THE EFFECT OF ACUTE ENDURANCE RUNNING EXERCISE ON CORTICOKINEMATIC COHERENCE: A MEG STUDY

Mila Nurminen

Master's Thesis in Biomechanics
Faculty of Sport and Health Sciences
University of Jyväskylä
Spring 2021
Supervisors: Janne Avela, Harri Piitulainen
& Tiina Parviainen

TIIVISTELMÄ

Nurminen, M. 2021. The effect of acute endurance running exercise on corticokinematic coherence: a MEG study. Liikuntatieteellinen tiedekunta, Jyväskylän yliopisto, biomekaniikan pro gradu -tutkielma, 101 s, 4 liitettä.

Kortikokinemaattisella koherenssilla (CKC) tarkoitetaan lineaarista riippuvuutta kinemaattisen signaalin (esim. nopeus tai kiihtyvyys) ja aivosignaalin välillä (Bourguignon et al. 2011; Bourguignon et al. 2012; Piitulainen et al. 2013b). CKC:n oletetaan kuvastavan proprioseptisen signaalin prosessointia aivokuorella. Ensisijaisia afferentin signaalin lähteitä ovat lihasspindelit sekä Golgin jänne-elimet ja koherenssin huippuarvo paikantuu sensorimotoriselle (SM1) korteksille (Piitulainen et al. 2013b; Bourguignon et al. 2015.) Edeltävissä tutkimuksissa on osoitettu eroja CKC:n voimakkuudessa ikäryhmien välillä ja joissain keskushermoston sairauksissa sekä korrelaatio tasapainon ja CKC:n voimakkuuden välillä (Piitulainen et al. 2018b; Marty et al. 2019). Viitteitä CKC:n eroista dominoivan ja ei-dominoivan raajan välillä on myös esitetty (Piitulainen et al. 2018b). Neuraaliset mekanismit ja koherenssin voimakkuuteen vaikuttavat sensorimotoriset hermoverkot on edelleen huonosti tunnettu. Tähän päivään mennessä ei ole tiedossa, onko fysiologisen tilan muutoksella, kuten väsymyksellä vaikutusta CKC:n voimakkuuteen ja voiko akuutti fyysinen urheiluharjoitus muokata sitä. Tutkimuksen tarkoituksena oli selvittää, vaikuttaako akuutti aerobinen juoksusuoritus CKC:n voimakkuuteen eli kortikaaliseen proprioseptiseen prosessointiin. Tutkimuksessa selvitettiin myös, onko tasapaino yhteydessä CKC:n voimakkuuteen, tai onko juoksuharjoituksen aiheuttamat muutokset tasapainossa tai CKC:ssa yhteydessä toisiinsa.

10 tervettä vapaaehtoista aikuista osallistui tutkimukseen, jossa mitattiin CKC:n voimakkuus ja tasapainokyky ennen 90 min juoksumattoharjoitusta ja sen jälkeen. Koherenssia nilkan kiihtyvyyssignaalin ja SM1 alueen magnetoenkefalografia-signaalin (MEG) välillä tarkasteltiin 2 Hz passiivisen nilkanliikutuksen aikana liiketaajuudella (F0) ja sen ensimmäisessä harmoniassa (F1). Koherenssi määritettiin arvona 0–1, jossa nolla tarkoittaa ei yhteyttä ja yksi täydellistä koherenssia signaalien välillä. Massakeskipisteen (COP) sijainninmuutoksen nopeutta mitattiin kahdella jalalla seisten tasapainolevyllä. Proprioseptiikan hyödyntämistä tasapainossa arvioitiin laskemalla suhdeluku huojuntanopeuksille silmät auki ja silmät kiinni seisten (RQ). 90 min juoksuharjoituksen kuormittavuutta arvioitiin juoksun aikana laktaattinäytteiden, sydämen sykkeen ja koetun kuormittuneisuuden asteikon avulla sekä isometrisellä maksimipolvenojennuksella ja suorin jaloin hyppelyllä ennen juoksua ja sen jälkeen. Hypoteesina oli, että 90 min aerobinen juoksuharjoitus heikentäisi proprioseptista prosessointia ja siten voimistaisi kortikokinemaattista koherenssia ja että CKC:n voimakkuus olisi yhteydessä tasapainokykyyn.

Koherenssi MEG-signaalin ja kiihtyvyyssignaalin välillä oli havaittavissa sekä ennen juoksua että sen jälkeen F0 ja F1 taajuuksilla. Mahdollisesti erittäin pienestä otoskoosta johtuen (F0: n = 4 ja F1: n = 8) tai pitkästä aikavälistä juoksun ja MEG-mittauksen välillä (26 min) ei pystytty osoittamaan, että akuutti juoksuharjoitus vaikuttaisi CKC:n voimakkuuteen. 90 min aerobisella juoksulla ei tämän tutkimuksen perusteella ole vaikutusta CKC:n voimakkuuteen F0 tai F1 taajuudella. Juoksu lisäsi huojuntaa tasapainotestissä, mutta ei vaikuttanut huojunnan määrän suhteeseen silmät kiinni ja silmät auki testien välillä. Anterior-posterior-suuntainen huojunta silmät kiinni oli yhteydessä CKC:n voimakkuuteen F0 taajuudella, mutta muita yhteyksiä tasapainon ja CKC:n väliltä ei löytynyt. Johtuen pienestä otoskoosta ja CKC-datan laatuongelmista, näitä tuloksia voidaan pitää vain suuntaa antavina.

Asiasanat: kortikokinemaattinen koherenssi; proprioseptiikka; juoksuharjoitus

ABSTRACT

Nurminen, M. 2021. The effect of acute endurance running exercise on corticokinematic coherence: a MEG study. Faculty of Sport and Health Sciences, University of Jyväskylä, Master's thesis in Biomechanics, 101 pp. 4 appendices.

Corticokinematic coherence (CKC) means linear dependence between kinematic signal (e.g. velocity or acceleration) and brain cortical signal (e.g. Bourguignon et al. 2011; Bourguignon et al. 2012; Piitulainen et al. 2013b). It is supposed, that CKC reflects cortical processing of proprioceptive feedback. CKC origins mainly from muscle spindles and Golgi tendon organs and peaks at contralateral SM1 cortex. (Piitulainen et al. 2013b; Bourguignon et al. 2015.) Previous studies have shown differences in the strength of CKC between age groups and with some central nervous system disorders, as well as association between postural balance and CKC (Piitulainen et al. 2018b; Marty et al. 2019). There are also some indications of the effect of limb dominance on CKC strength (Piitulainen et al. 2018b). Still, neural mechanisms of CKC and by which sensorimotor networks its strength is modulated are poorly understood. To date, it is unknown whether changes in physiological states, such as fatigue, affect the strength of CKC and whether CKC can be modulated by acute exercise. Purpose of this study was to investigate, does a single bout of aerobic running exercise have an effect on the strength of CKC, i.e. cortical proprioceptive processing. Secondary aim was to investigate if postural balance is correlated with the strength of CKC or if changes in these parameters due to running exercise associated with each other.

Ten healthy volunteer adults participated in the study, where CKC and postural sway was measured before and after 90 min treadmill running. Coherence between magnetoencephalography (MEG) signal in SM1 at movement frequency (F0) and its first harmonic (F1) and acceleration signal during passive 2 Hz ankle movement was evaluated in scale 0–1, where zero is no association and one is perfect coherence. Velocity of center of pressure (COP) displacement was measured during two feet standing on balancing board. Use of proprioception during standing was determined by calculating quotient between eyes open and eyes closed standing (RQ). For evaluation of 90 min running exercise, blood lactate levels, heart rate and rating of perceived exertion was monitored during running and maximal isometric contraction of knee extensors and straight-legged jumps was performed before and after running. Hypothesis was that 90 min running would impair proprioceptive processing and thus increase CKC and that CKC is connected to balance control.

