalool by repeated flash column chromatography and the identified racemic mixture of (*R*)-form (50.9%) and (*S*)-form (49.1%) with $[\alpha]_D = 0°$. The total significance score of 6.5 for (*RS*)-(±)-linalool was in good agreement with the value of 5 for commercial linalool (Figure 1c,d), the two profiles bearing a close resemblance, with a favorable correlation between inhalation and task assigned to subjects.

In a more detailed study in the view of this for other enantiometers of linalool, Figure 2 depicts such a complete diagram, when (*R*)-(–)-and (*S*)-(+)-forms were isolated using the same method described earlier from lavender oil and coriander oil respectively. As shown in Figure 2, the total significance score was 6.5 for (*RS*)-(±)-linalool, 7 for (*R*)-(–)-linalool and 4 for (*S*)-(+)-linalool in relation to hearing environmental sounds, and 4 for (*RS*)-(±)-linalool, 4.5 for (*R*)-(–)-linalool and 3.5 for (*S*)-(+)-linalool in relation to mental work respectively. It was remarkable that the value in all cases was ≥3.

When compared with the sensory evaluation spectrum of (*RS*)-(±)-linalool as a reference, it was suggested for hearing environmental sounds (Figure 2a–c) that the spectrum of (*R*)-(–)-linalool with a favorable trend was quite similar to that of (*RS*)-(±)-linalool but not to that of (*S*)-(+)-linalool, in which half of the descriptors marked as ** and * were upward on the vertical axis with the other half downward, and its unfavorable trend was more remarkable than that of (*R*)-(–)-linalool. As for mental work, each graph of Figure 2d–f showed an unfavorable trend, being the reverse of (*RS*)-(±)-linalool and (*R*)-(–)-linalool in the case of hearing environmental sounds. However, the resemblance between (*RS*)-(±)-linalool and (*R*)-(–)-linalool observed in hearing environmental sounds was not obvious in the case of mental work.

It is interesting to speculate from these findings that enantiometric stereospecificity of linalool may evoke a different odor perception not only with chiral dependence but also with task dependence. However, it is also evident that there is an inconsistency in the resemblance of sensory profiling of the (*R*)-(–)- and (*S*)-(+)-forms between the observation of hearing environmental sounds and mental work.

