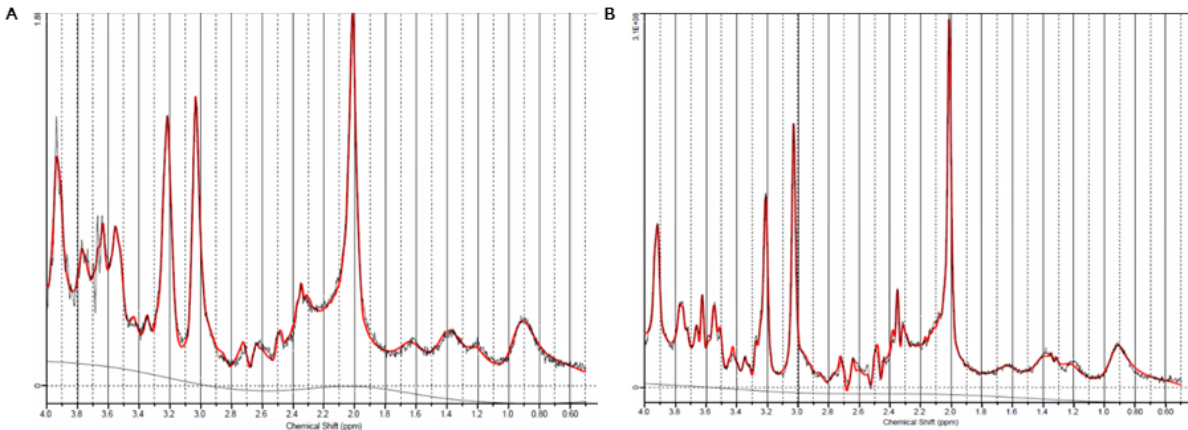


Supplements

1. Supplementary Methods

1.1. ¹H-MRS:

Supplementary Figure 1 | Representative spectra for one participant, measured in the **A**) hippocampus and **B**) dorsal anterior cingulate cortex (dACC).



Spectra were fitted using LCModel with a simulated basis set with a measured macromolecular baseline (using an sLASER dual inversion recovery sequence (Penner and Bartha, 2015)) and the following metabolites: alanine (Ala), aspartate (Asp), creatine (Cr), γ -aminobutyric acid (GABA), Gln, Glu, GSH, glycine (Gly), glycerophosphocholine (GPC), Inositol, Lac, phosphoethanolamine (PE), phosphocholine (PCh), phosphocreatine (PCr), inositol (Ins), choline (Cho), NAA, N-acetyl aspartyl glutamate (NAAG), taurine (Tau), scylloinositol (Sci), succinate (Suc), pyruvate (Pyr) and threonine (Thr).

The following control parameters were used for LCModel analyses:

```
deltat= 2.50e-04
doecc= F
dows= T
hzpppm= 2.9804e+02
nunfil= 2048
ppmend= 0.5
ppmst= 4.0
DKNTMN= 0.5
atth2o= 0.7
attmet= 1.0
chcomb(17)= 'Lac+Thr'
chcomb(18)= 'Cho+GPC+PC'
chomit(1)= 'MM09'
chomit(2)= 'MM12'
chomit(3)= 'MM14'
chomit(4)= 'MM17'
chomit(5)= 'MM20'
```

```

chomit(6)= 'Ala'
chomit(7)= 'Pyr'
chomit(8)= 'Suc'
ncombi= 18
neach= 50
nomit= 8
wconc= individual values
CHUSE1(1)='NAA'
CHUSE1(2)='PCr'
CHUSE1(3)='PC'

```

1.2. Statistical Analysis

Supplementary Table 1 | Evidence Categories for Bayes Factor BF (Jeffrey, 1961; Wagenmakers, 2007)

Bayes Factor	Interpretation
> 100	Decisive evidence for H_A
30 - 100	Very strong evidence for H_A
10 - 30	Strong evidence for H_A
3 - 10	Substantial evidence for H_A
1 - 3	Anecdotal evidence for H_A
1	No evidence
1/3 - 1	Anecdotal evidence for H_0
1/10 - 1/3	Substantial evidence for H_0
1/30 - 1/10	Strong evidence for H_0
1/100 - 1/30	Very strong evidence for H_0
< 1/100	Decisive evidence for H_0

