



Reduced sensorimotor lactate concentration and improved sleep efficiency following resistance training in older adults

Selin Scherrer¹ · Sven Egger¹ · Xinyu Liu² ·
Anna Zoé Wick¹ · Björn Rasch¹ · Lijing Xin² ·
Benedikt Lauber¹ · Wolfgang Taube¹

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Abstract As populations age worldwide, pathological neurodegeneration with subsequent cognitive decline has emerged as a pressing public health challenge. As effective treatments remain limited once neurodegeneration has occurred, prevention and delay of decline onset are crucial. While physical exercise is associated with improved cognition, exercise-specific mechanisms remain unclear. We therefore examined the effects of 12 weeks explosive lower-body resistance training (RT) in community-dwelling older adults on proposed markers associated with brain metabolism and sleep. Thirty-six participants (64–81 years) completed pre and post assessments consisting of sensorimotor lactate and N-acetylaspartate (NAA) levels via 7 T magnetic resonance

spectroscopy (analyzable lactate data: $n=24$; NAA: $n=32$), objective sleep architecture with wearable polysomnography ($n=34$), and subjective sleep quality of the recorded nights with the revised sleep questionnaire A ($n=25$) as well as of the preceding 4 weeks with the Pittsburgh Sleep Quality Index ($n=36$). Participants were assigned to RT (3 sessions per week) or a control group (CON; maintaining lifestyle). After significant Group $\times$ Time interactions via repeated-measures ANCOVA with sex as covariate, paired t -tests revealed that RT significantly ($p < 0.05$) reduced resting lactate concentration ($d=0.78$), improved objective sleep efficiency ($d=0.75$), and prolonged total sleep time ($d=0.61$). Our findings suggest that resistance training may be particularly beneficial for older adults experiencing fragmented sleep and impaired neural oxidative metabolism.

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S. Scherrer (✉) · S. Egger · B. Lauber · W. Taube
Department of Neuro- and Movement Sciences, University of Fribourg, Boulevard de Pérolles 90, CH-1700 Fribourg, Switzerland
e-mail: selin.scherrer@unifr.ch

X. Liu
Laboratory for Functional and Metabolic Imaging (LIFMET), Ecole Polytechnique Fédérale de Lausanne, CH-1015 Lausanne, Switzerland

X. Liu · L. Xin
CIBM Center for Biomedical Imaging,
CH-1015 Lausanne, Switzerland

X. Liu · L. Xin
MR Imaging and Technology, Ecole Polytechnique Fédérale de Lausanne (EPFL), CH-1015 Lausanne, Switzerland

A. Z. Wick · B. Rasch
Department of Psychology, University of Fribourg, CH-1700 Fribourg, Switzerland

L. Xin
Institute of Physics, École Polytechnique Fédérale de Lausanne, CH-1015 Lausanne, Switzerland

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Introduction

As the worldwide population ages, pathological neurodegeneration has become a major public health concern [1]. Progressive degeneration of the nervous system leads to cognitive decline resulting in reduced independence, impaired quality of life, and substantial economic costs for the individual, their family, and society. Neurodegenerative diseases affect more than 57 million people worldwide, with dementias like Alzheimer's disease being the most prevalent form [2].

Because effective therapies remain limited once neurodegeneration is established, prevention or at least onset delay has become central to public health strategy [3]. Notably, projection models demonstrate that delaying dementia onset by 5 years could result in saving more than \$500,000 per patient in the USA [4]. Lifestyle factors associated with healthy cognitive aging include regular physical activity, cognitive stimulation, social participation, and smoking abstinence, among others [5]. Among these, physical activity is the only lifestyle factor consistently included in brain health recommendations across major health organizations [for an overview, see 3]. This is supported, for instance, by a review of Sofi et al. [6] that included prospective studies of healthy participants and reported a significant risk reduction of cognitive decline. Compared to sedentary participants, high levels of physical activity reduced cognitive decline by 38% and low-to-moderate levels of physical activity by 35%. This reduced risk of cognitive decline aligns with evidence showing that physical activity supports several factors relevant to brain health, including a reduction in cardiovascular risk factors like hypertension, a decrease in brain volume loss, or an increase in neuronal growth factors [for review, see 3]. However, most studies refer to "physical activity" in general and do not distinguish between the specific effects of different, targeted exercise interventions. Clearly identifying which exercise modalities influence which dimensions of brain health, and in what ways, is essential for enabling

individualized and precise exercise recommendations as preventive medicine.

Resistance training represents an exercise modality with well-documented positive effects on cognitive function in healthy older adults [7]. In older adults with mild cognitive impairment (MCI), a condition associated with greater risk of dementia, resistance training appears to be particularly effective for improving global cognition [see umbrella review 8]. However, the specific neural processes underlying the beneficial impact on brain health remain incompletely understood.

Elevated brain lactate concentrations have emerged as a valuable biomarker for detecting altered brain energy metabolism [9]. Disrupted brain metabolism is a key driver of cognitive decline, and mitochondrial dysfunction plays a central role in the pathogenesis of Alzheimer's disease [10]. In older adults, mitochondrial dysfunction likely contributes to lactate accumulation by shifting metabolism toward glycolysis and reducing lactate utilization [11, 12]. Consequently, healthy older adults demonstrate higher resting-state lactate levels compared with younger adults, and adults with Alzheimer's disease display even greater concentrations compared with age- and sex-matched cognitively unimpaired controls [9]. Pre-clinical work suggests a positive effect of exercise on the brain lactate biomarker, as prolonged exercise has been shown to increase oxidative metabolic capacity in the motor cortex of rodents [13]. In humans, transient exercise-induced lactate elevation increases mitochondrial function through lactylation processes [14]. This mechanism might also occur in the brain, where exercise induces lactate elevations through lactate transport across the blood–brain barrier [15]. However, it remains unclear whether resistance training decreases resting brain lactate levels in humans.

A second biomarker relevant to neurodegeneration is N-acetylaspartate (NAA), one of the most prominent metabolites in the brain with diverse functions and close association with cognitive function [16]. NAA concentration declines with age and is especially reduced in patients with dementia [17, 18]. Aerobic exercise has been linked to increased NAA levels, and recent work suggests that 3 months of resistance training may mitigate declines in sensorimotor NAA levels in older adults [19, 20].

Sleep improvement represents another promising target to mitigate cognitive decline [21]. In their

recent meta-analysis, Wei et al. [21] showed that objective sleep parameters such as total sleep time (TST) and sleep efficiency (SE) were significantly worse in adults with MCI compared to healthy adults. Furthermore, participants with MCI showed less rapid eye movement (REM) and slow-wave sleep (SWS), while spending more time in light non-rapid eye movement sleep (N1). In a prospective study, wakefulness after sleep onset (WASO) showed a strong association (odds ratio=1.43) with increased cognitive decline 5 years later [22]. In this context, resistance training emerges as a promising intervention, as a 12-week resistance training program induced increased SE and reduced WASO in older adults living in an assisted facility [23]. However, the effect of resistance training on sleep in community-dwelling older adults remains unclear.

Herein, we investigated the effects of a 12-week explosive lower-body resistance training on relevant markers of cognitive decline in community-dwelling older adults. We assessed whether the training would (i) reduce resting lactate concentration and (ii) mitigate NAA decline in the sensorimotor cortex via 7 T magnetic resonance spectroscopy (MRS). We further assessed whether resistance training would (iii) improve sleep efficiency and other objective sleep measures assessed with wearable polysomnography (PSG), (iv) short-term subjective sleep quality (sSQ) of the PSG-recorded night with the revised sleep questionnaire A (SF-A/R), and (v) long-term sSQ over the preceding 4 weeks with the Pittsburgh Sleep Quality Index (PSQI).

