Mutual information analysis of EEG responses by odor stimulation

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Abstract: To investigate the changes of cortico-cortical connectivity during odor stimulation for subjects classified by occupations, we examined the mutual information of EEGs for general workers, perfume salespersons and professional perfume researchers. Analysis of the averaged cross mutual information (A-CMI) from the EEGs of the professional perfume researchers were more apparent in the frontal region of the brain, though for the general workers group and perfume salespersons group such changes were more conspicuous in the overall posterior temporal, parietal and frontal regions. These results indicate that the brains of professional perfume researchers respond to odors mainly in the frontal region, reflecting the function of the orbitofrontal cortex (OFC) due to the occupational requirement of these subjects to discriminate or identify odors. The perfume salespersons, although relatively more exposed to odors than the general workers, show similar changes to the general workers. A-CMI value is in inverse proportion to psychological preferences of the professional perfume researchers and perfume salespersons, but this is not the case with the general workers. This suggests that functional coupling for people who are occupationally exposed to odors may be related to psychological preference.

Key words: *odor stimulation; different occupation; mutual information; functional connectivity; frontal, temporal, posterior parietal regions; psychological preference*

1. Introduction

Henkin and Levy [1] reported that pleasant odors were more appreciated in the left hemisphere, while unpleasant odors were more appreciated in the right hemisphere. It is rare to find studies for EEG differences during odor stimulation for different occupational groups, especially workers in olfactory-related occupations. There has been limited research, through clinical case studies, on evaluating olfaction in workers occupationally exposed to chemicals [2, 3]. Dalton et al. [2] reported that both the perceived odor and cognitive expectations about a chemical could significantly affect how individuals respond to it. There was a statistically significant relationship between olfactory impairment and cadmium concentration in blood, urine and workplace air [3]. In the present study, we used the mutual information of EEGs to investigate the differences in response to odors in groups classified by occupations dealing with odors. Coherence analysis of the EEGs has been widely used to measure functional relationships between different brain regions. Harada et al. [4] suggested that EEG coherence mapping might provide a basis for the development of an objective test of olfactory function in humans. However, because coherence analysis only shows linear connectivity in a pair of electrodes, we cannot get the whole view of connectivity through this kind of analysis. To investigate the whole view of functional connectivity between a pair of electrodes, we used a measure of mutual information. Mutual information detects both linear and nonlinear statistical dependencies between two time series [5, 6]. This is used as a measure of functional connectivity [7, 8] or information transmission between the two time series [8]. The aim of this study is to use mutual information analysis of EEGs within each occupational group to investigate, according to occupations, the change in cortico-cortical functional connectivity during odor stimulation.

2. Method

2.1 Subjects

EEG recordings were obtained from 10 general workers (9 females and 1 male, mean age 27.3 years), 9 perfume salespersons (9 females, mean age 25.2 years), and 10 professional perfume researchers (5 females and 5 males, mean age 32.2 years). All subjects had a normal nasal anatomy; all had been in their present occupation for over 5 years; they were prohibited from drinking, smoking, or taking any drugs, including caffeine; and they were all right handed. All experiments were conducted in accordance with the Declaration of Helsinki.

2.2 Measurements and Analysis

Odors such as basil oil, lavender oil, lemon oil, jasmine oil, ylang-ylang oil (KIMEX Co. Ltd, KOREA) and skatole (Takasago Co. Ltd, JAPAN) were presented through an olfactometer, a device that scatters odor through Teflon tubes (with an inner diameter of 2mm), while subjects reclined with eyes closed. The odor stimulation was achieved by mixing pulses of the stimulants in a constantly flowing air stream. We set the scattering frequency of each odor in accordance with individual inhalation rate to avoid mismatching odor stimulation with respiration. Six kinds of odors were presented in random order for every 90 seconds. We ventilated the chamber between odor stimuli. A total of 630 seconds of recordings were acquired with a sampling frequency of 256 Hz; these were digitized using a 12-bit analog-digital converter on an IBM PC. EEGs were recorded from 8 scalp loci (F3/4, P3/4, T5/6, Fz, Pz, and Cz) referenced to the earlobes. All data were digitally filtered with a band pass of 0.3-60 Hz. After stimulation by each odor, subjects were asked to state their feelings through a questionnaire in order to obtain the individual psychological preference for the odors.

For every odor stimulus, we used 8 seconds of data. Let X be a set composed with measurement x_i and probability $P_X(x_i)$. The average amount of information gained from the measurement of X is the entropy H of a system, $H(X) = -\sum_{x_i} P_X(x_i)\log P_X(x_i)$. We also define the conditional entropy on X under the condition that Y has been measured and found to be y_i. $H(X \mid y_i) = -\sum_{xj} P_{X|Y}(x_j \mid y_i)\log P_{X|Y}(x_j \mid y_i) = -\sum_{xj} \frac{P_{XY}(x_i, y_j)}{P_Y(y_i)}\log \frac{P_{XY}(x_i, y_j)}{P_Y(y_i)}$, where $P_{X|Y}(x_j \mid y_i)$ is the probability that a measurement of X and Y produce the values of x_j is y_i. The averaged conditional uncertainty on X over y_i is $H(X \mid Y) = -\sum_{x_j, y_i} P_{XY}(x_j, y_i)\log[P_{XY}(x_j, y_i)/P_Y(y_i)] = H(X,Y) - H(Y)$, where $H(X,Y) = -\sum_{x_j, yi} P_{XY}(x_j, y_i)\log P_{XY}(x_j, y_i)$. We define mutual information as the amount by which the measurement of Y

reduces the uncertainty of *X*. The mutual information *I(X,Y)* is as follows:

$$I(X,Y) = H(X) - H(X|Y) = H(X) + H(Y) - H(X,Y) = -\sum_{i,j} P_{XY}(x_j, y_i) \log \frac{P_{XY}(x_j, y_i)}{P_X(x_j) P_Y(y_i)}$$

