

Headache pathophysiology: basic science

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CHARACTERISATION OF AN OROFACIAL PAIN ASSESSMENT DEVICE (OPAD) TO MEASURE FACIAL ALLODYNIA IN MICE

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Introduction: The Orofacial Pain Assessment Device (OPAD) is a behavioural test that measures changes in orofacial nociceptive behaviour (trigeminal nociceptive processing). It is a reward/conflict assay that allows the animal to choose between receiving a reward or avoiding a modifiable thermal stimulus. A decrease in the amount of licking suggests an avoidance behaviour, potentially due to an increased sensitivity to an aversive thermal stimuli. The nature of this method offers a more accurate and robust measure of the complex behaviour of choosing whether to withstand an aversive stimulus or not in freely-behaving mice, with the aim to complement this with other more subjective reflex based testing methods.

Objectives: To establish the utility of a novel orofacial pain assessment device (OPAD) as a sensitive tool to measure facial allodynia in freely behaving mice.

Methods: The effects of acute nitroglycerin (NTG) administration on thermal orofacial nociceptive withdrawal thresholds were studied. Mice were habituated to the OPAD for two weeks following acute (12 hour) food restriction. Following the demonstration of a stable baseline contact/licking profile mice were tested 10 minutes after intraperitoneal injection of NTG (10 mg/kg) or vehicle control at 30° and 55°. The total contact time and number of licks was recorded as a readout of orofacial thermal withdrawal thresholds. The difference between treatment groups was compared using an unpaired non-parametric Mann-Whitney test via GraphPad Prism 7.01 software (La Jolla, CA). $P < 0.05$ was considered significant.

Results: NTG-treated mice ($n=10$) showed a significantly lower orofacial thermal nociceptive withdrawal threshold compared to Saline-treated mice ($n=10$) at nociceptive temperatures (55°C), with a median amount of licking of 19 (9.17-29.42) and 73.5 (35-113.3), respectively ($p=0.0185$). There were no significant differences at non-aversive temperatures (30°C), with a median licking number of 155.5 (84.25-205.5) for the saline-treated ($n=10$), compared to 143 (108.3-165.8) for the NTG-treated mice ($n=10$) ($p=0.8132$).

Conclusion: Our data demonstrate that the OPAD is a viable behavioural model of orofacial thermal nociceptive thresholds. As such, we propose to use the OPAD as a sensitive method that can be used to test orofacial sensitivity in conscious freely-behaving mice that is not dependent on reflex behaviours. This will enable the determination of orofacial pain sensitivity in transgenic mice exposed to modulation of specific genetically defined neural-networks using novel chemogenetic approaches.

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