Not only to clarify such discrepancies but also to examine

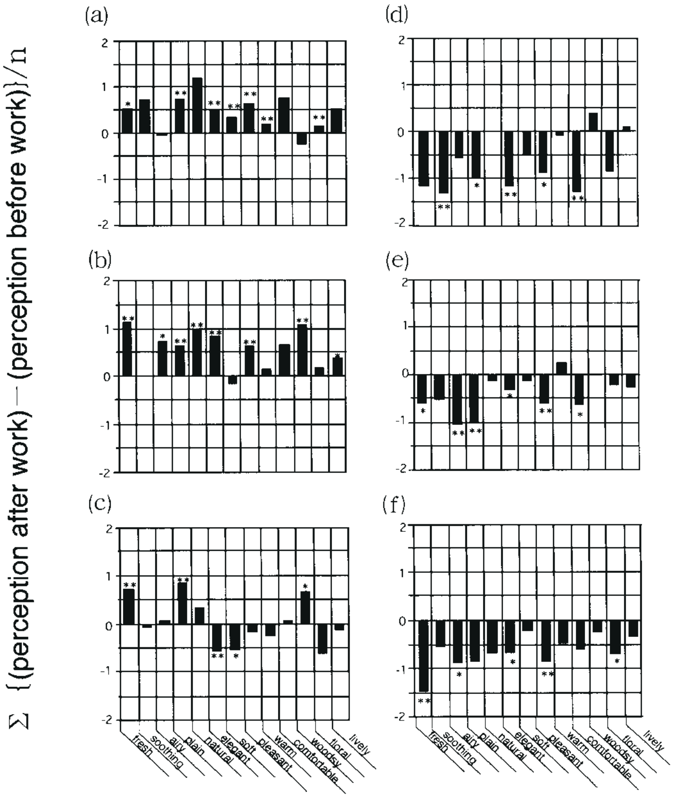

Figure 2 Bar graph for odor perception of enantiomeric linalools, (*R*)-(–)- and (*S*)-(+)-linalool with reference of (*RS*)-(±)-linalool, in relation to hearing environmental sounds and mental work. **(a)** (*RS*)-(±)-Linalool, **(b)** (*R*)-(–)-linalool and **(c)** (*S*)-(+)-linalool each versus hearing environmental sounds, and **(d)** (*RS*)-(±)-linalool, **(e)** (*R*)-(–)-linalool and **(f)** (*S*)-(+)-linalool each versus mental work respectively. Statistical significance by *t*-test was scored and marked with ** or * identical to Figure 1. Total significance score was calculated to be 6.5 for (a), 7 for (b) and 4 for (c) each in relation to hearing environmental sounds, and 4 for (d), 4.5 for (e) and 3.5 for (f) each in relation to mental work respectively. The number of subjects was (a) 21, (b) 24, (c) 23, (d) 18, (e) 23 and (f) 26. Concentration of each enantiomer was 20 mg/ml (in diethyl phtalate), which was loaded and moistened in an inhaler (300 ml) by applying 20 μl of this solution.

whether these different odor perceptions are accompanied with differences in odor response and whether the odor response is also dependent on a different content of tasks and on a difference of enantiomers, an IBVA-EEG was used for the inhalation study of linalool enantiomers in relation to both cases of hearing environmental sounds and mental work. IBVA-EEG is a portable unit with only three-point wave sensors on a headband equipped with a telegraphic system for recording and analysis on a Macintosh with receiver. Our previous study suggested that the system provides good reproducibility in contrast to poor reproducibility of fingertip temperature measurements and skin resistance measurements between the left thumb and left ear lobe (Sugawara *et al.*, 1998b).

Figure 3 shows a typical example of IBVA-EEG brain data after fast Fourier transformation, in which intensities

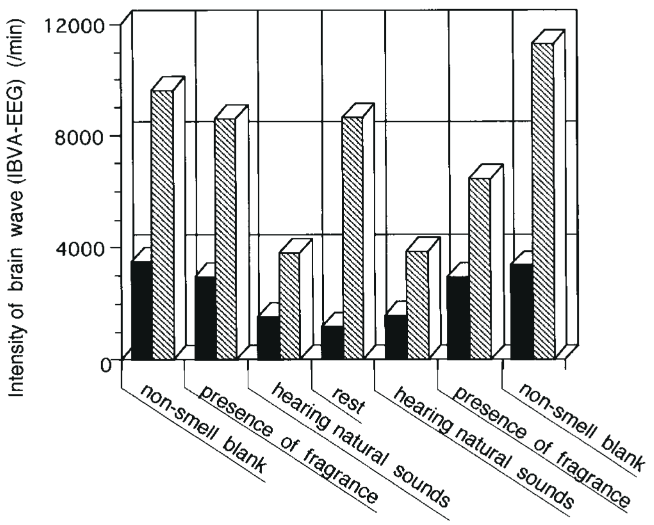

Figure 3 A typical example of IBVA-EEG brain data when optically active linalool was presented by inhalation before and after hearing environmental sounds with a non-smell blank as the control. After FFT analysis, intensities (per min) of 8–13 Hz for the alpha rhythm and those of 14–30 Hz for the beta rhythm were depicted according to the protocol described at the bottom of the graph in the case of (*R*)-(–)-linalool. Filled bars, alpha wave; diagonal shaded bars, beta wave.

of alpha and beta waves were depicted along the lines of the protocol described in the bottom of the graph, when (*R*)-(–)-linalool was presented by inhalation before and after hearing environmental sound with a non-smell blank as the control. As in the case after work, inhalation seemed to be accompanied by a tendency for the beta wave to be much more decreased with the non-smell blank as reference when compared with that before work. On the contrary, this tendency was quite opposite after mental work, in which the intensity of beta wave with inhalation of (*R*)-(–)-linalool resulted in an increase after work when compared with that before work with a non-smell blank as the control. This implies that even inhalation of the same enantiometric linalool evokes a different odor response with task dependence.

