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The central nervous system – an additional consideration in 'rotator cuff tendinopathy' and a potential basis for understanding response to loaded therapeutic exercise

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Abstract

Tendinopathy is a term used to describe a painful tendon disorder but despite being a well-recognised clinical presentation, a definitive understanding of the pathoaetiology of rotator cuff tendinopathy remains elusive. Current explanatory models, which relate to peripherally driven nocioceptive mechanisms secondary to structural abnormality, or failed healing, appear inadequate on their own in the context of current literature. In light of these limitations this paper presents an extension to current models that incorporates the integral role of the central nervous system in the pain experience. The role of the CNS is described and justified along with a potential rationale to explain the favourable response to loaded therapeutic exercises demonstrated by previous studies. This additional consideration has the potential to offer a useful way to explain pain to patients, for clinicians to prescribe appropriate therapeutic management strategies and for researchers to advance knowledge in relation to this clinically challenging problem.

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INTRODUCTION

Tendinopathy is a term commonly used to describe tendon pathology and/or pain. Despite being a well-recognised clinical presentation, a definitive understanding of the pathoaetiology of rotator cuff tendinopathy remains elusive (Lewis, 2009). Over recent years there has been a focus upon understanding pain associated with tendinopathy from the perspective of local tissue based pathology. But, in light of the well-recognised dissociation between pathology and pain (Cook and Purdam, 2009; Drew et al., 2012), it is becoming clear that additional explanatory models are now needed (Drew et al., 2012).

In view of this, the aim of this paper is to present a theoretical extension to current models incorporating the integral role of the central nervous system (CNS) in the pain experience. For the purpose of clarity within this paper and to aid clinical translation, the terminology 'rotator cuff tendinopathy' refers to a presentation where a person complains of shoulder pain with movement that is provoked further with load, for example lifting or through resisted tests performed by a clinician during a physical examination (Littlewood et al., 2012a).

We recognise that the reader might object to or question the appropriateness of the term rotator cuff tendinopathy for two reasons. Firstly, the criteria we use to define rotator cuff tendinopathy is broad and might include a range of biomedical diagnoses, including subacromial impingement, subacromial bursitis, rotator cuff tear, acromioclavicular joint osteoarthritis etc. However, in the absence of evidence to support the validity or reliability of such diagnoses (May et al., 2010), particularly in relation to the lack of association between pathology and pain, it is difficult to substantiate such an objection. Secondly, in the context of attempts to highlight the role of the CNS, such specific pathology or impairment

terminology might be regarded as a backwards step because of their reference to specific

peripheral tissue or mechanical mechanisms. However, such a broad definition of

tendinopathy in this translational paper is deliberate and purposeful to highlight how

current practice models can be interpreted and usefully enhanced without wholesale,

probably unrealistic, changes to practice and terminology; hence there is pragmatic value.

A secondary aim is to offer a potential rationale to explain the favourable response

to loaded therapeutic exercises demonstrated by previous studies (Jonsson et al., 2005;

Bernhardsson et al., 2010; Holmgren et al., 2012; Littlewood et al., 2012a). These further

considerations have the potential to offer a useful basis upon which to explain pain to

patients and for clinicians to prescribe appropriate therapeutic management strategies.

LOCAL TISSUE PATHOLOGY-PAIN MODELS

This paper will begin by offering a critique of local pain models as a basis upon which

to justify the need for greater consideration of the CNS. Tissue based pathology-pain models

have been proposed (Cook and Purdam, 2009) and adapted to the rotator cuff (Lewis,

2010). However, as mentioned, these models are confounded by the lack of association

between pathology and pain (Cook and Purdam, 2009; Drew et al., 2012). Using magnetic

resonance imaging, Frost et al. (1999) could not distinguish individuals diagnosed with

subacromial impingement from asymptomatic age-matched controls according to structural

pathology. In keeping with this, up to 40% of the general population have asymptomatic

rotator cuff tears (Templehof et al., 1999; Worland et al., 2003; Yamamoto et al., 2010).

Studies investigating prognosis (van der Windt et al., 1996; Bonde et al., 2003; Ekeberg et

al., 2010) have suggested that the biomedical diagnosis, relating to specific tissues at fault,

was not associated with clinical outcomes. Furthermore, it has been reported that structural

change does not explain response to therapeutic exercise because as clinical outcomes improve a corresponding change in observable structural pathology is not seen (Drew et al., 2012). Hence, in the context of this literature, traditional models that describe tissue injury/ structural pathology resulting in nocioceptive input and a pain response in proportion to the extent of injury seem inadequate, if considered in isolation.

