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Guest editorial

Working bitches and the neutering myth: Sticking to the science

In a recent issue of *The Veterinary Journal*, Dr. Hyeon H. Kim and colleagues from the College of Veterinary Medicine at Gyeongsang National University in the Republic of Korea, reported on the effects of ovariohysterectomy on reactivity in German Shepherd dogs (Kim et al., 2006). This is an important article for three reasons. Firstly, the paper clearly shows the advantage of a solid, albeit painstaking and low-technology, ethological analysis for understanding canine signalling and contextual behaviours. Secondly, it serves to remind us that when we say that there are no overt effects on behaviour of any procedure, caution is urged as so few potential outcomes have been rigorously measured. Thirdly, the rôle of myth – particularly as it pertains to sex and behaviour – can be enormous and can overwhelm that which is actually scientifically established. In no area is this risk more dangerous than for working dogs. That this study was carried out on military working dogs should be a credit to the authors and the Korean Air Force Dog Training Center.

Routine ovariohysterectomy is not globally universal, and yet few behavioural studies of either problem or normal behaviours have taken advantage of differences in application. Exceptions exist (O'Farrell and Peachey, 1990; Podbercsek and Serpell, 1996), and these tend to show that in females that had been neutered, aggression is more commonly reported than for the respective, intact cohort. Another study (Guy et al., 2001) examined odds ratios for biting household members and found that neutered females are two times more likely to have bitten than were intact females.

As noted in the paper by Kim et al. (2006), context matters. In one aggressive context, interactions with children, the dogs had shown no signs of aggression prior to ovariohysterectomy but did so after neutering (Podbercsek and Serpell, 1996). In contrast, O'Farrell and Peachey (1990) found that the effect was one of increased aggression only for the group of dogs already displaying a specific type of aggression prior to ovariohysterectomy (Overall, 1995). This difference in order of onset of aggression, developmental stage, and the apparent association with different types of aggression, may be related to the pattern reported by Kim and colleagues, and it suggests that hormonal effects on any behaviours are probably more complex than currently known.

When the focus is on a more general behaviour, like reactivity, that could lead to the dog entering a contextual situation where aggression might occur, there are few data on canids. One study of play in hyenas showed that females played more frequently, and more vigorously than males, but the category of play and the behaviours that were enhanced depended on the prevailing social context (Pedersen et al., 1990). An effect of sex on domestic dog activity has been noticed by those interested in evaluating the efficacy of early (seven months) and very early (seven weeks) neutering programs for reducing pet over-population and the problem of unwanted and abandoned pets. Salmieri et al. (1991) noted that of seven behavioural characteristics evaluated in a 15 month study of 32 mixed breed dogs, only general activity and excitability differed between treatment groups, and in both cases they increased in both neutered males and females.

As is often the case, better data exist for rodents than do for dogs, and suggest that hormonal effects on general behaviours affecting activity should be more closely examined in dogs. Rats are often used as models for drug addiction, depression, and other psychiatric conditions. As a result of the perturbations used to study the condition of focus many studies have noted sex differences in response. For example, when given cocaine, female rats exhibit considerably more locomotor activity and rearing than do males (Harrod et al., 2005). Interestingly, this increased activity is attenuated by ovariectomy, suggesting that another issue of interest is whether effects of sex on activity and reactivity vary among normal behavioural conditions, abnormal behavioural conditions, and treatment conditions. Effects of sex appear to be specific to type of activity, however, and true cocaine-stimulated stereotypic activity is not affected by ovariectomy, whereas overall activity on a horizonal surface is affected (Walker et al., 2001). These nuanced, context specific differences in activity may be important for our understanding of broader, sex-related behaviours.

