ISRCTN16744821 https://doi.org/10.1186/ISRCTN16744821

An integrated neuromuscular training intervention applied in primary schools induces epigenetic modifications in disease-related genes

Submission date
09/08/2024

Recruitment status
Recruiting

Registration date
27/09/2024

Overall study status
Ongoing

Last Edited
07/01/2025

Condition category
Other

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol
Background and study aims
Physical exercise has been shown to induce epigenetic modifications with various health implications, and directly affect DNA methylation. The objectives of the present study are: 1) to identify differently methylated genes in saliva of school-aged children following an integrated neuromuscular training; 2) to explore if any of these genes are considered core-genes, i.e., genes of essential importance within the human genome; and 3) to compare the effects of a 3 month and 10 month integrated neuromuscular training intervention on DNA methylation.

Who can participate?
The study population were apparently healthy children form 7 to 9 years, recruited in primary schools in Girona, Spain.

What does the study involve?
Schools are randomly assigned as control or intervention. The children from the intervention schools perform an integrated neuromuscular training as a warm-up activity during the physical education classes. More precisely, the integrated neuromuscular training consists of progressively structured exercises focusing on strength, coordination, dynamic stabilization, plyometrics, speed and agility, organized in circuits and games. On the other hand, the children from the control schools have traditional warm-up activities, i.e., exercises designed to prepare the cardiovascular system and increase the joint mobility for the up-coming physical effort during the class. Study outcome measures are DNA methylation (in saliva), physical fitness and fundamental motor skills. DNA methylation is assessed with the Illumina 900K microarray. Physical fitness and fundamental motor skills are assessed through validated and standardized testing batteries: endurance – assessed with 800 m run test; speed and agility – assessed with shuttle run 10 x 5 m test; explosive power of legs - assessed with the standing long jump test; handgrip strength – assessed with an analog hand dynamometer (TKK 5001, Grip-A, Takei, Tokyo, Japan); flexibility – assessed with the sit-and-reach test; balance – assessed with the closed eyes bipedal test performed on a Wii balance board platform; fundamental motor skills (locomotor,

control and manipulative) – assessed with the CAMSA test. All measurements are performed at baseline, after a 3 month integrated neuromuscular training intervention and will be performed after a 10 month integrated neuromuscular training intervention.

What are the possible benefits and risks of participating?
Participants recruitment is voluntary and there are no associated risk of participating. Conversely, the possible benefits of participating in this study are: increased physical activity, improved physical fitness, motor skills and overall health. The 3 month intervention has been realized in the academic 2016/17, and the 10 month intervention will be realized in 2024/25.

Where is the study run from?
University School of Health and Sport, University of Girona

When is the study starting and how long is it expected to run for?
January 2016 to May 2026

Who is funding the study?
The study is supported by the Ministry of Science and Innovation (Spain) (MCIN/AEI/ 484 10.13039/501100011033) and the ''ERDF A way of making Europe", funded by the European Union (ID2021-124162OA-I00)

Who is the main contact?
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
MCIN/AEI/ 484 10.13039/501100011033, ID2021-124162OA-I00

Study information

Scientific Title
An integrated neuromuscular training intervention applied in primary schools induces epigenetic modifications in disease-related genes: A genome-wide DNA methylation study

Acronym
PEHC

Study objectives
We hypothesized that a 3-month integrated neuromuscular training applied in schools will induce DNA methylation changes in saliva of healthy children and that this intervention may epigenetically modify some of the most important genes across the entire genome. Furthermore, we hypothesized that a 10-month integrated neuromuscular training will induce more prominent methylation changes as compared to the 3-month intervention.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 27/09/2016, Institutional Review Board of Dr. Josep Trueta Hospital, Girona, Spain (Avinguda de França, Girona, 17007, Spain; +34 972 40 51 30; aprats@euses.cat), ref: CEIm: 2016.134

Study design
Randomized controlled interventional study conducted in school settings

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
School

Study type(s)
Prevention, Quality of life

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
The study population is apparently healthy school-aged children.

Interventions
Schools are randomly assigned as a control or intervention school. An integrated neuromuscular training intervention is applied in the intervention schools during the physical education classes as a warm-up activity. More precisely, the children from the intervention school engage in progressively structured exercise sessions consisting of strength, coordination, dynamic stabilization, plyometrics, speed and agility exercises, organized in circuits and games. On the other hand, the children form the control school have the traditional warm-up activities i.e., exercises designed to prepare the cardiovascular system and increase the joint mobility for the up-coming physical effort during the class.

