



Département de psychiatrie
Centre de neurosciences psychiatriques
Site de Cery
CH-1008 Prilly - Lausanne

Centre de Neurosciences Psychiatriques

CNP SEMINAR

ANNOUNCEMENT

Monday, July 9, 2012, 11:00

“Neuropeptides & Reward Seeking”

Prof Andrew J Lawrence, PhD

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**Auditoire, Hôpital Psychiatrique de Cery
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For 15 years one of the interests of my laboratory has been examining the role that neuropeptides play in natural and drug rewards, including relapse. We established that isolation-rearing of rats from weaning resulted in an anxiety-like phenotype and the rapid acquisition of high ethanol preference. While the acquisition of ethanol use could be similarly attenuated by either diazepam or antalarmin, established ethanol use was only sensitive to antalarmin. These data suggested that isolation rearing resulted in a CRF-driven anxiety phenotype that facilitated high ethanol consumption. Subsequent molecular studies suggested the effect was likely mediated via modulation of dopamine D2 receptors throughout the extended amygdala. More recently, we were the first to demonstrate a role for orexins in both alcohol consumption and cue-induced reinstatement of alcohol-seeking. These effects were specific, and we demonstrated a differential effect of orexin1 receptor antagonism on the motivational strength of ethanol compared to sucrose. Moreover, in a model of reinstatement following extended abstinence, we also found evidence for a role of orexin1 receptors in this behaviour. Fos studies suggested that the prelimbic and orbitofrontal cortices were potential loci where ascending orexinergic input could modulate relapse-like behaviour. Subsequent microinjections confirmed that antagonism of orexin1 receptors in the prelimbic cortex can dramatically attenuate ethanol-seeking, with no effect on sucrose-seeking. In contrast to the orexin1 receptor system, which is implicated in both ethanol-seeking and consumption, our studies to date on the orexin2 receptor suggest a role in ethanol consumption but not ethanol-seeking. Collectively, these data provide strong evidence that orexins are implicated in both appetitive and consummatory drives for rewards.

Recent publications :

1. Madsen H, Brown RM, Short JL, Lawrence, AJ (2012) Investigation of the neuroanatomical substrates of reward-seeking following protracted abstinence in mice. *J. Physiol.*, 590, 2427-2442.
2. Jupp B, Krivdic B, Krstew E, Lawrence AJ (2011) The orexin₁ receptor antagonist SB-334867 dissociates the motivational properties of alcohol and sucrose in rats. *Brain Res*, 1391:54-59.
3. Jupp B, Krstew E, Deysi G, Lawrence AJ (2011) Discrete cue-conditioned alcohol-seeking after protracted abstinence: pattern of neural activation and involvement of orexin₁ receptors. *Br J Pharmacol*, 162(4):880-889.
4. Lawrence AJ, Cowen MS, Yang HJ, Chen F, Oldfield B (2006) The orexin system regulates alcohol-seeking in rats. *Br J Pharmacol*, 148(6):752-759.