LOCAL BIOCHEMICAL MODELS

In light of the shortcomings of local tissue pathology-pain models, others have suggested a local biochemical basis for the pain associated with tendinopathy where biochemical mediators in the tissue stimulate nocioceptive afferent fibres (Khan et al., 2000). Degenerative pathology is associated with neurovascular ingrowth and potential pain mediators such as substance P and acetylcholine. However, it remains unclear whether biochemical substances are a cause of tissue degradation and/ or pain or whether they are a by-product of tendinopathy (Danielson, 2009). But, because biochemical models make no assumption about the underlying pathology, such biochemically driven nocioceptive pathways might offer further understanding of symptomatic versus asymptomatic pathology. Further research in this area is on-going (Rees et al., 2013).

So, in light of what is currently known, local biochemical models appear to have the potential to enhance understanding and management of tendinopathy. But, neither these or local tissue pathology-pain models recognise the role of the CNS nor critically that nocioception is neither sufficient nor necessary for a pain experience (Moseley, 2007).

BACKGROUND TO THE ROLE OF THE CNS

A contemporary understanding of pain suggests that there might be other mechanisms involved in pain associated with tendinopathy that might act with the local

mechanisms outlined above or in isolation. The notion that the state of the tissue does not provide an adequate measure of pain is recognised in relation to other pain syndromes (Moseley, 2007; Melzack and Wall, 2008) but in tendinopathy local tissue/biochemical based models are predominantly used to explain pain (Cook and Purdam, 2009; Lewis, 2010; Liu et al., 2011). Such models continue to be developed but fail to adequately recognise the integral role of the CNS in the pain experience. This omission neglects a whole body of pertinent literature, that might offer some further explanation as to why attempts to link symptoms to peripheral structural pathology continue to fall short (Moseley, 2007; Wand et al., 2011).

We suggest here that the pain associated with rotator cuff tendinopathy, that persists beyond expected recovery times, should be evaluated within a framework that recognises the potential for altered processing and modulated output of the CNS rather than solely a product of peripherally driven nociception secondary to persistent tissue abnormality, for example tendon degeneration or tear. Note that we have used the term recovery time as opposed to healing time because many studies suggest that the rotator cuff does not always 'heal' from a structural perspective, even after attempts to surgically repair torn tissue (Galatz et al., 2004; Rees et al., 2006) although symptoms might still improve over time. In this context it is difficult to define a definitive time point by which we can assert that peripheral tissue recovery has been completed in terms of the inflammatory and proliferative stages. It is likely that this point will be highly individualised and compounded by factors specific to the rotator cuff including the relative hypovascularity of the tissue (Rees et al., 2006; Lewis, 2010). In practice, it might be more important to

consider factors other than time-course of symptoms when considering whether local or CNS pain mechanisms predominate.

EXPLAINING PAIN

The following section describes the potential mechanisms involved in pain associated with rotator cuff tendinopathy. The aim is to offer a reasoned explanation as to why pain state or output might persist and might not be proportionate to the state of the rotator cuff tissue. In addition to enhancing understanding of pain mechanisms, one further consequence of this might be a direct challenge to current practice where, for example, prescription of loaded exercise is limited due to fear of causing tissue damage (Littlewood et al., 2012b).

Central mechanisms

We begin by considering potential aberrations relating to processing of afferent inputs at the spinal cord level. Central sensitisation is a state that has been described in terms of altered processing where dorsal horn cells in the spinal cord become increasingly sensitised (Gifford, 1998a). In this altered state even non-noxious input, for example lifting the arm, can contribute to a painful output (Gifford, 1998a). Gwilym et al. (2011), recognising that anomalies existed between peripheral tissue structure and the degree of pain experienced, proposed the presence of central sensitisation in a significant proportion of their patients who underwent subacromial decompression. Furthermore, those patients who were regarded as having greater levels of central sensitisation pre-operatively reported worse outcomes three months following the operation. Clearly, pain mechanisms beyond peripherally driven nocioceptive mechanisms are in play here and the study by Gwilym et al.

(2011) casts further doubt upon the validity of tissue state as the sole basis upon which to understand pain.

Although central sensitisation is often described as being a product of a barrage of afferent impulses, maybe secondary to acute tissue injury, it is now well recognised that this hyper-reactive state of the dorsal horn cells can persist in the absence of on-going afferent input, known as pain memory (Gifford, 1998a). This reflects the plasticity or adaptability of the CNS. So, even in the presence of a recovered peripheral tissue, for example a rotator cuff tendon, central sensitisation can continue to contribute to an on-going pain state where non-noxious input contributes to a painful output.

