

TITLE PAGE

**Title: The association of psychological variables and outcome in tendinopathy:
a systematic review**

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The association of psychological variables and outcome in tendinopathy: a systematic review

ABSTRACT

Objective: Fear, anxiety, depression, distress and catastrophisation are all factors known to affect pain and disability levels. To date, the association of such psychological factors has yet to be established in tendinopathy. Therefore, the purpose of this paper was to determine if psychological variables are associated with tendinopathy and whether any such variables may be associated with pain and disability outcomes in conservative management of tendinopathy.

Design: A systematic review was undertaken and included studies were appraised for risk of bias using the Newcastle Ottawa Scale. Due to heterogeneity of studies, a qualitative synthesis was undertaken.

Data sources: An electronic search of MEDLINE, CiNAHL, SPORTDiscus, PsycINFO, EMBASE and PsycARTICLES was undertaken from their inception to April 2016.

Eligibility criteria for selecting studies: Any study design that incorporated psychological measures and clinical outcomes using participants with tendinopathy.

Results: Ten articles describing nine studies and 1108 participants were included. Conflicting evidence exists regarding the association of anxiety, depression and lateral epicondylalgia (LE). Strong evidence suggests LE is not associated with kinesiophobia. Moderate evidence links catastrophisation and distress with LE. Moderate evidence suggests distress is not associated with rotator cuff tendinopathy, but kinesiophobia and catastrophisation are. Limited evidence suggests patella tendinopathy is not associated with anxiety or depression and kinesiophobia may be linked with suboptimal outcomes in Achilles tendinopathy.

Summary/conclusions: Tendinopathy requires an individualised approach to management. Clinicians should consider using validated screening tools for the presence of psychological variables as a part their holistic management.

What are the new findings

- Psychological variables may be associated with tendinopathy and a suboptimal outcome
- Multi-dimensional factors influence the development and maintenance of pain and disability in tendinopathy

- The underlying factors for the presence of these variables and their amenability to change warrant further investigation

How might it impact on clinical practice in the near future

- Tendinopathy management should include an individualised, holistic assessment
- Management strategies may need to be adapted to address individual psychological variables and any underlying cognitive barriers.

INTRODUCTION

Tendinopathy is a widely accepted, generic term characterised by reduced loading capacity of a tendon associated with pain.[1] Thirty to fifty percent of all sports-related injuries are reported to be diagnosed as tendinopathy[2] with clinical symptoms including load-related pain, tenderness, localised swelling and disability.[3] Tendinopathy is frequently reported within the upper and lower limb.[4] Lateral epicondylalgia or tennis elbow affects up to 3% of the population[5] and whilst rotator cuff tendinopathy is considered a common problem, it is uncertain to what extent, with estimates of point prevalence ranging from 2.4% to 21%.[6] Twenty percent of knee injuries are diagnosed with patellar tendinopathy[7] and for top level runners Achilles tendinopathy is a 52% lifetime risk.[8]

Whilst tendinopathy is problematic to manage clinically,[1] there is a body of evidence to support a conservative management approach.[9–11] Current conservative management strategies for tendinopathy usually include strength training,[12,13] but may additionally include other interventions such as shock wave therapy or laser therapy.[14,15] However, tendinopathy can remain resistant to treatment, and peripheral tissue focused interventions are unlikely to address complex adaptations associated with persistent pain.[16] This suggests the need to include further considerations to management as current strategies appear sub-optimal. Load is considered a major pathoetiological component of tendinopathy. However, many factors are considered to modulate load. These include genes, age, circulating and local cytokine production, sex, biomechanics and body composition, with current management programmes suggesting the need to tailor to individual presentations.[1]

Tailoring management strategies to individual presentations has been suggested for other conditions which can also be resistant to treatment resulting in persistent pain states.[17] Strategies adopted include not only addressing physical factors such as loss of muscle strength or co-ordination, but also cognitive and psychological factors. Initial results from this approach, known as Cognitive Functional Therapy, have been encouraging.[18] Factors such as fear, anxiety, depression, stress and catastrophisation are all known to further affect the pain experience and disability levels.[19] To date, the association of such psychological factors has yet to be established in tendinopathy. Therefore, the purpose of this paper was to determine;

- 1) Are psychological variables associated with tendinopathy?
- 2) Are outcomes from conservative management of tendinopathy linked to the presence of psychological variables?