In spite of these trends, however, it seems to be quite difficult to achieve a full understanding of such olfaction and the olfactory response to a given enantiomer because each IBVA-EEG measurement showed a large individual variation. This may be attributable to sex difference, to the generation to which the subjects belong, to a particular linking for given linalool to olfactory memory and to the biorhythm of the subjects. To reduce such variability, a net intensity change due to inhalation was employed as follows, which can be expressed in terms of intensity of observed alpha and beta waves corrected by respective intensity of non-smell blank:

$$(I^{\alpha}_{obs} - I^{\alpha}_{o})/I^{\alpha}_{o} \text{ for alpha waves} \quad (1)$$

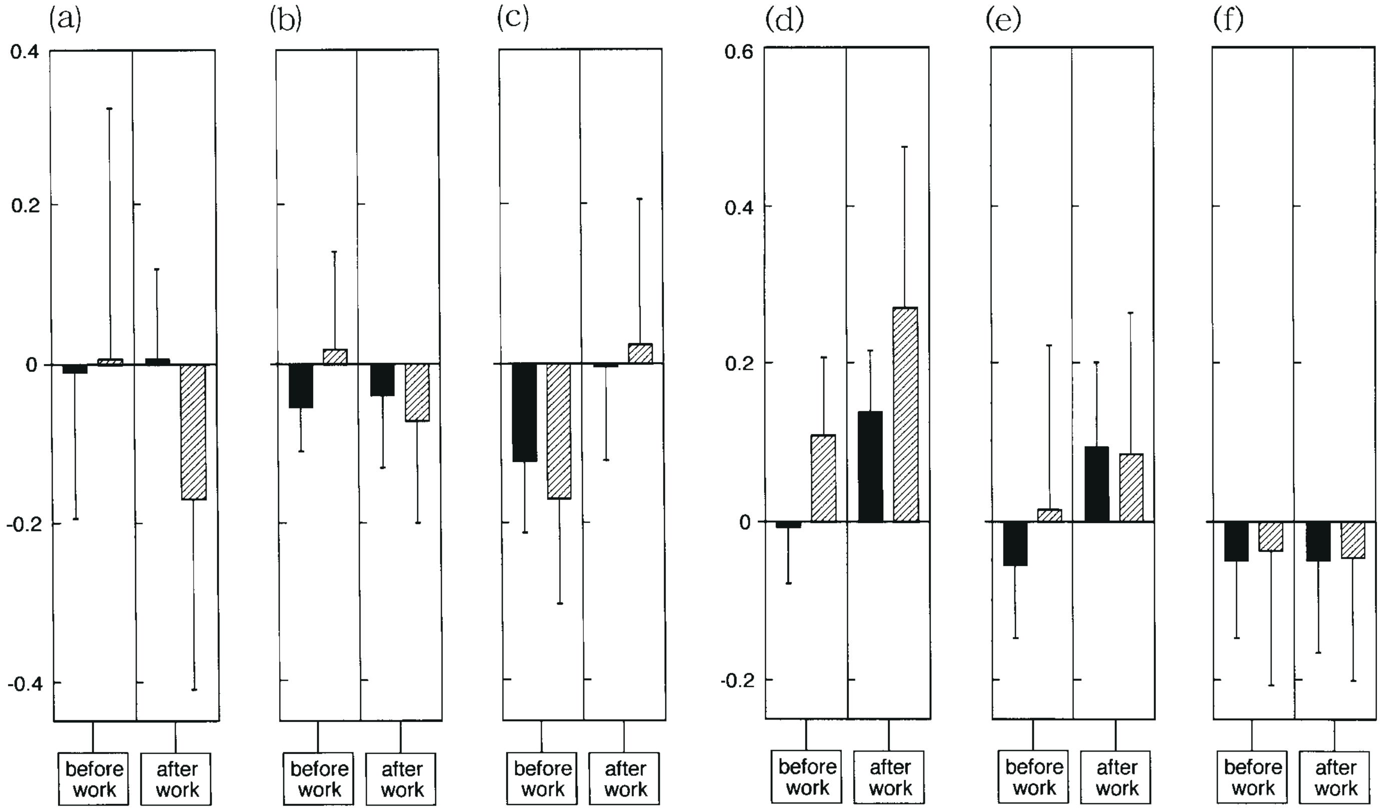

Figure 4 Changes of intensities of IBVA-EEG brain wave when optically active linalools were presented before and after hearing environmental sounds and mental work with non-smell blank as the control. **(a)** (*RS*)-(±)-Linalool, **(b)** (*R*)-(–)-linalool and **(c)** (*S*)-(+)-linalool each versus hearing environmental sounds, and **(d)** (*RS*)-(±)-linalool, **(e)** (*R*)-(–)-linalool and **(f)** (*S*)-(+)-linalool each versus mental work respectively. The number of subjects was (a) 9, (b) 10, (c) 10, (d) 8, (e) 8 and (f) 8. Filled bars, alpha wave; diagonal shaded bars, beta wave.

and

$$(I^{\beta}_{obs} - I^{\beta}_{o})/I^{\beta}_{o} \text{ for beta waves} \quad (2)$$

where I^{α}_{obs} and I^{β}_{obs} are the intensity (per min) of the observed alpha and beta waves and I^{α}_{o} and I^{β}_{o} are the respective intensity of the non-smell blanks. The summarized results of analysis using equation (1) and (2) are depicted in Figure 4, where the number of subjects was nine for (*RS*)-(±)-linalool, ten for (*R*)-(–)-linalool and ten for (*S*)-(+)-linalool for hearing environmental sounds, and eight for each linalool enantiomer for the case of mental work. The mean of the net intensity change due to inhalation of each enantiomer for the observed alpha and beta waves was plotted, with standard deviation, against that before and after work. In Figure 4 these were (a) (*RS*)-(±)-linalool, (b) (*R*)-(–)-linalool and (c) (*S*)-(+)-linalool each versus hearing environmental sounds, and (d) (*RS*)-(±)-linalool, (e) (*R*)-(–)-linalool and (f) (*S*)-(+)-linalool each versus mental work respectively.