Pain as an output

Pain as an output, in response to a threat, is regarded as a protective mechanism which might be helpful in some acute situations, where the primary aim is to minimise further threat, but unhelpful in other situations where unhelpful interpretation of a pain response serves as a barrier to recovery (Moseley, 2007; Melzack and Wall, 2008). An example of this would be resting a shoulder that needs movement to facilitate functional restoration. The key feature proposed here is that pain is a product of CNS processing, at the level of the spinal cord and the brain, which is modulated by other factors including thoughts and feelings, and does not necessarily reflect the state of the peripheral tissues, at least from an observable structural perspective. CNS modulation might be influenced by a range of intrinsic inputs, for example beliefs about what the pain means, or extrinsic inputs, for example societal context. To highlight this, a person who has been advised to rest, believing that their shoulder pain is caused by tissues being compressed and catching is likely to present in a different way to someone who has been reassured and given guidelines about how best to get their arm moving. In this context it is perhaps possible to see how the

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subacromial impingement model might adversely contribute to the pain experience and rightfully is now regarded as an outdated and unhelpful way to understand shoulder pain (Lewis, 2011).

The Mature Organism Model

To facilitate understanding and implementation, Gifford (1998b) proposed the mature organism model (MOM). This model describes a cyclical process beginning with an input to the CNS (sampling), for example nocioception. This is followed by CNS processing (scrutiny) before an output, for example an altered behaviour, is generated. The output subsequently serves as a further input to the sampling loop. The MOM suggests that the CNS is continually sampling tissue health, the surrounding environment and itself, consciously and unconsciously, before scrutinising this input in the context of past experience, knowledge, beliefs, culture, past successful behaviour, past successful behaviour observed in others (Gifford, 1998b; Jones et al., 2002).

This process of scrutiny before an output is generated is key and has the potential to create an environment for recovery or otherwise. For example, if this scrutiny takes place in the context of a subacromial impingement model, it is possible that an already de-conditioned tissue is allowed to de-condition further if any sign of pain is interpreted as impending tissue damage and is hence avoided. Considered in this context, Gifford (1998c) (p.58) suggests:

'It is perhaps far wiser to be involved in helping to establish the best possible conditions for natural recovery. This appears to involve a parallel and well balanced focus on functional restoration of best possible tissue health/ return of function in parallel with a recognition of and focus on relevant cognitive and affective factors'

The de-conditioned rotator cuff

Perhaps one immediate question that arises is: Why would the CNS generate a painful output that is not directly related to the pathological status of the tissue? We believe that this can be understood in terms of a protective pain output from the CNS in response to a perceived threat to a de-conditioned tissue. We use the term de-conditioned to describe a situation where the CNS perceives the tissue to have a reduced capacity to perform required tasks (Butler and Moseley, 2003). It is the *perceived* nature of the de-conditioning and hence protective pain output from the CNS that might offer an alternative explanation as to why observed structural changes do not adequately explain pain, although subtle mechanical changes to the tissue that might not appear on imaging cannot be fully discounted at this stage (Malliaras and Cook, 2006). It should be recognised that de-conditioning does not mean degeneration, although degenerated tissue might be de-conditioned and tissues that have been injured previously might become de-conditioned, but not necessarily so.

The source of de-conditioning in relation to the rotator cuff is open to debate but some speculative claims can be offered within a biopsychosocial framework. In terms of biology, factors including relative hypovascularity and adverse mechanical loading might be relevant. Also underuse, whereby physical stress levels perhaps secondary to a sedentary lifestyle, are lower than the maintenance range, and result in decreased capacity of the tissues (Mueller and Maluf, 2002; Rees et al., 2006; Lewis, 2010). A biological theory appears plausible where studies have reported a reduction in tendon capacity with age (Reeves, 2006) in tandem with an epidemiological perspective where studies have reported increasing prevalence rates of rotator cuff tendinopathy with age (Chard et al., 1991). In terms of psychology, a broad range of attitudes, beliefs and experiences might contribute to

this perceived de-conditioning. For example, a belief that; *'I've inherited weak shoulders so I'm limited in what I can do,'* or a past experience that resulted in a pain response might long be held in the memory and inform any future central scrutiny. From a social perspective, again many factors could contribute. The role of the health care professional and diagnostic labels was described above to demonstrate how a context can influence behaviour. Wandner et al., (2012) have also reported how the perception of pain varies across gender, race and age. It seems likely that a combination of these biopsychosocial factors might (mis)inform an individual's perception and hence pain response.