METHODS

Protocol

A systematic review was performed using a predetermined protocol in accordance with the PRISMA statement.[20]

Data sources and search strategy

An electronic search of MEDLINE, CiNAHL, SPORTDiscus, EMBASE, PsycINFO and PsycARTICLES was undertaken from their inception to April 2016. The keywords used are displayed in table 1. The electronic search was complimented by hand searching the reference lists of the papers identified. Citation searching using the identified papers was also carried out and recognised experts in the field of tendinopathy were consulted in an attempt to identify any further published or unpublished studies, although no unpublished studies were identified. The search, including the application of the selection criteria, was conducted independently by two reviewers (AM & TW) with any discrepancies resolved by discussion.

Table 1 Keywords used in the study selection process

Search Terms	
1	Tendin* or tendon* or jumper's knee or lateral epicondy* or rotator cuff or subacromial pain or subacromial impingement or tennis elbow
2	Psycholog* or fear or depression or emotion* or anxiet* or catastroph* or distress
3	1 & 2 Combined

Inclusion criteria

Population

Adult participants with a clear diagnosis of a tendon-related disorder, including tendinosis, tendinitis, tendinopathy or synonyms e.g. tennis elbow. In keeping with previous reviews, minimal diagnostic criteria of a largely preserved range of motion with pain provoked by loading of the tendon was required.[6] Studies with mixed or non-specific diagnoses, or those concerned with the risk of developing tendinopathy were excluded. Additionally, studies investigating tendinopathy considered to be as a result of an intervention e.g. fluoroquinolone, studies using participants with a known specific disease present (e.g. spondyloarthritis), or concerned with tendon rupture or post-surgical recovery were also excluded.

Outcome

Self-reported psychological measure(s) measuring emotional and cognitive variables known to be associated with persistent pain. These were namely; depression, anxiety, catastrophisation, fear and distress.[19] Measurements of pain and disability, plus any other clinical outcomes were included.

Study design

Any study design that incorporated measurement of psychological status and clinical measures of pain and / or disability. These included case study, case series, case-control, cohort, cross sectional, uncontrolled trials, quasi-experimental studies and randomised controlled trials (RCT). Narrative reviews, editorials or other opinion-based publications were excluded.

Language

Studies published in any language were included, however no identified studies published in a non-English language met the criteria for full review.

Risk of bias assessment

Risk of bias assessment of the included studies was undertaken independently by two authors (AM & TW) using the Newcastle-Ottawa Scale (NOS). The NOS is a tool designed for cohort and case-control studies, which is reliable and valid for assessing quality of non-randomised studies.[21] Criteria evaluate potential bias based on selection of participants, comparability of study groups and attainment of exposure (case-control studies) or outcome of interest (cohort studies).[21] The NOS uses a star rating system (semi-quantitative) where one star is awarded for each criterion of appropriate methods are reported, with the exception of comparability of cohorts where two stars are awarded if a study controls for more than one comparison factor.[21] The scale ranges from zero to nine stars.[22] Discrepancies in the awarding of a star were resolved by discussion with a third reviewer (CL). As the effectiveness of an intervention was not of interest to the review, but rather the association of other measures, the case-control scale and cohort study scale were also used to evaluate included cross-sectional, case-series and intervention studies, respectively.[23]

Data extraction

All data was extracted by a single reviewer (AM) and verified by a second reviewer (TW). Data included study characteristics, participant characteristics, source, sample size, intervention details, comparison group characteristics and results. Quantitative data relating to psychological measures, pain and disability were also extracted.

