Mid-report

December 2021

The effect of low-frequency pulsed electromagnetic field on inflammation and performance following high intensity exercise training: double-blind crossover clinical trial

Background: Blood markers, specifically those related to inflammation, are a useful tool to evaluate inflammation (Il-6, IL-10, TNF-a, IL1b) muscle damage (CK, LDH) and provide information about recovery status. During the first 24h post-exercise, macrophages and neutrophils act to clear cellular debris that accumulated in the muscle as a result of micro-structural damage. An accumulation of neutrophils observed at the injured areas leads to activation of myeloperoxidase, which promotes the inflammatory response. Interestingly, systematic elevation of bioactive substances may determine neutrophil mobilization and functional status, which may then affect local muscular tissue damage and related to injury in the long-run. The inflammatory response appears to have two phases, which include activation of both anti- and pro-inflammatory mediators, having antagonistic roles. Upon initial tissue insult from the exercise stimulus, the pro-inflammatory cytokines are activated. This response then leads to an increase in anti-inflammatory cytokines. The anti-inflammatory markers inhibit the expression of pro-inflammatory cytokines, thus controlling the magnitude of the inflammatory process. The influence of exercise intensity on the primary inflammatory response is highly relevant for elite athletes in term of faster recovery and injury prevention, and novel tools are needed to support the athletes.

Blood cells, skeletal muscle, and bone release glutamate into the blood under pathological condition and stress. Moreover, the blood-brain glutamate balance plays an important role in both peripheral organs and CNS. Recently, it has been demonstrated that strong physical exercise elevated blood glutamate, Alanine aminotransferase (ALT) and Aspartate Aminotransferase (AST) levels. However, the relationship between muscle damage caused by strong physical exercise and blood glutamate levels have not been examined.

Therapeutic treatment using extremely low frequency (ELF) electromagnetic field is a non-invasive therapy that uses a device generating EMFs with different physical parameters and pulse shapes. Electromagnetic field stimulation has complex effects on the physiological status of cultured cells. Previous studies have shown the induce effects on proliferation of stem cells,

oxidative stress, and human chondrocytes. Moreover, resent works on animal models have demonstrated the beneficial effects of magnetic stimulation at low frequency on recovery from cervical spinal cord injury. To date, no study evaluates the impact of ELF electromagnetic field on inflammation response to high intensity exercise. The anticipated results of this study will support use of ELF electromagnetic field as a novel and effective intervention to accelerate the rate of recovery and improve multistage exercise performance among athletes.

The overall objective of this original project is to determine the efficacy of extremely-low-frequency electromagnetic field (ELF-EMF) on recovery rate among elite cyclist.

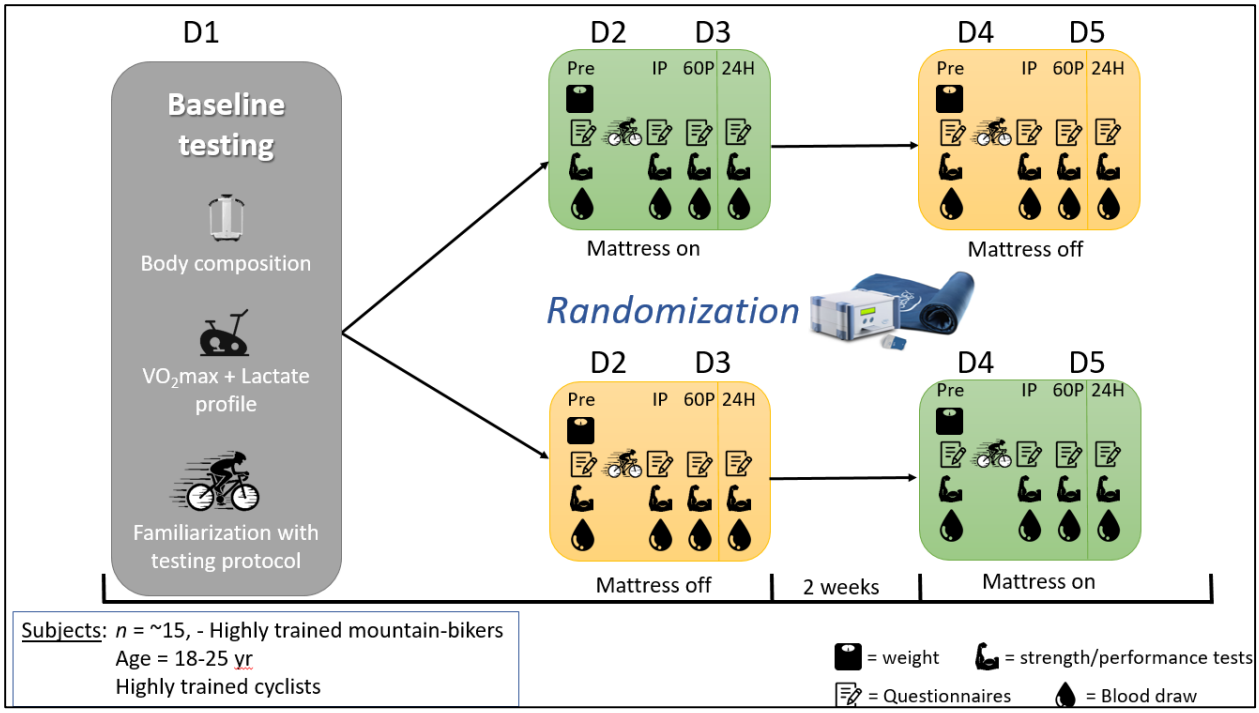
The following aims will be evaluate in this study:

Aim 1: The effect of ELF-EMF treatment (SEQEX) after high intensity exercise training on muscle damage markers and pro- and anti-inflammatory markers up to 24 hr.

Aim 2: To evaluate the effect of ELF-EMF treatment (SEQEX) after high intensity exercise training on Glu, AST and ALT levels up to 24 hr.

Aim 3: To evaluate the effect of ELF-EMF treatment (SEQEX) after high intensity exercise training on exercise performance and recovery up to 24 hr.

Study design: Fifteen young athletes (21-40 yr) without cardiac, pulmonary or metabolic disease will be requited for this double blind, crossover intervention study. Each volunteer will be asked to participate in five experimental visits in the new Sylvan Adams Sport Institute at Tel Aviv University. *Visit 1* will include informed consent and screening for eligibility criteria; measurement of anthropometrics and pulmonary function, including VO2max test. During *Visit 2 and 4*, following a brief standardized warm-up, participants will perform 30 min run on 85-90% VO2max. Immediately post-exercise, participants will ley for 60 min by intervention therapy of ELF electromagnetic field (a magnetic induction of 0.5 mT, with a frequency of 20-70 Hz) or sham only. The intervention or sham exposure will be on a random order. At *visits 3 and* 5 participants will come 24±2 hours following the exercise testing for lab assessment. Study measurements be conducted at *visits 2-5*, and will include muscle damage markers (CK and LDH), inflammation markers (IL-6, IL-10, TNF-a, IL1b), serum levels of glutamate, AST, ALT and exercise performance tests, including vertical jump, maximal voluntary contraction of the quadriceps. In addition, participants will be asked for pain and sourness via validate visual analog scale.



All participants will give their written informed consent prior to participation. This study will be executed according to the principles of the ethic declaration of Tel Aviv University committee.

Preliminary data:

The first three months were focus on protocol setup, pilots and calibration of analytic system. In addition, all ethical consideration have been approved.

We are currently recruiting professional cyclist from the national team in Israel, with fully support of the Israeli cycling federation. Out of 15 planned participants, 8 subjects has been recruited to participant in the study. They are currently in different stages of the research protocol. All study participants will be evaluated comprehensive physiological and biochemical assessment.

Below you can find summary results of one elite cyclist (26y, male, 71.9 kg, 185.9 cm, VO2 max 58.2 ml/kg/min) that completed the study protocol.

Program no.	Program 1				Program 2			
Time point	Pre	IP	60P	24H	Pre	IP	60P	24H
MVC (N)	506.4		436.5	465.5	464.7		406.9	396.8
VJ (cm)	28.6		27.5	27.3	28.6		28.1	25.3
Power output (W)	737	746		756	775	713		759
Work decrement (%)	2.3	3.5		2	4.4	3.5		10.8
Subjective VAS (scale)	1.4	1.9	5.3	1.5	1.2	2.1	1.3	2.5
Subjective ROF (scale)	2	0	3	2	2	2	2	4
Glutamate	21.75	55.08	25.08	21.27	20.58	74.7	45.81	20.79
Aspartate	4.26	4.59	3.18	2.16	3.57	7.5	2.4	1.95
GOT1	19.8	22.6	20.8	20.7	25	26.3	42.4	19.5
GPT	12.6	12.2	11.6	12.1	9.57	10.7	11.9	10.8

MVC: maximal voluntary contraction; VJ: vertical jump; VAS: visual analog scale; ROF: rate of fatigue; GOT1: glutamate-oxaloacetate transaminase;GPT: glutamate-pyruvate transaminase

Summary

Preliminary results demonstrated a different pattern of biochemical and physiological response to the active program of SEQEX (green) versus placebo (yellow). The decrease in blood glutamate and GOT1 levels immediately after SEQEX treatment was more significant compared with placebo treatment. Power output remain high with the active program, while significant decreased was observed for the placebo with lower level 24h post the activity. Similar patterns were found for dynamic (vertical jump) and static (maximal voluntary contraction) strength assessment.