RATIONALE FOR RESPONSE TO LOADED THERAPEUTIC EXERCISE

From a biological perspective initially, tendons are regarded as being mechanosensitive, which means they are capable of responding to mechanical stimuli (Maffulli and Longo, 2008). The term 'mechanotherapy' has been coined to describe how a programme of structured exercise might stimulate human tissue and reverse tendon de-conditioning (Reeves, 2006; Abate et al., 2009; Khan and Scott, 2011). It is proposed that a progressive exercise regime will stimulate a process of re-conditioning and improve the capacity of the rotator cuff to withstand greater load and stress (McKenzie and May, 2000; Reeves, 2006; Kjaer et al., 2009). This idea has been substantiated in the literature where tendon tissue has been shown to become stronger through increases in tensile strength and elastic stiffness in response to programmes of structured exercise (Abate et al., 2009).   Due to the paucity of evidence, the optimal load to stimulate re-conditioning remains unclear. However, when reporting favourable outcomes, recent studies have encouraged load prescription according to symptom response where pain was produced during exercise (Jonsson et al., 2005; Bernhardsson et al., 2010; Holmgren et al., 2012). Such an approach

might initially appear counter-intuitive within the context of the framework described here but we suggest that quite the opposite is true.

Drew et al., (2012) reported that observable structural change does not adequately explain response to therapeutic exercise and that other mechanisms are more likely to be responsible. In addition to local biological changes, it is feasible that appropriate prescription of loaded therapeutic exercise has an impact upon CNS scrutiny or processing with a resultant modified output. From a psychological perspective, the prescription of painful loaded exercise within a framework that suggests hurt does not equal harm; hurt, in some circumstances, equals a tissue that is de-conditioned and needs using/exercising, has the potential to reframe the meaning of pain. In addition to this, a progressive exercise programme has the capacity to address the hypothesised de-conditioning as the frequency and load of exercise increases over time. Basically, if the way a person conceives their shoulder pain is adapted then there is potential for beneficial change in CNS output to be realised, particularly if the prescribed exercise programme resembles their usual functional activities. Clearly in this context, intelligent but individualised prescription of painful loaded therapeutic exercise and return to normal function is required that does not provoke a threat response from the CNS in terms of a lasting and exaggerated pain output. In practice this requires that our patients have an understanding of why the exercise has been prescribed, that hurt does not equal harm, in their circumstance, and it requires an understanding of the patient's acceptable pain response. Although an inexact science for which the boundaries have not yet been adequately defined, acceptable pain responses can be elicited through simple questioning, for example; 'Is that amount of pain acceptable to you while you are exercising or after you have exercised? Should we add more/ less load?'

For such exercise prescription to be effectively implemented, the therapist must be mindful of the perspectives held by the patient. We suggest simple exploratory questions such as: What do you understand is the cause of your problem? (Littlewood et al., 2013 – see for further information relating to assessment and management). Such questioning can help to elicit understanding and begin to identify potential barriers to implementation.

Finally, from a social perspective, in terms of the influence of surroundings and significant others, the prescription of loaded exercise within this framework challenges diagnostic and therapeutic approaches that promote fear avoidance, for example *'the pain is a sign of further tissue damage so don't move it if it is painful.'* Such prescription also has the potential to challenge public perception that hurt equals harm in all circumstances. As opposed to some previous approaches, a constructive, non-threatening means around which restoration of function can be achieved is offered.

Clearly the pain associated with 'rotator cuff tendinopathy' has a multi-dimensional basis. The key to future success will be to discover indicators of each dimension along with reasoned and relevant multi-dimensional management strategies.

Summary

This primary message of this paper is summarised in figure 1. It can be conceptualised as a process beginning with perceived tissue de-conditioning, secondary to a known or unknown cause, for example chronic underuse. An episode of relative overuse or overload results in short term tissue responses that are scrutinised by the CNS in the context of other inputs and the surrounding environment and if the input is regarded as a threat, a painful output as a means of protection will ensue. In this situation this might promote avoidance of shoulder movement if the pain is believed to be indicative of harm, and will

also result in a unique pain experience, for example absence from work and low mood due to activity withdrawal. Such fear avoidance might result in further tissue de-conditioning and a continuation of the cycle. However, appropriate contextualisation and intervention might result in a different outcome. If pain is regarded as a sign of de-conditioning rather than actual or impending tissue damage then an alternative process of CNS scrutiny might result in an active output, for example engagement with a structured exercise regime, with the potential to re-condition peripheral (tendon) and central tissue. Additionally, active engagement and 'permission' to resume normal activity without fear of causing harm to self might facilitate an improved outcome in contrast to existing approaches.

CONCLUSION

The cause of pain associated with rotator cuff tendinopathy remains uncertain and there are clear limitations associated with current explanatory models that rely on a peripheral tissue based understanding. A theoretical addition to these pre-existing models has been presented with reference to current literature incorporating the integral role of the CNS in any pain experience. This additional consideration offers an accessible way to understand the pain associated with rotator cuff tendinopathy and to understand potential mechanisms underpinning therapeutic response to loaded exercise.

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