Methods

Participants

We recruited 40 volunteers aged 64 to 81 years and randomly allocated them to either the resistance training group (RT) or the control group (CON). Randomization was performed using the online randomization tool randomizer.org with simple allocation. Participants and study personnel only knew about group allocation after PRE tests. Given the nature of the intervention, participants and study personnel could not be blinded to group assignment after PRE tests. Interested people who reacted to our newspaper advertisements were invited to an information

session, where they were provided with more detailed information about the study procedures, screened for exclusion criteria, and where they confirmed availability for the required time commitment. Participants were free of any known sleep disorder, depression/anxiety, neurological and orthopedic diseases, and injuries as well as contraindications to MRS and did not take any medication affecting sleep. The participants were financially compensated in accordance with the guidelines of the ethics commission. The study was performed in accordance with the Declaration of Helsinki, except for pre-registration in a publicly accessible database. All procedures were approved by the local ethics committee (Commission cantonale d'éthique de la recherche sur l'être humain (CER-VD); ID: 2021-00378). Participants provided written informed consent before preparation for the adaptation night.

Two participants per group had to drop out before POST tests because of health or personal reasons (Fig. 1). An overview of analyzable sample sizes per outcome can be found in supplementary material (Table S1).

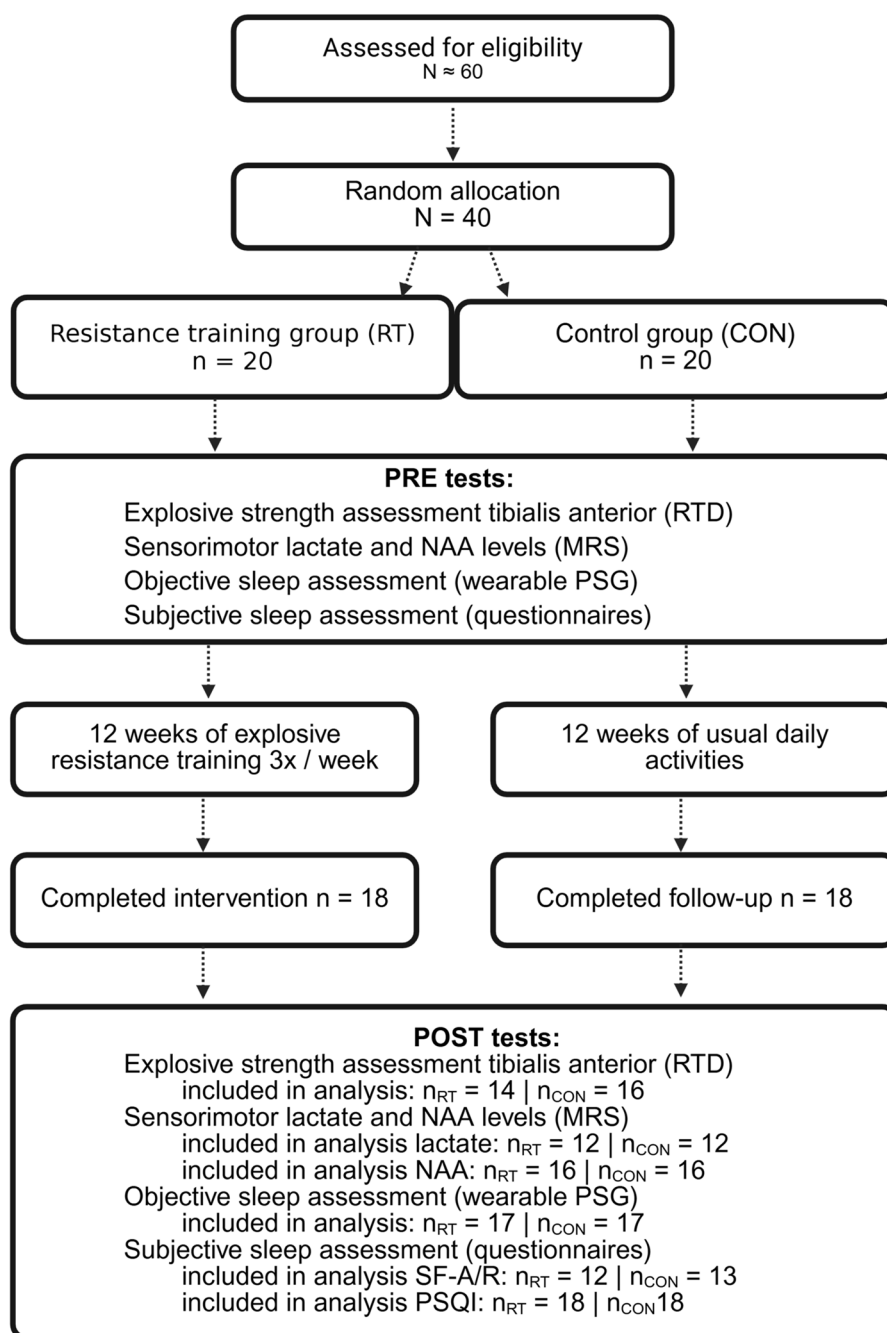
Study design

The study design comprised PRE tests, followed by a 12-week intervention period, and was terminated by POST tests (Fig. 1). PRE and POST tests assessed explosive strength performance, lactate, and NAA levels in the left sensorimotor cortex, and both objective SE and sSQ. During the intervention, the RT group completed a supervised lower-body resistance training program, while the CON group maintained their regular lifestyle. To monitor physical activity in the CON group throughout the study, participants reported exercise frequency (sessions per week), weekly exercise duration, and activity type(s) at PRE and POST. Participants were asked to avoid vigorous activity on the days of MRS or PSG assessment and the interval between the final training session and the POST tests ranged from 1 day to 1 week.

Explosive lower-body resistance training

Participants in the RT group attended three resistance training sessions per week, totaling at least 30 sessions within 12 weeks. The training was conducted in groups and supervised by a certified personal coach

Fig. 1 Study design. Following the study process from top to bottom with N showing the number of participants included in the corresponding step. RTD, rate of torque development; MRS, magnetic resonance spectroscopy; PSG, polysomnography; SF-A/R, one-night subjective sleep quality questionnaire; PSQI, Pittsburgh Sleep Quality Index



and students in movement sciences (one coach per 6 ± 3 participants). Each 45-min session included a warm-up, the main part, and a cool-down. The warm-up and cool-down together lasted approximately 15 min and the main part approximately 30 min. The main part focused on high-speed resistance training, as these interventions promote greater functional

improvements in older adults compared to exercises performed at slower velocities [24, 25]. Each session consisted of four exercises targeting the lower extremities, including one exercise each for ankle dorsiflexion (lying on the back with a resistance band attached to a wall bar and weight cuffs around the foot; seated with weights on foot), ankle plantarflexion (loaded

calf raises seated with weights on their lap; loaded calf raises in standing position with weights in a backpack), knee extension (barbell back squat; single-leg squat with weights in backpack), and knee flexion/hip extension (leg curl with weighted cuffs; loaded glute bridge). The two exercises per movement alternated between sessions to add variety. External training load was progressively increased through adjusting repetitions, sets, weight, or resistance and adding jump movements to provide optimal stimuli [26]. The first 3 weeks consisted of traditional training (1–3 sets of 10–15 repetitions, increasing resistance). Over the following 9 weeks, the training program comprised alternating sessions of explosive training (2–3×6–10 repetitions, contraction as fast as possible—hold shortly—slow eccentric movement back) and traditional training (2–3×8–12 repetitions, slow concentric and eccentric movement). The participants added weight cuffs or weight plates to increase the weight by 0.5 to 1 kg every week, depending on the exercise. The weight was reduced to the weight from 2 weeks prior for explosive movements. Participants and coaches individually regulated the training to reach RPE scores between 4 and 7 of 10 for each exercise. One-repetition maximum testing was not performed given time and safety considerations in this age group. Rest intervals between sets were 1–2 min. Attendance was recorded at each session by the supervising coach, and participants were supported in tracking their training content on prepared documents stored at the university.

Explosive strength performance assessment: rate of torque development

For the assessment of rate of torque development (RTD) during explosive isometric ankle dorsiflexion, the participant sat on an isokinetic dynamometer (Cybex Norm, HUMAC, CA, USA). The right foot was placed in a customized shoe directly bolted to the foot pedal of the machine and additionally attached with Velcro straps to achieve direct power transmission. Participants executed isometric ankle dorsiflexion in neutral zero position and were verbally encouraged to maximize peak RTD by contracting as fast as possible. After two familiarization trials, five maximal trials were executed with at least 15 s rest between trials [following the recommendations of 27]. Peak RTD was identified as the steepest 20-ms

interval on the rising torque-time curve using a 20-ms moving window. Valid trials were averaged for PRE to POST comparisons. Invalid trials (~15% of all trials), for example, due to changes in execution strategy (e.g., countermovement or upper body movement) were excluded from the analysis.

