

# The Neural and Endocrinological Mechanisms of the Salt Reduction Effect Induced by Oregano Odor

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## Summary

**Background and Objective:** Previous studies have demonstrated that exposure to oregano and its major active component, carvacrol, in male and female C57BL/6J (B6) mice exhibits a salt-sparing effect. Additionally, olfactory stimulation by oregano was shown to significantly activate the ventral part of the bed nucleus of the stria terminalis, a region involved in salt intake regulation. In this study, we aimed to elucidate the neurophysiological mechanisms underlying the inhibitory effects of olfactory stimulation with oregano and carvacrol on salt intake and conducted the following experiments.

**Methods:** Female mice were fed a low-sodium diet and presented with the odor of oregano (1 g) or carvacrol (1  $\mu$ l) for 2 hours while performing a two-bottle choice experiment with pure water and 0.3 M saline. Following the two-bottle choice experiment, brain tissue from mice was collected, including regions related to olfactory stimulation and salt regulation, such as the olfactory bulb, amygdala, and hypothalamus. mRNA expression was then analyzed using quantitative PCR. Additionally, after presenting oregano 1 g or carvacrol 1  $\mu$ l for one hour, the changes in Fos-positive cell density in central regions related to sodium regulation in the brains of male and female mice were evaluated using immunohistochemical techniques.

**Results and discussion:** In the behavioral experiment, the odor-exposed group showed a consistently lower saltwater intake rate compared to the control group. Immediately after the behavioral experiment, brains were sampled from mice, and quantitative PCR was performed on 17 types of neurotransmitters and hormones in the brain. The results showed that olfactory stimulation by Oregano and Carvacrol increased the signal intensity of the serotonin and oxytocin systems. Additionally, in the oregano-exposed group, a decrease in the orexin system, which promotes salt intake, and an increase in corticotropin-releasing hormone and norepinephrine systems, which have inhibitory effects, were confirmed. These changes in gene expression suggest that they may induce a salt-regulating effect. Furthermore, the increase in dopamine receptors 1, 2, and 3 in the amygdala suggests that the odor of oregano may regulate sodium preference.

Olfactory exposure to oregano and carvacrol extensively activated multiple neural nuclei involved in salt regulation pathways, including the ventral part of the bed nucleus of the stria terminalis, the central nucleus of the amygdala, and the raphe nucleus, which is the origin of serotonin neurons, in both male and female B6 mice. These results suggest that this exposure induces inhibitory effects on salt intake. Furthermore, stimulation of the nucleus accumbens and ventral tegmental area, which are neural nuclei of the dopamine system, in female mice alone suggested that this may be directly stimulated by these odor components and indirectly promote salt-regulating effects.