Data synthesis

There was considerable clinical heterogeneity within the included studies with regard to study design, patient populations and measures of psychological variables.[24] Therefore, a qualitative synthesis was deemed the most appropriate means to analyse the data. As threshold scores to differentiate between 'good' and 'poor' studies using NOS have yet to be established[21] the qualitative synthesis of data was informed by a scoring system to rate studies included in this review. The score for each was calculated by dividing the number of stars achieved by the number of items. Each study was graded as low, moderate or high quality based on this score. Cut-off points were designated *a priori* as: 0.00-0.44 low methodological quality, 0.45-0.70 moderate quality, and 0.71-1.00 high quality. Such cut-off points are often used to determine reference values for level of association / agreement by

researchers and have been acknowledged as acceptable by experts in research methods[25,26] and utilised by previous studies.[27] In order for both quality and quantity of the available evidence to be taken into account, a rating system for levels of evidence, was used to summarise data relating to psychological factors, tendinopathy and outcome (table 2).[28]

Table 2 Levels of evidence

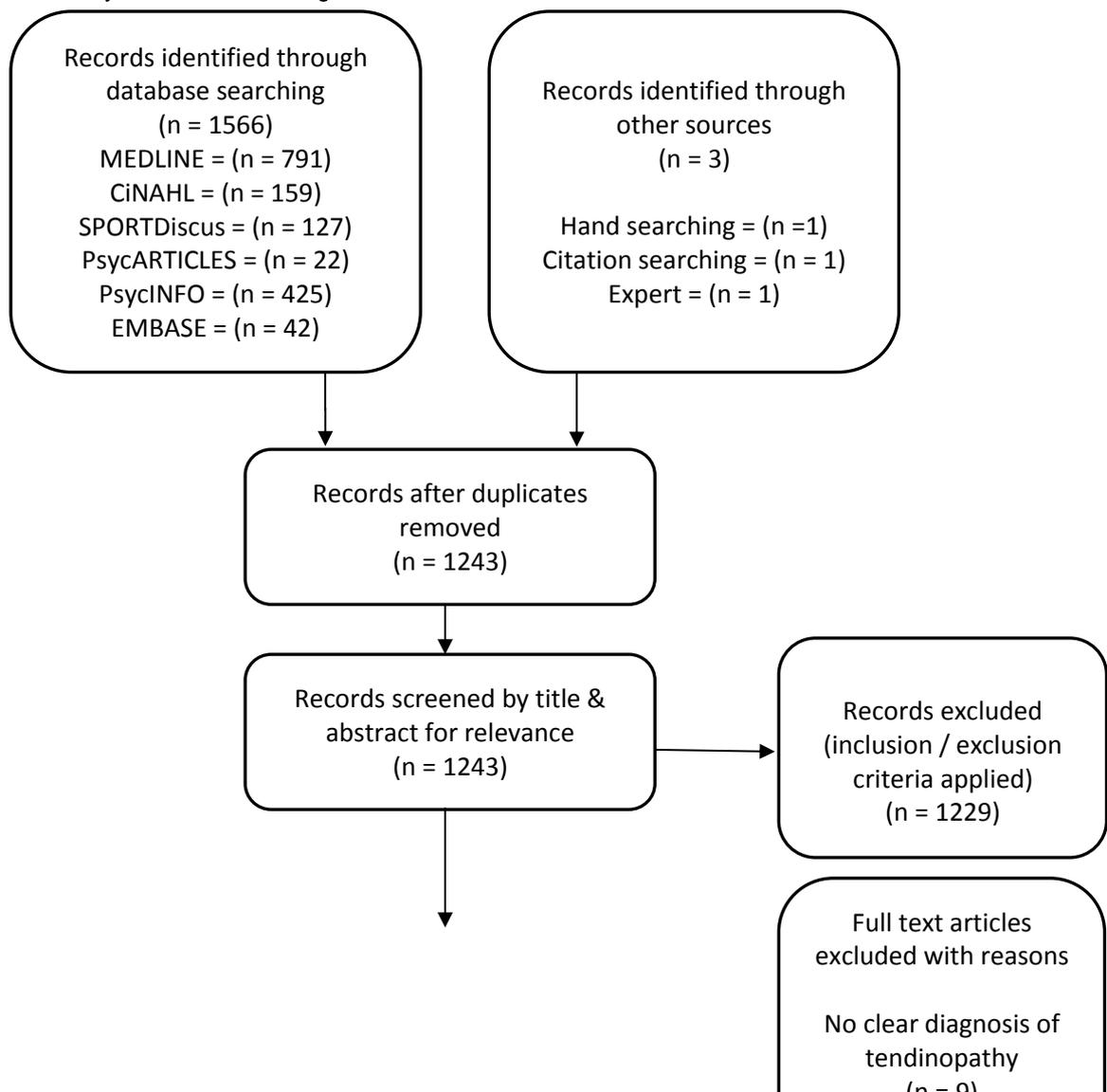
Strong evidence	Consistent findings in high-quality studies (n≥2)
Moderate evidence	Consistent findings among lower-quality studies (n>2) and / or one high quality study
Limited evidence	≤ relevant low quality studies
Conflicting evidence	Inconsistent findings amongst multiple studies
No evidence	No studies