Quantification of lactate and NAA levels: ¹H magnetic resonance spectroscopy

Metabolite levels were measured in the left sensorimotor cortex, a proposed key region for metabolic changes after resistance training [13, 20]. Individuals were measured at the same time of day to ensure prevention of possible circadian effects [28]. MRS measurements were performed on a 7 T/68 cm Siemens Magnetom scanner (Siemens Medical Solutions, Erlangen, Germany) equipped with 80 mT/m gradients and with a single-channel quadrature transmitter and a 32-channel receiver coil (Nova Medical Inc. MA, USA). A high-resolution MP2RAGE [29] sequence was used to acquire 3D anatomical images for MRS voxel placement (voxel size=0.6×0.6×0.6 mm³, TR/TE=6000/4.94 ms, TI1/TI2=800/2700 ms, slice thickness=0.6 mm, field of view=192×192×154 mm³, acquisition time=10 min 8 s).

Metabolite spectra were acquired in the left sensorimotor cortex using the semi-adiabatic Spin Echo full Intensity Acquired Localized (sSPECIAL) sequence (TR/TE=4000/16 ms, average number=100, number of datapoints=2048, spectral width=4000 Hz, volume of interest=30×20×20 mm³) [30]. The outer volume suppression was interleaved with VAPOR water suppression [31]. MR spectra were averaged after frequency drift and phase correction using FID-A [32] and analyzed by LCModel [33] for quantification. An experimentally measured macromolecule spectrum and simulated spectra of the following 21 metabolites were included in the basis set for LCModel analysis: alanine (Ala), ascorbate (Asc), aspartate (Asp), creatine (Cr), γ -aminobutyric acid (GABA), glucose (Glc), glutamine (Gln), glutamate (Glu), glycerophosphorylcholine (GPC), glycine (Gly), glutathione (GSH), lactate (Lac), myo-inositol (mIns), NAA, NAAG, phosphocreatine (PCr), phosphorylcholine (PCho), phosphorylethanolamine (PE), scyllo-inositol (sIns), serine (Ser), and taurine (Tau).

A smooth spline baseline was included in the fit, with a minimum knot spacing (DKNTMN) of 0.25 ppm to account for residual broad background signals.

Metabolite concentrations were determined using the unsuppressed water signal as a reference. To account for inter-individual differences in tissue composition, all metabolite concentrations were corrected based on voxel tissue segmentation using SPM12 (<https://www.fil.ion.ucl.ac.uk/spm/software/spm12/>) and transverse (T_2) relaxation time and tissue-specific water concentration values [34]. Data of one person could not be analyzed because of heavy head motion, three individuals were absent from at least one of the MRS measurements, and for an additional eight individuals, lactate concentration could not be analyzed because of Cramér-Rao lower bound (CRLB) > 30%. To ensure that data quality was comparable between time points, we calculated water linewidth, signal-to-noise ratio (SNR) for all measurements, and performed statistical comparisons of linewidth, SNR, average CRLB and fractions of grey matter, white matter, and cerebrospinal fluid (CSF) using *t*-tests between PRE and POST measurements in both groups. Voxel placements were also visually examined during experiment to ensure consistency of location. The SNR is calculated by dividing the signal intensity of NAA by the noise between 9.5 and 10 ppm. In addition, visual inspection was performed to ensure comparable spectral quality for all PRE and POST measurements used for analysis.

Objective sleep parameters: wearable polysomnography

We assessed objective sleep architecture with wearable PSG devices (SOMNOtouch RESP, SOMNO-medics, Randersacker, Germany) at the participant's home. Participants had one adaption night to avoid the First Night-Effect, followed by one sleep recording at PRE and one at POST [35]. Participants refrained from caffeine from 2 pm on the experimental day and from alcohol for 2 days. Six single gold-cup electroencephalographic (EEG) electrodes were positioned according to the international 10–20 system (Fpz, Fz, Cz, Pz, M1, M2) [36]. Electromyographic (EMG) and electrooculographic (EOG) electrodes were attached following AASM recommendations [37]. Recorded data were processed using BrainVision Analyzer 2.2 (Brain-Products, Ing., GmbH). EEG recordings were

referenced to the average of the two mastoid signals and filtered according to AASM guidelines [37]. Recordings were segmented from “lights off” (i.e., when the participant attempted to sleep) to “lights on” (i.e., when the participant stopped trying to sleep). This interval corresponded to the participant's time in bed (TIB). Sleep scoring was performed by the deep learning-based sleep staging algorithm U-Sleep [38] and verified by a sleep scoring expert who was blinded to group allocation. Each 30-s epoch was classified as wake, N1 sleep, N2 sleep, SWS, or REM sleep according to AASM criteria [37]. Objective sleep parameters included sleep onset latency (SOL), TST, SE (TST/TIB), percentage in each sleep stage, and WASO. SE was the main parameter to assess objective sleep. We also reported the Apnea-hypopnea index (AHI) calculated from the DOMINO software via the PSG respiratory channels. One person in each group did not have two valid assessments because of lost electrodes during the night and had to be excluded from this analysis.

Subjective sleep quality assessment: subjective sleep quality questionnaire and Pittsburgh Sleep Quality Index

We assessed sSQ of the PSG-assessed night with the *sleep quality* subscale of the SF-A/R after waking up in the morning [39]. The scale comprises four indices reflecting difficulty initiating sleep, difficulty maintaining sleep, early morning awakening with inability to return to sleep, and general sleep characteristics. The score ranges from one to five, with one indicating the absence of and five indicating pronounced characteristics of good sSQ. Because the questionnaires were completed on paper at participants' homes, which resulted in incomplete responses, only 12 participants in the RT group and 13 in the CON group could be included in the analysis.

Additionally, the PSQI questionnaire was administered as a measure of general sSQ and completed before the PSG-assessed nights [40]. The questionnaire is validated, clinically relevant, and widely used [41, 42]. It assesses sSQ over the 4 weeks preceding completion, providing a stable measure of sSQ. The 19 included questions evaluate the components of perceived *sleep quality*, *sleep latency*, *sleep duration*, *sleep efficiency*, *sleep disturbances*, *use of sleep medication*, and *daytime dysfunction*. The sum of these

seven components gives a total score ranging from 0 to 21 points, with lower scores indicating better ratings. Individuals with a maximum of five points are considered healthy sleepers, bad sleepers typically reach scores between six and ten, and individuals with chronic sleep disturbances more than ten points.

Statistical analysis

As this study was not prospectively registered, we explicitly distinguish between pre-specified and exploratory analyses. Pre-specified analyses, based on our study aims and power calculation, comprised RTD, resting lactate and NAA concentrations, objective SE, and short-term and long-term sSQ. Resting lactate and NAA concentration were each treated as a single primary outcome testing a distinct hypothesis (oxidative metabolism and neuronal integrity, respectively). Within the objective sleep domain, SE was designated the primary outcome, all other PSG-derived parameters (WASO, SOL, TST, TIB, and sleep percentages) are reported as secondary/exploratory outcomes to characterize the pattern underlying SE and were not independently corrected for multiplicity. Short-term (SF-A/R) and long-term (PSQI) sSQ were treated as two separate, independent primary outcomes reflecting distinct constructs (perceived quality of a single PSG-recorded night vs. habitual sleep quality over 4 weeks). RTD was analyzed as a single, independent primary outcome confirming training efficacy. All other analyses, described below under the “Additional sub-analyses” section, were exploratory.