Significant coherence between MEG and acceleration signal was observed before and after running at F0 and at F1. Possibly due to extremely small sample size (n = 4 at F0 and n = 8 at F1) or time between running and CKC measurement (26 min) this study could not show that acute running exercise would alter the strength of CKC. Results from this study suggest that 90 minutes moderate intensity aerobic running exercise has no effect on corticokinematic coherence at F0 or at F1. Moreover, running exercise disturbed postural balance control when standing on two feet eyes closed and eyes open, but did not have effect on quotient between eyes closed and eyes open sway. Only antero-posterior sway during eyes closed standing correlated with the strength of CKC at F0, but further evidence about associations between the strength of CKC and postural balance was not found. Because of small sample size and problems in CKC data quality, these results must be considered only preliminary.

Key words: corticokinematic coherence; propriocetion; running exercise

ABBREVATIONS

Bal	Balance
BLa	Blood lactate
BPM	Beats per minute
cHPI	Constant head position indicator
CKC	Corticokinematic coherence
CMC	Corticomuscular coherence
CNS	Central nervous system
CON	Control condition
COP	Center of pressure
DC-ML	Dorsal column - medial lemniscus pathway
EC	Eyes closed
ECG	Electrocardiography
EEG	Electroencephalography
EMG	Electromyography
EO	Eyes open
EOG	Electrooculography
fMRI	Functional magnetic resonance imaging
GTO	Golgi tendon organ
Hop	Straight-legged jumping
HR	Heart Rate
M1	Primary motor cortex
MEF	Motor evoked field
MEG	Magnetoencephalography
MRI	Magnetic resonance imaging
MSR	Magnetically shielded room
MVC	Maximal voluntary contraction
ROM	Range of motion
RPE	Rating of perceived exertion
RS	Resting state

RUN	Running condition
S1	Primary sensory cortex
SAI	Short-latency afferent inhibition
SD	Standard deviation
SEP	Somatosensory-evoked potential
SM1	Primary sensorimotor cortex
SQUID	Superconducting quantum interference device
SSS	Signal-space-separation
VO_2	Oxygen consumption
VO_{2max}	Maximal oxygen consumption
VPL	Ventral posterior lateral nucleus

CONTENT

1 INTRODUCTION

Corticokinematic coherence (CKC) refers linear dependence between kinematic signal (e.g. velocity or acceleration) and brain cortical signal, measured with magnetoencephalography (MEG) (e.g. Bourguignon et al. 2011; Bourguignon et al. 2012; Piitulainen et al. 2013b) or electroencephalography (EEG) (Smeds et al. 2017; Piitulainen et al. 2020). CKC peaks at primary sensorimotor (SM1) cortex and reflects processing of proprioceptive afferent input (Piitulainen et al. 2013b; Bourguignon et al. 2015). Currently, it is unknown what mechanisms operate the alteration of CKC strength, but it has been proposed that less specific activation of cortical neural populations increases coherence between limb kinematics and SM1 brain signals. With healthy subjects the direction of adaptation is that weaker coherence indicates more accurate and targeted proprioceptive processing and stronger coherence reflects less efficient processing. (Piitulainen et al. 2018b.) It is not known whether CKC can be modulated acutely or does it require long-term adaptation in the brain. Along with sensorimotor deficit in peripheral proprioceptors and spinal circuits, changes in thalamocortical loops and primary somatosensory (S1) and motor (M1) cortex circuits has been argued to explain stronger coherence observed with older, compared to younger subjects and with non-dominant, compared to dominant limb (Piitulainen et al. 2018b; Bardouille et al. 2019). It should be noted that CKC has been shown to reflect proprioceptive processing at the group level, but at the individual level, it may not be effective (Piitulainen et al. 2018a).

Origin of corticokinematic coherence is proprioceptive afference, primarily from muscle spindles, but also from Golgi tendon organs (GTO), while skin receptors have negligible effect (Piitulainen et al. 2013b; Bourguignon et al. 2019). Physical exercise has number of acute effects on proprioceptors and spinal circuits (e.g. Hagbarth & Macefield 1994; Pedersen et al. 1998; Taylor et al. 2000; Taylor et al. 2016), which may modulate afferent feedback from proprioceptors to sensorimotor cortex and alter the strength of coherence. Thus, proprioception can be impaired when muscle fatigue disturbs proprioceptors and modulates afferent signal.

However, general, whole body exercise, can alter central processing of proprioceptive inputs and impair proprioception without local muscle fatigue (Miura et al. 2004.) Whole body aerobic exercise has been shown to increase afferent conduction velocity together with decreased S1 cortex excitability (Bulut et al. 2003) or without changes in excitability (Nakata et al. 2016). Reduced inhibition in motor cortex circuits without changes in corticospinal excitability (Smith et al. 2014), as well as reduced inhibition in sensorimotor integration (Yamazaki et al. 2019) has been noted. Acute exercise can also increase (Rajab et al. 2014; Raichlen et al. 2016) or decrease (Schmitt et al. 2019) connectivity of sensorimotor related areas in resting state brain activity. Changes in cortical neural circuits may alter cortical processing of somatosensory feedback and thus strength of CKC. It is well recognized that aerobic exercise can alter postural stability (Lepers et al. 1997; Nardone et al. 1997), and it has been argued that changes in proprioception may cause this alteration (Nardone et al. 1997; Paillard 2012). Increase in Romberq quotient (RQ), referred as ratio of postural sway during eyes closed and sway during eyes open is considered to indicate impaired proprioception (Nardone et al. 1997). Some evidence about connection between poorer balance control and stronger CKC has been found (Piitulainen et al. 2018b).

To date, CKC has been studied in group level and it has been shown that the strength of CKC is altered by ageing, as older age group demonstrated stronger CKC than younger group (Piitulainen et al. 2018b). However, it is unknown whether changes in physiological states, such as fatigue, affect the strength of CKC. Purpose of the study was to examine effect of acute aerobic running exercise on the strength of CKC, expecting it to indicate efficiency of proprioceptive processing. Secondary aim of this study was to investigate if postural balance or alteration in postural balance after exercise is associated with the strength of CKC or changes in CKC-level due to running exercise. Hypothesis was that running exercise would disturb cortical proprioceptive processing and strengthen CKC. It was also expected to impair postural balance. Further expectation was that stronger CKC is connected to impaired control of balance.

2 MAGNETOENCEPHALOGRAPHY

Magnetoencephalography (MEG) is a non-invasive brain imaging technique that detects ongoing brain activity in time resolution of milliseconds. Since Cohen (1968) first measured magnetic fields generated by alpha rhythm currents, MEG has been used for studying brain activity during different cognitive processes, neurophysiological processes under external stimuli, for localizing brain function, as well as in clinical settings.

2.1 Principles of MEG

MEG measures magnetic fields. MEG-sensors detect magnetic fields that are generated by activity of large neuron populations. Primary source of MEG signals are postsynaptic currents in the pyramidal neurons' apical dendrites (Fig. 1). (Da Silva 2010, 1–23.) These weak magnetic fields are measured with very sensitive, superconducting quantum interference device (SQUID) sensors. Because small diameter of SQUID and thus poor coupling with magnetic fields, superconductive flux transformers are used for enhancing collection of magnetic flux. Typical configurations of flux transformers are magnetometers, which consist of single pick-up coil, or axial or planar gradiometers, which in addition to pick-up coil, comprise also a compensation coil. By combining different magnetometers and gradiometers, more comprehensive range of signal detection from different sources and directions is achieved. (Parkkonen 2010, 24–34).

Inverse problem and magnetic noise. Measuring neuronal activity from outside the skull causes inverse problem of source modelling. Externally measured MEG signal is generated by activity of several distinct neuron populations. Thus, the exact source of the electrical activity cannot be localized without making some assumptions about unknown parameters. There are different models that are trying to solve this inverse problem, but the localization of externally measured signal is always an estimate. Another main issue is that brain signals are weak compared to other magnetic fields (e.g. earth's geomagnetic field and electronics). For avoiding external

sources of magnetic fields, measurements must be conducted in magnetically shielded room (MSR). Besides external sources, there are several sources in human itself that generate similar electrical activity as brain neurons. Electrical activity from heart beats and eye movements are usually recorded for that non-brain source activity can be removed from MEG signal. For the same reason, muscle activity and excessive movement must be voided during MEG measurements. Despite mentioned actions, MEG signal must be averaged from several trials for better signal to noise ration. Further analyses of MEG signal require several steps of signal processing and filtering to distinguish external signals and components from non-brain sources. (Hämäläinen et al. 1993.)