An integrated neuromuscular training intervention is applied to children during physical education classes. The physical education classes in both groups are conducted twice weekly (60 min each) and are structured into an introductory segment (20 min), main segment (30-35 min) and concluding segment (5-10 min). While the main and the concluding segments are the same across both groups, the introductory segment is different.
For the control group, the introductory segment consists of traditional warm-up activities i.e., exercises designed to prepare the cardiovascular system and increase the joint mobility for the up-coming physical effort during the class. On the other hand, the integrated neuromuscular training group during the introductory segment of the classes engages in integrated neuromuscular training sessions as warm-up activities for 3 months, i.e., progressively structured exercises focusing on strength, coordination, dynamic stabilization, plyometrics, speed and agility, organized in circuits and games. Following the 20-minute warm-up during the introductory segment, the children from both groups proceed to the main segment of the class. The main segment of the physical education classes in both groups covers specific curricular content outlined in the national curricula for physical education, which is didactically delivered by the teacher: 1) aerobic activities (running, jumping a rope) and activities that include solving motor tasks in environmental conditions (outdoor circuits and polygons, orienteering activities); 2) activities that will induce development of fundamental motor skills, motor abilities and motor competence (motor challenges that contain elements from individual sports: athletics, gymnastics, tennis); 3) activities that will induce development of interaction skills and team-work (cooperative motor challenges that contain elements from sport games: football, basketball, handball, volleyball); 4) traditional and contemporary dances; and 5) outdoor activities in the natural environment (hiking, cycling, rollerblading, skating).
Finally, the concluding segment of the physical education classes in both groups covers a short period with less dynamic activities that allow children to cool-down gradually, and also provides an opportunity for reflection of the acquired skills during the class.

Intervention Type
Behavioural

Primary outcome measure
DNA methylation is assessed with the Illumina 900K microarray at baseline, after a 3 month integrated neuromuscular training intervention and will be assessed after a 10 month integrated neuromuscular training intervention

Secondary outcome measures
Physical fitness and fundamental motor skills are assessed through validated and standardized testing batteries:
1. Endurance – assessed with 800 m run test before and after the intervention
2. Speed and agility – assessed with Shuttle run 10 x 5 m test before and after the intervention
3. Explosive power of legs - assessed with the standing long jump test before and after the

intervention
4. Handgrip strength – assessed with an analog hand dynamometer (TKK 5001, Grip-A, Takei, Tokyo, Japan) before and after the intervention
5. Flexibility – assessed with the sit-and-reach test before and after the intervention
6. Balance – assessed with the closed eyes bipedal test performed on a Wii balance board platform before and after the intervention
7. Fundamental motor skills (locomotor, control and manipulative) – assessed with the CAMSA test before and after the intervention

Overall study start date
01/01/2016

Completion date
30/05/2026

Eligibility

Key inclusion criteria
1. No evidence of chronic or acute illness in the month preceding potential enrollment
2. Age between 7 and 9 years

Participant type(s)
Healthy volunteer, Learner/student

Age group
Child

Lower age limit
7 Years

Upper age limit
9 Years

Sex
Both

Target number of participants
A minimum of 68 participants should be included in the study. Forty participants were already recruited for the 3 month intervention (20 in the control and 20 in the intervention group). Forty participants more are planned to be recruited for the 10 month intervention.

Total final enrolment
40

Key exclusion criteria
1. Major congenital abnormalities
2. Illness or chronic use of medication
3. Musculoskeletal, neurological disorder and/or a medication therapy that could alter postural stability and cardiorespiratory function
4. Attending fewer than 80 % of the physical education classes

Date of first enrolment
01/10/2017

Date of final enrolment
01/10/2026

Locations

Countries of recruitment
Spain

Study participating centre
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University/education

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Funder(s)

Funder type

Government

Funder Name
Ministerio de Ciencia e Innovación

Alternative Name(s)
CienciaGob, Ministerio de Ciencia e Innovación de España, Ministry of Science and Innovation, Spanish Ministry of Science and Innovation, Ministry of Science and Innovation of Spain, Spain, Ministry for Science and Innovation, Ministeri de Ciència i Innovació, MCIN, MICINN

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Spain

Funder Name
European Commission

Alternative Name(s)
European Union, Comisión Europea, Europäische Kommission, EU-Kommissionen, Euroopa Komisjoni, Ευρωπαϊκής Επιτροπής, Европейската комисия, Evropské komise, Commission européenne, Choimisiúin Eorpaigh, Europskoj komisiji, Commissione europea, La Commissione europea, Eiropas Komisiju, Europos Komisijos, Európai Bizottságról, Europese Commissie, Komisja Europejska, Comissão Europeia, Comisia Europeană, Európskej komisii, Evropski komisiji, Euroopan komission, Europeiska kommissionen, EC, EU

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Results and Publications

Publication and dissemination plan
Planned presentation of the results on national and international scientific congresses and publication in peer-reviewed journals.

Intention to publish date
01/09/2027

Individual participant data (IPD) sharing plan

The datasets generated during the study will be stored in a publicly available repository (https://www.ncbi.nlm.nih.gov/geo/).

IPD sharing plan summary

Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		07/01/2025	07/01/2025	Yes	No