Additional file 1: Oxytocin in the hypothalamic osmostat (a physiologic strain system viewed as 'the first stress system')

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Oxytocin in the hypothalamic osmostat 'stress system'

M. Bouchon

The hypothalamus is a crucial governing centre for physiologic homeostasis. It regulates body temperature, sleep, and appetite, and is involved in the dysautonomic and neuro-cognitive-emotional manifestations of multi-factorial chronic syndromes, especially in women. It produces corticotropin-releasing hormone (CRH), and contains cells that produce the oxytocin hormone (OT) and antidiuretic hormone (ADH), which regulates the fluid balance and water metabolism. These peptides act both as peripheral hormones and as central neuro-hormones or neurotransmitters in the brain. ADH, also known as arginine vasopressin (AVP), or vasopressin, is a peptide closely related to OT, a similar molecule differing only by two amino acids that play a role in protein metabolism (figure 1).

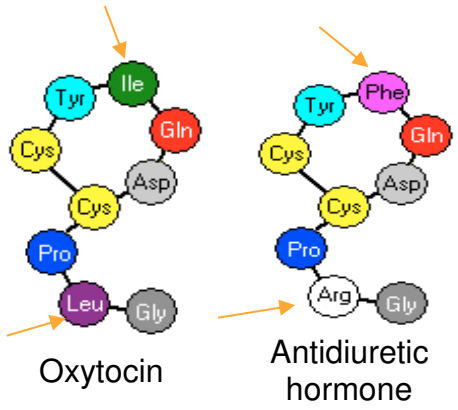

Figure 1. Oxytocin and arginine vasopressin (AVP or ADH) differ by two amino acids.

OT and ADH evolved from a universal family of substances crucial to physical survival [I]. Both participate in the adaptive capacity and are considered stress hormones. Both peptides are produced primarily in the anterior hypothalamus, in a group of cells called the 'hypothalamic osmostat'. Research in recent years has shown that ADH, is affected by OT; how, exactly, at what dosage, and in which circumstances, is still unclear [II]. ADH ensures water conservation during dehydration, in response to increased plasma osmotic pressure. The similarity of their receptors can cause cross-reactions.

OT can have completely opposite effects [II] on the HPA axis, the autonomic nervous system, and stress/arousal. This is under investigation: the complex interactions are being researched [III, IV, V], but less for peripheral action (systemic, hormonal), than for their central role in the brain as neuropeptides, and interest tends to focus on biosocial anti-stress, pain-killing, and socialisation effects [I], or on the global 'integrative' role of OT [VI] (a similar role that has also been ascribed to histamine). Medical research also uses mostly chemical analogs, in large doses.

The hypothalamic osmostat modulates vital functions such as the body's metabolic 'thermostat' and other homeostasis functions, by activating the 'vertical axis' (autonomic, endocrine, and HPA axes, but also the brain-kidney axis of fluids regulation). OT initiates the stress reaction (which manifests in part in behaviours driven by the emotional 'rheostat'), and maintains the adaptive physiological capacity. It also governs the sensitivity to stress, and aspects of pain perception and tolerance. Furthermore, the threshold of response of the osmostat itself, involving both OT and ADH, is set at birth, influencing lung function, but can be reset, for example during pregnancy and in the 'reset osmostat syndrome' [VII]. Thus, it

also determines the level of sensitive reaction of vital functions and behaviours, other than pain.

A recent approach to treating menopausal and ageing symptoms, yet supported by little research, consists in using 'natural' or bio-identical hormones, such as progesterone (becoming popular) or oxytocin (yet little used). The term 'bio-identical' is used for hormonal preparations of the same molecule as is produced in the body, as opposed to agonists and chemical analogs. Bio-identical OT has a different structure from that of the chemical analog drug named Syntocinon (or Pitocin) (figure 2), and therefore, effects are bound to display some differences.

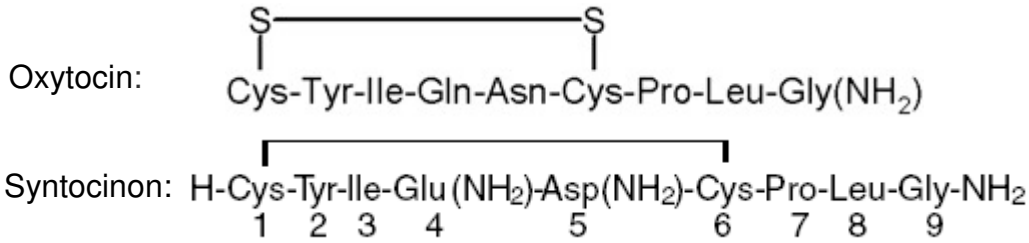

Figure 2. Different formulas for oxytocin and its chemical analog.

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