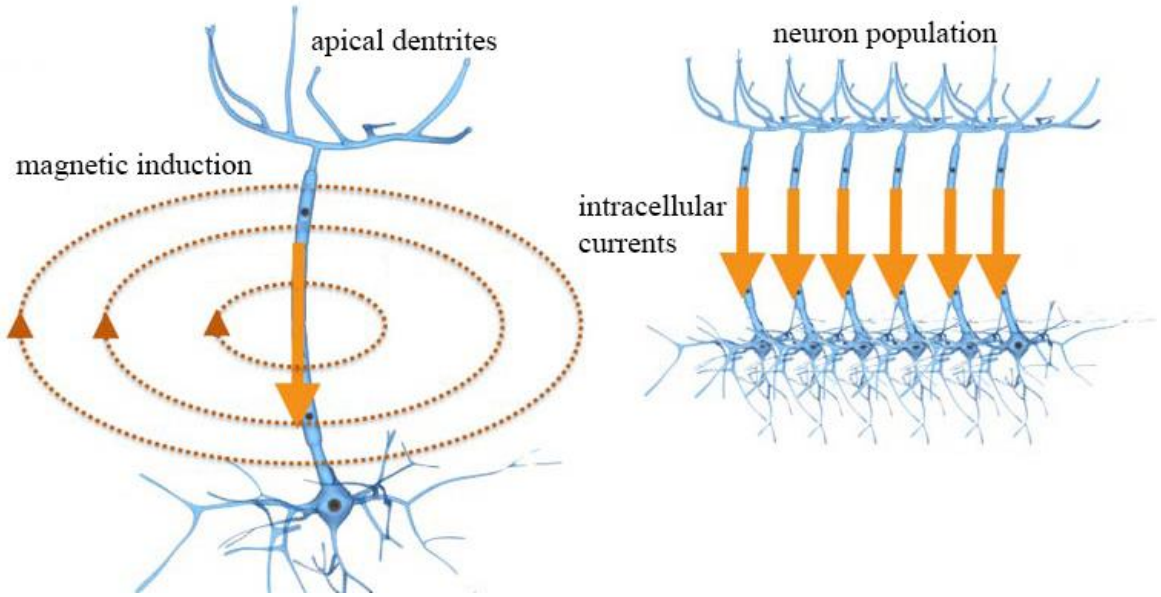

FIGURE 1. Postsynaptic potentials of pyramidal neurons' apical dendrites generate electrical current which produces magnetic field. Modified from Baillet (2017).

2.2 Studying sensory and motor functions with MEG

The advantage of MEG in measuring brain sensory and motor function after physical activity, is that MEG detects signal outside of the skull and is not sensitive to skin-electrode conductance

that can be affected by sweating. Besides spontaneous brain activity after sensory and motor system has been stressed, MEG can be used for studying human brain function under different sensory stimuli. External stimulations, such tactile stimulation by pressure and temperature changes can be applied for studying neurophysiological processes of somatosensory system (Parkkonen 2010, 57–58). Somatosensory evoked fields, evoked by electrical stimulations and motor evoked fields (MEF), evoked by voluntary or passive movement can be detected in sensory cortex. MEG detects currents that are tangential to scull, which makes source localisation difficult in certain brain areas. Therefore, brain activity evoked by electrical stimulation can be easily detected from the wall of postcentral gyrus, (Brodmann area 3b), while afferent signals evoked by voluntary or passive movement that are carried to bottom of central sulcus (Brodmann area 3a) are not as easily detected in MEG signal. Sensory afferents to primary motor cortex in wall of the precentral gyrus are also easily detected with MEG. (Kakigi & Forss 2010, 300–345.)

Synchronous activity of large populations of cortical neurons generates oscillation of electrical and concomitant magnetic fields. In addition to evoked fields, oscillatory cortical activity can be measured during rest or under different activities. Level of co-activation of neuron populations between brain regions and relationship between time-series of neuronal signals can be studied with MEG. (Marzetti et al. 2019.) Coherence between brain oscillations and kinematic signals (Bourguignon et al. 2011; Bourguignon et al. 2012; Piitulainen et al. 2013b) or muscle activity (Conway et al. 1995; Liu et al. 2019) at same frequency has been used for studying encoding of sensory and motor functions. Limitation in coherence analyses with MEG is its sensitivity to even small magnetism. As MEG measures all magnetic fields, weather they are from brain or non-brain sources, even small magnetism which is connected to stimulus (e.g. acceleration of movement) will produce MEG signal that is coherent with kinematic signal. Thus, before conducting MEG measurements subject should be cleaned from all objects that contain metal and from hair and face products that could contain magnetic metal particles (Parkkonen & Salmelin 2010).

3 PROPRIOCEPTION IN HUMAN SENSORIMOTOR SYSTEM

The somatosensory system plays an important role in controlling movement. It is responsible for internal body perception and its relation to environment and together with motor system it is controlling movement for proper outcome. Sensory system includes sensory receptors, parts of the brain responsible for processing sensory information and neural pathways carrying this information. Sensation of touch, pressure, temperature, pain, body position and movement arise from peripheral receptors located in muscles, joints and skin (Fitzpatrick & Mooney 2019, 181). At the spinal cord level, sensory inputs from the environment can activate reflexes, modulate locomotor pattern generators and other spinal cord pattern generators, as well as descending commands of movement from higher levels of central nervous system (CNS) (Shumway-Cook & Woollacott 2010, 51).

Proprioception reflects sense of position (static proprioception) and sense of rates of movement (dynamic proprioception). Together with vision and vestibular system, proprioception is important part of sensorimotor system and crucial for appropriate motor control. (Kandel et al. 2000, 345; Gandevia et al. 2002.) According to Shields et al. (2005), the term was first classified in 1906 by Sherrington in his book "The Integrative action of nervous system". However, sense of movement has been under the interest before Sherrington's classification of proprioception. Bastian (1887) classified the term kinaesthesia and defined it as a sense of movement. Kinaesthesia is sometimes referred as dynamic proprioception.

3.1 Sensory pathways for proprioception

Movement coordination utilizes position sense and requires information from peripheral receptors, such as muscle spindles. Conscious position sense is processed in cerebral cortex and information from peripheral receptors is carried through dorsal column - medial lemniscus pathway (DC-ML). Automatic movement coordination, such as timing of contraction is

processed in cerebellum and information is transported through dorsal spinocerebellar tract. Tactile information is also carried to somatosensory cortex through DC-ML, (Fitzpatrick & Mooney 2019, 190–193), while painful and thermal sensations are carried to cortex through Anterolateral system (Kandel et al. 2000, 448).

3.1.1 Dorsal column - medial lemniscus pathway

First order neurons to dorsal column nuclei. Proprioceptive information from muscle spindles and GTOs, along with other sensory information from tactile receptors is carried to cerebral cortex via dorsal column - medial lemniscus pathway (DC-ML). Information from receptors is entering to spinal cord via dorsal root. Small branches of these axons terminate grey matter and modulate spinal reflexes, but majority of the axons continue ascending to medulla. Proprioceptive axons are carried in ventral side of dorsal column. Axons from lower limbs are bunded in fasciculus gracilis, while axons from upper limbs, trunk and neck are in fasciculus cuneatu. In caudal medulla, first order neurons from lower body synapse to second order neurons in medial subdivision of dorsal column nuclei, called nucleus gracilis, while axons from upper body synapse in nucleus cuneatus. (Kandel et al. 2000, 446–448; Fitzpatrick & Mooney 2019, 190–193.)

Second order neurons to thalamus. Second order neurons cross the midline of spinal cord and continue their way via medial lemniscus pathway to ventral posterior lateral nucleus (VPL) of thalamus. Again, axons from lower body are located ventrally, whereas axons from upper body are located dorsally, until they pass pons and midbrain and rotate 90 degrees. Axons from lower body terminate to thalamus in lateral and upper body axons in medial side. (Kandel et al. 2000, 446–448.) Thalamus is located in the dorsal portion of diencephalon and consist of several different nuclei. Specific, nonspecific, and reticular nuclei of thalamus receive input from varied areas and have projections to different sites of the brain modulating the information that is passing through thalamus. Neurons in specific nuclei modulate and pass information of specific sensation, as somatosensory, auditory and visual inputs, while nonspecific nuclei are

affecting to state of brain. Sensory and motor functions are modulated in ventral group of specific nuclei. Reticular nucleus is covering the thalamus and is sending axons to other nuclei of thalamus instead of to cerebral cortex and modulates the activity of thalamus itself mostly with inhibitory neurons. (Kandel et al. 2000, 341–344.)