In determining the significance of an observed sample mean difference, Student's *t*-test was used on the basis of Welch's method, $P < 0.05$ being considered statistically significant. Among the samples shown in Figure 4, a significant difference in change of beta waves was observed between the following cases: (1) for hearing environmental sounds, before work versus after work each for (*S*)-(+)-linalool [$|t| = 2.6096 \geq t(18, 0.05) = 2.101$] with $P < 0.05$ (Figure 4c) and (2) for mental work, before work for (*RS*)-(±)-linalool versus after work for (*S*)-(+)-linalool [$|t| = 2.1882 \geq t(14, 0.05) = 2.145$] with $P < 0.05$ (Figure 4d,f). For hearing environmental sounds, there was also a highly significant difference in beta waves between the case of (*RS*)-(±)-linalool versus (*S*)-(+)-linalool each for after work [$|t| = 3.245 \geq t(15, 0.01) = 2.947$] with $P < 0.01$ (Figure 4d,f). At this point, if the level of significance is elevated to $P < 0.1$, it appears to become significant in the case of mental work between after work for (*RS*)-(±)-linalool versus after work for (*S*)-(+)-linalool [$|t| = 1.8775 \geq t(10, 0.1) = 1.812$] (Figure 4d,f).

When compared between each isomer and between before and after work assigned to subjects, the results showed: (1) as for hearing environmental sounds, inhalation of the (*R*)-(–)- and (*RS*)-(±)-forms produced a decrease in the intensity of the beta wave, while the feature was different in the case of (*S*)-(+)-linalool; (2) as for mental work, similarly, smelling of (*R*)-(–)-and (*RS*)-(±)-linalool showed a trend to evoke an increase in beta waves, whereas the feature was the reverse of (S)-(+)-linalool, although increasing the intensity of the beta wave with inhalation of (R)-(–)-linalool in mental work was the complete opposite of hearing environmental sounds.