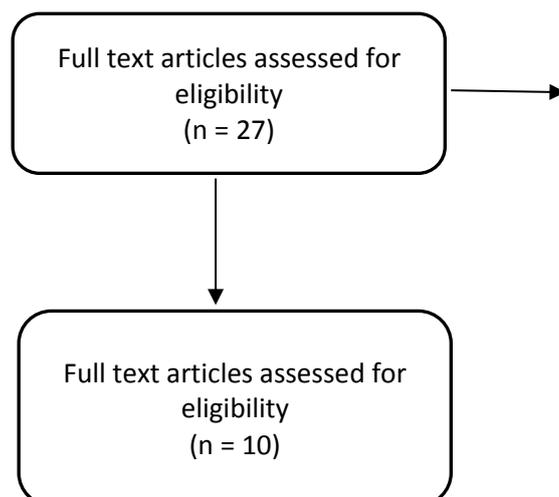
RESULTS

Study selection

Figure 1 represents the results of the study identification process. Initially, 1243 citations were identified once duplications were removed. After screening, 27 articles were considered for full review. Applying the eligibility criteria, 10 articles, describing 9 studies were included for risk of bias assessment.

Figure 1 Study selection flow diagram





Newcastle-Ottawa Scale assessment

The results of the risk of bias assessment are shown in table 3. From the possible nine stars available, five studies were awarded eight stars[29–33] and deemed of high quality, three studies were awarded seven stars[34–36] and also deemed of high quality and two studies were awarded six stars,[37,38] deemed moderate quality.

Table 3 Risk of bias assessment using the Newcastle-Ottawa Scale

Author / Year	Selection	Comparability	Exposure / Outcome	Total Stars	Quality of study
Alizadehkhayyat et al (2007)	****	*	**	7	HIGH
Coombes et al (2015)	****	*	***	8	HIGH
Coombes et al (2012)	****	*	***	8	HIGH
Engebreetsen et al (2010)	****	*	**	7	HIGH
Garnevall et al (2013)	****	*	**	7	HIGH
Haahr & Andersen (2003)	****	*	***	8	HIGH
Kromer et al (2014)	****	**	**	8	HIGH
Lee et al (2014)	****	*	***	8	HIGH

Silbernagel et al (2011)	***	*	**	6	MODERATE
van Wilgen et al (2013)	***	*	**	6	MODERATE

Study characteristics

A summary of the characteristics of the included studies is presented in online supplementary appendix 1.

Study design

The most frequently used study design was cross sectional (n=5).[29,32,35,36,38] Other study designs were case control (n=1),[34] case series (n=1),[37] randomised control trial (n=1),[31] and cohort (n=2).[30,33]

Participants

Two studies reported data utilising one set of participants.[29,30] Thus, the ten articles included for review identified nine studies. The studies included 1108 participants, 580 women and 528 men. The mean age of the participants was 48.8 years, ranging from 18[36] to 82 years.[33] Six studies included participants with lateral epicondylalgia (LE), [29–31,33–35] two studies included participants with rotator cuff tendinopathy (RT),[32,36] one study included participants with Achilles tendinopathy (AT)[37] and one study included participants with patella tendinopathy (PT).[38]

CLINICAL FINDINGS

Psychological variables and tendinopathy

Overall, there is conflicting evidence relating the presence of psychological variables and their association with tendinopathy. Six studies (5 of high quality and 1 of moderate quality) support a statistically significant positive association between the presence of psychological variables and tendinopathy.[31–35,37] Four of these investigated LE, one RT and the other AT. Four studies (3 of high quality and 1 of moderate quality) demonstrated no statistically significant association between psychological variables and tendinopathy.[29,30,38] Two of these investigated LE, one RT and the other PT.

