Alterations in the central opioid system following acute swim stress and olfactory bulbectomy in the rat

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Introduction: Stress is a major component of many animal models of depression, induced acutely as in the forced swim test, or more long-term in the olfactory bulbectomy (OB) and chronic mild stress models [1]. The central opioid system has been implicated in regulating the stress response in rodents [2]. The objective of this study was to examine the effects of acute swim stress, and OB, alone or in combination, on opioid receptors and the precursors for their endogenous ligands in a number of brain regions implicated in stress/depression.
Methods: Male Sprague Dawley rats (200-250g on arrival) underwent surgery (sham or OB) using isoflurane anaesthesia, and were pair-housed thereafter (n=9/group). Four weeks following surgery, rats were placed in the forced swim test apparatus for 15 min, or left undisturbed in their homecage. Behaviour (immobility, swimming and climbing) was manually scored using Ethovision® video-tracking technology, and 45 min later, rats were euthanised and brains removed. The expression of mRNA for the mu (OPRM1), delta (OPRD1) and kappa opioid (OPRK1) receptors, and their precursor peptides pro-opiomelanocortin, preproenkephalin and preprodynorphin was examined using RT-qPCR in the hippocampus, amygdala, hypothalamus and prefrontal cortex (PFC). Data are expressed as mean ± standard deviation and analysed using two-way ANOVA (with surgery and swim stress exposure as factors), followed where appropriate by post-hoc Student Newman-Keuls test; $p<0.05$ was deemed statistically significant.
Results: Behaviours were not altered in OB rats during the 15 min acute swim stress exposure. The main effects in the opioid system after acute forced swim exposure and OB are summarised in Table 1. OPRK1 mRNA level was significantly reduced in OB rats in the hippocampus and prefrontal cortex ($p<0.05$); similar reductions were observed in OPRK1 mRNA level in these brain regions following acute swim stress. In addition, OB was associated with a significant reduction in OPRD1 mRNA expression and its precursor peptide preproenkephalin in the PFC ($p<0.05$); these OB-related effects were not altered by acute swim stress. No change in mRNA expression was observed in the hypothalamus or amygdala, or in pro-opiomelanocortin or preprodynorphin.
Conclusions: We have found that both acute (forced swim) and chronic (OB) stressors produce qualitatively similar effects on the central kappa opioid system, acknowledging the role that this system has in regulating stress-related function [2]. In both cases, the reduction in OPRK1 mRNA level might represent an adaptive response to increased activation of OPRK1 by endogenous dynorphin release [3]. The OB-related alterations in the delta opioid system suggesting longer-term alterations extending beyond the kappa opioid system.

Table 1. Expression of OPRK1 mRNA in the hippocampus and prefrontal cortex following OB and acute swim stress exposure. Data are expressed as mean ± standard deviation and as a percentage of the Sham Non-Swim group.

		OPRK1 mRNA expression Hippocampus	OPRK1 mRNA expression Prefrontal Cortex
Sham	**Non-swim**	100 ± 29%	100 ± 28%
	Swim	51 ± 18%*	72 ± 28%*
OB	**Non-swim**	61 ± 14%*	51 ± 19%*
	Swim	77 ± 23%	58 ± 26%

*$p<0.05$ vs. respective sham non-swim group.

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P.129 Effect of Propofol in a mouse model of despair

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Introduction: Propofol (2,6-diisopropylphenol) is an intravenous anesthetic agent commonly administered in ambulatory settings because of its rapid onset, dose-related hypnotic effect, rapid recovery and favorable safety profile. Propofol's anesthetic effects are felt to derive principally from modulating the inhibitory function of the neurotransmitter gamma-aminobutyric acid (GABA) through GABA-A receptors [1]. However, propofol also inhibits NMDA receptors, although it is unclear if this occurs apprecia-