Third order neurons to cerebral cortex. From thalamus, internal capsule carries third order somatosensory neurons to primary somatosensory cortex (Fitzpatrick & Mooney 2019, 190). Besides somatosensory cortex, primary motor cortex receives direct inputs from proprioceptive afferents (Goldring & Ratcheson 1972). Figure 2 represents dorsal column medial lemniscus pathways from lower and upper body.

3.1.2 Spinocerebellar tract

Proprioceptive information is also transported to cerebellum, where information is used in modulating the timing of contraction of voluntary movement. As was the case with DC-ML, proprioceptive information from upper and lower body are transported via different pathways in spinocerebellar track. Axons from upper body are carried to medulla via dorsal column. In medulla, they make synapses in external cuneate nucleus and continue to ipsilateral side of cerebellum. Unconscious information from muscle spindles and GTOs of lower body is carried to cerebellum through dorsal spinocerebellar tract. First order neurons from mid-lumbar and thoracic levels (L2–T1) enter in dorsal root and synapse on neurons in Clarke's nucleus, located in dorsal horn. Neurons from lower body parts first ascend through dorsal column to Clarke's nucleus and synapse to second order neurons. From Clarke's nucleus, neurons travel in dorsal spinocerebellar tract to cerebellum. In their way to medulla, axons give collaterals to dorsal column nuclei, where they synapse to other proprioceptive neurons and continue to cortex via medial lemniscus. (Fitzpatrick & Mooney 2019, 192–193.)

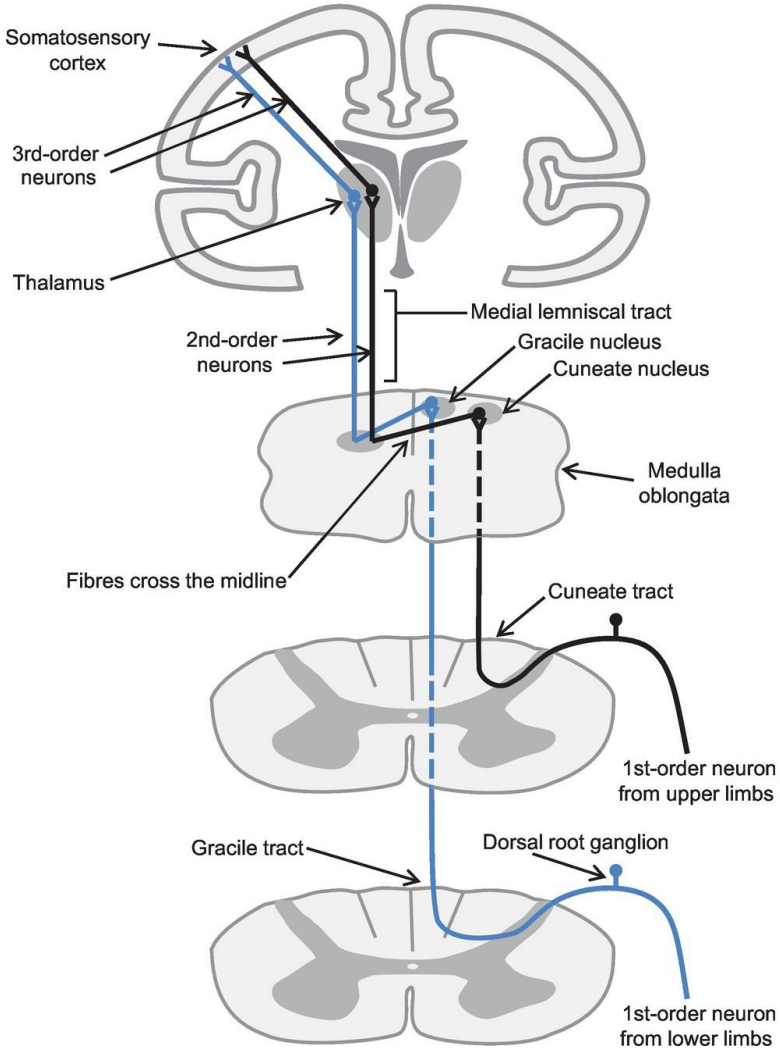

FIGURE 2. Dorsal column - medial lemniscus pathways from lower (blue) and upper (black) body. (Chambers et al. 2019.)

3.2 Proprioceptive receptors and reflex regulation

Receptors in muscles, tendons and joints react to mechanical stimuli and provide information about the body position and movement, as well as sense of effort, force and heaviness. Primary information of proprioception arises from muscle spindles, which sense both static position and dynamic movement. Skin and joint receptors seem to offer some, but limited information for

sense of movement, while Golgi tendon organs sense muscle tension and offers information about force and heaviness (Proske & Gandevia, 2012.)

3.2.1 Muscle spindle

Structure of muscle spindle. Muscle spindles are located in the skeletal muscle. Spindles consist of nuclear bag fibers (divided into static and dynamic types) and less elastic nuclear chain fibers (static type). These so called intrafusal fibers are parallel with extrafusal fibers and are stretch when skeletal muscle is stretched. Stretching activates mechanically-gated ion-channels of intrafusal fibers, and two types of sensory neurons are ascending from the central regions of the spindle to central nervous system (CNS): Fast conducting and fast adapting primary afferents (Ia) are connected to both bag and chain fibers and react to rate of the muscle length changing. Slower, secondary afferents (II) are mostly connected to chain fibers. They are less sensitive to stretch and are specialized to recognize static muscle length. (Shumway-Cook & Woollacott 2010, 51.) Figure 3 illustrates structure of muscle spindle.

Function of muscle spindle. Intrafusal fibers of muscle spindle are not only passively stretched or shortened with length changes of extrafusal fibers. As extrafusal fibers are innervated by alpha-motoneurons, intrafusal fibers also receive input from motor efferents: static gamma-motoneuron innervate nuclear chain fibers and statig nuclear bag fibers, while dynamic gamma-motoneuron innervate dynamic nuclear bag fibers. Alpha-gamma coactivation theory states that alpha-motoneuron activates extrafusal fibers to contract and, gamma-motoneuron, which activates intrafusal fibers, is activated parallel. Whenever there is voluntary contraction, the efferent neurons are activating both alpha-motoneuron and gamma-motoneuron. With this motor innervation, intrafusal fibers length is regulated, and muscle spindle sensitivity is monitored. (Kandel et al. 2000, 713–736.) In very simplified model, muscle spindle firing rate is increasing when muscle is stretch, as the stretch-activated channels depolarize and firing rate decreases when muscle is shortening (contracting). Slowly adapting II afferents from static

nuclear bag fibers transmits information about muscle length in static contraction. Both spinal and supraspinal regions use information from muscle spindle. (Kandel et al. 2000, 713–736.)

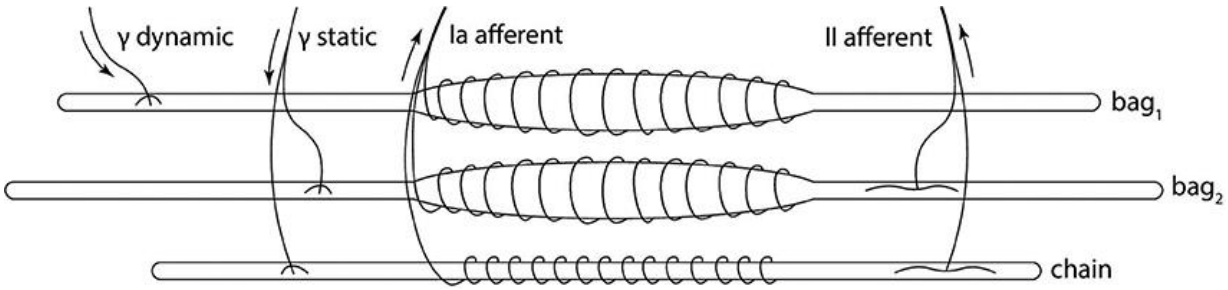

FIGURE 3. Three types of muscle spindle fibers (dynamic nuclear bag (bag_1), static nuclear bag (bag_2), and nuclear chain fibers) are stimulated by static and dynamic gamma-motoneurons (γ dynamic and γ static), which activate Ia and II afferents. (Vannucci et al. 2007.)