Discussion

It is well known that humans can distinguish between 4000 and 10 000 different odors (Roderick, 1966; Firestein, 1991). Consequently, theories attempting to explain the perception for such numerous odors have been presented by several authors with a variety of views such as vibrational energy levels, intermolecular interaction, and molecular size and shape (Roderick, 1966), but no physiologic clue to this olfactory discrimination has been presented in these studies.

This study was undertaken to examine odor distinctiveness of optically active linalools through investigations to assess the possible effects on humans of their inhalation in terms of sensory tests and IBVA-EEG measurements. As illustrated typically in Figure 4, a large standard deviation against a smaller value of the mean was observed in cases of IBVA-EEG measurements. To reduce such variability and maintain consistency of data, subtraction was made of the sensory score between before work and after work to further minimize the effect of internal and extraneous influences of subjects, and equations (1) and (2) were employed for minimizing individual differences between IBVA-EEG measurements.

Although these were insufficient for an odor incongruity study, our study clearly indicated that (1) enantiomers of linalool could be regarded as significantly different odors and (2) they consequently evoked different odor reactions with dependence not only on species of enantiomer but also on tasks assigned to the subjects. Though these points are open to future study, they might contribute toward resolving some conflicting conclusions surrounding odor incongruity and perception.

The calming and relaxing effects of lavender flowers, the oil derived from them and the main constituents of linalool and linalyl acetate are better documented by experimental studies than other odorants (Imaseki and Kitabatake, 1963; Atanassove-Shopova *et al.*, 1974; Buchbauer *et al.*, 1991; Sugawara, *et al.*, 1998a,b). Torii *et al.* (1991) demonstrated that human subjects who had inhaled lavender oil showed a significant decline in selective EEG potential (contingent negative variation) that correlated with vigilance and expectancy alertness. They also demonstrated that it had no effect on heart rate or reaction time, unlike nitrazepam. At the same time, however, there have been two reports that such calming and relaxing effects of lavender were not observed. Schwartz *et al.* (1986) reported that smelling of lavender was accompanied by increase in alertness and increase in respiration parameters such as inspiration amplitude. Lorig and Schwarz (1988) showed that lavender odorants tended to cause an increase in theta activity in EEG, which is associated with emotion- and anxiety-provoking stimuli, together with an increase in the scale of self-report differences of anxiety and tension.

Our previous sensory tests (Sugawara, *et al.*, 1998a,b) showed that the total significance score for lavender oil was 1.5 for hearing environmental sounds, 0 for mental work and 1 for physical work. But, as shown in Figures 1 and 2, the situation was very different in the case of linalool and its enantiometric isomers. As for the case of enantiomers, for example, inhalation (*R*)-(–)-linalool after hearing environmental sounds produced a much more favorable impression in the sensory test in association with a consequent decrease in the beta wave, implying a sedating and relaxing effect on subjects. This was in sharp contrast to the case for mental work, which resulted in a tendency for agitation and alertness associated with an increase in the beta wave, as the subjects had inhaled the same enantiomeric isomer.

Even when the variability in our study was taken into account, our findings suggested some important aspects of the salience of odors as neurophysiological stimuli, which cause a different perception and lead in turn to a diverse odor reaction depending on internal and extraneous conditions of the subject. As Lorig and Schwartz (1988) have pointed out, because of this salience, together with the ability to modify limbic system activity, odor may have an application in the alteration of perception, mood state and odor reaction in humans.

Conclusion

Sensory profiling and IBVA-EEG measurements for enantiomers of linalool revealed that (1) enantiomers could be regarded as significantly different odors and (2) they consequently evoked different odor reactions with dependence not only on species of enantiomer but also on tasks assigned to the subjects. Moreover, the subjects who had inhaled (*R*)-(–)-linalool after hearing environmental sounds produced a much more sedating and relaxing profile in the sensory evaluation spectrum associated with a consequent decrease in beta waves. This was in sharp contrast to the case of mental work, which resulted in a tendency of agitation and alertness with an increase in the intensity of the beta wave as the subjects had been taking the same enantiometric isomer. Our findings thus indicated some important aspects of the salience of odors as neurophysiological stimuli, which cause a different perception and lead to diverse odor reactions with dependence on the internal and extraneous conditions of the subject.

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