Statistical analyses were conducted using RStudio version 4.4.1 [43]. Descriptive statistics were expressed as means (M) and standard deviations (SD). Analyses with p -values smaller than $\alpha=0.05$ were considered significant. Baseline differences between groups were assessed using independent samples t -tests. Group differences across timepoints were examined using two-way repeated-measures analysis of covariance (ANCOVA), with sex included as a covariate to account for sex differences in sleep measures and brain metabolism in older adults [44, 45]. In case of baseline group differences of a parameter, we additionally assessed changes with POST values as dependent variable and PRE values as additional covariate. Some parameters were Box-Cox transformed before statistical analysis to ensure normality

of residuals ($\lambda_{\text{RTD}}=-0.303$, $\lambda_{\text{NAA}}=-2$, $\lambda_{\text{SE}}=2$, $\lambda_{\text{WASO}}=-0.141$, $\lambda_{\text{SOL}}=0.343$, $\lambda_{\text{REM}}=1.111$). All estimates of interaction between Group $\times$ Time were reported with the effect size partial eta squared (ηp^2), interpreted as negligible (<0.01), small ($0.01-0.059$), moderate ($0.06-0.139$), or large (≥ 0.14) effects [46]. To assess direction of changes within groups, paired t -tests with Bonferroni-adjusted p -values for two groups were calculated. Changes were reported using absolute changes and the standardized effect size Cohen's d , interpreted as negligible (<0.2), small ($0.2-0.5$), moderate ($0.5-0.8$), or large (≥ 0.8) effects [46]. For outcomes with significant Group $\times$ Time interaction, we additionally derived the sex-adjusted between-group difference in change (difference-in-differences) with 95% confidence intervals from estimated marginal means using the *emmeans* package to complement the within-group paired t -tests with a direct estimate of the intervention effect. Power analysis was performed using G*Power 3.1 for a two-way repeated-measures ANOVA with two time points and two groups (Group $\times$ Time interaction) [47]. Assuming a medium effect size (Cohen's $f=0.25$), $\alpha=0.05$, power=0.80, and correlation among repeated measures $r=0.6$ for objective sleep parameters, $r=0.7$ for lactate, and $r=0.86$ for NAA, we calculated a required total sample size of $N=28$ participants ($N=14$ per group) [48]. To account for dropouts during the intervention period, we recruited 40 participants. For outcomes with fewer than 14 participants per group (lactate: $n=12$ per group; SF-A/R: $n=12-13$ per group), we calculated post-hoc power with G*Power 3.1, based on the observed values. Post-hoc power was 98.4% for lactate levels and 82.7% for SF-A/R.

Additional sub-analyses

Previous literature has shown that training interventions are more effective to improve sSQ in participants with worse baseline sSQ [7]. Our sample size was too small to divide between poor and good sleepers. Instead, we assessed a similar effect in our data using Pearson correlation analysis between baseline PSQI values and change in PSQI in the RT group.

Additionally, as a sensitivity analysis, we ran the Group $\times$ Time ANCOVA models for the parameters that showed significant interactions with baseline sleep status (poor sleeper [PSQI > 5] vs. good sleeper

[PSQI $\leq$ 5]) included as an additional covariate to assess whether these findings were robust to baseline differences in sSQ.

We further performed a supplementary analysis to examine changes of the same parameters in a different group that did 12 weeks of balance training with paired *t*-tests. The balance training intervention and the detailed results are described in the supplementary material (Online Resource).

Results

Participant characteristics can be found in Table 1. The CON group reported no change in exercise frequency from PRE to POST ($t(17)=0.00$, $p=0.999$, $d<0.01$ [−0.46; 0.46]), nor in weekly exercise duration ($t(17)=-0.62$, $p=0.542$, $d=-0.15$ [−0.61; 0.32]), nor in reported types of sports. These self-reported measures suggest that the CON group maintained their habitual exercise behavior over the study period.

Analysis of baseline differences showed that only NAA baseline levels were different between RT and CON (Table S2), with RT showing greater prior NAA decline compared to CON. At baseline, 7 of 18 participants (39%) in the RT group and 9 of 18 participants (50%) in the CON group had PSQI

scores above 5, indicating poor sSQ. This proportion did not differ significantly between groups (Fisher's exact test, $p=0.748$).

Participants in the RT group attended 32.11 ± 2.63 of the 36 prescribed sessions ($89.2\%\pm7.3\%$) with everyone attending at least 30 sessions (83.3%). No injuries occurred during the resistance training sessions, including explosive and jump exercises.

Explosive strength performance

The analysis of explosive strength performance in the tibialis anterior ($n_{RT}=14$, $n_{CON}=16$; Fig. 2A) revealed a significant Group $\times$ Time interaction of RTD ($F(1,27)=9.91$, $p=0.004$, $\eta p^2=0.27$; Fig. 2B). This interaction was driven by a significant increase in the RT group by 21.11 Nm/s ($t(13)=2.75$, $p_{\text{bonf.}}=0.034$, $d=0.73$ [0.13; 1.32]), while the CON group showed no significant change ($\Delta=-14.78$ Nm/s, $t(15)=1.90$, $p_{\text{bonf.}}=0.152$, $d=0.48$ [−0.05; 0.99]). The sex-adjusted between-group difference in RTD change was 36.4 Nm/s (95% CI [12.2; 60.5]). Together with the significant interaction, this pattern is consistent with a beneficial effect of resistance training on explosive strength performance relative to the control condition.

Table 1 Participant characteristics

Characteristic	RT ($n=18$)	CON ($n=18$)	Group comparison
Age (years) , Mean $\pm$ SD	70.1 $\pm$ 4.00	69.72 $\pm$ 4.64	$t(33.206)=0.19$, $p=.847$
Height (cm) , Mean $\pm$ SD	171.33 $\pm$ 9.82	168.56 $\pm$ 8.57	$t(33.392)=0.90$, $p=.372$
Body mass (kg) , Mean $\pm$ SD	71.26 $\pm$ 14.76	72.89 $\pm$ 16.15	$t(33.728)=-0.32$, $p=.753$
BMI (kg/m²) , Mean $\pm$ SD	24.17 $\pm$ 3.97	25.44 $\pm$ 4.30	$t(33.778)=-0.92$, $p=.365$
Sex , n (%) female	7 (39%)	10 (56%)	Fisher's exact, $p=.505$
Chronotype (MEQ score) , Mean $\pm$ SD			Fisher's exact, $p=.443$
— Morning type , n (%)	14 (78%)	12 (67%)	
— Intermediate type , n (%)	3 (17%)	6 (33%)	
— Evening type , n (%)	1 (5.6%)	0 (0%)	
Physical activity h/week (score 1–6), Mean $\pm$ SD	4.61 $\pm$ 1.85	4.39 $\pm$ 1.58	$t(33.16)=0.39$, $p=.701$
Physical activity n/week (score 1–5), Mean $\pm$ SD	3.2 $\pm$ 1.17	3.06 $\pm$ 0.80	$t(30.152)=0.50$, $p=.621$
Apnea-Hypopnea Index (events/h) , Mean $\pm$ SD			Fisher's exact, $p=.465$
— Normal , n (%)	13 (76%)	10 (59%)	
— Mild , n (%)	4 (24%)	7 (41%)	

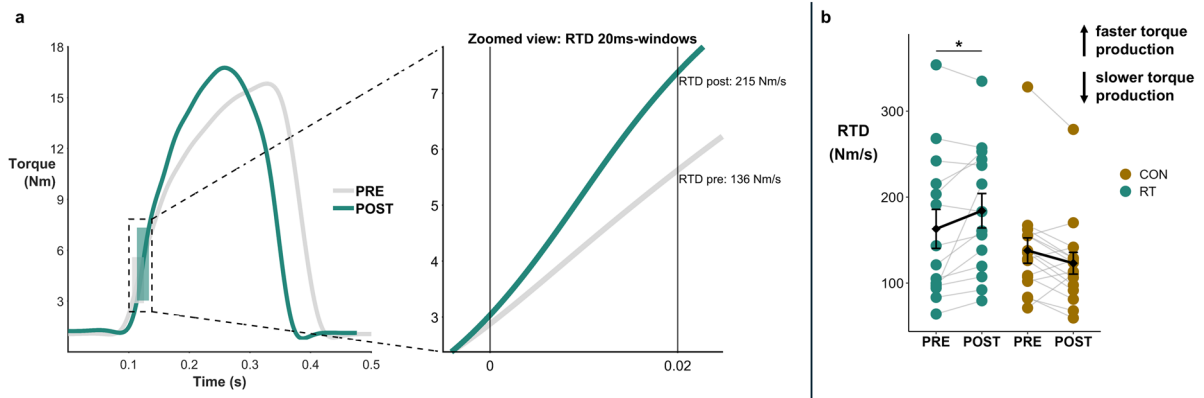


Fig. 2 Faster rate of torque development for explosive performance assessment. **a** Data from a representative participant of the RT group illustrating one trial of torque production during explosive ankle dorsiflexion at PRE (grey) and POST (green) test. The shaded boxes indicate the 20 ms window of peak torque development. **b** Colored dots show individual data points of participants; mean and standard error of the mean