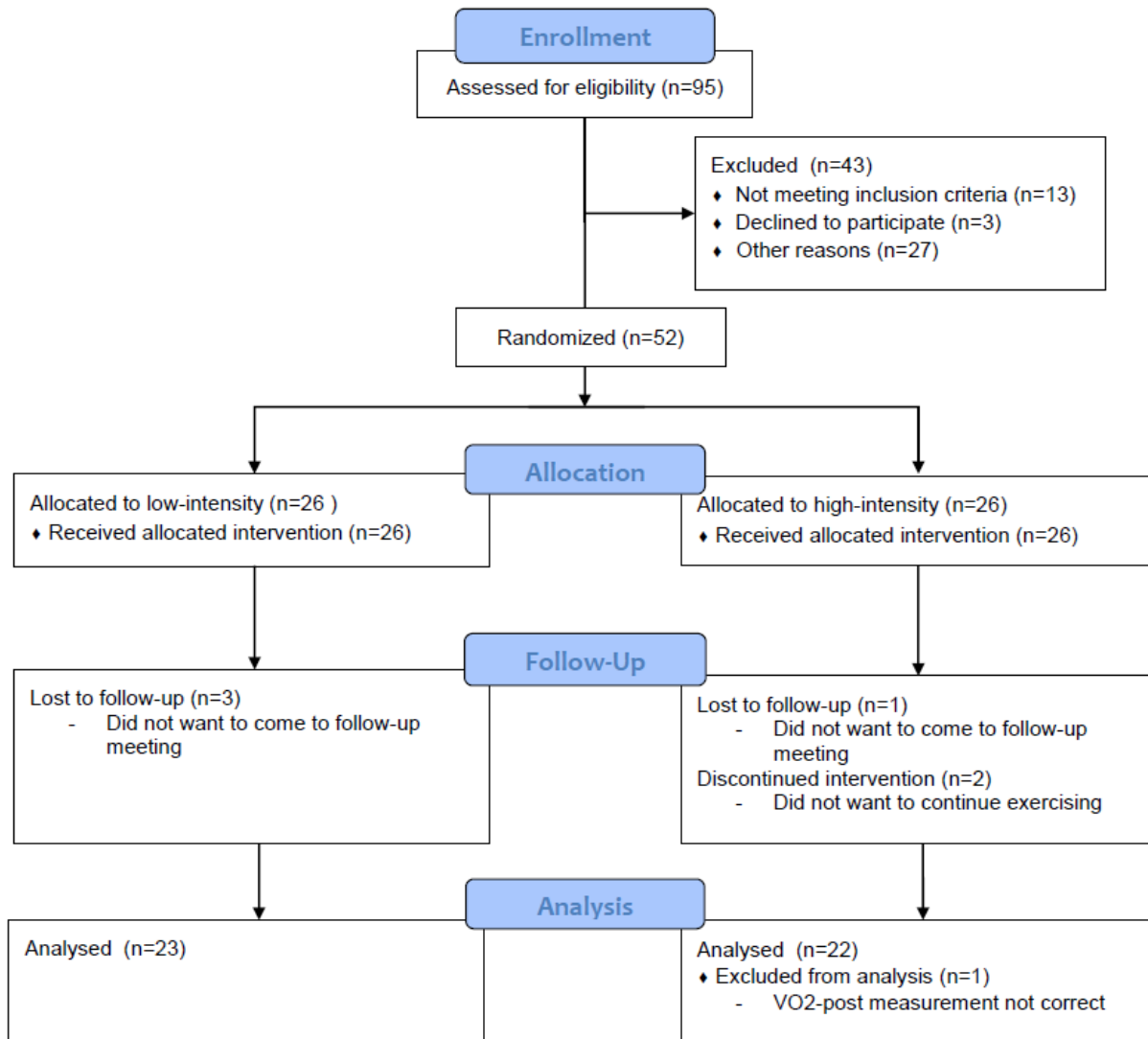
1.3. Sample Size Calculations

We aimed to investigate the neural mechanisms underlying brain volume changes resulting from exercise interventions. First, we determined the sample size to assess a hypothesized effect on neurometabolite signaling. A previous study investigating exercise effects on anterior cingulate cortex glutamate concentration changes reported an effect size of $d=1.48$ (Cohen d) in young participants (Maddock et al., 2016). As this study used an acute exercise intervention, we expected a more moderate effect size for a longitudinal exercise intervention of $d=1.0$. To detect the effect of exercise, with a power of 80% and an α of 0.05, we would need 12 participants per

exercise intervention group. Taking a 20% dropout into account (due to MRI data quality), we would need at least 15 subjects in each exercise intervention group.

Secondly, we calculated the required sample size to assess the effect of exercise on vascular outcome measures. A previous study using contrast-enhanced MRI assessed the effect of a dietary intervention with flavanol on CBV in the hippocampus (Brickman et al., 2014). This study detected an increase in CBV with an effect size of $d=0.75$. We expect the dietary intervention to have effects of a similar magnitude as the exercise intervention. With an effect size of $d=0.75$, a power of 80%, and an α of 0.05, we would need 16 subjects to detect a difference before and after the exercise intervention. Taking a 20% dropout into account, we would need at least 20 subjects in each exercise group.

1.4. CONSORT flow chart



1.5. Exercise intervention

Recommended exercise group classes per exercise intensity group (translated from Dutch):

Low-Intensity Group:

- BBB - The class consists of a short warm-up followed by various exercises that focus on the belly, buttocks, and legs.
- Body power* - This is a group workout to music using simple and effective exercises with barbells and dumbbells. It is focused on the muscular endurance of the whole body.
- Essentrics - At Essentrics you get an effective toning workout to music using dynamic stretches and fluid movements without using gear. The main goals are a slimmer silhouette, more flexibility, and better posture.
- Pilates - In this class the focus is on: posture and control, flexibility, breathing, and awareness. In Pilates, you do floor exercises that target all postural muscles in the body, especially the abdominal and back muscles. You do the exercises slowly, fluently and in collaboration with your breath. You concentrate on doing the exercises carefully and accurately, and not on the number of repetitions. The result is better posture and flexibility.
- TrippleShape barre workout - Ballet Barre workout is a combination of ballet, pilates, and yoga to contemporary music.
- Yoga basic - This is a basic yoga class. The focus lies on: stretching and holding postures.
- Kinesis - Kinesis Training takes traditional exercises (like chest press, lat pull, row) and combines them with functional movements (like reaching, squatting, bending). It develops balance, core/overall strength, and flexibility for people of all fitness levels.
- Abs - 15 minutes of abs training using own-body weight.
- Basic movement - In this class good technique of the most basic exercises using own-body weight is being practiced. This lesson focuses on questions such as: How do I perform the squat correctly? What is a pull-up and how do I do it? What variations are there for a deadlift?
- Mobility class - This lesson focuses on increasing flexibility in muscles and joints.
- Calisthenics - This is a class to practice exercises like a handstand, muscle up, human flag, front and back lever.
- Core*- This lesson focuses on posture and strengthening the abdominal and back muscles in a controlled manner. The training does not only consist of floor exercises but is also offered in challenging circuit forms.
- W.A.C.* - Weightlifting Aerobic Circuit: this workout is originally based on Olympic weightlifting, a valuable full-body workout.

***For Core, W.A.C., and body power, participants were only allowed to do a maximum of 1 of these 3 per week for this sports program.**

High-Intensity Group:

- Combat - In this class you train your entire body during circuit training. It includes techniques from (kick) boxing, self-defense techniques, strength, and conditioning to increase your heart rate.
- Fitness training - This is circuit training in which all available materials are used. Walking and jumping are used a lot in this training, the intensity is largely determined by the participants themselves. A high-intensity training involving both strength and condition.
- Fit Fight - This is a powerful cardio workout inspired by Eastern martial arts such as karate, boxing, taekwondo, and Muay Thai to music.
- Kick & shape - This is an intensive class in which participants learn various punching and kicking techniques against the punching bag to music.
- Spinning - In this class participants sit on a spinning bike, on which, under the guidance of the teacher, they go on a 'bike tour' in which different speeds alternate. The resistance is chosen by the participants themselves.
- Step & dance - Step & dance is a choreographically challenging, advanced step class, with the goal of increasing aerobic fitness.
- Total body workout - This class is a short piece of aerobics hi/low impact after a warm-up. This is followed by exercises for all muscle groups: back, arms, abdomen, shoulders, chest, and legs. This class improves the participant's overall fitness, both cardio and muscle endurance are trained.
- Synrgy - Synrgy is a large device, with rods, ropes, bells, and whistles. Participants can follow group training sessions of 30 minutes several times a day, in which they do high-intensity interval training in circuit form.
- H.I.I.T. - High-Intensity Interval Training consists of short periods of intense effort, followed by short recovery moments. Participants train their general condition but also strength and speed, using simple materials or body weight.
- Crossfit - This small group training is based on the principles of a fitness concept from the USA: functionality, variation, and high intensity. Participants train speed, (muscle) endurance, strength, flexibility, and coordination.

Details about the exercise intervention:

Exercise progression was monitored by tracking their sports center visits using an automated fingerprint entrance system and by using weekly questionnaires on exercise duration and activities. Additionally, participants received an HR monitor (Polar, Finland) to measure HR during each training session. In case the regularity of participants' training sessions was

decreasing, participants were contacted and motivated to continue exercising by one of the experimenters.

No home-program or non-exercise components were added to the intervention. No adverse events occurred during the exercise intervention in this study.

2. Supplementary Results

2.1. Quality Control Spectra

Quality metric	Left Hippocampus BL <i>Mean ± std</i>	Post <i>Mean ± std</i>	dACC BL <i>Mean ± std</i>	Post <i>Mean ± std</i>
SNR	30.76 ± 6.05	28.85 ± 7.03	46.64 ± 2.96	47.41 ± 2.79
FWHM	14.41 ± 2.26	15.68 ± 3.71	7.55 ± 0.71	7.55 ± 0.72
Glu CRLB	3.17 ± 0.66	3.49 ± 0.76	2.0 ± 0	2.02 ± 0.15
Gln CRLB	29.41 ± 6.19	27.91 ± 6.69	19.97 ± 6.04	20.72 ± 5.98
GSH CRLB	7.48 ± 1.91	7.13 ± 1.49	7.67 ± 0.81	7.74 ± 0.83
NAA CRLB	1.02 ± 0.15	1.05 ± 0.22	1.0 ± 0	1.0 ± 0

2.2. Exploratory Analysis:

Supplementary Table 2 | Statistical tests for all variables: Linear mixed-effects models were used to investigate the condition (high- vs. low-intensity exercise) x time (pre- vs. post-intervention) x sex (female vs. male) interaction in Rv.3.5.3 using the lme4 package. Multiple comparison corrections using Sidak's resulted in an $\alpha^*=0.02$. Model selection was based on an adjusted top-down procedure, in which the resulting models were compared using the Bayesian information criterion (BIC); the model was consequently tested using chi-square (χ^2) tests.

