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Commentary

Could titin have a role in strain-induced injuries?

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It has been known for some time that strain injuries occur through the excessive lengthening of a muscle.[1–3] However, the precise mechanism for strain injury remains elusive and has been the subject of recent debate in the *Journal of Sport and Health Science*,[4–9] but it seems sensible to consider mechanisms at the level of the muscle fiber. It was previously believed that damage was the result of non-uniform stretching of sarcomeres on the descending limb of the length–tension curve, with the weakest sarcomeres undergoing the greatest deformation and ultimately damaging the myofibril.[10] This non-uniform lengthening was also believed to explain the residual force enhancement observed during lengthening contractions, as the rapid lengthening of some sarcomeres gives rise to passive tension whilst allowing the remaining sarcomeres to operate closer to their optimal length.[11] While it has been shown sarcomeres do lengthen non-uniformly, it does not appear to be dependent on the strength of the sarcomere.[12] Furthermore, the increase in sarcomere length non-uniformity after active stretching is not correlated to the residual increase in force ($r = -0.309$).[12] Although this does not disprove the notion that sarcomere lengthening is responsible for muscle damage and injury, it does contradict the idea that the weakest sarcomeres lengthen first as suggested by the sarcomere popping theory.[10]

An alternative explanation is the winding filament theory, which proposes titin binds to actin upon the presence of calcium, in turn reducing titin's "free length".[13] Therefore, the strain placed on titin, and its associated contribution to force, is greater for an absolute increase in length. In the absence of calcium (passive stretch), titin does not bind to actin and has a greater free length.[13] Thus, whilst the increased force from titin during active contractions may be useful in an isolated event to prevent further lengthening, it may also accumulate muscle damage due to the excessive lengthening of the unbound or free part of titin. Furthermore, after a bout of eccentric exercise the content of titin in a myofibril is depleted, most likely due to direct damage to titin and removal by proteolysis.[14] Considering that titin also helps stabilize myosin in a sarcomere,[15] any damage to titin could also potentially leave myosin vulnerable to deformation and possibly injury. Indeed, it has been demonstrated that maximally stimulated fibers require just a 30% increase in length for injury to occur whereas passively stretched fibers can reach up to a 50% increase in length before injury.[16]

Greater fiber strain is observed in contractions initiated at longer lengths compared to those initiated at shorter lengths ($p < 0.002$),[17] which is believed to increase injury risk. However, we propose the strain placed on titin should also be considered, which might be greater in contractions initiated at shorter muscle lengths. Indeed, when the absolute lengthening is equal between groups, the stimulation of a muscle preceding lengthening results in greater reductions in peak torque after a bout of eccentric exercise ($p = 0.003$),[17] which suggests greater muscle damage. In theory, the stimulation of a muscle preceding contraction would bind titin to actin earlier, placing more strain on titin during lengthening and may explain the greater muscle damage. Although further reductions in peak torque are observed in contractions initiated at longer lengths, this is likely due to the absolute muscle length also being greater. This observation also explains why peak torque during an exercise bout is larger in contractions initiated at long compared to short muscle lengths ($p > 0.05$).[17]

It has been observed that sprinters suffer injuries to the bicep femoris (BF) long head (active contraction),[18] whereas dancers, performing movements such as the splits,[19] often suffer injuries to the semimembranosus (SM) (passive contraction).[20] In passive conditions, the BF may have greater extensibility, which leaves the SM vulnerable to injury, but in active contractions, the BF may become the shortest due to the shortening of titin when titin binds to actin. Perhaps the extensibility of titin under active conditions is a risk factor for hamstring strain injuries. Indeed reduced active flexibility appears to be a risk factor for hamstring strain injuries,[21] which is in contrast to passive measures of flexibility.[22] Interestingly, the length of the muscle (fascicle length) should not differ between active and passive contractions and so a variable that is mediated by active contractions, such as titin, is likely responsible for this finding. Furthermore,

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it appears that the isoform of titin alters and becomes stiffer with age, resulting in larger passive tension ($p < 0.05$), independent of collagen.[23] This may be part of the reasons older athletes are more susceptible to hamstring strain injuries.[24]

Continuing with the specific case of the hamstrings, isokinetic testing of hamstring eccentric strength is a weak risk factor for injury (odds ratio = 1.37; $p = 0.04$);[25] yet, strength measured during the Nordic curl (an eccentric movement) is a much stronger risk factor (relative risk = 2.9; $p = 0.01$).[26] It would be logical to assume that isokinetic tests may be a more specific tests of hamstring injury risk due to the longer muscle lengths used (hip in 90° flexion and knee achieving full extension)[25] compared to the Nordic curl (typically 50° joint amplitude with hip in neutral);[27] yet this is not the case. Tests at short muscle lengths may be a measure of eccentric strength from the active component of the sarcomere, which may be more meaningful for injury prevention. At long muscle lengths, the role of structural components such as titin may increase torque production.[13] Future research should determine whether passive tension, for which titin is believed to be a large contributor, in the hamstrings is a risk factor for injury. In essence, strain injuries could be dependent on not only the strain experienced by the muscle but also the contraction type and the length contraction it is initiated from.

It is acknowledged this would be a complicated hypothesis to test directly with respect to occurrence of hamstring strain injuries. However, we would expect to observe greater muscle damage in the hamstrings from contractions that are initiated at shorter muscle lengths than contractions that are initiated at longer lengths, provided that the absolute lengthening of the muscle is equal. Furthermore, it would be expected that strength toward the end of the range of motion would be greater in contractions initiated at short lengths possibly due to titin's greater contribution.

Authors' contributions

CP conceived of the idea and wrote the initial draft; JS and KN provided feedback and assisted with the completion of the manuscript. All authors have read and approved the final version of the manuscript, and agree with the order of presentation of the authors.

Competing interests

The authors declare that they have no competing interests.

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