Brain metabolites

We assessed changes in brain metabolism and neuronal integrity indirectly through resting sensorimotor lactate ($n=12$ per group) and NAA ($n=16$ per group) concentrations via MRS (Fig. 3A). ANCOVA revealed a significant Group $\times$ Time interaction in lactate levels ($F(1, 21)=6.35$, $p=0.020$, $\eta^2=0.23$; Fig. 3B). Statistical comparisons of quality metrics suggested no data quality difference between PRE and POST measurements in both groups (individual values and uncorrected p -values for PRE-POST comparisons are reported in supplementary material Table S3; a representative LCModel fit for MRS spectra is reported in supplementary material Fig. S1). On average, participants in the RT group reduced their lactate levels by 0.36 mmol/L ($t(11)=-2.70$, $p_{\text{bonf.}}=0.042$, $d=-0.78$ [-1.42 ; -0.11]), while there was no significant change in the CON group ($\Delta=0.06$ mmol/L, $t(11)=0.49$, $p_{\text{bonf.}}=0.99$, $d=0.14$ [-0.43 ; 0.71]). The sex-adjusted between-group difference in lactate change was 0.45 mmol/L (95% CI [0.06; 0.84]).

Analyses further revealed no significant Group $\times$ Time interaction for NAA levels ($F(1, 29)=1.78$, $p=0.192$, $\eta^2=0.06$, Fig. 3C). Given the baseline imbalance in NAA between groups, we additionally performed baseline-adjusted analyses,

(SEM) per group and time are presented in black. The RT group in green ($n=14$) showed a significant improvement in explosive strength. The mean RTD of CON in yellow ($n=16$) did not change significantly. CON, control; RT, resistance training; RTD, rate of torque development. $*p_{\text{bonf.}}=.034$ for paired t -test after significant Group $\times$ Time interaction

which yielded consistent conclusions (Group effect: $p=0.768$). Descriptively, average NAA concentration slightly increased in RT ($\Delta=0.11$, $t(15)=0.59$, $p_{\text{bonf.}}=0.99$, $d=0.15$ [-0.35 ; 0.64]), while it slightly decreased in CON ($\Delta=-0.22$, $t(15)=1.54$, $p_{\text{bonf.}}=0.290$, $d=-0.38$ [-0.13 ; 0.89]).

These results are consistent with an effect of resistance training on brain lactate levels, whereas changes in NAA remain inconclusive in this dataset.

Sleep parameters

We analyzed whether resistance training positively affected sleep, a key factor for maintaining brain health. AHI did not indicate severe sleep apnea in any participant at PRE or POST (Table 1). Participants adhered to the caffeine instructions and did not take sleep medications for any recorded night. No participant consumed alcohol on the day of a recorded night. The change in SE ($n=17$ per group; Fig. 4A), our primary objective sleep outcome, differed significantly between groups ($F(1, 31)=4.87$, $p=0.035$, $\eta^2=0.14$; Fig. 4B). This interaction was driven by an increase in SE in participants in the RT group by 7.55 percentage points (pp) ($t(16)=3.10$, $p_{\text{bonf.}}=0.014$, $d=0.75$ [0.20 ; 1.28]), while the participants of the CON group showed no significant change ($\Delta=0.73$ pp, $t(16)=0.23$, $p_{\text{bonf.}}=0.99$, $d=0.05$

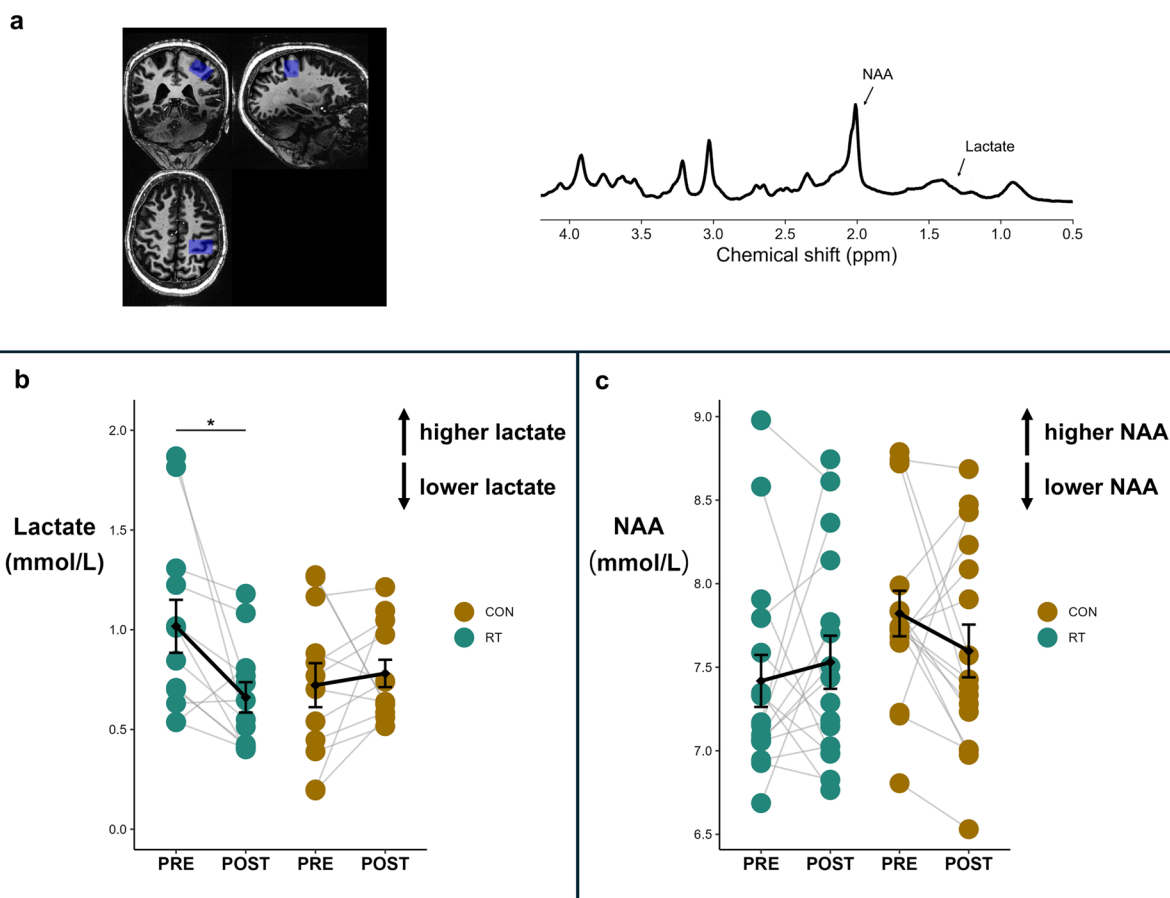


Fig. 3 Brain metabolite concentrations. **a** MRS voxel in the left sensorimotor cortex marked in blue (Left). Lactate and NAA concentrations determined by single-voxel MRS with an exemplary spectrum of a measurement sequence (Right). **b** RT in green ($n=12$) showed a significant decrease in lactate levels; the lactate levels of CON in yellow ($n=12$) did not change

significantly. **c** There was a slight increase in NAA levels in the RT group ($n=16$) and decrease in the CON group ($n=16$), though both are non-significant. CON, control; NAA, N-acetylaspartate; RT, resistance training. * $p_{\text{bonf.}}=.042$ for paired t -test after significant Group $\times$ Time interaction

$[-0.42; 0.53]$). The adjusted between-group difference in SE change was 7.48% (95% CI [0.40; 14.6]).