Variables	Interaction effects <i>Group * Time</i>	Main effects <i>Time</i>	Sex	Tukey Post-Hoc test
Fitness measures				
VO2max	$\chi^2(5)=4.51, p=0.48, \Delta BIC=-18.42$	$\chi^2(1)=15.43, p<0.001, \Delta BIC=11.15$	$\chi^2(1)=21.26, p<0.001, \Delta BIC=17.32$	Female<Male; pre<post
Bike-resistance	$\chi^2(5)=11.84, p=0.04, \Delta BIC=-11.09$	$\chi^2(1)=38.92, p<0.001, \Delta BIC=34.34$	$\chi^2(1)=36.23, p<0.001, \Delta BIC=31.64$	Female<Male; pre<post
HR during VO2max	$\chi^2(7)=1.35, p=0.25, \Delta BIC=-3.21$	$\chi^2(1)=4.03, p=0.04, \Delta BIC=-0.53$	$\chi^2(1)<0.01, p=0.97, \Delta BIC=-4.56$	-
Volume measures				
Left Hippocampus				
Whole	$\chi^2(6)=5.70, p=0.45, \Delta BIC=-21.54$	$\chi^2(1)=2.68, p=0.10, \Delta BIC=-1.82$	$\chi^2(1)=24.97, p<0.001, \Delta BIC=21.54$	Female<Male
Dentate Gyrus	$\chi^2(6)=4.61, p=0.59, \Delta BIC=-22.39$	$\chi^2(1)=2.14, p=0.14, \Delta BIC=-2.35$	$\chi^2(1)=18.23, p<0.001, \Delta BIC=14.27$	Female<Male
CA1	$\chi^2(6)=2.68, p=0.85, \Delta BIC=-24.20$	$\chi^2(1)=0.08, p=0.77, \Delta BIC=-4.40$	$\chi^2(1)=23.46, p<0.001, \Delta BIC=19.00$	Female<Male
CA3	$\chi^2(6)=2.08, p=0.91, \Delta BIC=-9.92$	$\chi^2(1)=0.95, p=0.33, \Delta BIC=-1.05$	$\chi^2(1)=15.75, p<0.001, \Delta BIC=11.26$	Female<Male
WM	$\chi^2(5)=7.55, p=0.18, \Delta BIC=-14.83$	$\chi^2(1)=5.18, p=0.02, \Delta BIC=0.69$	$\chi^2(1)=6.31, p=0.01, \Delta BIC=1.83$	Male<Female; Post<pre
GM	$\chi^2(6)=2.83, p=0.83, \Delta BIC=-24.17$	$\chi^2(1)=0.04, p=0.83, \Delta BIC=-4.46$	$\chi^2(1)=31.79, p<0.001, \Delta BIC=27.28$	Female<Male
Right Hippocampus				
Whole	$\chi^2(5)=5.00, p=0.43, \Delta BIC=-18.39$	$\chi^2(1)=8.47, p<0.01, \Delta BIC=4.03$	$\chi^2(1)=22.72, p<0.001, \Delta BIC=18.22$	Female<Male; Post<pre
Dentate Gyrus	$\chi^2(6)=10.59, p=0.10, \Delta BIC=-16.41$	$\chi^2(1)=4.08, p=0.14, \Delta BIC=-2.08$	$\chi^2(1)=13.04, p<0.001, \Delta BIC=8.54$	Female<Male
CA1	$\chi^2(6)=7.45, p=0.28, \Delta BIC=-5.40$	$\chi^2(1)=0.84, p=0.36, \Delta BIC=-4.30$	$\chi^2(1)=23.46, p<0.001, \Delta BIC=20.60$	Female<Male
CA3	$\chi^2(6)=2.08, p=0.91, \Delta BIC=-24.85$	$\chi^2(1)=0.95, p=0.33, \Delta BIC=-3.66$	$\chi^2(1)=15.75, p<0.001, \Delta BIC=11.26$	Female<Male
WM	$\chi^2(6)=10.22, p=0.12, \Delta BIC=-6.72$	$\chi^2(1)=2.89, p=0.08, \Delta BIC=-0.4$	$\chi^2(1)=5.34, p=0.02, \Delta BIC=0.96$	Male<Female
GM	$\chi^2(6)=3.74, p=0.71, \Delta BIC=-23.26$	$\chi^2(1)=0.50, p=0.48, \Delta BIC=-4.00$	$\chi^2(1)=27.06, p<0.001, \Delta BIC=23.44$	Female<Male
dACC	$\chi^2(6)=7.03, p=0.95, \Delta BIC=-20.10$	$\chi^2(1)=0.005, p=0.95, \Delta BIC=-5.5$	$\chi^2(1)=5.4, p=0.02, \Delta BIC=1.1$	Female<Male
1H-MRS				
Hippocampus				
GLU	$\chi^2(7)=4.22, p=0.74, \Delta BIC=-26.44$	$\chi^2(1)=0.82, p=0.36, \Delta BIC=-3.55$	$\chi^2(1)=0.84, p=0.36, \Delta BIC=-3.53$	-
GLN	$\chi^2(6)=4.60, p=0.60, \Delta BIC=-21.54$	$\chi^2(1)=1.92, p=0.17, \Delta BIC=-3.56$	$\chi^2(1)=4.57, p=0.03, \Delta BIC=0.21$	Female<Male
NAA	$\chi^2(7)=6.37, p=0.50, \Delta BIC=-24.13$	$\chi^2(1)=2.71, p=0.10, \Delta BIC=-1.65$	$\chi^2(1)=0.32, p=0.57, \Delta BIC=-4.04$	-
GSH	$\chi^2(6)=6.37, p=0.46, \Delta BIC=-21.46$	$\chi^2(1)=9.21, p<0.01, \Delta BIC=4.83$	$\chi^2(1)=2.72, p=0.09, \Delta BIC=-2.65$	Pre<post
dACC				
GLU	$\chi^2(6)=10.48, p=0.11, \Delta BIC=-16.32$	$\chi^2(1)=1.85, p=0.17, \Delta BIC=-2.61$	$\chi^2(1)=8.87, p<0.01, \Delta BIC=4.41$	Male<Female
GLN	$\chi^2(7)=7.59, p=0.37, \Delta BIC=-23.67$	$\chi^2(1)=0.01, p=0.91, \Delta BIC=-5.05$	$\chi^2(1)=2.43, p=0.12, \Delta BIC=-2.03$	-
NAA	$\chi^2(6)=5.52, p=0.48, \Delta BIC=-22.72$	$\chi^2(1)=3.77, p=0.05, \Delta BIC=-1.3$	$\chi^2(1)=6.05, p=0.01, \Delta BIC=5.95$	Male<Female
GSH	$\chi^2(7)=5.68, p=0.58, \Delta BIC=-34.41$	$\chi^2(1)=0.05, p=0.83, \Delta BIC=-3.69$	$\chi^2(1)=2.27, p=0.13, \Delta BIC=-2.81$	-
Vasculature				
CBF				
Left Hippocampus	$\chi^2(6)=5.59, p=0.47, \Delta BIC=-21.13$	$\chi^2(1)=0.19, p=0.66, \Delta BIC=-4.33$	$\chi^2(1)=0.74, p=0.39, \Delta BIC=-4.32$	-
Right Hippocampus	$\chi^2(7)=5.65, p=0.58, \Delta BIC=-25.36$	$\chi^2(1)=0.95, p=0.33, \Delta BIC=-3.48$	$\chi^2(1)<0.01, p=0.94, \Delta BIC=-4.42$	-
GM	$\chi^2(7)=13.60, p=0.06, \Delta BIC=-18.67$	$\chi^2(1)=2.84, p=0.09, \Delta BIC=-2.42$	$\chi^2(1)=0.85, p=0.36, \Delta BIC=-4.43$	-
CBV				
Left Hippocampus	$\chi^2(6)=4.34, p=0.63, \Delta BIC=-22.24$	$\chi^2(1)=5.97, p=0.01, \Delta BIC=2.05$	$\chi^2(1)=15.21, p<0.01, \Delta BIC=10.78$	Male<Female
Right Hippocampus	$\chi^2(6)=6.86, p=0.33, \Delta BIC=-20.21$	$\chi^2(1)=3.57, p=0.06, \Delta BIC=-1.12$	$\chi^2(1)=6.45, p=0.01, \Delta BIC=2.00$	Male<Female
GM	$\chi^2(7)=8.23, p=0.31, \Delta BIC=-22.70$	$\chi^2(1)=0.98, p=0.32, \Delta BIC=-3.43$	$\chi^2(1)=1.71, p=0.19, \Delta BIC=-3.31$	-
Myelination (R1)				
WM left Hippocampus	$\chi^2(7)=8.90, p=0.26, \Delta BIC=-23.1$	$\chi^2(1)=0.20, p=0.65, \Delta BIC=-5.6$	$\chi^2(1)=0.32, p=0.57, \Delta BIC=-5.7$	-
WM right Hippocampus	$\chi^2(7)=12.76, p=0.08, \Delta BIC=-21.0$	$\chi^2(1)=0.42, p=0.52, \Delta BIC=-4.1$	$\chi^2(1)=0.63, p=0.43, \Delta BIC=-4.1$	-
Neurotrophic factors				
BDNF	$\chi^2(7)=11.06, p=0.14, \Delta BIC=-20.20$	$\chi^2(1)=0.95, p=0.33, \Delta BIC=-4.50$	$\chi^2(1)=0.05, p=0.82, \Delta BIC=-4.40$	-
VEGF	$\chi^2(7)=8.10, p=0.32, \Delta BIC=-23.32$	$\chi^2(1)=0.40, p=0.53, \Delta BIC=-4.09$	$\chi^2(1)=0.83, p=0.36, \Delta BIC=-4.34$	-
IGF	$\chi^2(7)=4.49, p=0.72, \Delta BIC=-17.06$	$\chi^2(1)=0.01, p=0.94, \Delta BIC=-5.52$	$\chi^2(1)=1.59, p=0.21, \Delta BIC=-3.10$	-

