

Exercise, by the Evidence

Recent research on the brain, mood, immunity, muscle and the molecular signals between them. A thirty-minute review for clinicians.

October 2026



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Brain and cognition

01

Exercise and cognition across 2,724 trials



Standardised mean differences from 133 systematic reviews covering 2,724 randomised trials and 258,279 participants of all ages. Benefits held across healthy and clinical populations.

45%

of dementia cases worldwide are attributable to 14 modifiable risk factors, by the 2024 Lancet Commission's estimate. Physical inactivity carries a relative risk of 1.4 and is now classed as a midlife factor, alongside depression, diabetes and smoking.



The EXERT trial in MCI

- 296 sedentary adults with amnesic MCI, randomised for twelve months.
- Aerobic exercise or stretching and balance: neither arm declined.
- No inactive control, so aerobic intensity alone cannot be credited.



Mood and depression

02

Exercise modalities for major depression



Walking, jogging, yoga, and strength training reduced depressive symptoms compared with active controls. Confidence in the estimates was low to very low. Hedges' g, 218 randomised trials, 14,170 participants.



Intensity, severity and tolerability

- Effects were larger when exercise was vigorous.
- Equally effective with or without comorbidity, at any baseline severity.
- Yoga and strength training were the best tolerated.

Immunity and inflammation

03

The ageing immune system

- Fewer CD14^{low} CD16⁺ inflammatory monocytes, with lower TLR4 expression.
- More NK-cell activity and T-cell proliferation; less Th17 skewing.
- Stronger influenza-vaccine antibody responses in regularly active men.





“We found that exercise induces a mild local inflammatory response and, at the same time, accumulation of Tregs to control the inflammation.”

— Diane Mathis, Harvard Medical School, on
Langston et al., Science Immunology, 2023

Exercise-mobilised lymphocytes

- One bout mobilises effector lymphocytes via β 2-adrenergic signalling; in mice this curbed lymphoma via NK cells.
- In older adults, moderate exercise activated classical monocytes; intense exercise raised CD56^{bright} NK cells.
- Exercise-mobilised donor lymphocytes are in early clinical trials for allogeneic cell therapy (NCT06643221).



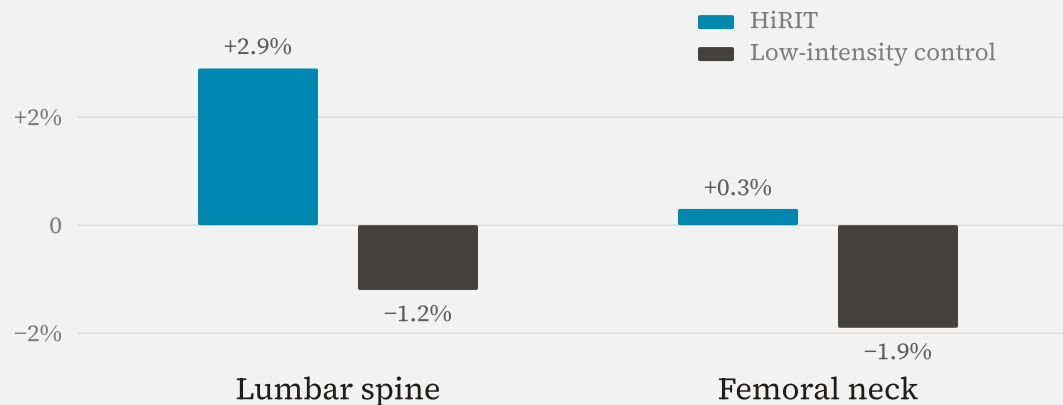
Muscle, bone and ageing

04

Heavy resistance training at retirement age

ARM	ONE-YEAR PROTOCOL	ISOMETRIC LEG STRENGTH AT FOUR YEARS
Heavy resistance training	Supervised full-body lifting, three sessions a week	Maintained: 149.7 → 151.5 Nm
Moderate-intensity training	Body-weight and band circuits, three sessions a week	Declined
Control	Usual activity	Declined

Bone density under load



Change in bone mineral density over eight months in 101 postmenopausal women with low bone mass; HiRIT was twice weekly, 30 minutes, supervised.