The remaining PSG parameters, reported here as secondary/exploratory outcomes to contextualize the SE finding, showed a consistent pattern. Participants in the RT group demonstrated lower WASO ($F(1, 31)=4.47$, $p=0.043$, $\eta^2=0.13$; Fig. 5A) and longer TST ($F(1, 31)=5.19$, $p=0.030$, $\eta^2=0.14$; Fig. 6A), while SOL did not differ ($F(1, 31)=0.56$, $p=0.460$, $\eta^2=0.02$, Fig. 5B). Looking at within-group changes, the individuals in the RT group spent a significantly higher amount of time in REM

sleep after the training ($t(16)=2.48$, $p_{\text{bonf.}}=0.049$, $d=0.60$ [0.08; 1.11]; Fig. 6B; Table S2). This increase was not accompanied by a significant Group $\times$ Time interaction, indicating that it cannot be attributed to the intervention with the same confidence. No significant Group $\times$ Time interaction was found for short-term ($n_{\text{RT}}=12$, $n_{\text{CON}}=13$) or long-term ($n=18$ per group) sSQ (Table 2).

In summary, 3 months of resistance training improved SE compared to the control group. However, this improved objective sleep did not go along with improved subjective sleep.

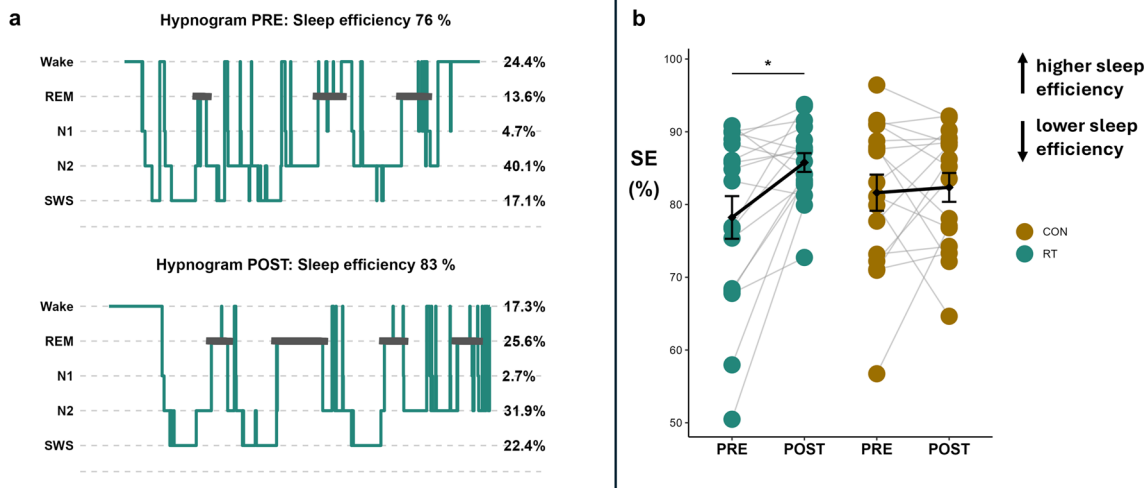


Fig. 4 Improved sleep efficiency. **a** Illustrative hypnogram from a representative participant of the RT group at PRE (top) and POST (bottom) showing how the participant's sleep was less fragmented after intervention. **b** The RT group ($n=17$) in green increased SE, while SE in the CON group ($n=17$) in

yellow did not change significantly. CON, control; N1, non-rapid eye movement 1 sleep; N2, non-rapid eye movement 2 sleep; REM, rapid eye movement sleep; RT, resistance training; SE, sleep efficiency; SWS, slow-wave sleep. $*p_{\text{bonf.}}=.014$ for paired t -test after significant Group $\times$ Time interaction

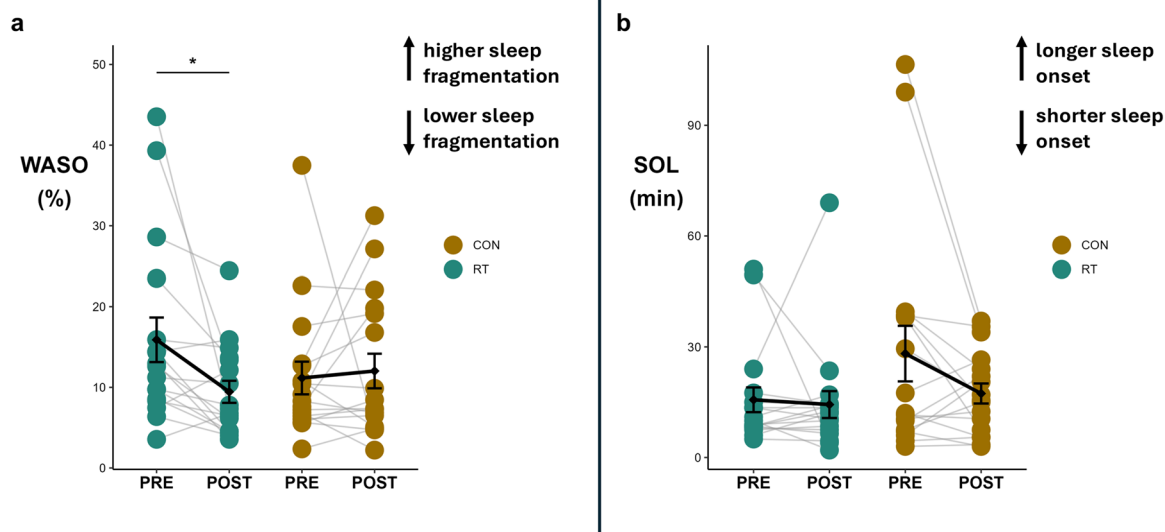


Fig. 5 Decreased wakefulness after sleep onset but no change in sleep onset latency. SE was improved through fewer and/or shorter awakenings during the night and not through shortened SOL. **a** WASO was fewer and/or shorter after RT ($n=17$ per group). **b** SOL was not significantly changed after RT ($n=17$

per group). CON, control; RT, resistance training; SE, sleep efficiency; SOL, sleep onset latency; WASO, wakefulness after sleep onset. $*p_{\text{bonf.}}=.016$ for paired t -test after significant Group $\times$ Time interaction

Sensitivity analysis

To assess whether the observed improvements were dependent on baseline sSQ, we repeated the

ANCOVA models with baseline sleep status (poor vs. good sleeper) as an additional covariate. The Group $\times$ Time interactions for RTD, SE, WASO, TST, and lactate levels remained significant after this

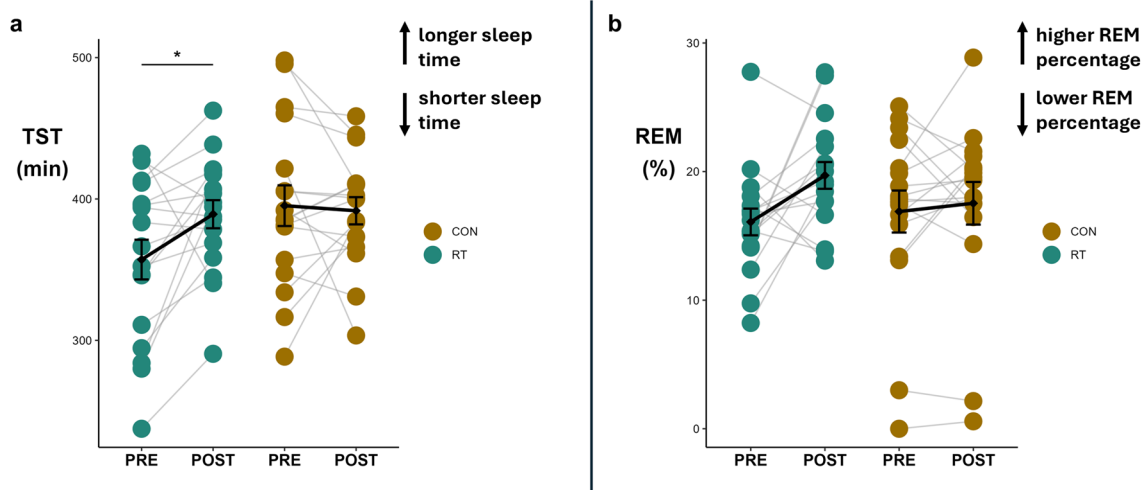


Fig. 6 Longer total sleep time and within-group increase in REM sleep. **a** Increased TST in the RT group in green ($n=17$ per group). **b** No significant Group $\times$ Time interaction for percentage of REM sleep, but the RT group showed an increased

percentage of REM sleep. CON, control; REM, rapid eye movement sleep; RT, resistance training; TST, total sleep time. $*p_{\text{bonf.}}=.046$ for paired t-test after significant Group $\times$ Time interaction

adjustment ($F_s \geq 4.59$, $p \leq 0.040$), indicating that the observed improvements were not driven by baseline differences in sSQ.

