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Letter to the Editor

Beyond the social stereotypes of hormones

Stereotyping, despite its bad reputation, makes the world simpler to deal with. We constantly label and categorize in order to make cognitive and emotional processes more efficient. The drawback is that stereotypes are oversimplified notions of reality. As scientists, we are challenged to venture beyond stereotypes, so that they do not hinder our progress and limit our understanding. Here, we wish to debunk three common stereotypes concerning hormones and their relationship to social behaviour.

First, it is commonly believed that testosterone is a male hormone that is only relevant to male behaviour, and therefore should only be studied in males. This notion is based on an anthropocentric male-biased view of nature. Indeed, in humans, men have on average tenfold higher circulating concentrations of testosterone relative to women (Longcope, 1986; Mazur and Booth, 1998; Staub and DeBeer, 1997). However, this view of male testosterone dominance is not universal across nature (e.g., Koren et al., 2006), and individual variation is vast. Testosterone is an androgen, produced by both sexes mainly in the gonads and the adrenal cortex (Mazur and Booth, 1998). It is required for basic physiological and anatomical functions such as muscle and bone development, neuronal growth, and immune reaction in both sexes (Staub and DeBeer, 1997). Testosterone is also involved in female reproduction by stimulating follicle growth, development, and responsiveness to follicle stimulating hormone (González-Comadran et al., 2012; Walters et al., 2008), although it may also be associated with reproductive challenges (Rutkowska et al., 2005; Ryan et al., 2014; Searcy, 1988). Additionally, testosterone is associated with behaviour in both sexes, although the relationship is often context related and complex (Christiansen, 2001; De Vries and Villalba, 1997; Eisenegger et al., 2011; Koren and Geffen, 2009; Mazur et al., 1997; McGlothlin et al., 2008; McGlothlin et al., 2004; McGlothlin et al., 2010). Another mode of action for testosterone is via its conversion to estradiol (that is commonly stereotyped as the 'female hormone'). Both testosterone and estradiol may be involved in sexual, social, and aggressive behaviour in both sexes (Ball and Balthazart, 2006; Balthazart and Surlemont, 1990; Carlson et al., 2004; Cashdan, 2003; Soma et al., 2000; Tramontin et al., 2003), and a combination of androgenic and estrogenic metabolites of testosterone is needed to stimulate and modulate sexual behaviour in males (Meisel and Sachs, 1994). Thus, preconceptions as to what steroids are expected to be significant according to sex are limiting scientific investigations and minds.

Second, cortisol and stress have been used synonymously in psychophysiology, cultural, and layman references. Glucocorticoids are part of the classic stress response (Boonstra et al., 2014; Sapolsky et al., 2000). However, cortisol is not the only 'stress hormone' (Wasser et al., 2000). Corticosterone is present in all vertebrates as part of the mineralocorticoid synthesis pathway. It is synthesized via the same enzymes that synthesize cortisol, androgens, and estrogens (Freking et al., 2000), and is found in higher concentrations than cortisol in multiple species (Wasser et al., 2000). Both cortisol and corticosterone may act independently or in concert (Koren et al., 2012b), possibly responding to various stressors. In addition to its role in the hypothalamic-pituitary-adrenal (HPA) axis, cortisol has multiple roles in alerting and focusing individuals in social contexts and in times of change, in order to sustain fitness-related behaviours (e.g., movement (Breuner et al., 1998)), and maintain homeostasis (Goymann and Wingfield, 2004). Glucocorticoids are involved in coping and adaption to changing environments (Boonstra et al., 2001; Romero et al., 2009; Wingfield, 2005; Wingfield et al., 1994; Wingfield and Sapolsky, 2003) by mediating energy balance (Vera et al., 2017), in addition to daily changes and circadian rhythms (Bottoms et al., 1972; Curtis and Fogel, 1971; Garrick et al., 1987). Glucocorticoids are also related to and modulate social status (Creel, 2001; Creel et al., 1996; Creel, 2005; Goymann and Wingfield, 2004; Koren et al., 2008; Sapolsky, 1990) and social behaviours (Abbott et al., 2003; Remage-Healey et al., 2003), possibly through their influence on arousal and responsiveness (Fleming, 1990). This is especially crucial for mating and maternal behaviour, which necessitate high attention and reaction. For example, in humans, first time mothers with higher salivary cortisol were better at identifying their infants and found them more appealing (Fleming et al., 1997).

Last, oxytocin is usually referred to as the love hormone. Traditionally, oxytocin was labeled a maternal hormone through its role in inducing birth and the milk-let down reflex during breastfeeding (Carter, 2014; Gimpl and Fahrenholz, 2001). The last decade marks an exponential rise in the study of oxytocin's effects on sociality. In both men and women, most studies utilized an acute intranasal oxytocin administration as a means of manipulating oxytocin levels in the central nervous system (Bakermans-Kranenburg and van, 2013; Macdonald and Macdonald, 2010). Results are highly variable and context-dependent (Guastella and MacLeod, 2012). This has led several researchers to doubt the effects of intranasal oxytocin, claiming them as underpowered with low replicability and merit (Nave et al., 2015; Walum et al., 2016). In addition, since the mechanism by which oxytocin is delivered to the brain following such nasal administration has not been established (Leng and Ludwig, 2016), researchers have been cautious of oxytocin's potential effects (Miller, 2013). This is especially true for populations with atypical development, such as individuals with autism spectrum disorders (Alvares et al., 2017). Despite these concerns, there is evidence that intranasal oxytocin administration can indeed lead to cerebral spinal fluid oxytocin elevations (e.g., Striepens et al., 2013), and exude significant central effects (Quintana and Woolley, 2016). There is also substantial research linking peripheral oxytocin levels to behavior, especially in the context of attachment and bonding (Feldman et al., 2013; Gordon et al., 2010). Here we suggest that some of the seemingly contradicting results regarding oxytocin may be due to its highly interactive nature and interactive role. In part, researchers may be perplexed by oxytocin's effects, because they expect it to have a pro-social main effect, when in fact its crucial role is that of a modulator. Thus, the nature of its effects on sociality will depend on the social context and individual differences (Bartz et al., 2011; Shamay-Tsoory and Abu-Akel, 2016), as well as interactions with other neurohormones and endocrine systems. For instance, cortisol (and the HPA axis) interacts with both testosterone (via the HPG axis) and oxytocin in individual- and context-specific manners (i.e., (Evans et al.,

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2000; Perez-Rodriguez et al., 2006; Roberts et al., 2004)), further highlighting the need to progress beyond stereotypes.

When attempting to understand hormone interactions, it is also crucial to choose the appropriate time-frame, state (e.g., basal, reactive, integrated, free, bound) (Breuner and Orchinik, 2002; Malisch et al., 2010), and matrix (e.g., blood, saliva, hair) (Koren et al., 2002) to sample in order to properly analyze, compare, and discuss hormonal levels. Depending on the tissue, hormones that are measured may be related to specific time points or reflect chronic versus reactive or acute levels. In addition, there are multiple challenges involved with extracting hormones from different matrices, and validating their presence (Sheriff et al., 2011). Finally, single hormones can be quantified using sensitive biological antibody based assays such as RIAs or EIAs, or via more specific chemical and physical methods (e.g., based on their mass to charge ratios in LC–MS/MS) that allow multiple hormones to be quantified from a single sample (Koren et al., 2012a). Such novel methods produce a rich profile that can be used to investigate the hormones that are involved in processes without sex, species, or context biases, opening exciting opportunities to understand the underlying hormonal mechanisms behind social behaviour.

Conflict of interest

The authors declare no conflict of interests.

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