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Guest Editorial

Keeping joints healthy: The Goldilocks effect of exercise



Efficient functioning of diarthrodial joints is essential for frictionless, pain-free locomotion. Integral to this is the structure of the joint and the interrelationship between its component parts. Although much study has been focussed on individual tissues (especially articular cartilage), it is important to realise that the joint should be viewed as a whole organ, with key relationships existing between cartilage, subchondral bone and synovium. Appropriate responses of these components to internal and external factors influence the ambient physiology or homeostasis of the joint. Of the factors known, exercise appears to be a vital element. The review article published in a recent issue of *The Veterinary Journal* by Nikae te Moller and René van Weeren, of Utrecht University, The Netherlands, highlights the importance of exercise for joint homeostasis in the horse (te Moller and van Weeren, 2017); too little or too much can result in joint derangement, whereas just the right amount of exercise (akin to Goldilocks and her porridge requirements) will provide optimal functioning of the joint.

We are often told of the health benefits of exercise on a number of body systems. Longitudinal studies in human beings report reduced morbidity and mortality following regular exercise (Schnohr et al., 2015), but studying the effects of exercise can be problematic; the level and amount of exercise seen as beneficial can be difficult to determine and other factors (e.g. age, diet, type of activity) can confound investigations. This is highlighted by te Moller and van Weeren (2017), where they bring to light differences, such as those between juvenile and adult horses, in the response of extracellular matrix maturation to exercise (te Moller and van Weeren, 2017).

But what are the mechanisms involved? The influence of exercise is most likely to be a direct effect through mechanical loading leading to a cellular response. This effect has been studied primarily in articular cartilage, but load will also lead to responsive adaptations of the underlying subchondral bone (Brama et al., 2009), which can also influence chondrocyte behaviour (Amin et al., 2009). Indeed, it has become apparent in recent years that cross-talk between subchondral bone and articular cartilage is essential for joint function and, although originally deemed to be an impenetrable barrier, there is now an increasing body of evidence for direct communication between the calcified and non-calcified cartilage layers, and the underlying bone and marrow spaces (Lyons et al., 2006). In addition to effects on bone and cartilage, exercise will affect other articular tissues, such as the synovium and fibrous joint capsule, likely through changes to local vascular flow regulating delivery of nutrients and oxygen to target tissues.

Defining what load is can also be an issue and makes studies difficult to compare. Mechanical forces and cell responses differ with the type (e.g. static or dynamic), amount and frequency of load (Chen et al., 2013). What is clear though is that cells have the ability to sense and modulate behaviour in response to load. This is called mechanotransduction and loss of the ability to mechanosense is an important event in joint disease (Salter et al., 2002). Cellular mechanotransduction may be through a variety of mechanisms, including shear stress, fluid flow and electrical field alterations resulting in cell membrane deformation and activation of membrane transporters (Mow et al., 1999). Changes in ion flux may have direct cellular effects (e.g. calcium influx), but can also lead to cellular volume changes (e.g. through sodium influx and associated water flow). Other mechanisms include cytoskeletal re-arrangements from direct (e.g. surface integrin receptors) or indirect (e.g. phosphorylation of second messengers by protein kinases) pathways. Articular chondrocytes have even been shown to respond to mechanical stimuli through cilia (Muhammad et al., 2012). Not only does load affect the cell directly, but dynamic changes in the matrix itself will also influence cell behaviour; for example, when loaded, movement of water results in increases in pH and osmolality in the local environment of the matrix, resulting in a cell response (Bush and Hall, 2001).

The response to loading during exercise can be seen as a classic feed-forward mechanism; alterations in extracellular matrix following loading will alter the properties of the matrix, thereby influencing its mechanical properties and hence the way it responds to subsequent load. However, inappropriate load (or lack of load) can lead to inappropriate responses; for example, acute overload injuries cause mitochondrial dysregulation, calcium influx and activation of caspases, resulting in chondrocyte apoptosis (Huser and Davies, 2007). This may be akin to what happens in post-traumatic osteoarthritis (PTOA), as is often seen in sports injuries with high impact/torsional forces (Anderson et al., 2011).

It is clear from the review by te Moller and van Weeren (2017) that exercise is a critical factor in maintaining a healthy joint and that early adaptation of tissues to exercise will influence the longevity of the joint. It is a fine line in getting the level right though; get the balance wrong and irreparable damage to the joint may occur, to the detriment of the animal, whereas get it right and happy joints will ensue!

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