Local administration of the orexin receptor antagonist MK-4305, but not orexin-A, into the nucleus accumbens increases accumbal dopamine efflux in freely moving rats

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The nucleus accumbens (NAc), a major terminal area of mesolimbic dopaminergic projections, receives inputs from orexin neurons. Behavioural studies suggest that accumbal orexin receptors (-Rs) play modulatory roles in the regulation of accumbal dopaminergic activity-dependent locomotion in rats (Kotani et al., 2008). We studied the effects of intra-accumbal application of orexin-R ligands on accumbal dopamine (DA) efflux in freely moving rats, using *in vivo* microdialysis, to analyse the roles of orexin-Rs in regulating accumbal dopaminergic neural activity. Orexin-R ligands were applied into NAc though a microinjection needle attached with a dialysis probe. The OX_1- and OX_2-R agonist orexin-A failed to alter DA levels in NAc. However, the OX_1- and OX_2-R antagonist MK-4305 induced a dose-related increase in DA levels. This MK-4305-induced increase in accumbal DA levels was suppressed by infusion of TTX through the probe and was inhibited by local co-administration of orexin-A. These results suggest that intra-accumbal application of MK-4305 could enhance accumbal DA efflux by antagonism of OX_1- and/or OX_2-Rs. The present study also indicates that accumbal OX_1- and/or OX_2-Rs could play inhibitory roles in the regulation of accumbal dopaminergic neural activity.