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Editorial Comment

Neuro-musculoskeletal interactions in bed rest, hibernation and stroke

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News from people who stay in bed long

While the idea to 'stay in bed all day' is intuitively appealing when the alarm goes off in the morning, staying there for a consecutive 56 days is not everyone's notion of a good time. A horizontal lifestyle comes with many inconveniences, and a loss in muscle mass is not the least of them. Surprisingly, however, nobody seems to have examined which muscles waste away fastest, until Belavy et al. looked into the matter[1]. These authors measured the cross-sectional area of individual lower extremity muscles during 8 weeks of strict bed rest and found striking differences between muscles. Atrophy proceeded most rapidly in the medial gastrocnemius, soleus and vastii muscles, but was much slower in the ankle dorsiflexors and anteromedial hip muscles. Muscles thus are not only weaker but also imbalanced after prolonged bed rest. The authors speculate that this issue could be addressed by a targeted training program.

When muscles waste, bones are usually not long to follow. Stay in bed for three days and your bone resorption markers start to increase[2]. After just a few weeks more, bone mass is measurably on the decline. This bone loss is faster and larger in the epiphyses than in the diaphyses, which is because epiphyses contain a lot of trabecular bone whereas diaphyses are made up of cortical bone. That is at least what everyone said until Rittweger et al. started to poke a hole into this explanation[3]. These authors found that it is cortical rather than trabecular bone that gets lost in the epiphyses of bed-resting people. They think that epiphyseal cortex is lost faster than diaphyseal cortex because its larger endocortical surface makes it more vulnerable to osteoclast attack. If so, they argue, skeletal sites where the bone is large and the cortex thin should receive 'specific clinical attention'.

What kind of specific clinical attention might help those wasting muscles and bones is not immediately obvious from this paper. However, a few publications later, the same authors become more explicit: Their preferred mode of clinical attention is 'resistive vibration exercise'[2,4]. In a randomized study they observed that resistive vibration exercise during bed rest restricted the increase in bone resorption markers and boosted bone formation markers. It also inhibited the loss of lower extremity lean mass and bone mass, whether measured by dual-energy X-ray absorptiometry or by peripheral quantitative computed tomography. The study design did not allow deciding whether these beneficial effects were due to the resistive or the vibration component of the resistive vibration exercise. To find an answer to this question, more people will have to populate the beds of the authors' laboratory.

Why not hibernate altogether?

Lying still for 8 weeks may sound like an awfully long time, but if you were a bat or an ursus arctos horribilis (also known as grizzly bear), you would probably consider it a piece of cake. These species spend 3 to 6 months per year in almost motionless torpor. Why do they not lose their muscle and bone mass? Lee et al. think that bats do not lose muscle mass during hibernation because they periodically wake up for a few hours and start shivering[5]. This shivering activity is violent enough to increase muscle temperature from 5ºC to 35ºC within half an hour and to activate anabolic pathways in muscle cells. As catabolic pathways remain at a low level throughout the hibernation period, these bouts of shivering exercise ensure that bats make it through the winter in good shape.

Hibernating grizzly bears apparently maintain their cortical and trabecular bone mass by slowing down bone turnover, as new histomorphometric studies by McGee et al. demonstrate[6,7]. You do not see grizzly bear histomorphometry every day, so histomorphometry aficionados should definitely throw a glance at these studies. Intracortical activation frequency is down by 75% in hibernating bears. Due to this decreased intracortical remodeling activity, hibernating bears have lower cortical porosity than active bears. In trabecular bone, remod-

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eling activity seems to be similarly decreased, as both formation and resorption indices are low. In both cortical and trabecular bone, the remodeling balance is apparently zero, so no bone gets lost. This is different from acute disuse osteoporosis, where bone turnover is high and remodeling balance is negative. So do grizzly bears hold the key to the prevention of disuse osteoporosis, as McGee et al. propose? Perhaps, but there is a little caveat: Hibernation comes with a low body temperature. Treatments of disuse osteoporosis that require lowering body temperature to around 30ºC may not find many takers.

Bone resorption before and after stroke

The skeletal effects of stroke are an important example of neuro-musculo-skeletal interactions. It appears though that most people who study this topic have yet to discover JMNI, as manuscripts submissions on 'stroke and bone' are few and far between. Nevertheless, it is clear that acute stroke leads to inactivity and disuse, and so bone density is expected to decrease in the presence of sluggish bone formation and vigorous bone resorption. The first histomorphometric study on stroke patients has just appeared and describes this expected pattern of bone metabolism[8]. However, another study by Szulc et al. shows that elevated bone resorption is not necessarily the consequence of stroke but may actually precede it[9]. In a longitudinal study these authors observed that men who subsequently suffered a stroke had elevated markers of bone resorption at baseline. Presumably, there are underlying factors that increase both bone resorption activity and the incidence of stroke, even though the nature of these factors remains in the realm of speculation for now.

As bone density decreases after stroke and fracture rates increase, it is intuitive to connect the dots and to conclude that it is the post-stroke bone loss that leads to fracture. However, a new study on fracture epidemiology after stroke casts some doubt on this conclusion. Pouwels et al. had a large enough study population to assess the time course of hip/femur fracture after stroke[10]. They found that the risk of hip fracture was highest in the first three months following stroke. Thereafter, fracture risk diminishes even though bone density keeps decreasing. Thus, it is hard to blame the observed pattern of fracture risk on the low bone density. The propensity for falls seems to be a more plausible explanation.

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