Catastrophisation

Two studies investigated the association of catastrophisation and tendinopathy.[32,33] One high quality study investigating RT supported a statistically significant positive association of the presence of catastrophisation and tendinopathy at baseline.[32] The other study investigating LE was also of high quality and showed a statistically significant positive relationship between a reduction in catastrophisation and a reduction in the need for additional treatment.[33]

Distress

Two high quality studies investigated the association of distress and tendinopathy.[31,36] One study investigated RT and showed no statistically significant association between the presence of distress and pain and function associated with tendinopathy.[36] The additional study investigated LE and supported a statistically significant positive association of the presence of distress and tendinopathy.[31]

Anxiety & Depression

Four studies investigated anxiety in conjunction with depression.[29,30,34,38] One study investigated anxiety without depression, but instead included aggression and extraversion factors.[35]

Two high quality studies[29,30] investigating LE and one moderate quality study[38] investigating PT demonstrated no statistically significant association between the presence of anxiety, depression and tendinopathy.

One high quality study investigating LE supported a statistically significant positive association between the presence of depression and tendinopathy.[34] Two high quality studies both investigating LE supported a statistically significant positive association of the presence of anxiety and tendinopathy.[34,35]

Kinesiophobia

Three studies investigated the association of fear-avoidance and tendinopathy.[29,32,37] One high quality study investigating LE demonstrated no

statistically significant association between kinesiophobia and tendinopathy.[29] Another high quality study investigating RT supported a statistically significant association of the presence of fear-avoidance beliefs and disability at baseline.[32] One moderate quality study investigated AT and showed a statistically significant negative correlation between levels of kinesiophobia and heel-rise work recovery (a battery of tests consisting of two jump tests, two strength tests, and one endurance test), suggesting a negative effect on the effectiveness of treatment.[37]

Psychological variables and prognosis

Overall, there is conflicting evidence relating the presence of psychological variables and their association with outcome in tendinopathy. Three studies (2 of high quality and 1 of moderate quality), two investigating LE and the other AT support a statistically significant positive association.[31,33,37] Two studies (both of high quality), one investigating LE and the other RT showed no association.[30,32]

Catastrophisation

Two studies investigated the association of catastrophisation and outcome in tendinopathy.[32,33] One high quality study, investigated RT and showed high baseline catastrophisation scores were not predictive of disability at 3 months.[32] The other, also of high quality investigated LE and showed a statistically significant positive relationship between a reduction in catastrophisation and a reduction in the need for additional treatment at 12 months.[33]

Distress

One high quality study investigated the association of distress and outcome in LE.[31] This study showed a statistically significant association with continued high pain scores and a less than 50% reduction in pain scores at 12 months associated with high baseline distress.

Anxiety & Depression

One high quality study investigated the association of anxiety and depression and outcome in LE.[30] This study found no statistically significant association between anxiety, depression and pain and disability scores at 12 months. One high quality study investigated the association of depression and LE.[33] This study showed depression was independently statistically significant for an association with seeking additional treatment at 12 months.