3.2.2 Golgi tendon organ, joint and cutaneous receptors

Golgi tendon organ. GTO sends information about changes of tension to spinal cord, cerebellum, and cerebral cortex. GTO is very sensitive to even small changes in tension caused by muscle contraction. (Fitzpatrick & Mooney 2012, 196 - 198.) However, GTO does not detect small changes during static or passive movement, indicating that GTO is not crucial in position sense during passive movement. (Paillard & Brouchon 1968). GTOs are connected to 15–20 muscle fibers and are located at muscle-tendon junction. Stretch or contraction of muscle may cause tension, which GTO responds. GTO is involved in the regulation of muscle activity with its disynaptical connection to motoneurons its own muscle via inhibitory interneuron and to its antagonist via excitatory interneuron. (Shumway-Cook & Woollacott 2010, 53.)

Joint receptors. Joint receptors lie in different parts of joint capsule. Information of joint receptors ascends to cerebral cortex, where the joint position is processed based on which receptors are activated (Shumway-Cook & Woollacott 2010, 53). Joint receptors have only minor role in limb proprioception, but they seem to have important role in position sense of fingers (Fitzpatrick & Mooney 2019, 189–190.)

Cutaneous receptors. Pacinian, Merkel cell, Meissner and Ruffini are the type of cutaneous receptors that detect tactile stimuli. They are stimulated by skin motion, stretch and vibration, and together with proprioceptive receptors, they help recognizing motion and body position. (Fitzpatrick & Mooney 2012, 196 - 198.) Other kind of cutaneous receptors are thermoreceptors, detecting temperature changes and nociceptors, detecting skin damaging. (Shumway-Cook & Woollacott 2010, 55).

3.2.3 Regulation of spinal circuits and ascending information

Proprioceptive reflex regulation. When entering to spinal cord, majority of proprioceptive axons are ascending to the cerebral cortex, cerebellum, and other supraspinal structures, but small branches of these axons terminate grey matter and modulate spinal reflexes (Wardman et al. 2014). These branches synapse to other spinal neurons in both, dorsal and ventral root. They regulate interneurons and motoneurons, which modulates spinal activity and thus reflexes. (Fitzpatrick & Mooney 2019, 192.) Primary afferents (Ia) of muscle spindles are monosynaptically connected to motoneurons of the muscle itself and its synergists, and via inhibitory interneuron to motoneuron of its antagonists (Kandel et al. 2000, 713–736). Muscle afferent populations of single muscle or muscle groups provide crucial information about a movement. Thus, proprioception plays an important role in reflexive regulation of motor control.

Changes in receptor sensitivity. Sensitivity of peripheral receptors and thus the ascending proprioceptive information may be altered depending on the type of the muscle activity. When

considering proprioceptive signals from muscle spindle in different kind of activities, the role of fusimotor system must be noted. Muscle spindle can be activated by muscle stretch or by contraction of intrafusal fibers. Meaning that these receptors may send ascending signals not only when muscle is stretch, but also when muscle fibres are contracting and gamma-motoneurons activates intrafusal fibers (Fitzpatrick & Mooney 2012, 197–198). Thus, the level of the gamma-motoneuron activity must be noted when considering positional signals from periphery. Because of the modulation of spindle sensitivity via activity of gamma-motoneuron, spindle is more sensitive to changes in position during active than in passive movement (Gandevia & Burke 1992). Repeated stretch-shortening cycles may cause mechanical changes in the extrafusal and/or intrafusal fibers, reduce spindle sensitivity and thus modulate spinal reflex loops and affect motor control in spinal level (Horita et al. 1996; Avela et al. 1999) and potentially ascending feedback and supraspinal control.

3.3 Supraspinal processing of proprioception

Proprioceptive input from DC-ML is conducted to several cortical and subcortical areas through thalamus, which is an essential modulator of afferent information (Goble et al. 2011; Goble et al. 2012, Shumway-Cook & Woollacott 2010, 58 – 59). Both, S1 and M1 receive direct afferent proprioceptive projections through thalamus (Goldring & Ratcheson 1972; Lucier et al. 1975). Areas of cerebral cortex have projections to other cortical and subcortical areas, and with these networks, sensory proprioceptive information is integrated for coordinated motor functions (Shumway-Cook & Woollacott 2010, 58 – 59).

3.3.1 Sensory and motor cortex

Somatosensory cortex, located in the parietal posterior site of central sulcus receives information from joint, muscle and cutaneous receptors. It covers Brodmann areas 1, 2, 3a, and 3b of primary somatosensory cortex (S1), and secondary somatosensory cortex (S2) (Fitzpatrick & Mooney 2019, 194–195). From VPL of thalamus, proprioceptive information is

carried to primary sensory cortex area 3a, while inputs from skin are carried to area 3b (Fig. 4). These two types of sensory information are integrated in Brodmann area 2, and area 1 is for higher order processing of cutaneous information. (Kandel et al. 2000, 384–387.) From somatosensory cortex, neurons project to motor regions, as well as to somatosensory association areas in parietal cortex, from where information continues to unimodal association areas of premotor cortex and posterior parietal cortex, from where it continues to higher order association areas and to premotor cortex (Kandel et al. 2000, 344–345). However, primary motor cortex, Brodmann area 4 receives proprioceptive information not only from sensory areas, but also directly from muscle spindles through thalamus (Goldring & Ratcheson 1972). Figure 4 represents organization of Brodmann areas 1, 2, 3a, 3b and 4.

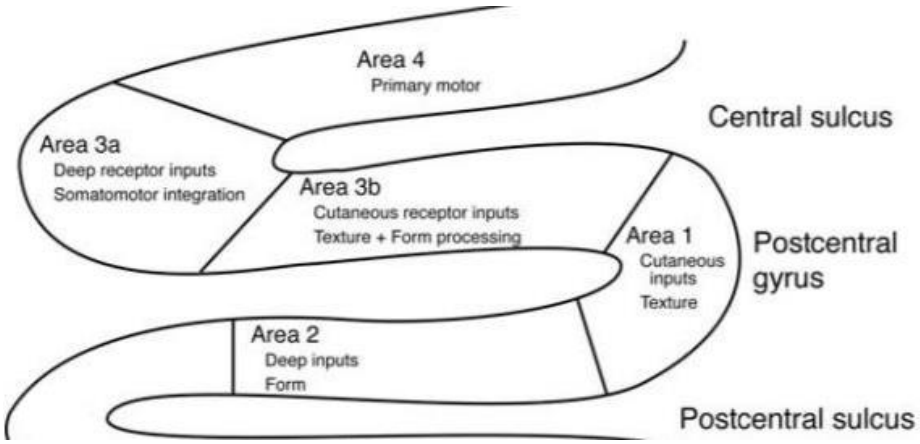

FIGURE 4. Primary somatosensory areas 1, 2, 3a, and 3b on postcentral gyrus and primary motor area 4 on precentral gyrus. Adapted from James et al. (2007).

Both S1 cortex and M1 cortex have homunculus that represents certain areas of body (Penfield & Boldrey 1937). Each Brodmann areas on S1 cortex represent different types of sensory information but have similar body maps. For sensing movement in space, it is essential to be able to separate information from different body parts and sense location of body parts relative to each other. (Shumway-Cook & Woollacott 2010, 58 - 59). Figure 5 represents both sensory and motor homunculus.

