An investigation of oxytocin’s effects on measures of amygdala and DMN connectivity following intranasal and intravenous modes of administration.

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**Background:** Animal and human studies highlight the role of oxytocin in social cognition and behaviour and the potential of intranasal oxytocin to treat social impairment in individuals with a range of neuropsychiatric disorders characterised by social dysfunction, such as autism. Aiming to understand the mechanisms underpinning intranasal oxytocin’s effects, a number of studies have used resting state BOLD fMRI and shown that intranasal oxytocin modulates connectivity between the amygdala, a key region in the processing of social emotional stimuli, and core nodes of the default mode network (e.g. medial prefrontal cortex and precuneus) involved in self-processing and the processing of social and affective stimuli. Importantly, intranasal oxytocin has been shown to modify patterns of resting state connectivity associated with neuropsychiatric disorders such as PTSD and generalised anxiety disorder. What still remains uncertain is whether the effects of intranasal oxytocin on brain connectivity are solely mediated from its direct action on central targets or can be accounted for by intranasal oxytocin’s engagement of peripheral oxytocin receptors. The current study aims to address this question by comparing changes in brain connectivity following the intranasal and intravenous administration of oxytocin.

**Methods:** We used a double-blind, cross-over, placebo controlled design whereby 17 healthy male volunteers received, in counterbalanced order over four different visits about a week apart, either 40IU of oxytocin with an intranasal spray (standard method), 40IU of oxytocin with a nebulizer that maximizes oxytocin deposition in the areas of the nasal cavity underpinning direct nose-to-brain transportation, 10IU of oxytocin intravenously, or placebo. While participants experienced all three different modes of administration in each visit, the active substance was delivered through a single mode of administration in three of the visits (using placebo for the remaining two modes), with placebo being delivered through all modes in a fourth visit. We used an 8-minute multi-echo resting state BOLD fMRI scan on a 3T GE scanner with a 32-channel coil to examine changes in resting state connectivity. We further measured oxytocin concentration levels in blood plasma on 8 time points over 2 hours to characterize the pharmacokinetic profile associated with each mode of administration.

**Results/Conclusions:** The study has been completed but the data have not been analyzed yet. We will investigate the effects of oxytocin on measures of intraregional and interregional brain connectivity focusing on the centromedial and basolateral parts of the amygdala and the nodes of the default mode network. To the extent that intranasal oxytocin directly reaches the brain via postulated direct nose-to-brain pathways we would predict that changes in brain connectivity induced by intranasal oxytocin are not observed following the intravenous administration of an amount of oxytocin that achieves comparable pharmacokinetic profiles as intranasal oxytocin.