Kinesiophobia

Three studies investigated the association of fear avoidance and tendinopathy.[30,32,37] One high quality study investigated LE and found no statistically significant association between kinesiophobia and pain and disability at 12 months[30] and another high quality study investigating RT found high baseline kinesiophobia scores were not predictive of disability at 3 months.[32] One moderate quality study investigating AT found at 5 year follow up, increased fear of movement

was statistically significant for an association with reduced heel-rise work recovery.[37]

SUMMARY OF KEY FINDINGS

Lateral Epicondylalgia

There is conflicting evidence from multiple study designs surrounding the association of anxiety, depression and LE.[29,30,33–35] Strong evidence from one high quality cross-sectional study and one high quality cohort study, suggests kinesiophobia is not associated with LE.[29,30] Moderate evidence from one high quality RCT links distress with LE.[31] Moderate evidence from one high quality cohort study links catastrophisation with LE.[33]

Rotator Cuff Tendinopathy

There is moderate evidence from one high quality cross-sectional study suggesting distress is not associated with RT.[36] There is moderate evidence from one high quality cross-sectional and longitudinal study to suggest that kinesiophobia and catastrophisation are associated with RT at baseline, but are not associated with a suboptimal outcome.[32]

Patella Tendinopathy

There is limited evidence from one moderate quality cross-sectional study to suggest anxiety and depression are not associated with PT.[38]

Achilles Tendinopathy

There is limited evidence from one moderate quality case series to suggest kinesiophobia is associated with AT.[37]

DISCUSSION

This systematic review suggests overall there is conflicting high quality evidence relating to the association of psychological variables and outcome in tendinopathy. Previous systematic reviews considering features of tendinopathy have investigated structural changes[39] and central nervous system (CNS) changes,[40,41] but consideration to psychological variables has been limited to other conditions such as low back pain.[42,43] The review was undertaken in accordance with published guidelines.[20] Whilst it is acknowledged criteria for ‘good’ and ‘poor’ studies have yet to be established for the NOS,[21] according to the scoring system and cut off points designated *a priori*, the majority of studies were considered to be of a high quality, whilst two studies were considered of moderate quality. The conflicting high quality evidence as to the association of psychological features in tendinopathy could potentially be explained by several factors.

Firstly, the variance in population under investigation. Although most of the participants were around the mean age of 50yrs, one study[38] had a mean age of 23.3yrs. Additionally, participants were recruited from various settings ranging from

specialist hospital settings[34] to university populations[38] and general care.[31] Two studies (from three articles) investigated anxiety and depression in LE and utilised the Hospital Anxiety and Depression scale.[29,30,34] One population[29,30] was recruited via advertising from the general population and the other from consecutive attendance at an upper limb clinic.[34] While inclusion criteria for both populations were similar, the study[34] whose population was taken from attendees at an upper limb clinic found a positive association between LE and anxiety and depression whilst the population who self-selected for inclusion did not.[29,30] Reasons behind these contrasting findings may consequently lie in the population studied. Those attending a specialist service may have a longer duration of symptoms or failed previous interventions and consequently represent a separate sub-population of LE which appear more vulnerable to associated psychological variables alongside tendinopathy. Whilst it is acknowledged the variation in population may contribute to discrepancies between the studies, it was considered that the inclusion of all study types represents the evidence base as a whole; thus allowing the clinician to make their clinical reasoning based on a synthesis of all the available evidence.[44]

Secondly, the heterogeneity of outcome measures; for example, symptoms of anxiety and depression were measured by five studies and four different outcome measures were used. Although this in itself does not reduce the quality of the individual studies as they are justified choices, comparability between studies is made more difficult. Thirdly, the majority of studies investigated tendinopathy of the upper limb; six investigated tennis elbow,[29–31,33–35] two investigated rotator cuff tendinopathy,[32,36] one patellar tendinopathy[38] and one Achilles tendinopathy.[37] The efficacy of treatment, and potential relationship of psychological variables, will likely be dependent on the specific tendon's anatomical and biomechanical properties.[45] For example, with Achilles tendinopathy most commonly manifesting in the mid-portion and patellar tendinopathy occurring as an enthesopathy.[46] In addition, there is growing evidence of CNS changes that may contribute to pain and disability in tendinopathy, but to date these data have been predominately considered in the upper limb,[40,47] with lower limb data limited[38] or even negating.[48] Changes in the CNS or central sensitisation is much more than generalised hypersensitivity to pain and includes increased responsiveness to stress, emotions and mental load.[49] Consequently, differing dominant states of sensitivity (peripheral or centrally driven) may have influenced the association of psychological variables. A possible area for further study would be to investigate this potential influence.

