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**Recent Literature Review**

# What is new in neuro-musculoskeletal interactions?

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## Bye-bye, density?

Imagine an extraterrestrial bone scientist whose knowledge about earthly affairs stems from reading clinical literature. She/he might be excused for coming up with the following synthesis: "The skeleton is a soup of more or less dense mineral. Its purpose is to serve as a target organ for hormones". Yet, some signs for change are on the horizon, as clinical researchers are rediscovering the fact that bones actually have a structure that is somehow related to mechanical requirements.

You do not need sophisticated equipment and still make it into the New England Journal of Medicine with this insight. Ahlborg and colleagues used old-fashioned single-photon absorptiometry to analyze the distal radius in 108 postmenopausal women[1]. After 15 years of annual measurement, they discovered that bone mass decreased and bone diameter increased with time. "Well, young man", you might say, "I have known this even before you were born. Smith and Walker have shown periosteal expansion for the femur in 1964, and Garn for the second metacarpal a couple of years later[2,3]. So what's the news here?" According to the authors, the new thing is that this is a longitudinal study and that they not only looked at outer bone size, but also at the inner surface of the cortex. This enabled them to calculate a "strength index", which they say is similar to Ferretti's bone strength index[4]. This strength index decreased with time and was associated with the occurrence of radius fractures.

Curiously, Ahlborg et al. do not refer to Tom Beck's work, who has published similar data for the proximal femur. His hip structural analysis program has been applied to a number of large DXA-based longitudinal studies[5-7]. In the latest of these it is reported that the femoral neck expands more rapidly in elderly women than in men[7]. This periosteal expansion is interpreted as an effort to maintain bone strength in the face of endocortical bone loss. Larger bones should be stronger bones, so why do women have a higher incidence of hip fracture than men? The authors propose that the compensatory periosteal expansion has its limits. When cortical thickness decreases below a certain point, the cortex will become unstable due to buckling, leading to catastrophic structural failure.

Thus, it looks like 'strength' and 'structure' are becoming the new buzz words in the field, even though the demise of the bone density paradigm is not for tomorrow. Yet, some day analysts may refer to Beck's and Ahlborg's work when they say: "This was when the bone density bubble started to burst."

## Falls or no falls, this is a neglected question

Bone researchers like to think of fractures primarily as a consequence of weak bones, no matter whether they prefer to talk density or structure (unpublished observation). For example, several high-profile publications have shown that vitamin D and calcium supplementation reduce the incidence of nonvertebral fractures in elderly persons, an effect that was of course attributed to changes in BMD[8,9]. The sober truth is that bones are only part of the story. The other part is the event that leads to the fracture, typically a fall. Vitamin D clearly has an influence on muscles, so could the vitamin D-associated decrease in fracture rates not simply be explained by fewer falls? Bischoff et al. pursued this idea in a double-blind trial of 122 long-stay geriatric care patients[10]. Participants received either 1200 mg of calcium alone or the same amount of calcium plus 800 IU of vitamin D. During the 3-month treatment period, women receiving vitamin D had 49% fewer falls than women on calcium alone. They also had better "overall musculoskeletal function". Thus, future fracture studies might benefit from giving a serious consideration to factors associated with fall rates.

These results fit in nicely with data from the Nurses Health Study[11,12]. In an 18-year prospective analysis of 72,327 postmenopausal women Feskanich et al. found that women consuming more than 500 IU of vitamin D had a 37% lower risk of hip fracture than women who consumed less than 140 IU. Calcium intake had no effect on hip fracture incidence.

Eating vitamin D evidently is not the only way to prevent hip fractures. In another analysis of 12-year longitudinal data

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from more than 60,000 participants of the Nurses Health Study, the same authors evaluated the effect of walking and leisure-time activity on hip fracture risk. The most interesting result perhaps was that walking for at least 4 hours per week was associated with a 41% lower incidence of hip fracture, compared with walking for less than 1 hour per week. But note that you have to keep walking to enjoy the protective effect. Hip fracture risk increased among women who were actively exercising at first but then became sedentary.

## Good vibrations?

"Those new whole-body vibration plates, doctor, are they good for my health?" A simple question begs for simple answers, but as is true more often than not, things become confusing when you look at them closely. "Vibrations? It all depends" is the correct response. "What frequency, amplitude and duration are you talking about? Vertical or angular movements? With or without extra weight or additional exercise?" Even researchers who use similar settings in healthy people do not agree on what they find. Does a single whole-body vibration session make muscles more powerful? Some believe so[13], others don't[14,15]. De Ruiter et al. found no beneficial effect of vibration on the maximal isometric force or maximal rate of force rise. Quite to the contrary, these parameters decreased after the vibration session and took more than 3 hours to normalize thereafter. This negative result was to be expected anyway, the authors write, because "it is difficult (...) to see, how whole-body vibrations would lead to (...) enhanced performance."

Torvinen and colleagues looked at the effects of an "8-month vertical whole body vibration" program[16]. No worries, despite the title of the paper, the young and healthy study subjects did not have to vibrate for an uninterrupted eight months, but rather for 4 minutes per day, 3 to 5 times per week, for eight months. Peripheral quantitative computed tomography of the tibia did not reveal any changes in mass, structure or estimated bone strength during this time. The only measurable effect was an 8% higher vertical jump height. As the authors dryly comment, apparently "the musculoskeletal tissues of these young adults had no particular physiological need to adapt themselves to this kind of loading."

## Reported sex differences an artifact?

One of the most often cited papers on muscle-bone relationships is an article by Schiessl et al. where the authors replotted published Argentinean reference data for total body bone mineral content and lean body mass in children and adolescents[17,18]. This revealed that prepubertal boys and girls had a similar relationship between bone mineral content and lean body mass, whereas postpubertal girls for a given level of lean body mass had a higher bone mass than boys. The authors took this as an indication that estrogen lowers the modeling threshold on internal bone surfaces, thus making those bone surfaces more sensitive to mechanical strain in girls. No way, such conclusions are "unwarranted", say Tothill and Hannan[19]. They compared total body DXA data from a number of publications and detected that the Argentinean study had "unusual" soft tissue results which differed from the other European and North American studies. Schiessl et al. thus had based a new concept of bone development on an artifact? As the plot thickened, Wang et al. set out to resolve the question in a rat study[20]. They measured bone mineral content of the L4 vertebra and the cross-sectional area of surrounding muscles by peripheral quantitative computed tomography (pQCT). They found that from 1 to 6 months of age bone mineral content increased faster in females than in males with similar muscle cross-sectional area. At maturity, female rats therefore had more bone mass per muscle cross-sectional area than male rats. By the way, we had similar findings in a pQCT study on human forearm development[21]. So, whatever there may be unusual about that Argentinean paper, the conclusions derived from it can be supported by other data as well.

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