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Because drug addiction is thought to be associated with novelty seeking, the extent to which rats explore novel and possibly threatening environments has been used as one assay of potentially important behaviours. In most studies, intact females have been shown to be consistently more active than males (e.g., Slob et al., 1981), and in a recent study designed to measure exploration and anxiety, females explored more, were more active, and exhibited fewer behaviours associated with anxiety (Ray and Hensen, 2004). Gonadectomy reduced these behaviours in females, but it also reduced the baseline for these behaviours in males. Fewer females have a low-harm avoidance to high-novelty-seeking profile, a finding that may be an important one to examine if one is interested in breeding military working dogs. These data are interesting in light of the findings that ovariectomised female rats have significantly lower basal and stress-induced cortisol levels that do intact females or males, regardless of reproductive state (Seale et al., 2004). It should not surprise us – especially given the associations of sex and novelty seeking – that gonadal steroids appear to play a major role in the regulation of hypothalamic–pituitary–adrenal (HPA) axis, which is also intimately involved in reactive behaviours. Receptors for corticosterone and estradiol can heterodimerise which results in decreased responsiveness to estrogen (Stromstedt and Waterman, 1995). This is not a trivial finding now that it is postulated that cortisol acts as a hormone response element (HRE) and greatly affects how and what we learn (Yau et al., 1995), and whether new proteins are transcribed and translated, primarily in the hippocampus, the region of the brain responsible for most associative learning.

There are now some extremely provocative data – again primarily from rats – that suggest that sex matters when effects of neurochemicals associated with impulsivity and learning are assessed. Impulsivity increases in rats that are serotonin-depleted (Svensson et al., 2000), a finding that should be intuitive, given that serotonin-enhancing drugs are used to treat impulsivity. Gonadectomy of males reduces this impulsive effect, and the effect of testes removal is reversed by testosterone. These data provide clear and tantalizing evidence that gonadal hormones exert effects on the serotonergic system. This effect could be direct, or indirect through the HPA axis. No where is this complex association more clearly laid out than in a recent paper reviewing all of the hormonal data available for situations involving learning (McCarthy and Konkle, 2005). This re-evaluation suggests that long-term potentiation (LTP) – learning at the cellular level that involves making new proteins and synaptic connections in the hippocampus and the frontal cortex – involving dendritic spine density and fear conditioning is a hormonally modulated response in females. In the female rats examined, dendritic spine density, a measure of protein production associated with synaptic connection, and the associated ability to develop conditioned/learned fear correlated positively with estradiol. So, we have evidence at the level of cellular anatomy that sex hormones can affect the regions in which most learning occurs. Evidence of such modulation removes us from the realm of absolutes that is implied when we use terms like 'increased' or 'decreased'. This new focus on modulation allows us to appreciate the relative effects of estradiol on various neurochemicals, and to begin to ask questions about the mechanism of subsequent effects on behaviours.

Estradiol prevents the age-associated diminution that occurs in the cellular response to γ-aminobutyric acid (GABA), an inhibitory neurotransmitter that aids in prevention neurocytotoxicity (Perrot-Sinal et al., 2001). In experimental rodent models, estradiol also depresses the potential excytotoxicity associated with the excitatory neurochemical glutamate in the hippocampus early in development (Hilton et al., 2003, 2004). This finding is particularly important because the hippocampus is exquisitely sensitive to hypoxia and ischemia induced injury that results from excytotoxicity. One can easily see that there could be differential gender effects on peri-parturient infant trauma, a situation that is a concern for anyone who breeds dogs.

Finally, we need to remember that all of these putative mechanisms can be affected by selection, and there is no stronger imposed selection in dogs than for those intended for military service. As part of selecting for ever-alert and forceful dogs, it is possible that we have selected for a more reactive dog, in general, and that manner in which these females are affected by ovariohysterectomy may not be the same as for breeds or families of dogs who have not undergone the same selection (Lucki et al., 2001). We also have no clue about the effects of this reactivity on future performance or behavioural profiles, but the implications are important for those interested in dogs with certain skills (e.g., the military) or with a decreased propensity for reactivity associated with behavioural problems (e.g., the population committed to pet dogs).

In any case, the findings presented by Kim et al. (2006) should be viewed as a beginning and a warning. They should caution us that what we assume is better measured, and that we need to invest in an understanding of various mechanisms involved in producing different reactivities.

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