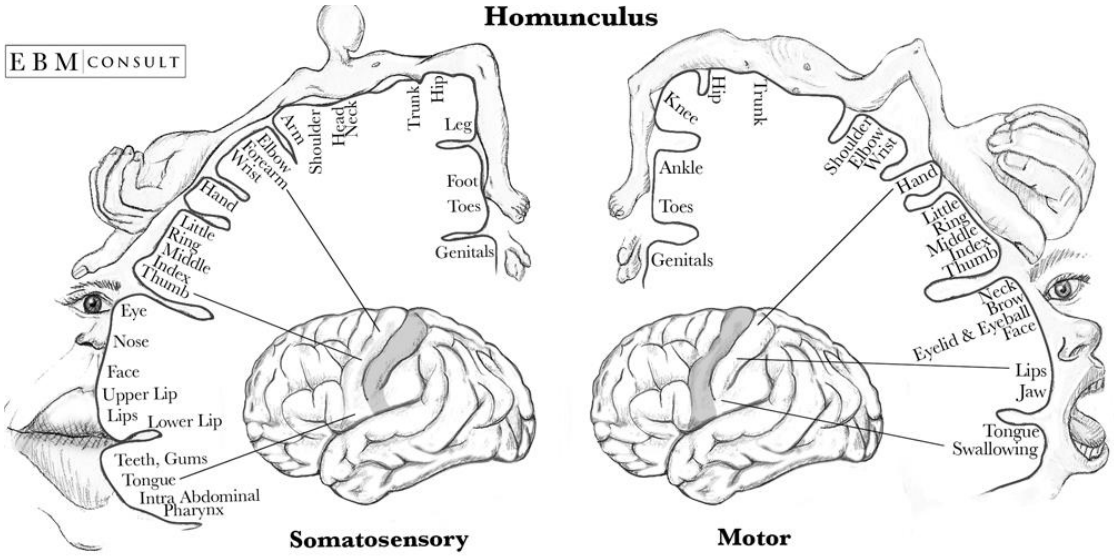

FIGURE 5. Sensory and motor homunculus. (Anthony & Kellogg 2005.)

3.3.2 Cortical, subcortical, and thalamo-cortical connections

Perception of sensory information and its integration for coordinated movement activates several structurally and functionally connected brain areas. Proprioceptors is processed in parietal (for example, primary somatosensory cortical areas), frontal (motor areas), secondary-associative areas and insular cortical areas, as well as structures within the basal ganglia (putamen) and several areas are activated simultaneously (Goble et al. 2011; Goble et al. 2012). For example, during active and passive dorsi-plantar flexion movements, activation in contralateral M1 and S1 but also in the premotor cortical regions, as well as in the subcortical regions (ipsilateral cerebellum and contralateral putamen) can be seen (Ciccarelli et al. 2005).

S1 and M1 are anatomically connected to each other, but have also monosynaptic, reciprocal functional connections (Miyashita et al. 1994; Mao et al. 2011). Somatosensory input elicits feed-forward and feedback loops between the sensory and motor cortices (cortico-cortical S1-M1 connection). These reciprocal feedback and feedforward connections are essential for sensorimotor integration and coordinated movement. Both inhibitory and excitatory neurons are activated in sensorimotor processing and modulation of M1 excitability (Tokimura et al.

2000). S1 cortex has also feedforward glutamatergic projection, so direct communication pathway to S2 cortex. Further, activity of Brodmann areas 1 and 2 can be modulated through inputs not only from thalamus, but also from areas 3a and 3b. (Shumway-Cook & Woollacott 2010, 58 – 59.)

Processing of somatosensory information use not only cortico-cortical connections, but also cortico-thalamo-cortical (trans-thalamic) networks (Mo & Sherman 2019). Before passing input to S1, proprioceptive information can be modulated in thalamus by inputs from brainstem, excitatory feedback from neocortex and inhibitory feedback from the reticular nucleus. (Kandel et al. 2000, 341–344; Shumway-Cook & Woollacott 2010, 58 – 59.) Several cortical regions are activated by direct inputs from S1, but also trans-thalamic pathways are involving in processing of somatosensory information. Ascending information from thalamus can be modulated by descending pathways from S1 to thalamus, dorsal column nucleus and spinal cord (Shumway-Cook & Woollacott 2010, 58 – 59). As said, S1 can communicate with M1 via monosynaptic direct pathway. Parallel to direct S1-M1, sensorimotor cortical circuit from S1 to thalamus and from thalamus to M1 also involve in modulation of sensory inputs. (Mo & Sherman 2019). Sensory information has also trans-thalamic pathway from S1 to S2 (Theyel et al. 2010).

3.4 Proprioception in motor control

Proprioception is critical source for adjustment of goal-directed movement. Proprioceptive feedback of body position and movement is used for error detection of ongoing movement. Sensory proprioceptive signals are used in CNS to modulate motor actions (Kandel et al. 2000, 345). Sensitivity of peripheral receptors, and inhibitory and excitatory modulation in spinal circuits have a role in modulating the ascending proprioceptive signal. For final motor output, proprioceptive signals are integrated with information from other brain areas, such as basal ganglia and cerebellum. Several brain regions are activated for processing of proprioceptive and other sensory inputs. (Shumway-Cook & Woollacott 2010, 45–82.)

Voluntary movement requires integration of sensory feedback from discharge of skin, joint, and muscle receptors caused by the movement. By sensing the body's internal state and kinematics of executed movement, motor command can be adjusted for proper outcome. In the absence of peripheral feedback, there is a deficiency in the motor control. Importance of peripheral feedback is highlighted in precise movements, during disturbances of movement and during learning process. It has been argued that importance of sensory feedback is reduced in simple or automated movements (Gandevia & Burke 1992) and that the role of proprioceptive feedback among other sensory cues is increased during fine motor control tasks and accurate postural control (Sanes et al. 1985).

Although, even simple motor actions, like postural balance is controlled by integrating information about body position in external environment (Fitzpatrick & McCloskey 1994; Fitzpatrick et al. 1994). Postural balance is controlled with information from proprioceptive afferences (e.g. Goble et al. 2011), but maintaining postural balance utilizes also visual and vestibular systems (Poole 1992; Lord et al. 1999; Wiesmeier et al. 2015). The role of vestibular system, visual and proprioceptive feedback may vary between individuals and between tasks or environments. Postural stability can be measured for example by the amplitude, velocity, or frequency of displacement of centre of pressure (COP) during upright standing (Lafond et al. 2004). Romberg quotient (RQ), defined as a ratio between eyes closed and eyes open sway demonstrates use of proprioceptive clues by eliminating visual clues (Nardone et al. 1997). Higher age (Goble et al. 2009), or some diseases, as Parkinson's disease (Vaugoyeau et al. 2007; Vaugoyeau et al. 2011) may cause deficit in proprioception, that in turn may lead to increased role of visual cues in balance control (Lord et al. 1999). Elderly people seem to process proprioceptive feedback insufficiently, and impairment in proprioceptive perception can be seen in reduced ability to sense joint position (Adamo et al. 2007). Errors in proprioceptive perceptions, like sense of joint position, are related to poorer balance control (Lord et al. 1991). Similarly, Parkinson's decease has negative effect on proprioceptive processing, resulting impaired balance control (Lefaivre & Almeida 2015).

4 CORTICOKINEMATIC COHERENCE

Corticokinematic coherence (CKC), a linear dependence between kinematic signal (e.g. acceleration or velocity) and brain cortical signal, measured with MEG (e.g. Bourguignon et al. 2011; Bourguignon et al. 2012; Piitulainen et al. 2013b) or EEG (Smeds et al. 2017; Piitulainen et al. 2020), reflects cortical processing of proprioceptive afference. CKC could provide information about the function of spino-cortical pathway in health and disorders (after a stroke, after injury, in motor disorders or in rehabilitation) and neuronal mechanisms of proprioception in aging, balance control, motor-skill acquisition, etc. (Bourguignon et al. 2013b; Piitulainen et al. 2018b; Marty et al. 2019). It can also be used in functional mapping of sensorimotor cortex (Bourguignon et al. 2011; Bourguignon et al. 2013b; Pitkänen et al. 2019).

CKC, at least during passive finger movement is well reproduced and thus, it can be useful tool in longitudinal studies (Piitulainen et al. 2018a). In group level, CKC is robust tool and coherence between kinematic and cortical signals can be found in most cases: CKC was visible with all participated 10 healthy subjects in passive finger movement (5 male, 5 female) (Piitulainen et al. 2015), with all 10 healthy subjects (5 male, 5 female) in active finger movement (Bourguignon et al. 2011) and all 23 subjects (15 from group of young individuals and 8 from group of older individuals) in passive ankle movement (both dominant and non-dominant legs) (Piitulainen et al. 2018b).

