



## Intermittent drinking, oxytocin and human health



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### ABSTRACT

Looking at a waterhole, it is surprising that so many animals share the same space without visible signs of anxiety or aggression. Although waterholes are the preferred feeding locations of large carnivores, waterholes are shared by all type of herbivores of all sizes and shapes, including elephants. Recent research shows that the homeostatic disturbances leading to the “thirst feeling” not only activate specific substances regulating water and mineral household, but also the “trust and love” hormone oxytocin, while decreasing the production of the typical stress hormone cortisol. People using drugs, seem to be in search for oxytocin, as evidenced in studies with individuals on drugs such as ecstasy and gamma-hydroxybutyrate. Hot environment, drought and increased sweating also activate specific oxytocin-producing parts of the hypothalamus, just as breastfeeding does in mother *and* infant. Water homeostasis is the only allostatic system activating trust neuro-anatomy and we suggest that this is due to the fact that all animals depend on water, whereas food type is species specific. Our hypothesis; regulating drinking behaviour through intermittent bulk drinking could increase oxytocin signalling, recover human trust and increase health by down-regulation of stress axis activity and inflammatory activity of the immune system. Intermittent bulk drinking should be defined as water (including tea and coffee) drinking up to a feeling of satiety and regulated by a mild feeling of thirst. This would mean that people would not drink less quantity but less frequently and that’s how all animals, but also human newborns behave. It is the latter group, which is probably the only group of humans with a normal fluid homeostasis.

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### 1. Introduction

Stress, broadly defined as a real or perceived threat to homeostasis, activates neural circuits that alter the body’s physiology and behaviour to ensure survival and well-being. Physical stressors are real threats that create signals within the internal environment that communicate deviations from homeostasis to the brain. In contrast, perceived threats or psychogenic stressors create signals that arise within the brain itself as it interprets stimuli in the external environment as potential insults [1]. Both type of stress factors activate allostatic systems, including the sympathetic nervous system and hypothalamic circuits, leading to stressful and even aggressive behaviour [2]. Starvation, infection, dehydration, violence and climate are ancient stressors producing severe danger to the body and have therefore shaped ultimate survival function producing proximate homeostatic feelings to induce behaviour at service of the ultimate purpose [3]. Perhaps the best example is

humans crying. The ultimate explanation of crying is that it elicits care and defence from mothers and other care-givers; if infants do not cry when in need of assistance, it will be less likely to survive. Proximate explanations include both the external triggers of crying, for example physical separation from the caregiver, cold, or a lack of food, and also the internal mechanisms, such as the limbic system and the endogenous opioids involved in the cessation of crying. These are proximate explanations because they describe the immediate causal triggers of crying [4]. In this context, the ultimate explanation for hunger is to signal the body for possible starvation and death. The proximate value of hunger is that it leads to eating, although eating is also stimulated by looking at, smelling of and thinking in food, which are therefore all proximate causes of eating [5]. This so-called thought-shaped fusion can be so strong that individuals can gain weight just looking at food [6]. Food deficiency as a stress factor activates a complex systemic response, which should lead to gluconeogenesis, changes in energy distribution and spontaneous physical activity [7,8]. Starvation may induce a certain level of aggressive behaviour, which should be considered adaptive when hunting big game or when suffering from a lack of high-energy nutrients [9,10], whereas food sharing behaviour is

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more beneficial once the animal has been hunted (see [11] and the references herein).

Overall, stress responses activate the sympathetic nervous system, together with the HPA axis exerting a range of effects in benefit of solving the homeostatic disturbance as fast as possible. Of all stress factors dehydration occupies a special place in animal evolution. It seems to be the only homeostatic disturbance leading to attenuation of stress axis responses, decrease of fear feelings, anxiety and aggressive behaviour [12]. Drinking, caused by regulatory thirst, could be considered proximate behaviour at service of preventing dehydration, an ultimate purpose [13]. Nevertheless it is regulatory or also physiological drinking, which is regulated by oxytocin and therefore drinking could also stand at the service of another ultimate purpose; bonding. These are the reasons which made us formulate our hypothesis; Could bulk drinking recover human health, trust and mental well being? In this hypothesis “bulk drinking” is defined as non-frequent drinking up to satiety and only when thirsty; like drinking visiting a waterhole.

## 2. Thirst, trust, oxytocin and bonding

Animals drink up to satiety every time they drink, just as infants do. So infants and animals “suffer” real thirst (regulatory/physiological thirst, 14) based on hypernatremia, hypovolemia and/or hyperosmolality [15,16] and these conditions induce increased oxytocin signalling (Olszewski, 2010). Oxytocin has numerous effects on multiple physiological mechanisms and oxytocin influences behaviour significantly (see below). The mentioned up to satiety-drinking behaviour of infants every time they are breastfed, is opposite to modern adults who drink small amounts of liquid, often numerous times every day.

