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Prevention and/or Recovery Effects by Green Odor(s) on Fatigue and Green-odor-responsible Brain Regions as Revealed by PET

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Introduction

Green odor (we used a mixture of 3*Z*-hexenol and 2*E*-hexenal in this study) has many physiological functions. Stress-induced hyperthermia was attenuated by green odor in rats (Akutsu *et al.*, 2002). Sano *et al.* (2002) reported that a mixture of hexenol and hexenal was accepted as a pleasant odor and it decreased the amplitude of an event-related potential (P300). However, the neural mechanisms of the effect of hexenol and hexenal are almost completely unknown. We studied its effect on prevention and/or recovery from fatigue, through analyzing the behavioral performance (reaction time, RT) of monkeys during repetition of a simple visual discrimination task and the autonomic function as judged by acceleration plethysmography (APG) during a mental task [advanced trail making test (ATMT), continuously loaded for 4 h] in human volunteers. Moreover, we investigated changes in regional cerebral blood flow (rCBF) during green-odor stimulation using positron emission tomography (PET) in monkeys.

Anti-fatigue effects of green odor

Exposure of monkeys to green odor throughout the tasking period resulted in a reduction of delay of RT during the task. In the human study, the RT of ATMT just after the start and before the end of a task in the control group was delayed ($P < 0.05$). The height of the wave A of APG decreased by 0.36 times ($P < 0.005$) in a comparison between before and after ATMT. On the other hand, the RT in the group that inhaled green odor had little delay throughout the task. The wave A decreased by 0.77 times ($P < 0.05$) after the task. This reduction in the green odor group showed a significant difference as compared with the control group ($P < 0.05$). In conclusion, 'green odor' has fatigue-mitigation effects in monkeys and humans; this effect might be via an autonomic function, such as a healing effect on the sympathetic nervous system.

Activation of the anterior cingulated gyrus by green odor: a monkey PET study

Functional neuroimaging using PET makes it possible to localize functional brain regions in humans and primates brains by detecting changes in regional cerebral blood flow (rCBF). Performing PET studies in monkeys and humans will aid in integrating the electrophysiological studies in monkeys. We have examined changes in rCBF during olfactory stimulation using PET in alert monkeys (Kobayashi *et al.*, 2002). Olfactory stimulation by acetic acid or apple odor increased rCBF in the prepyriform area, substantia innominata and amygdala. Apple odor or flavor stimuli increased rCBF in the inferior occipital gyrus, which is the visual area, in addition to the above areas. These findings suggest that the increases in rCBF in response to neural activities in the primary olfactory cortices are detectable by use of PET. In addition, the regions activated by apple stimuli suggest that higher brain function, in this case perhaps visual imagery, might be detected with PET in alert monkeys. The equivalent mixture of 0.03% *cis*-3-hexenol and 0.03% *trans*-2-hexenal (hexenol/hexenal; Soda Aromatic, Japan) diluted with triethyl citrate—'green odor'—is known to have a healing effect on psychological damage caused by stress. The behavioral studies described above in humans and monkeys revealed that hexenol/hexenal prevents the prolongation of reaction time caused by fatigue. In this study, we investigated which brain regions are activated by the odor of hexenol/hexenal using PET with alert monkeys. rCBF in the prepyriform area was commonly increased by passive application

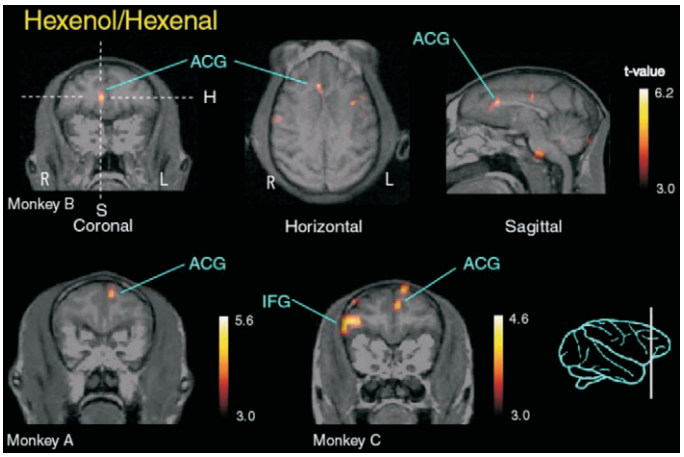

Figure 1 Areas of activation responsible for hexenol/hexenal stimuli superimposed upon MRI slices. Hexenol/hexenal commonly increased rCBF in the anterior cingulate gyrus. Lateral view of schematic monkey brain indicates coronal slice location. Horizontal (H) and vertical (S) broken lines in the left top coronal slice represent the position of the horizontal and sagittal slices, respectively. The color scales indicate the range of t-values. ACG, anterior cingulate gyrus; IFG, inferior frontal gyrus; L, left; R, right.

of odor: acetic acid, *iso*-amylacetate, or hexenol/hexenal. We observed rCBF increases in the orbitofrontal cortex (the secondary olfactory cortex) by these olfactory stimuli in two of three monkeys and found no predominance of laterality of the activated hemisphere. In addition to these olfactory-related regions, the anterior cingulate gyrus was activated by the odor of hexenol/hexenal (Figure 1) (Sasabe *et al.*, 2003). These findings suggest that the increase in rCBF in the anterior cingulate gyrus causedby the odor of hexenol/hexenal may contribute to its healing effects observed in the monkey.

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