4.1 Background of CKC

CKC is a fairly new method for studying proprioceptive processing, but for much longer, it has been under the interest to examine how we sense our position and how different sensory inputs are transformed to motor actions. For example, Soechting (1982) studied, weather our sense of limb position is based on intrinsic (sensed by joint angles with joints and muscles) or extrinsic cues (orientation in surrounding space). Later, it became under the interest to study the intrinsic

sensorimotor coordination system of movement. Single cell activity recordings pointed that firing rate of M1 neurons was correlated with several movement kinematics. M1 cortex encoding for example movement direction (Georgopoulos et al. 1982), and speed (Moran & Schwartz 1999) was observed in non-human studies.

After 2010s several MEG-studies have demonstrated significant coupling between movement kinematics and brain activity. To date, significant coupling between SM1 brain signal and kinematic signals has been seen in active, passive (Piitulainen et al. 2015; Piitulainen et al. 2018a; 2018b) and observed movement (Bourguignon et al. 2013a). CKC during finger movement (Piitulainen et al. 2015; Piitulainen et al. 2018a), as well as ankle movement (Piitulainen et al. 2018b) has been studied in various movement frequencies between 1 and 10 Hz. CKC can be measured also in isometric contraction (Bourguignon et al. 2017).

4.2 Features of CKC

Principles of coherence. Coherence reflects correlation of amplitude and phase between two signals, within selected frequency band (Pitkänen et al. 2019). Coherence quantifies the rhythmic association between two signals (linear dependence of signals) in certain frequency and reflects the information flow within these frequencies. Coherence is quantified in scale 0 to 1, where 0 is no association and 1 is perfect coherence between two signals. (Halliday et al. 1995; Kramer 2013.)

Coherence in cortex-kinematic interaction. Among anatomical connections, coherence of two signals from distinct areas, is a way of neural communication (Singer 1999; Womelsdorf et al. 2007). Coupling or synchronization between two signals illustrates statistical dependence between ongoing oscillations. In case of corticokinematic coherence (corticokinematic coupling or cortex-kinematic interaction), coherence illustrates coupling between brain signal and body's kinematic signal. Kinematic signal can be e.g. velocity (Jerbi et al. 2007) or acceleration (Bourguignon et al. 2011) that is driven by rhythmicity of repetitive movement.

Interaction of movement rhythmicity and brain signal can also be demonstrated with other action related peripheral signals, such as force, pressure and rectified electromyographic (EMG) signals (Piitulainen et al. 2013a). Synchronous activity of neuron populations, rather than individual neurons in areas such as somatosensory, motor, and premotor cortex, as well as cerebellum, which are active during movement (Ciccarelli 2005), can give us information about how parameters of movement modulate firing of neuron populations. Features of this interaction can provide information about functionality of human sensorimotor system. Coupling between body kinematic signals and frequency of brain signals in sensorimotor areas measured with MEG or EEG, is considered to reflect somatosensory perception, primary from proprioceptors (Piitulainen et al. 2013b).

Direction of information flow. Findings from M1 neurons encoding movement kinematics in non-human studies (Georgopoulos et al. 1982; Moran & Schwartz 1999) first led to assumption, that coupling between SM1 MEG signal and limb kinematic signal represent encoding of motor output (Jerbi et al. 2007). However, the current view is that CKC is driven by afferent signals and reflects ascending flow of sensory information from peripheral receptors to sensorimotor area in cortex. Piitulainen et al. (2013b) and Bourguignon et al. (2015) demonstrated, that efferent signals had no effect on the strength of CKC. They compared the strength of CKC during active and passive dynamic movement and found, that the strength was at similar or higher level when joint was moved with external force, compared to condition where joint was moved voluntarily. Directionality analyses of signal being dominated by afferent direction supports this afferent direction view. (Piitulainen et al. 2013b; Bourguignon et al. 2015.)

Origin of afferent information. CKC is thought to primarily reflect proprioceptive processing in the SM1 cortex, rather than any other sensory information (Piitulainen et al. 2013b; Bourguignon et al. 2015). The fact, that CKC is visible without visual or auditory feedback, and evidence about CKC during both active and passive movement supports this hypothesis, as well as reduction of CKC strength when measuring patients with Friedreich ataxia (impairment in spino-cortical proprioceptive afferent and cerebellar pathways) (Marty et al. 2019). Even

though tactile evoked responses can be seen as an additional afferent information flow to the SM1 cortex (Bourguignon et al. 2015), cutaneous inputs seem to have marginal or negligible effect on the strength of CKC (Piitulainen et al. 2013b). Thus, primary source of corticokinematic coherence is thought to be muscle spindles and GTOs (Bourguignon et al. 2019), from which muscle spindles are the preferred sources for proprioception (Goodwin et al. 1972). More specifically, SM1 signal, coherent with the limb kinematic signal originates from proprioceptors, which detect changes in internal state of moving joint and from which spino-cortical pathway passes information synchronously with the movement frequency to SM1 cortex. In other words: mechanical stimulus of joint movement opens mechanically gated channels of stretch- or tension sensitive receptors, leading afferent neurons to fire and SM1 cortex to receive this proprioceptive input. This chain of events evokes synchronous activity of proprioceptive signals, which can be measured in SM1 cortex on the movement frequency.

Cortical sources of MEG-signal. Passively or actively moved limb's kinematic signal and brain signals peak coherence is located at contralateral sensorimotor area of moving limb (Bourguignon et al. 2012; Piitulainen et al. 2013a; Piitulainen et al. 2015; Piitulainen et al. 2018b). Primary somatosensory cortex receives information from muscle spindles and GTOs via DC-ML pathway (Kandel et al. 2000, 387) and thus, proprioceptive inputs can be measured from S1. However, besides S1, anatomically and functionally adjacent M1 also receives direct inputs from muscle spindles (Goldring & Ratcheson 1972; Lucier et al. 1975). S1 and M1 being reciprocally connected to each other and having strong functional connectivity complicates the separation of these areas in the manner of source localization. For example Piitulainen et al. (2013b) tried to localize CKC on either side of central sulcus, but in addition to inverse problem with all MEG signals, location of M1 and S1 on the walls of both sides of central gyrus and both areas receiving directly afferent proprioceptive projections, the exact location could not be defined. In addition to SM1 cortex, similar coupling has been demonstrated between kinematics and other somatosensory integration related brain areas, such as dorsolateral prefrontal cortex, posterior parietal cortex (Bourguignon et al. 2012) and cerebellum (Bourguignon et al. 2013a).

CKC peaks at movement frequency and its harmonics. CKC peaks at movement frequency and its first harmonic (F0 and F1) in S1 and M1 cortex (Bourguignon et al. 2012). It has been studied in various movement frequencies and movement rate seems to have no effect on the strength of CKC (Marty et al. 2015). The neural basis of CKC peaking not only at movement frequency, but also at its first harmonic is still unclear. It is supposed, that F1 represents afferent proprioceptive signals during both flexions and extensions from agonist and antagonist muscles, while F0 reflects afferent proprioceptive signal from single cycles of flexion–extension movement (Bourguignon et al. 2012; Piitulainen et al. 2013b; Marty et al. 2019). During passive movement, coupling seems to be stronger at F1 than F0, while during active movement there is no difference between F1 and F0. (Piitulainen et al. 2013b; Bourguignon et al. 2015.) Piitulainen et al. (2013) explained this phenomenon by the fact that passive movement frequency was by a third more regular than active movement, which in turn enhances coherence between signals. And because of twice as high frequency of F1 compared to F0, this regularity has twofold effect to coherence at F1.

4.3 Strength of CKC

CKC is visible with almost all subjects, but some differences in the strength of coupling have been seen between groups and within individuals. At least age, and some evidence suggest that also limb dominance appears to affect to the strength of CKC (Piitulainen et al. 2018b).

Piitulainen et al. (2018b) found variation in the strength of CKC between older and younger individuals. They hypothesized weaker CKC to indicate worse proprioceptive processing and thus expected older individuals to have less coherent signals between SM1 MEG and limb acceleration signals. Contrary to hypothesis, Piitulainen et al. (2018b) found CKC to be stronger among older than younger individuals. After unexpected findings, they suggested that stronger CKC could reflect insufficient proprioceptive processing, instead of more efficient processing.