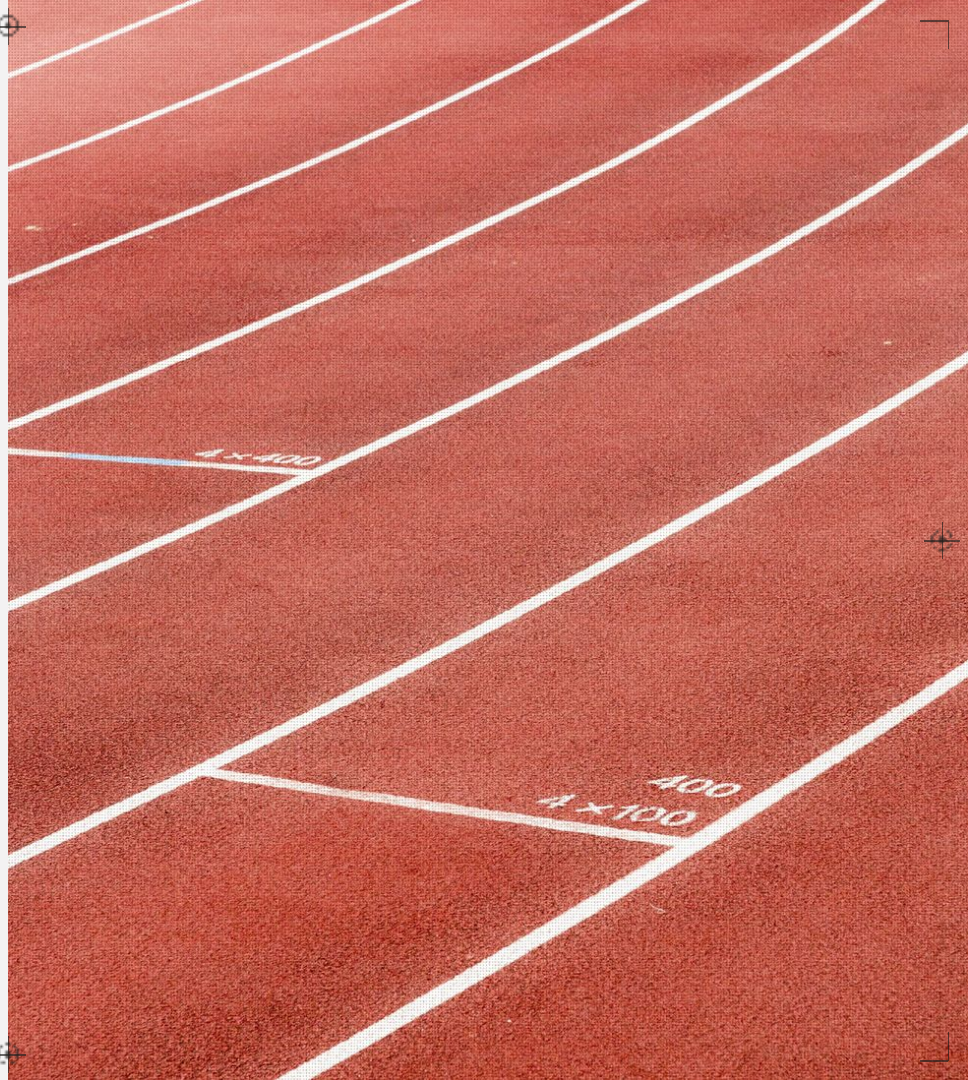


Molecular mechanisms

05

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tissues profiled by the Molecular Transducers of Physical Activity Consortium across eight weeks of treadmill training in male and female rats: 9,466 assays on 25 molecular platforms, showing shared, tissue-specific and sex-specific changes in immune, metabolic, stress-response and mitochondrial pathways.



Exerkines, the signals between organs

EXERKINE	REPORTED ACTION	STUDY
Irisin (FNDC5)	Raises hippocampal BDNF in mice	Cell Metabolism, 2013
Cathepsin B	Tracks running-induced memory gains	Cell Metabolism, 2016
Lac-Phe	Suppresses feeding and obesity in mice	Nature, 2022
Platelet factor 4	Restores cognition in aged mice	Nature Communications, 2023

Open questions

- Publication bias: an earlier umbrella review saw the exercise–cognition effect fall from $d = 0.22$ to 0.05 after correction.
- Comparators: in EXERT both the exercise and stretching arms held steady, so the control condition shapes the conclusion.
- Translation: a 2025 rodent multi-omics analysis found brain-targeting exerkines unchanged in brain tissue after exercise.

Summary for practice

Cognition

Exercise improves general cognition, memory and executive function across ages and conditions; effects are small to moderate.

Immunity

Regular activity lowers inflammatory monocytes and preserves NK- and T-cell function in older adults.

Depression

Walking, jogging, yoga, and strength training reduced depressive symptoms compared with active controls. Confidence in the estimates was low to very low.

Muscle and bone

Heavy resistance training around retirement preserves leg strength for years; high-intensity loading raises lumbar spine density.

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Thank you

Questions and discussion.

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