Regarding the baseline sex imbalance between groups, sex was included as a covariate in our models to account for known sex differences in sleep and brain metabolism in older adults. None of the models revealed a significant Sex $\times$ Time interaction. Only main sex effects for RTD ($p=0.004$, $\text{Mean}_{\text{males_pre}}=186.82$ Nm/s, $\text{Mean}_{\text{females_pre}}=117.05$ Nm/s) and relative amount of N1 sleep ($p=0.024$, $\text{Mean}_{\text{males_pre}}=6.09\%$, $\text{Mean}_{\text{females_pre}}=4.30\%$) were significant. These analyses did not provide evidence for sex-specific responses to resistance training in the present sample.

Additional sub-analysis: PSQI changes dependent on baseline levels

To assess whether changes in PSQI scores were dependent on baseline scores, we calculated Pearson's correlation between baseline scores and change scores in the intervention group. This analysis showed that also in our study, participants with worse sSQ at baseline showed greater improvements in sSQ after 3 months of resistance training ($r=-0.53$, $p=0.024$).

Additional training group: balance training

The supplementary analysis within the balance training group showed that the same parameters (RTD, lactate concentration, NAA concentration, SE) did not change significantly after 3 months of balance training (see Table S4). Meanwhile, general sSQ assessed with PSQI was improved after 3 months of balance training (Table S4).

Discussion

As of today, there is no cure once neurodegeneration sets in, and thus, prevention and delay of neurodegenerative onset are crucial. In this study, we examined the effects of explosive resistance training in healthy older adults on their sleep and brain metabolism, which are both critically affected in brain aging. Our findings indicate that 3 months of resistance training were associated with reduced lactate levels in the sensorimotor cortex and improved SE.

After resistance training, age-related lactate accumulation was significantly attenuated in the sensorimotor cortex. Previous studies have shown that lactate levels increase with aging and in neurodegenerative diseases [9], which has been attributed

Table 2 Sleep parameters per group and timepoint

Parameter	RT PRE, Mean $\pm$ SD	RT POST, Mean $\pm$ SD	CON PRE, Mean $\pm$ SD	CON POST, Mean $\pm$ SD	ANCOVA, Group $\times$ Time
SE^t (%)	78.22 $\pm$ 12.09	85.77 $\pm$ 5.32	81.62 $\pm$ 10.24	82.35 $\pm$ 8.19	$F(1, 31) = 4.87$, $p = .035$, $\eta p^2 = .14$
SOL^t (min)	15.65 $\pm$ 13.83	14.35 $\pm$ 15.04	28.18 $\pm$ 31.07	17.35 $\pm$ 11.20	$F(1, 31) = 0.56$, $p = .460$, $\eta p^2 = .02$
WASO^t (%)	15.90 $\pm$ 11.39	9.45 $\pm$ 5.64	11.16 $\pm$ 8.36	12.03 $\pm$ 8.84	$F(1, 31) = 4.47$, $p = .043$, $\eta p^2 = .13$
N1 (%)	5.06 $\pm$ 2.01	5.19 $\pm$ 3.45	5.5 $\pm$ 2.28	5.23 $\pm$ 2.36	$F(1, 31) = 0.33$, $p = .571$, $\eta p^2 = .01$
N2 (%)	50.84 $\pm$ 11.89	54.21 $\pm$ 9.89	53.53 $\pm$ 8.14	51.86 $\pm$ 8.25	$F(1, 31) = 3.08$, $p = .089$, $\eta p^2 = .09$
SWS (%)	12.12 $\pm$ 6.10	11.46 $\pm$ 7.50	12.92 $\pm$ 4.84	13.35 $\pm$ 6.10	$F(1, 31) = 0.51$, $p = .482$, $\eta p^2 = .02$
REM^t (%)	16.08 $\pm$ 4.28	19.70 $\pm$ 4.29	16.89 $\pm$ 6.74	17.53 $\pm$ 6.83	$F(1, 31) = 3.40$, $p = .075$, $\eta p^2 = .10$
TST (min)	357.15 $\pm$ 57.90	389.24 $\pm$ 40.92	395.26 $\pm$ 59.34	391.68 $\pm$ 39.69	$F(1, 31) = 5.19$, $p = .030$, $\eta p^2 = .14$
TIB (min)	457.74 $\pm$ 38.48	453.79 $\pm$ 39.17	487.03 $\pm$ 64.59	479.5 $\pm$ 63.59	$F(1, 31) = 0.11$, $p = .737$, $\eta p^2 < .01$
SF-A/R (1–5)	2.86 $\pm$ 0.87	3.39 $\pm$ 0.84	2.76 $\pm$ 0.90	2.96 $\pm$ 0.76	$F(1, 22) = 1.72$, $p = .204$, $\eta p^2 = .07$
PSQI (0–21)	5.78 $\pm$ 4.29	5.22 $\pm$ 3.69	6.11 $\pm$ 3.38	5.83 $\pm$ 2.87	$F(1, 33) = 0.24$, $p = .630$, $\eta p^2 < .01$

Mean $\pm$ SD per group and timepoint for each sleep parameter and corresponding Group $\times$ Time interaction. Bold rows highlight parameters with significant interaction. SE is the primary objective sleep outcome; WASO, SOL, TST, TIB, N1, N2, SWS, and REM are reported as secondary/exploratory outcomes

SOL sleep onset latency, WASO wake after sleep onset, N1 non-rapid eye movement 1 sleep, N2 non-rapid eye movement 2 sleep, REM rapid eye movement sleep, SWS slow-wave sleep, TST total sleep time, TIB time in bed, SE sleep efficiency, SF-A/R one-night subjective sleep quality questionnaire, PSQI Pittsburgh Sleep Quality Index

^tData was Box-Cox transformed to ensure normality of residuals for ANCOVA

to a metabolic shift from oxidative phosphorylation toward glycolysis [49]. Therefore, the reduction seen in our data may suggest improved mitochondrial function and a return toward more efficient oxidative metabolism in older adults. Animal studies showing that exercise increases brain oxidative metabolism [50, 51], and previous work linking glymphatic clearance inversely to brain lactate [52], provide a

plausible but speculative framework for interpreting our finding, particularly given that RT participants also showed improved sleep efficiency in our study, and glymphatic clearance is highest during sleep [53–55]. In summary, we observed lower resting-state lactate levels in the sensorimotor cortex after resistance training.

Our findings did not provide statistical evidence that resistance training mitigates the decline in sensorimotor NAA levels in older adults. Nonetheless, the trend aligned with previous work reporting a protecting effect of resistance training on NAA levels [20], with reduced NAA levels in CON and a slight increase in RT. A possible explanation for the discrepant results is statistical power. Sheoran et al. [20] included PRE and POST data of 20 participants per group, whereas our final sample comprised 16 participants per group. Baseline differences between groups may be another explanatory factor, as NAA levels were lower in the RT group at baseline. Given that NAA has been linked to neurodegenerative processes in prior work [16], this may reflect greater age-related neurodegeneration in the RT group, although this remains speculative. At this possibly more advanced neurodegenerative stage, restoring neuronal integrity may be more challenging and could require a longer intervention period than the one implemented here. Future studies should examine whether initiating resistance training earlier in life could be more effective in preventing age-related reductions in NAA. So far, results about the effect of resistance training on NAA in the sensorimotor cortex remain inconclusive.

