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Amg9810- a trpv-1 receptor antagonist, in contrast to trpv-1 ko mice, shows similar antidepressant properties to citalopram in burrowing test

L. Nabi, J. Keeble. Institute of Pharmaceutical Sciences, Kings College London, London, United Kingdom.

Depression will be the leading cause of disease and disability by 2020 (1) therefore it is important to understand the pathophysiology of the disorder and to find new therapeutic targets. Transient receptor potential vanilloid type-1 receptor (TRPV-1R), an ionic channel involved in inflammation and nociception, plays a role in depression possibly due to its presence in several brain regions and or being part of the inflammatory response system (2). The study aim was to investigate antidepressant properties of TRPV-1R by manipulating it pharmacologically and genetically and comparing its effects with citalopram- a known antidepressant using burrowing.

Method: Burrowing method by Deacon (3) was used to assess functionality. 8-10 weeks old male C57bl/6 mice were injected (I.P) with Citalopram (10mg/kg), TRPV-1R antagonist AMG9810 (50 mg/kg) or vehicle an hour before testing; 2 X two-hour tests , and 2 baseline tests, for pharmacologically manipulated mice and 3X two-hour test for the KO mice. Burrowing (n=5) was measured as weight of gravel displaced from the tube.

Results: Data was analysed using Two-way ANOVA followed by post-hoc tests when necessary. Citalopram and AMG9810 did not reduce burrowing significantly, although citalopram showed a trend in reducing the behaviour. However, in contrast to TRPV-1 antagonist, TRPV-1R knock out (KO) mice burrowed significantly ($P \leq 0.05$) over 30% more than the WT mice in both tests 1 and 2 but not test3.

Discussion: Burrowing test was used as it has been employed to measure several parameters such as systemic inflammation or ‘sickness behaviour’ (4) which are associated with depression. The trend of reduced burrowing seen with citalopram may be due to a decrease in motivation to engage in non-essential behaviours which is in line with unpublished observation of Deacon (1) that antidepressants reduce burrowing behaviour. TRPV-1R KO mice burrowed significantly more than WT mice which may be due to hyperactivity (5) or 'enhanced functionality'. Furthermore, the burrowing difference between TRPV-1R KO (present throughout development) and acute pharmacological manipulation during adulthood could be due to differential development of stress pathways and thus stress reactivity.

References:
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