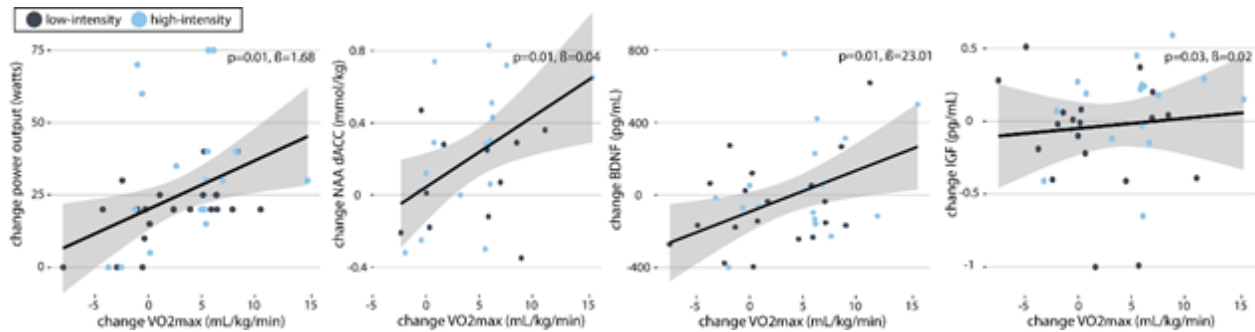
Supplementary Table 3 | Exploratory analyses testing the association of all variables with VO2max, and hippocampal or dACC volume change were conducted using linear models in R, including the baseline measure of the explanatory variables, VO2max, and sex as covariates ($\alpha=0.05$).