This latter way of drinking should be considered evolutionary novel and might affect the water homeostasis and even health [14]. We think that this constant drinking decreases oxytocin signalling through chronic low NaCl levels, leading to salt- and sugar craving, whereas dehydration/hypernatremia increases oxytocin induced water-craving and inhibition of hunger and carbohydrate intake [17,18].

Recent research shows that in spite of the expected typical stress response, mild hypernatremia as a state of dehydration decreases the activity of the HPA axis (less cortisol production) and increases the production of oxytocin and arginine-vasopressin significantly [12]. This study further showed that hypernatremia as a psychogenic/physical stress factor attenuates the heart limb of the stress response and increases social engagement. Oxytocin and vasopressin are important hormones for development of trust, love and bonding neuroanatomy ([19] and the references herein). Oxytocin further influences the immune response through context-based interactions. It maintains peripheral homeostasis during acute inflammation [20], has anti-inflammatory protective effects on the heart muscle [21], increases the production of salivary IgA [22] and has overall anti-inflammatory effects [23]. Breast-feeding is the most significant example of how a homeostatic need induces bonding, in this case between mother and baby, through the massive release of oxytocin [24] and affective-bonding mechanisms are responsible for neuro-anatomical development and immune function later in life [25,26]. It is even so that long term breastfeeding prevents the development of criminal and overall anti-social behaviour in later adults [62].

Paediatricians agree that hydration in children may be optimal only in breastfed infants. However, their hydration status is very peculiar. Total water intake per unit of body weight is four times higher in infants compared to adults. Breast milk has higher water content per energy unit than the diet of adults. Nevertheless, urine

volume per unit energy is almost identical. Infants retain water for growth and have higher non-renal water losses due to a higher body surface area related to body mass. However, osmolar load per unit of energy is four times lower which corresponds to a very low urine osmolality of 130 mosm/kg and leaves only a small renal dilution capacity to excrete an extra water load [27]. Breastfeeding is normally a topic studied in relationship with eating behaviour, although we and others [28] think that it much more reflects fluid needs, water and sodium homeostasis.

Water is an essential nutrient for all animals and plants across lifespan and maintaining chronic hydration is recognised to provide multiple health benefits and enhance quality of life [29]. Modern diseases are mostly caused by the cause of causes, low-grade inflammation or metaflammation [30–32]. The actual environment seems to be pro-inflammatory and the sum of novel anthropogenic factors, including food and drinking behaviour, might give a plausible explanation for the increase of people suffering from chronic non-communicable disorders [30,33,34]. Optimal water-intake, based on a certain rhythm might optimise oxytocin signalling, recover human character and regulate immune activity [35]. Recent research on the relations of personality to well-being shows that the people who are most healthy, happy and fulfilled are those who are *high in all three* of the character traits of *self-directedness, cooperativeness, and self-transcendence* as measured by the Temperament and Character Inventory [36]. All three traits are related with the functionality of oxytocin [37,38] and disruption might cause pathological dominance of one of them, leading to several disorders such as autism [39]. We suggest that intra- and interspecies behaviour at the waterhole could serve as example of how to recover health, trust and mental well being in and between modern humans, which is the hypothesis we present in this review paper.

## 3. People at search for oxytocin; the pandemic use of oxytocin-ergic drugs and the need for new interventions; our hypothesis

Prosocial and empathogenic behaviour depend on endogenous oxytocin systems, which might be disturbed in people engaging in drug use and addiction [40]. It has been shown recently that the rate of parental bonding and attachment in childhood is directly related with adult psychosocial behaviour including drug use and abuse [41]. It might even be so that drug users become “bonded” to their drugs and the environmental triggers related with the use of drugs [40].

On the other hand, stable social bonds and happy relationships, perhaps associated with higher levels of oxytocin, might be protective against addiction to drugs [42]. Social reintegration and rehabilitation are important factors to promote drug abstinence and recovery from addiction [43] and family management seems to be of specific significance [44]. These studies suggest that the role of oxytocin signalling is central to drug use and abuse and that successful interventions should focus on recovery of dysfunctional oxytocin mechanisms, which perhaps is the secret behind Alcoholics Anonymous [45] and group therapy [46]. An enormous amount of young and not so young people are engaging in the use of a wide range of oxytocinergic drugs such as ecstasy, fantasy, cannabis and cocaine and not all of them suffered childhood abuse, lack of parental bonding or neglect (World Drug Report 2012). We think that they are “searching” people for normal social interaction in a society dominated by “egoistic hawks” and very few social “doves” [3,47]. As stated by Blum et al. [48]: “people provide the real “highs”. People need people. However, in today’s screwed up, financially unstable (1.4 million bankruptcies 2009), and very scary world, loneliness and alienation are commonplace. Everything would look perfect if we were all living in a vacuum,

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