Development Of A Neurogenic Flare Model Measurable By Laser Doppler In The Anaesthetised Rat

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Activation of skin nociceptors by strong electrical stimulation has been shown to induce an increase in local blood flow, which is termed the neurogenic flare. This has been demonstrated in numerous species including rat, pig and man (1, 2) and can be measured and quantified using the laser Doppler imaging technique. This study aims to establish and validate a non-invasive model of neurogenic flare in the anaesthetised rat which may be used to provide a translatable biomarker.

Primarily the optimal parameters with which to induce a neurogenic flare were identified, with the effects of both stimulation intensity and duration investigated. Male Sprague-Dawley rats were anaesthetised using an Isoflurane/O2 mixture and maintained via nose cone for the duration of the procedure. Baseline images were recorded for 35minutes using a Moor Scanning laser Doppler (Moor Instruments, Axminster, UK). Subsequently electrical stimuli were applied at 5Hz for 30seconds at a range of intensities up to 300 Current Perception Thresholds (CPT) using a Neurometer CPT (Neurotron Inc, Baltimore, USA) and the skin blood flow response followed for 1hour. Data shows that electrical stimulations of 100, 200 and 300CPT result in an intensity dependent increase in skin blood flow (7.1 ± 3.7%, 25.8 ± 4.4% and 37.2 ± 11.6% respectively). Further work investigating the effects of altered stimulation duration showed that increasing the duration to 1minute elicits a larger neurogenic flare when compared to 30second stimulation, however variability is greatly increased (200CPT 31.5 ± 9.0% vs. 25.8 ± 4.4%; 300CPT 41.7 ± 8.1% vs. 37.2 ± 11.6%). From this work 200CPT, at 5HZ for 30seconds were selected as the stimulation parameters eliciting a reproducible neurogenic flare of suitable magnitude for future use.

In order to validate this work the ability of the local anaesthetic Lidocaine to block the neurogenic flare was investigated. Following 35minutes of baseline scans 10ul of 2% Lidocaine or saline vehicle were subcutaneously injected into the centre of the scan area. 30 minutes later animals were stimulated with 200CPT, at 5Hz for 30seconds and the response of skin blood flow followed for 1 hour. Animals treated with 2% Lidocaine displayed a statistically significant reduction in the neurogenic flare induced when compared to saline treated animals (9.9 ± 5.6% vs. 33.8 ± 6.9% P<0.05).

In conclusion we have hereby established a model of neurogenic flare in the anaesthetised rat and optimised the parameters with which to induce this flare. We have also demonstrated that within this model the flare may be blocked with the local anaesthetic Lidocaine.

1. Lynn B., Cotsell B. Blood flow increases in the skin of the anaesthetised rat that follow antidromic sensory nerve stimulation and strong mechanical stimulation Neuroscience Letters 137 (1992) 249-252