<i>Variables</i>	<i>Regression with VO2max</i>
SPORT	
<i>VO2max</i>	-
<i>Bike-resistance</i>	F(1,38)=7.46, p=0.01 , $\beta=1.68$
Volume measures	
Left Hippocampus	
<i>Whole</i>	F(1,41)=0.51, p=0.48, $\beta=1.74$
<i>Dentate Gyrus</i>	F(1,42)=1.81, p=0.19, $\beta=0.38$
<i>CA1</i>	F(1,40)=0.82, p=0.37, $\beta=-0.95$
<i>CA3</i>	F(1,41)=0.88, p=0.36, $\beta=0.17$
<i>WM</i>	F(1,37)=0.03, p=0.86, $\beta=-0.43$
<i>GM</i>	F(1,38)=0.10, p=0.75, $\beta=-1.06$
Right Hippocampus	
<i>Whole</i>	F(1,40)=0.51, p=0.48, $\beta=2.18$
<i>Dentate Gyrus</i>	F(1,42)=1.80, p=0.19, $\beta=1.76$
<i>CA1</i>	F(1,40)=0.08, p=0.78, $\beta=0.33$
<i>CA3</i>	F(1,41)=0.88, p=0.36, $\beta=-0.20$
<i>WM</i>	F(1,37)=0.04, p=0.84, $\beta=0.46$
<i>GM</i>	F(1,36)=1.22, p=0.28, $\beta=-3.47$
dACC	F(1,40)=0.30, p=0.59, $\beta=3.22$
1H-MRS	
Hippocampus	
<i>GLU</i>	F(1,26)<0.01, p=0.95, $\beta=-0.002$
<i>GLN</i>	F(1,27)=0.38, p=0.55, $\beta=0.02$
<i>NAA</i>	F(1,25)=0.07, p=0.80, $\beta=-0.006$
<i>GSH</i>	F(1,25)=0.99, p=0.33, $\beta=0.007$
dACC	
<i>GLU</i>	F(1,25)=0.08, p=0.78, $\beta=0.006$
<i>GLN</i>	F(1,26)<0.01, p=0.98, $\beta=0.001$
<i>NAA</i>	F(1,27)=7.14, p=0.01 , $\beta=0.04$
<i>GSH</i>	F(1,26)=0.26, p=0.61, $\beta=-0.002$
Vasculature	
CBF	
<i>Left Hippocampus</i>	F(1,27)=1.08, p=0.31, $\beta=-0.002$
<i>Right Hippocampus</i>	F(1,27)<0.01, p=0.96, $\beta=0.001$
<i>GM</i>	F(1,28)=3.06, p=0.06, $\beta=0.35$
CBV	
<i>Left Hippocampus</i>	F(1,27)=0.63, p=0.44, $\beta=-0.01$
<i>Right Hippocampus</i>	F(1,27)=1.86, p=0.18, $\beta=-0.02$
<i>GM</i>	F(1,27)<0.01, p=0.94, $\beta=-0.01$
Myelination (R1)	
<i>Left</i>	F(1,37)=0.02, p=0.88, $\beta=0.001$
<i>Right</i>	F(1,36)=0.33, p=0.57, $\beta=-0.001$
Neurotrophic factors	
<i>BDNF</i>	F(1,36)=6.84, p=0.01 , $\beta=23.01$
<i>VEGF</i>	F(1,36)=0.02, p=0.89, $\beta=-0.04$
<i>IGF</i>	F(-1,36)=5.19, p=0.03 , $\beta=0.02$

Supplementary Table 4 | Mean and standard deviation for pre- and post-exercise intervention per variable.