Improved SE along with decreased WASO and longer TST represent key objective markers of better sleep. A recent meta-analysis concluded that aerobic exercise has the strongest positive impact on objective SE in the general population [56]. However, evidence indicates that resistance training particularly benefits sleep in older adults. For instance, Li et al. [23] reported that 12 weeks of resistance training significantly improved SE among residents of assisted facilities. Building on this work, our study extends these findings to independent, community-dwelling older adults. Consequently, incorporating resistance training in older adults of diverse levels of independence may help prevent disturbed sleep, a major contributor to cognitive decline and dementia later in life [22, 57, 58]. PSG analysis enabled us to investigate the different sleep phases in greater detail than common actigraphy studies. Within the RT group, the percentage of bedtime spent in REM sleep increased by 3.6 pp after the intervention (Table S2), although this within-group change was not accompanied by a significant Group×Time interaction. If replicated in future studies, such a shift toward REM sleep would be of interest, as REM sleep has been linked to emotional

regulation, and reduced risk of anxiety or depression could represent an additional pathway relevant to cognitive decline [59]. Herein, objective sleep analysis suggests that resistance training may improve SE in healthy, independently living older adults.

The improvement in objective sleep did not go along with an improvement in sSQ that night (SF-A/R), nor with an improvement in general sSQ over a 4-week interval (PSQI). This seems surprising, as 12 weeks of resistance training have previously been shown to improve sSQ assessed with PSQI in older adults [7]. One explanation for our results is that our participants exhibited better baseline sSQ compared to the poor sleepers in Cunha et al. [7]. In their study, only the group of poor sleepers (PSQI > 5) showed a significant improvement in PSQI scores. In line with this observation, our correlation analysis showed a larger positive impact of the training intervention on poor sleepers, but our sample size was too small to conduct a separate analysis only with poor sleepers. Taken together, these findings suggest that the improvement in sSQ following resistance training cannot be generalized to the healthy, independently living older population.

To place our findings in a broader context, prior literature has proposed several mechanistic pathways connecting brain lactate and sleep to neurodegenerative risk. However, the present study was not designed to assess long-term effects on neurodegenerative risk, and the mechanistic links below should be read as speculative background. In addition to its role as marker of mitochondrial function, lactate has been described as a pro-inflammatory signaling molecule [60], and neuroinflammation is considered a key driver of cognitive decline [see 61]. Fragmented sleep (i.e., reduced SE and increased WASO) has similarly been linked to pro-inflammatory states through microglial hyperactivation and reduced glymphatic clearance [55, 62], and chronic sleep disruption has been associated with blood–brain barrier breakdown in prior work [55, 61]. In conclusion, we observed significant changes in two markers that, based on previous literature, may be relevant to mechanisms proposed to support brain health, including neuroinflammation, oxidative metabolism, and blood–brain barrier integrity.

Our findings suggest that even 3 months of explosive resistance training in community-dwelling older adults may benefit markers of brain health. This study

adds an important dimension to previous research that has focused on the effect of exercise on cognitive performance and has given little attention to neural mechanisms. Gaining clearer understanding of the neural mechanisms specifically driven by resistance training, and how these differ from adaptations produced by other exercise modalities, is essential for designing interventions that are more precisely tailored to the needs of distinct target groups. For example, our supplementary analysis shows that balance training did not result in the same adaptations as resistance training but seems to have more potential in improving general sSQ (Table S4).

This study has some limitations that should be considered when interpreting our findings. (1) Our assessment of brain health was restricted to a limited set of markers, resting sensorimotor lactate and NAA concentrations and objective and subjective sleep parameters, and we did not directly measure the underlying mechanisms (e.g. neuroinflammation, mitochondrial function, glymphatic clearance, or blood–brain barrier integrity) that we propose link these markers to brain health. We also did not assess cognitive performance. These connections are therefore inferred from prior literature and not demonstrated directly. (2) Objective sleep was assessed via a single PSG night per timepoint, which may not fully capture habitual sleep given known night-to-night variability. Future studies could incorporate multi-night recordings per timepoint (e.g., using actigraphy to complement PSG) to better characterize habitual sleep and account for variability. In our study, this was partially mitigated by an adaptation night controlling for the first-night effect, and by asking participants to avoid alcohol, caffeine, and vigorous activity before the recorded nights. Nonetheless, PSG remains the gold-standard method for objective sleep assessment, representing a methodological strength relative to studies relying on actigraphy or only self-report. (3) Simple randomization allowed for baseline imbalances between groups. Baseline tests were completed on a rolling basis as we could only test one person per day. Individual participants started the intervention immediately after completion of baseline assessments to minimize time between baseline assessments and intervention and reduce attrition. Therefore, stratified randomization was not possible, which may have contributed to the observed baseline imbalance in NAA levels between groups (RT showing lower NAA

values). Another baseline imbalance was the sex distribution, although this difference was not statistically significant. While our analyses point towards no sex-specific effects, we cannot fully exclude any contribution of the sex imbalance to the observed results. Simple randomization also led to numerically lower baseline SE and TST in the RT group compared with CON (Table 2). Even though these differences were not statistically significant, we cannot fully exclude that some regression to the mean appeared in our sample. However, several observations argue against regression to the mean as the single explanation for the observed changes. The CON group, which also underwent repeated testing and could equally be subject to regression to the mean, showed no comparable changes, the BAL group similarly did not replicate the pattern seen in RT (Table S4), and the magnitude and consistency of changes across three related parameters (SE, WASO, TST) align with the physiological rationale and prior resistance training literature [23]. Nonetheless, future studies with larger samples and baseline-matched groups are needed to disentangle true intervention effects from statistical artifacts of baseline imbalance. (4) Data loss reduced sample size for several outcomes: eight participants were excluded from lactate analyses due to poor spectral quality, and incomplete paper-based questionnaires reduced the SF-A/R sample to 12 (RT) and 13 (CON) participants. Our final sample size for NAA analysis (16 participants per group) was smaller than in comparable prior work [20]. Furthermore, the *p*-values of our main results were close to significance threshold (lactate $p=0.020$, SE $p=0.035$), warranting replication in a larger sample. (5) Study personnel, except the sleep scoring expert, were not blinded to group allocation, which may have introduced bias. However, as outcomes were objective measures obtained using predefined protocols, the absence of blinding is unlikely to have influenced the results. (6) The comparison with the passive control group cannot fully rule out that changes in the RT group might partially be attributed to social and general activity benefits, rather than purely training-specific benefits. However, the lacking within-group changes in the same parameters in the balance group suggest at least training-specific contributions. (7) This study was not prospectively registered in a publicly accessible database. Therefore, the hypotheses described above cannot be independently verified by readers as

pre-specified. (8) We did not assess education level, comorbidities beyond our neurological and orthopedic exclusion criteria or cognitive status. Future studies should incorporate more comprehensive baseline characterization to better evaluate generalizability and control for potential confounding.

Overall, this study suggests that 3 months of structured resistance training improves sleep and reduces sensorimotor lactate accumulation in community-dwelling older adults. These findings provide further evidence that resistance training can influence physiological markers associated with brain health in older age. Future studies additionally incorporating direct measures of cognition and neurodegeneration are needed to determine the clinical significance of these changes. So far, our findings suggest that resistance training could particularly benefit older adults with fragmented sleep and impaired oxidative brain metabolism.

Author contribution The study was conceptualized by Wolfgang Taube, Lijing Xin, and Benedikt Lauber. All authors contributed to the study design. Material preparation, data collection and analysis were performed by Selin Scherrer, Sven Egger, and Xinyu Liu. The first draft of the manuscript was written by Selin Scherrer and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data Availability Data are available from the corresponding author on reasonable request.

Declarations

Competing interests The authors declare no competing interests.

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