



Early survival factor deprivation in the olfactory epithelium enhances activity-dependent survival

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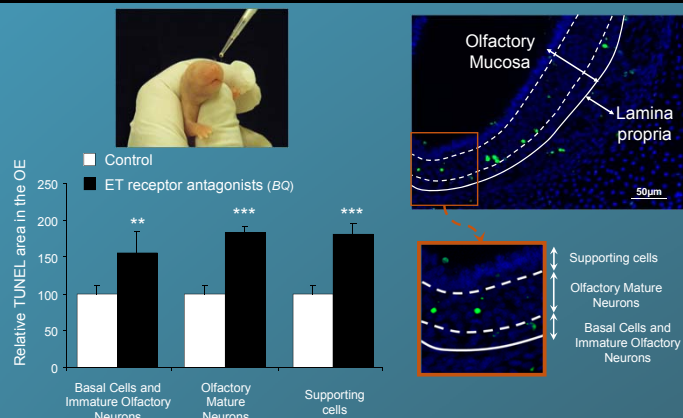
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Early survival factor deprivation in the olfactory epithelium enhances activity-dependent survival

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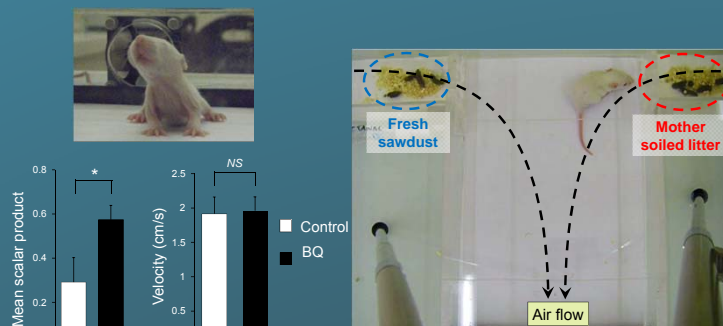
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Apoptosis level in the olfactory mucosa of rats treated by intranasal antagonists of endothelin receptors : **TUNEL**



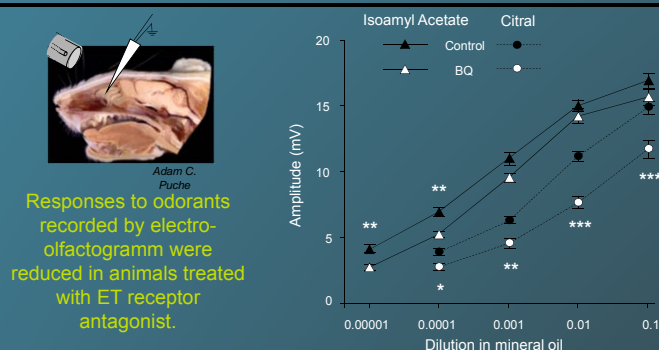
TUNEL signal was enhanced in all layers of the olfactory epithelium after the ET receptor antagonist treatment (twice a day during 7 days).

Olfactory driven orientation behaviour of rats treated with ET receptor antagonists : **Behaviour Test**



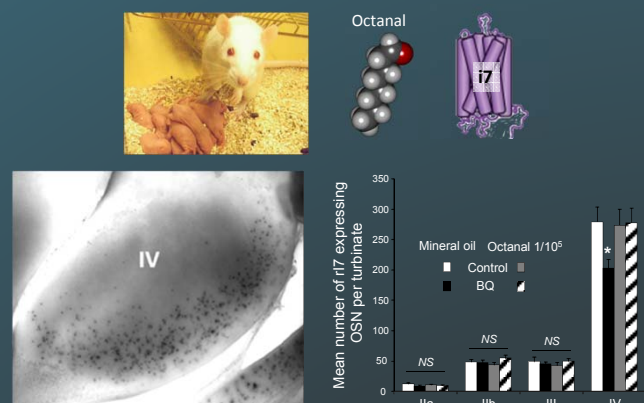
10 days old rats treated or not with ET receptor antagonist were monitored for their orientation toward mother's bedding. Treated animals scored better despite their lower EOG amplitude response to odorant and higher level of apoptosis in the olfactory neuron layer of their olfactory epithelium.

Responses of olfactory mucosa to odorants from rats treated by intranasal antagonist of endothelin receptors : **EOG**



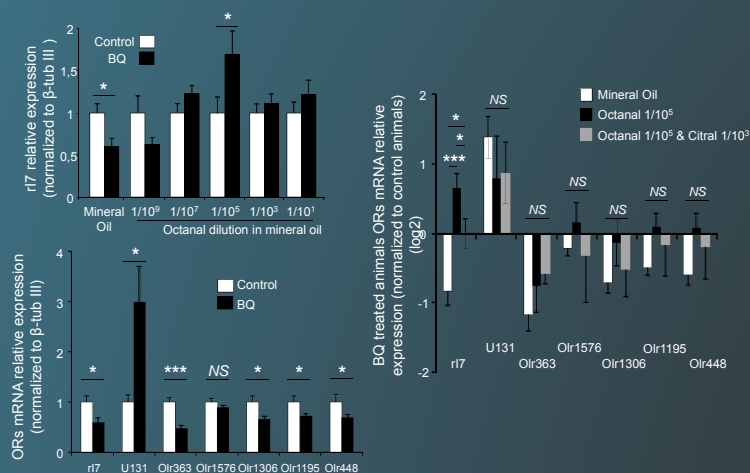
Responses to odorants recorded by electro-olfactogram were reduced in animals treated with ET receptor antagonist.

Quantification of r17-expressing OSNs population **Whole mount in situ hybridization (WISH)**



While the number of OSNs on turbinates Ila, Ilb and II was stable between control and treated animal, it was significantly affected in turbinates IV. When the dam is odorized with octanal the increased r17-expressing neurons apoptosis in the OE of BQ treated animal is reversed.

Indirect quantification of OSNs population **Real-time quantitative PCR**



r17 mRNA level is decreased after treatment. Odorization with octanal significantly reversed this decrease in a dose-dependent manner. The mRNA expression levels of 3 other ORs were statistically decreased by BQ treatment, one (U131) was significantly increased (odorant present in rat milk). The effect of BQ treatment was affected by octanal odorization only for r17. Finally, co-odorization with citral, a known antagonist of r17, limited the effect of octanal odorization.

- Endothelin system inhibition in young rats leads to
- Increased apoptosis in all cell layer
- Decreased amplitude of odorant response recorded by EOG
- Improved odour based orientation behaviour toward maternal smell
- Modulation of OR mRNA level dependent of odorant presence
- Endothelin acts as an anti-apoptotic factor in the olfactory mucosa. Its inhibition could lead to improved detection of odorants already present in the animal's environment by increasing their relative OSN sensitive population.