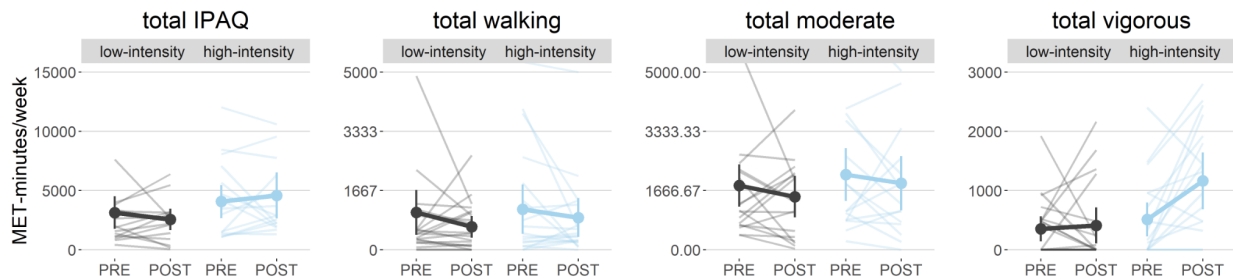
	<i>HIGH-INTENSITY</i>		<i>LOW-INTENSITY</i>	
	<i>PRE</i> <i>Mean ± SD</i>	<i>POST</i> <i>Mean ± SD</i>	<i>PRE</i> <i>Mean ± SD</i>	<i>POST</i> <i>Mean ± SD</i>
Participant characteristics:				
<i>Age (years)</i>	23.12 ± 2.52	23.25 ± 2.31	24.19 ± 3.25	24.43 ± 3.14
<i>Body Mass Index (kg/m²)</i>	23.30 ± 2.80	22.96 ± 2.75	23.96 ± 3.24	23.78 ± 3.17
Fitness measures:				
<i>VO2max (kg/mL/min.)</i>	37.21 ± 7.39	41.60 ± 6.69	37.32 ± 6.58	39.39 ± 7.38
<i>Max. Heart Rate (beats/min.)</i>	186.60 ± 8.41	186.01 ± 8.26	189.12 ± 7.53	187.48 ± 7.31
<i>Resistance pre (watts)</i>	240.33 ± 61.94	273.54 ± 67.56	244.62 ± 45.54	262.17 ± 45.45
Volume measures:				
<i>Left hippocampus</i>	3025.33 ± 428.42	3024.76 ± 432.52	3082.54 ± 350.55	3076.88 ± 346.14
<i>Right hippocampus</i>	3128.94 ± 484.38	3123.99 ± 461.99	3095.15 ± 334.10	3063.12 ± 335.44
<i>dACC</i>	3984.78 ± 832.14	4053.26 ± 848.16	4241.57 ± 682.49	4254.65 ± 875.18
Vasculature				
CBF				
<i>Left Hippocampus</i>	42.24 ± 7.85	43.81 ± 5.42	47.03 ± 9.40	44.88 ± 7.75
<i>Right Hippocampus</i>	41.08 ± 7.89	42.73 ± 6.07	45.28 ± 9.15	42.90 ± 8.17
<i>GM</i>	46.41 ± 7.29	46.61 ± 6.41	48.44 ± 6.43	46.33 ± 7.02
CBV				
<i>Left Hippocampus</i>	2.19 ± 0.96	2.15 ± 0.85	2.11 ± 1.08	1.74 ± 0.59
<i>Right Hippocampus</i>	2.13 ± 0.78	1.93 ± 0.75	1.90 ± 0.77	1.82 ± 0.56
<i>GM</i>	2.44 ± 0.57	2.86 ± 0.84	2.49 ± 0.43	2.59 ± 0.64
Myelination (R1)				
<i>Left</i>	8.49E-04 ± 2.90E-05	8.49E-04 ± 2.90E-05	8.51E-04 ± 3.97E-05	8.41E-04 ± 2.28E-05
<i>Right</i>	8.47E-04 ± 3.75E-05	8.47E-04 ± 3.75E-05	8.60E-04 ± 4.85E-05	8.49E-04 ± 3.00E-05
1H-MRS				
Hippocampus				
<i>GLU</i>	7.80 ± 0.77	7.80 ± 0.65	7.60 ± 0.51	7.75 ± 0.54
<i>GLN</i>	1.17 ± 0.56	1.31 ± 0.67	1.06 ± 0.39	1.28 ± 0.59
<i>NAA</i>	1.79 ± 0.38	1.92 ± 0.30	1.71 ± 0.31	1.97 ± 0.64
<i>GSH</i>	10.23 ± 0.99	10.20 ± 0.48	9.95 ± 0.55	10.12 ± 0.31
dACC				
<i>GLU</i>	11.67 ± 0.91	11.75 ± 0.93	11.89 ± 0.66	11.98 ± 0.60
<i>GLN</i>	1.56 ± 0.51	1.56 ± 0.48	1.53 ± 0.34	1.46 ± 0.40
<i>NAA</i>	0.92 ± 0.07	0.92 ± 0.10	0.90 ± 0.31	0.91 ± 0.63
<i>GSH</i>	10.88 ± 0.76	10.93 ± 0.69	10.87 ± 0.64	11.10 ± 0.08

Supplementary Figure 2 | Exploratory analysis – associations with VO2max: Significant associations of the change in power output during the VO2max test, NAA concentration in the dACC, blood BDNF levels, and blood IGF levels with change in VO2max.



