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Letter to the Editor
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Oxytocinergic Tonus, Addictions and Affiliative Human Behaviour

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Letter to the Editor

The future of addiction psychiatry is likely to become enriched by advances in biological treatments. The management of the patient with addictions is often contingent upon the therapeutic alliance as influenced by engagement and positive empathy. The concepts of Motivational Interviewing [1] and the Prochaske and De Clemente [2] cycle of change are essential paradigms to embed in one's clinical practice, but may lead some clinicians to consider acting more decisively only when the patient is "ready to change". With today's expanding repertoire of biological treatments we may be able to more opportunistically or consistently harm minimize, or give trials of medications which may inadvertently lead to abstinence or enhancing readiness for more definitive treatments. If more variegated biological approaches existed, greater promotion of health services could occur, possibly enhancing intake commensurate with the hope such news promotes.

There are so many complex systems and circuits in the human nervous system, involved in a complex interplay with other organ systems such as hormonal axes. The brain is the most complex and least understood organ. To claim that we have a good understanding of it is naïve at best.

One of the (neuro hypophysial) neuropeptide systems which is poorly understood, but with great therapeutic potential, is the Oxytocinergic system. It may exert a countervailing influence over neural circuitry coopted by addictive disorders, due to being linked to Affiliative behavior and by mediating the effects of drug reward.

There is animal and human evidence suggestive of oxytocin's pro-social and entactogenic effects, which are hypothesized to be protective against addictive disorders. Sexual activity is known to induce the release of oxytocin into the central nervous system and increases mesolimbic dopaminergic release [3-5]. Gamma-Hydroxy Butyrate (GHB) is licensed in some parts of the world for management of Alcohol Use Disorder [6,7] and GHB is known to increase oxytocin levels in the supraoptic and para ventricular nuclei [8]. Neurobiological plausibility may exist if exogenous oxytocin is ever comprehensively demonstrated to mediate dopaminergic tonus in the ventral striatum and/or nucleus accumbens in the human brain to inhibit drug reward.

Meyer-Landenberg [9] (Figure 1), Wei [10] and Herpertz [11] have eloquently described some of the proximal and distal targets for endogenous oxytocin, and how this putatively links to overt behaviors and moderates other neurotransmitter systems.

Pedersen et al [12] have demonstrated how oxytocin can reduce the features of alcohol withdrawal in humans, and Bowen [13] showed it reduces the intoxicating effects of alcohol in rodents. Intra peritoneal oxytocin in rodents improves sociability, and reduces anxiety and alcohol use [14]. According to a placebo controlled double-blind crossover trial [15], intranasal oxytocin has potential to improve social perception, reduce cue-induced alcohol cravings, and reduce appetitive approach bias in subjects with alcohol abuse, and can be safely tolerated in this population.

There is a growing body of evidence suggesting functional and symptomatic benefits can be derived from oxytocin administration in patients with a range of conditions other than addictive disorders, such as neurodevelopmental disorders, psychotic disorders, sexual dysfunction induced by psychotropic medication, and anxiety disorders such as Post-Traumatic Stress Disorder and Social Anxiety Disorder. It is beyond the scope of this editorial to examine these conditions also.

Oxytocin is primarily secreted from the para ventricular nucleus of the hypothalamus, however, is also secreted from peripheral organs [3]. Only 1-2% of peripherally secreted oxytocin readily crosses the blood brain barrier to alter central dopamine secretion [3]. Intranasal administration of oxytocin allows exogenous oxytocin to rapidly travel to the central nervous system along the

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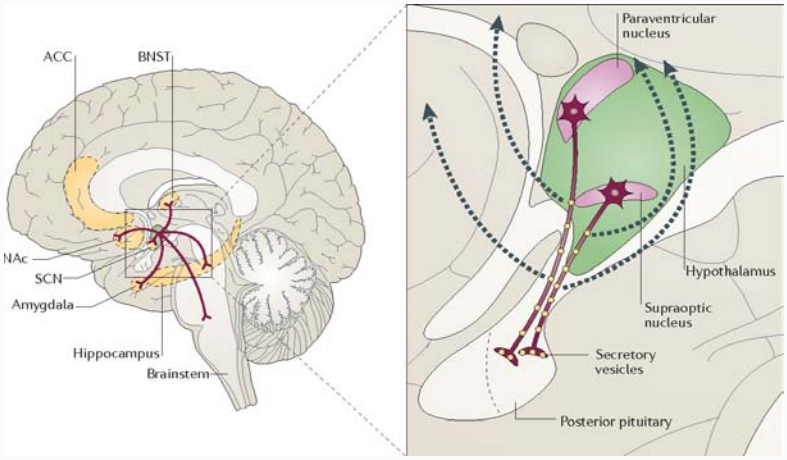

Figure 1: Neurophysiology of Oxytocin and Arginine Vasopressin [9]. BNST, bed nucleus of the stria terminals; NAc, nucleus accumbens; SCN, suprachiasmic nucleus; ACC, anterior cingulate cortex.

olfactory and trigeminal nerves [16].

There are multiplicities of determinants which could theoretically, or practically, alter intranasal bioavailability of oxytocin, such as those related to delivery or local absorption. Galvez et al. [17,18] presented recent findings of intranasal ketamine administration resulting in rather unpredictable absorption, which those considering prescribing oxytocin should take heed of. There is likely to be sexual dimorphism for the oxytocin gene [3] which further complicates this. There is no consensus statement or treatment algorithm which includes oxytocin for any condition which the author is privy to.

With respect to the pharmaco-economics of prescribing oxytocin, the neuropeptide itself is relatively cheap, but compounding costs and excipients/preservatives may vary depending on the compounder, based on the author's local prescribing experience. Some oxytocin products from health food shops or sourced online may or may not have reasonable claims to contain the neuropeptide. The final product may need to be stored at low temperatures after compounding, and can form a precipitate, perhaps determined by temperature or concentration, that can irritate the nasal passages. The systemic side effect profile is poorly described.

Despite the uncertainties and demonstrably unproven nature of such an exogenous neuropeptide treatment, any further pharmacological research or industrious delivery/device designs could offer more hope to those who might feel trapped in the cycle of addiction.

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