Letters

Link between brain and bone

Congratulations Mughal and colleagues for the excellent study on the underestimated crosstalk between bone and brain in the orthogeriatric setting (*AJGP* January–February 2019).[1] In the introduction, the authors named the direct costs related to osteoporosis in Australia at $1.9 billion per year. However, this amount was estimated for the financial year 2000–01. In 2017, the annual total direct healthcare system cost of osteoporosis in Australia was $3.44 billion.[2] General practitioners (GPs) should know these current costs. And considering that the total annual direct cost of dementia is expected to reach $9.6 billion in Australia in 2019 (plus $5.9 billion in indirect costs of dementia),[3] the relevant bidirectional interplay between osteoporosis and dementia as well as the implications for GPs identified by the authors take an even greater significance.

The following shared/intermediate risk factors were evaluated for both common degenerative diseases in the elderly population: ageing, female sex, lack of physical activity and mobility, falls, genetic susceptibility factors (eg apolipoprotein E4 allele – a major cholesterol carrier), lower vitamin K levels, vitamin D/calcium deficiencies and oestrogen or androgen deficiency.[4,5] As a potential driving mechanism for bone loss in Alzheimer's disease pathogenesis, a systemic dysfunction of signalling in the complex canonical Wnt (wingless-type mouse mammary tumour virus integration site)/beta-catenin pathway has also been discussed in recent years. The complex Wnt signalling plays a fundamental part in the regulation of cellular function in most tissues – including the maintenance of homeostasis of the bone and brain (eg facilitating bone formation in bone tissues, promoting synaptogenesis and neurogenesis in the brain).[4,5] Furthermore, the exercise-induced myokine irisin and its membrane-bound precursor protein, fibronectin type III domain-containing protein 5, appear to have an important interconnected mediator function in age-related bone loss and Alzheimer's disease–associated neurodegeneration.[4] Some examples: irisin stimulates new bone formation, enhances brain-derived neurotrophic factor gene synthesis and release, protects the nervous system by facilitating hippocampal proliferation and suppressing amyloid-beta aggregation, and stimulates Wnt/beta-catenin signalling through downregulation of sclerotin (a Wnt pathway inhibitor).[4,6,7]

Among the pathophysiological brain–bone interactions, a recent Australian review by Yuan et al also discussed bone-related modulators that may influence the progression of Alzheimer's disease: bone-derived cellular secretory proteins including osteocalcin, osteopontin and sclerostin, as well as bone marrow–derived cells including microglia-like cells, hematopoietic stem cells and mesenchymal stem cells.[5] Further studies are urgently needed to bring more scientific evidence into the complexities of this age-related brain–bone comorbidity and – hopefully as soon as possible – more prevention into clinical practice.[4–7]

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References

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Retraction

Dixon AJ, Steinman HK, Nirenberg A, Anderson S, Dixon JB. Cutaneous melanoma: Latest developments. Aust J Gen Pract 2019;48(6):349–53.

Dixon AJ, Steinman HK, Nirenberg A, Dixon ZL, Anderson S, Dixon JB. Management of invasive melanoma. Aust J Gen Pract 2019;48(6):368–72.

These articles have been retracted by the *Australian Journal of General Practice* for the following reason: A Letter to the Editor from Professor John Thompson, Melanoma Institute, reported that these articles contained a large number of factual errors that undermined the reliability of the overall articles. After consultation with our expert independent advisory panel, we have decided to retract both articles. Pending publication of an updated version, we refer readers to the published Australian guidelines for clinical practice for the diagnosis and management of melanoma (https://wiki.cancer.org.au/australia/Guidelines:Melanoma).