An analysis of the activity-temperature relationship in transient potential receptor vanilloid 1 (TRPV1) wild type mice for the study of TRPV1-antagonist-induced hyperthermia.

Khadija Alawi[1], Johannes Van Baardewijk[2], Julie Keeble[1,2]. *[1]Institute of Pharmaceutical Science, King's College London, Franklin-Wilkins Building, 150 Stamford Street, SE1 9NH, London, UK, [2]Centre for Integrative Biomedicine, King's College London, Franklin-Wilkins Building, 150 Stamford Street, SE1 9NH, London, UK*

The transient potential receptor vanilloid 1 (TRPV1) receptor is a non-selective cation channel that is activated by capsaicin, (the pungent component of hot peppers), temperatures within the noxious range (>43 degrees C) and low pH (<pH 6.0). TRPV1 receptors are expressed in primary afferent fibres, such as A-delta and C-fibres, and non-neuronal cells such as vascular smooth muscle (Kark et al., 2008). TRPV1 antagonists are analgesic, but have recently been shown to cause an increase the body temperature, as seen in man, rodents and monkeys (Gavva et al., 2007). The precise mechanism underlying the hyperthermia is, however, unknown. Activity levels are not significantly different between vehicle- and antagonist-treated rodents (Gavva et al., 2007; Alawi et al., unpublished data). However, changes in activity in individual mice can significantly affect body temperature. The current study aims to take a systems approach to researching the activity-body temperature relationship in order to determine the component of TRPV1 antagonist-induced hyperthermia that is dependent on the drug alone in future studies.

Male TRPV1 wild type (WT) mice (n = 9) were used in all radio-telemetry studies (30-40 g of body weight); All mice were implanted with radio-telemetry transmitters to monitor core body temperature and activity for a 24 h period (ambient temperature 22 ± 2 ºC). Radio-telemetry surgical implantations were undertaken one week prior to drug administration. Buprenorphine (10µg/kg, *i.m.*) was administered 10 min prior to surgery. The mice were anaesthetised and the radio-telemetry transmitter (TA10TA-F20; DSI, St Paul, MN, USA) was inserted into the abdominal cavity. Surgery was performed under isoflurane anaesthesia (2-3% vol. isoflurane; 2-3% vol. O_2). A statistical analysis of the relationship between activity and temperature was performed, incorporating an appropriate correction factor for the time-delay in temperature change following either an increase or decrease in activity. The correlation profile between temperature and activity in the naïve mice will be subtracted from the correlation profile of the antagonist-treated mice in order to isolate the effect of activity on antagonist-induced hyperthermia in subsequent studies.

In conclusion, this study has produced a statistical method suitable to establish correlation patterns between body temperature and activity in antagonist-treated mice as a tool for studying the effect of TRPV1 in subsequent studies. Activity, quantified in the present study using telemetry, should be regarded as an *indicative* measure of locomotor changes. The correlation patterns found could be tested in further studies using different observational measures of locomotor activity.

References: Gavva *et al.* (2007) *J Neurosci. 2007 27(13):3366-74.*

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