2.3. Physical activity besides the intervention:

Minutes spent on physical activity did not change for either low- or high-intensity condition from pre to post (low: $t(37)=0.26, p=0.79$; high: $t(36)=-0.12, p=0.91$). When splitting these hours up into different categories we also did not find any changes from pre to post intervention in: minutes spent walking (low: $t(43)=0.85, p=0.40$; high: $t(45)=1.43, p=0.16$); minutes spent on intermediate activities (low: $t(40)=0.80, p=0.43$; high: $t(41)=0.77, p=0.45$). Minutes spent on vigorous activities significantly changed only in the high-intensity group (low: $t(43)=-0.24, p=0.81$; high: $t(47)=3.46, p<0.01$).



3. Supplementary References

- Beck AT, Ward C, Mendelson M, Mock J, Erbaugh J. 1961. Beck depression inventory (BDI). *Arch Gen Psychiatry* 4:562–571.
- de Beurs E, van Dyck R, Marquenie LA, Lange A, Blonk RWB. 2001. De DASS: een vragenlijst voor het meten van depressie, angst en stress. *Gedragstherapie* 1:35–54.
- Brock Kirwan C, Hartshorn A, Stark SM, Goodrich-Hunsaker NJ, Hopkins RO, Stark CEL. 2012. Pattern separation deficits following damage to the hippocampus. *Neuropsychologia* 50:2408–2414.
- Carver CS, White TL. 1994. Behavioral Inhibition, Behavioral Activation, and Affective Responses to Impending Reward and Punishment: The BIS/BAS Scales. *J Pers Soc Psychol* 67:319–333.
- Eriksen BA, Eriksen CW. 1974. Effects of noise letters upon the identification of a target letter in a nonsearch task. *Percept Psychophys* [Internet] 16:143–149. Available from: <https://link.springer.com/article/10.3758/BF03203267>
- Fujii T, Saito DN, Yanaka HT, Kosaka H, Okazawa H. 2014. Depressive mood modulates the anterior lateral CA1 and DG/CA3 during a pattern separation task in cognitively intact individuals: A functional MRI study. *Hippocampus* [Internet] 24:214–224. Available from: <http://doi.wiley.com/10.1002/hipo.22216>
- Gaumer Erickson AS, Noonan PM. 2018. Self-efficacy formative questionnaire. In: *The skills that matter: Teaching interpersonal and intrapersonal competencies in any classroom.* . p 175–176.
- Hartman DE. 2009. Test review Wechsler Adult Intelligence Scale IV (WAIS IV): Return of the gold standard. *Appl Neuropsychol* [Internet] 16:85–87. Available from: <https://www.tandfonline.com/doi/abs/10.1080/09084280802644466>
- Jeffrey H. 1961. *The Theory of Probability*. Available from: https://books.google.nl/books?hl=nl&lr=&id=vh9Act9rtzQC&oi=fnd&pg=PA1&ots=feYALYY1nW&sig=18DCw5ZHgMYz8SO5WKZp_ttZRtl&redir_esc=y#v=onepage&q&f=false
- Marteau TM, Bekker H. 1992. The development of a six-item short-form of the state scale of the Spielberger State-Trait Anxiety Inventory (STAI). *Br J Clin Psychol* [Internet] 31:301–306. Available from: <http://doi.wiley.com/10.1111/j.2044-8260.1992.tb00997.x>
- Penner J, Bartha R. 2015. Semi-LASER 1H MR spectroscopy at 7 Tesla in human brain: Metabolite quantification incorporating subject-specific macromolecule removal. *Magn Reson Med* 74:4–12.

- Saan RJ, Deelman BG. 1986. The 15-Words Test A and B.(a preliminary manual). Groningen Univ Groningen, Dep Neuropsychol.
- Skinner EI, Fernandes MA. 2007. Neural correlates of recollection and familiarity: A review of neuroimaging and patient data. *Neuropsychologia* 45:2163–2179.
- Snaith RP, Hamilton M, Morley S, Humayan A, Hargreaves D, Trigwell P. 1995. A scale for the assessment of hedonic tone. The Snaith-Hamilton Pleasure Scale. *Br J Psychiatry* 167:99–103.
- de Sonneville LMJ. 1999. Amsterdam Neuropsychological Tasks: A computer-aided assessment program. In: *Cognitive Ergonomics, Clinical Assessment and Computer-assisted Learning*. . p 187–203.
- Stark SM, Kirwan CB, Stark CEL. 2019. Mnemonic Similarity Task: A Tool for Assessing Hippocampal Integrity. *Trends Cogn Sci* 23:938–951.
- Suwabe K, Hyodo K, Byun K, Ochi G, Yassa MA, Soya H. 2017. Acute moderate exercise improves mnemonic discrimination in young adults. *Hippocampus* [Internet] 27:229–234. Available from: <http://doi.wiley.com/10.1002/hipo.22695>
- Wagenmakers EJ. 2007. A practical solution to the pervasive problems of p values. *Psychon Bull Rev* [Internet] 14:779–804. Available from: <https://link.springer.com/article/10.3758/BF03194105>
- Yassa MA, Mattfeld AT, Stark SM, Stark CEL. 2011. Age-related memory deficits linked to circuit-specific disruptions in the hippocampus. *Proc Natl Acad Sci U S A* [Internet] 108:8873–8878. Available from: www.pnas.org/cgi/doi/10.1073/pnas.1101567108