Mutual information has a maximum value when the two time series are completely the same. We computed the time-delayed mutual information

$$I(X(t), Y(t+\tau)) = -\sum_{X(t), Y(t+\tau)} P_{X(t)Y(t+\tau)}(x(t), y(t+\tau)) \log \frac{P_{X(t)Y(t+\tau)}(x(t), y(t+\tau))}{P_{X(t)}(x(t)) P_{Y(t+\tau)}(y(t+\tau))}$$

The averaged CMI (A-CMI) values were used as a mutual coupling measure between different brain regions. To investigate the brain functional connectivity of the brain we estimated the CMI of each EEG as a function of time delay for F3F4, P3P4, T5T6, F4F3, P4P3, and T6T5 pairs over time delays of 0-500 ms. The detailed derivation of these equations is presented elsewhere [10, 11]. The A-CMI values for 6 pairs of two different cortical areas were estimated from three different occupation groups between all odor stimuli.

The normally distributed data (Kolmogorov-Smirnov test) was subjected to an unpaired Student's t-test (SPSS 6.0) to evaluate the statistical differences in the pairs of electrodes within each group. All significant results quoted are significant to at least $P<0.05$.

3. Results and Discussions

The higher A-CMI value suggests the mutually stronger functional coupling between two different time series. In the F3F4 and F4F3 pairs, an increased mutual coupling was observed during lavender and lemon stimuli, relative to a no-odor baseline (fig.1). General workers had a higher A-CMI in the pairs of P3P4 and P4P3 during the lavender stimulus compared to a no-odor baseline. They also had a higher A-CMI in the T6T5 pair during the lemon stimulus in comparison with the ylang-ylang. A-CMI values had no correlation with the psychological preference. In the F3F4 pair, the perfume salespersons group had a higher A-CMI value during the basil stimulus than during presentation of the odorless stimulus and the lavender (fig.2). The A-CMI value increased more during the skatole stimulus than during the lavender stimulus. The salespersons had a higher A-CMI value in the F3F4 and F4F3 pairs in response to the skatole stimulus than during the odorless stimulus and the lavender. In the P3P4, P4P3, T5T6, and T6T5 pairs, this group's A-CMI value was higher in response to basil than to jasmine.

In the T6T5 pair, their A-CMI value was significantly higher during the basil stimulus than during the lavender. The A-CMI of the salespersons had a lower value when stimulated by an odor for which they had a higher preference in comparison to the other odors. There was a lower A-CMI value in the F3F4 and F4F3 pairs for the lavender stimulus than for the basil stimulus or an odorless. In this group, the significantly different results were

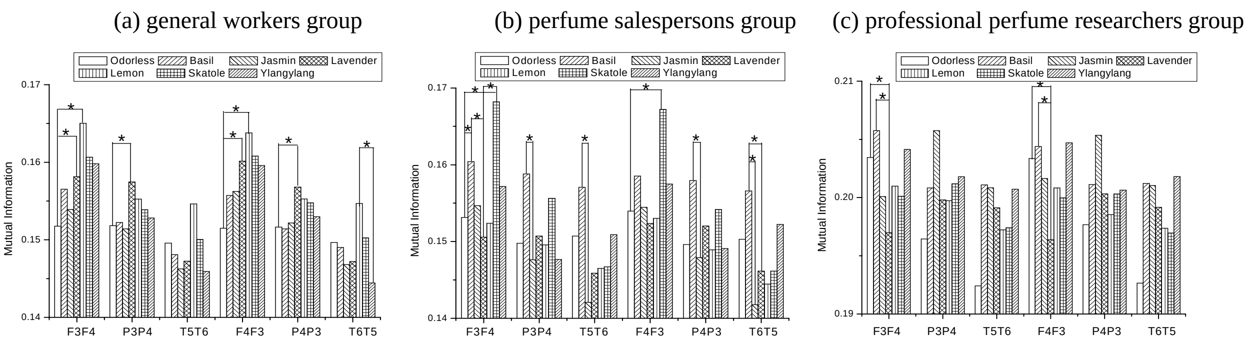

Figure 1. The pairs with significant changes in the A-CMI values for all cases. (* $P<0.05$)

revealed in the mid-frontal pairs. The group had a lower A-CMI value when stimulated by an unpleasant odor in comparison with other odors, as was the case for the perfume salespersons group. There was no correlation between sex differences in the significantly different pairs of electrodes; we excluded sex difference in our study. For the group of professional perfume researchers, the dominant change in the frontal region may reflect the effects of functional coupling in the OFC when being stimulated by an odor (fig.3). These results indicate that the brains of professional perfume researchers respond to an odor mainly in the frontal region, reflecting the function of the OFC due to the occupational requirement of these subjects to discriminate or identify odors. Although relatively more exposed to odors in their occupation, the perfume salespersons responses to odor stimulation were similar to those of the general workers. The A-CMI value is in inverse proportion to psychological preference among the professional perfume researchers and the perfume salespersons, but this is not the case for the general workers. This suggests that functional coupling for people who are occupationally exposed to odors may be related to psychological preference. The regions of the brain where changes in A-CMI appear, however, differ according to occupational specialty.

Although mutual information is an indicator of functional cortico-cortical connections in the brain, including linear and nonlinear properties, the A-CMI does not reveal the actual mechanism or pathways. But by using the A-CMI we can quantify the information transmission at one site from the time series at another site. So we can obtain the functional connectivity to an odor for subjects classified by occupations.

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