学 位 論 文 の 要 旨

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学 位 論 文 名　Development of Olfactory Epithelium in the Human Fetus: Scanning Electron Microscopic Observations

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論 文 内 容 の 要 旨

INTRODUCTION

The olfactory epithelium is distributed over the superior wall of the nasal cavity, representing the sensory epithelium, which manages the olfactory sense. Odor has great significance throughout human life and plays an important role in the suckling of newborns. Human olfactory epithelium therefore becomes functional at birth, but its prenatal development remains unclear.

In the present study, we observed the detailed prenatal developmental process of the human olfactory epithelium, particularly for olfactory vesicles, under scanning electron microscopy (SEM) and compared the results with reported findings in other fetal and adult animals.

MATERIALS AND METHODS

All fetuses used in the present study belong to the 'Kyoto collection' and were obtained through collaboration with obstetricians in Japan, in accordance with Japanese laws. Twenty-four externally normal human fetuses with a crown-rump length (CRL) of 102-336 mm (ca gestational weeks 14-38) were used (10 males, 14 females). For SEM, the olfactory mucosa was

dissected from the superior wall of the nasal septum near the choana and specimens were post-fixed with 1% OsO_4 in phosphate buffer (pH 7.2), then stained with 2% tannic acid solution followed by 1% phosphate-buffered OsO_4. After dehydration, critical-point dried with liquid CO_2, and sputter-coated with platinum-palladium, the specimens were observed with an S-800 scanning electron microscope (Hitachi, Hitachi-naka, Japan) at 15 kV. We observed the surface structure of the olfactory epithelium to determine the general surface configuration, the number and size of the olfactory vesicle, and the length and number of olfactory cilia.

The fetuses were grouped by the hierarchical clustering with four normalized variables, the number and size of the olfactory vesicles and the number and length of the olfactory cilia. In addition, the correlation between CRL and each measurement was assessed by regression analysis. Values of $P<0.05$ were considered statistically significant.

RESULTS AND DISCUSSION

The present fetuses were clustered into the following three groups by the hierarchical clustering with four variables; group 1 in which CRL of the fetuses is 102 -140 mm, group 2 in which CRL is 150 – 220 mm and group 3 in which CRL is 225 – 336 mm.

In fetuses of group 1, the number of olfactory vesicles was 22.3 ± 7.87 (mean ± standard deviation) per unit area (1000 μm^2). These vesicles have a diameter of 0.94 ± 0.14 μm. They existed separately from each other above the olfactory epithelium and displayed 1-2 short cilia that were 0.73 ± 0.20 μm long. In fetuses of group 2, the number of olfactory vesicles was increased to 34.2 ± 4.78 per unit area. The olfactory vesicle diameter was 1.24 ± 0.15 μm. The olfactory vesicles were present in small clusters of 3-6. The number of cilia increased to 6.91 ± 0.65 per vesicle, and the olfactory cilia were 1.24 ± 0.16 μm long. In fetuses of group 3, the number of olfactory vesicles was 33.5 ± 6.51, remaining nearly the same that in group 2, with a diameter, 1.62 ± 0.15 μm. The number of cilia was 11.65 ± 0.78 per vesicle, and the cilia were 1.51 ± 0.24 μm long. In the fetuses with CRL 225 and 233 mm, some of the olfactory vesicles

exceeded 2 μm in diameter with more than 10 cilia per vesicle, and some of the cilia exceeded 2 μm in length.

Pyatkina (1982) suggested that the human olfactory epithelium becomes capable of sensory performance by the end of organogenesis (first trimester), based on TEM observations of single olfactory vesicles. However, previous SEM studies reported that the olfactory epithelium in mice and rats attains morphology almost the same as that of adults much later than the end of organogenesis. In the present SEM study, the fetus with CRL 225 mm (ca gestational week 26) was the minimum size among the present fetuses showing the morphological findings similar to the olfactory epithelium of adults. The present study thus suggested that fetal olfactory epithelium becomes morphologically almost the same to that in adults much later in gestation than previously suggested.

CONCLUSION

In summary, the present SEM study revealed the detailed developmental progress of the surface ultrastructure of human fetal olfactory epithelium and suggested that olfactory epithelium continues to grow after organogenesis, reaching a state morphologically similar to that of adults much later in gestation than previously suggested, and with function possibly occurring later as well.