Finally, differing cognitive factors which may underpin the psychological variables and their amenability to change could also help explain the conflicting high quality studies results. Complex mental events such as hope, beliefs, information and expectations have all been shown to influence the pain experience.[50,51] The relationship between the patient and the practitioner has been shown to be useful in predicting and influencing outcomes in other chronic conditions such as low back pain[52,53] and a positive alliance is seen to have an overall positive influence on rehabilitation.[54] The influences on this relationship or 'working alliance' include a

mix of interpersonal skills, practical skills and individualised patient centred care.[55] Working alliance involves technical skill and the reflective capacity of the therapist to respond to the patient, but extends beyond good communication to a sense of collaboration, warmth and support.[56,57] Consideration to the aforementioned mental events and investigation into the influence of working alliance has yet to be explored and may be an area for future study.

For the clinician, being aware that psychological variables may be associated with tendinopathy may assist in optimising management by utilising strategies to help overcome or reduce their influence. Although future testing by research is required, adopting strategies which aim to influence hope and positive beliefs, [51] place emphasis on neuroscience education[58] or address individual cognitive behavioural barriers[18] whilst maximising working alliance[52–54] are all plausible strategies to adopt in conjunction with a graded loaded programme.[13,59] These psychological variables may be particularly important when considering more invasive procedures such as surgery, as they are associated with negatively influencing outcomes.[60–62]

Change in psychological status may offer another explanation as to the response to commonly used loading programmes for the management of tendinopathy. A confrontational graded exposure intervention, resembling education and a progressive loading programme (a combined cognitive and behavioural intervention), may serve to reduce fear, anxiety and catastrophisation and consequently enhance performance by reducing pain and disability. This type of approach has been utilised successfully in other persistent pain conditions,[18] where changes in tissue state also do not appear to correlate with reductions in pain and disability.[39,63]

FUTURE DIRECTIONS

The findings of the current review suggest that taken as a whole, there is conflicting evidence as to the significance of psychological variables in tendinopathy. However, specific psychological variables may be associated with tendinopathy and suboptimal outcomes from treatment. As such, clinicians should be vigilant as to the possibility of the presence of such variables and the possibility to need to adapt management accordingly.

While a clear explanation for the response of tendinopathy to therapeutic exercise is lacking, further studies to identify the underlying mechanism are warranted. Theories surrounding the potential influence of the CNS, biochemical and myogenic factors have been proposed.[16,47,64–66] Whilst acknowledging the likelihood of a multifactorial explanation,[67] to date psychological response explanations have lacked consideration and the findings of this review suggest further research is warranted. Currently it is unknown why people with tendinopathy may also present with psychological variables which link with suboptimal outcome. One possible explanation might be those with fear of pain might perform less exercise with less intensity.[37] Given the conflicting high quality evidence of psychological variables

presented in the review, further exploration of cognitive processes connected with psychological variables and means of influencing these is warranted.

CONCLUSIONS

Conflicting evidence exists surrounding the significance of the association of anxiety, depression and LE. However, strong evidence suggests LE is not associated with kinesiophobia. Moderate evidence links catastrophisation and distress with LE, with distress being associated with a less than 50% reduction in pain at twelve months. Conflictingly, moderate evidence suggests distress is not associated with RT, but kinesiophobia and catastrophisation are. However, this may not lead to a suboptimal outcome. Limited evidence exists linking psychological variables and AT and PT, but current evidence suggests PT is not associated with anxiety or depression and kinesiophobia may be linked with suboptimal outcomes in AT.

Tendinopathy requires an individualised approach to management. As such, when a person is suspected to have tendinopathy, clinicians should consider using validated screening tools for the presence of psychological variables which may contribute to suboptimal outcomes. Management to address the presence of specific variables would need to be tailored for the individual's circumstances, but consideration should be given to providing neuroscience education and addressing cognitive behavioural barriers.

STATEMENTS

Competing interests: There are no competing interests

Contributorship: All authors listed have made substantial contributions to the conception, design, acquisition, analysis and interpretation of data. All authors have revised it critically for important intellectual content and approved the final version. In doing so, we agree to be accountable for all aspects of the work.

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