Older group had stronger CKC at F0 without differences in amplitudes of MEG or acceleration signal or the amount of cortical activation. Stronger CKC without increased afferent input or cortical activation was argued to indicate differences in the strategy of cortical proprioceptive processing, rather than in the amount of afferent feedback. It was argued that stronger coherence between kinematic and cortical signals could indicate activation of wider neuronal networks. More specific activation of action related neuronal population by younger subjects would indicate efficient processing of the action, while wider activation could represent insufficient processing. This compensation mechanism by activation of wider neuronal populations is also supported by evidence of reduced neural activity of skill trained athletes during upright standing, indicating more selective involvement of task related cortical networks (Del Percio et al. 2009). Similar findings about more precise activation in the sensorimotor related cortical areas and smaller recruited population of neurons with motor training has been done for example by Krings et al. (2010) and Jäncke et al. (2000). That is, stronger coherence indicates impaired cortical proprioceptive processing. It is known, that ageing affects to movement related oscillations and evoked responses of primary somatosensory and motor cortex. In case of different strength of CKC between age groups, changes in thalamocortical loops and S1 and M1 circuits with ageing has been argued to explain differences in CKC strength. (Bardouille et al. 2019.)

In the same study by Piitulainen et al. (2018b), where they found age difference in CKC, difference in CKC strength was found between dominant and non-dominant leg. CKC at F1 with non-dominant leg was significantly higher than with dominant leg in younger group. CKC and balance control tests with dominant leg showed that stronger F1 was connected to poorer balance control. However, at movement frequency, CKC seems to be as strong with dominant as with non-dominant limb. Piitulainen et al. (2018b) argued, that younger subjects, who had weaker CKC than older subject, activated smaller neuronal population during balance control and smaller neuronal population was also argued to explain stronger CKC with non-dominant leg, compared to dominant leg. (Piitulainen et al. 2018b.)

This evidence has led to current view, that along with possible deficits in the peripheral proprioceptors and spinal circuits, processing of proprioception can be impaired in cortical level, and reflected with stronger CKC. In summary, CKC represents cortical processing of proprioceptive afferent information and the strength of CKC indicates efficiency of proprioceptive processing. Stronger corticokinematic coherence may represent compensation mechanism of insufficient information processing, when sensorimotor deficit occurs in level of peripheral proprioceptors, spinal circuits, or cortical processing.

4.4 Phenomena related to CKC

Corticomuscular coherence. Two different interactive oscillatory activities can be measured between sensorimotor related brain areas and body in motor actions: corticokinematic coherence (CKC) and corticomuscular coherence (CMC). Both phenomena reflect communication between sensorimotor cortical areas and peripheral signals in motor actions, but they represent different neural pathways. CMC quantifies coupling between mainly M1 cortex activity and skeletal muscle electromyogram (EMG) (Conway et al. 1995). Coupling is usually measured in weak isometric contraction and primarily within beta band (13–35 Hz) (Conway et al. 1995; Mima & Hallett 1999; Bourguignon et al. 2019). Communication of SM1 and skeletal muscles has been proposed to reflect efferent corticospinal pathway and cortical recruitment of motor units (Conway et al. 1995; Mima & Hallett 1999; Bourguignon et al. 2019). However, neural basis of coherent signals is not solely explained by efferent corticomuscular communication. It has been supposed that CMC could also reflect reciprocal communication of afferent feedback in motor control (Mima & Hallett 1999; Baker 2007). As described in review by Liu et al. (2019), several studies have shown that the level and band range of CMC is varied by age, in some motor disorders and by the level of force applied. Like with CMC, age (Piitulainen 2018b) and some CNS disorders (Marty et al. 2019) are known to affect the strength of CKC. Like the properties that affect the strength of signal coupling in CKC, the representation of CMC is also not fully understood. To conclude, CMC and CKC

reflects different brain–body interactions and the mechanisms of either are not yet fully understood.

Motor evoked fields. Another phenomenon related to CKC is movement evoked fields (MEFs). While CKC reflects movement evoked changes in neuromagnetic fields, measured as coherent oscillatory activity between SM1 and periphery, MEF represents single component of these neuromagnetic fields. Kristeva et al (1991) found six different event related components related to voluntary finger flexions. Besides "readiness field" prior to movement onset, "motor field" shortly before onset of muscle activity and "post-movement field" after the movement, three different components of movement evoked fields (MEFs) were found. MEFs were found at 100 msec, 225 msec and at 320 msec after EMG onset. MEFs, measured at SM1 area are thought to reflect sensory feedback and/or sensorimotor modulation of movement. (Kristeva et al. 1991). MEF at 100 msec is supposed to reflect similar afferent feedback from muscle, joint and tendon receptors as CKC (Cheyne et al. 1997; Hoshiyama et al. 1997; Piitulainen et al. 2015). Piitulainen et al. (2015) stated, that cortical mechanisms underlying CKC and movement evoked fields are likely closely related as the latency of peak CKC corresponds to the timing of movement evoked field. Latency of peak CKC has been shown to be 50 – 100 ms. In active joint movement 59–104 ms and in passive movement 64–78 ms apparent latency between acceleration and MEG signal in sensorimotor area was shown in the study by Bourguignon et al. (2015).

5 FATIGUE INDUCED BY ENDURANCE EXERCISE

Exercise acutely affects several body functions. Depending on the type, duration and intensity of the exercise, the exercise effect on central and peripheral sites of neuromuscular system varies widely. Changes can be detected for example in subcellular level, muscle metabolism and energy supply, in neural pathways on supraspinal and spinal level, respiratory system, neurochemistry and brain activity (Gandevia et al. 1994).

Changes in above-mentioned sites may have positive or negative effects on physical performance and cognitive functions. Fatigue, the negative influence on physical performance can be defined as reduction in maximal force or torque output or inability to maintain certain effort. Reduction in force production is considered as dysfunction in muscle or neuromuscular junction (peripheral fatigue) or at spinal or supraspinal stages of efferent corticospinal tract (central fatigue) (Gandevia 2001). However local (directed to certain muscle) and general (involving the whole body) exercises may also affect to sensory system and indirectly alter motor performance via modulated sensory inputs. Changes in sensory system can occur in the level of sensory receptors, central afferent pathway and in networks in cortical and subcortical levels (Bulut et al. 2003; Yamazaki et al. 2019).

5.1 Type, duration and intensity of the exercise

The type of the exercise performed, duration and intensity of exercise, participant fitness level and type and timing of tests in regard to exercise modulates the effect of performance on physiological and cognitive factors (Lambourne and Tomporowski 2010; Chang et al. 2012). Acute effect of exercise is not always linear with the intensity of the exercise. It is supposed that the effect of intensity of physical exercise on information processing and cognitive function is a shape of inverted U. Very low and very high intensity exercise seems to have negative effect or no impact, while medium intensity exercise seems to have increasing effect on

cognitive functioning. (Tomporowski 2003.) Thus, information processing can be modulated differently depending on the exertion of exercise and level of fatigue.

Intensity of endurance exercise can be defined e.g. based on changes in blood lactate level (BLa), heart rate (HR) as beats per minute (BPM) with respect to maximal HR or ventilatory thresholds (Seiler & Tønnessen 2009). Table 1 illustrates Seiler & Tønnessen's (2009) five intensity zone scale for typical endurance exercise, which takes oxygen consumption (VO_2), heart rate and blood lactate into account and shows typical duration of certain exercise intensity. Zone 3 corresponds training between first and second lactate threshold, setting continuous exercise on first lactate turn point somewhere on the upper edge of zone 2. Heart rate on zone 2 set typically between 75–85% of maximal heart rate, while blood lactate is between 1.5 and 2.5 mmol/l. By monitoring oxygen consumption, heart rate and blood lactate, effect of exercise on different intensities can be detected. Along with physiological measures, effect of exercise can be measured with subjective rating of perceived exertion (RPE) (Foster et al. 2001).

TABLE 1. Five-zone intensity scale based on VO_2, HR and BLa. Intensity zone 3 corresponds training between the first and second lactate threshold. (Seiler & Tønnessen's 2009.)

zone	VO_2 (%max)	HR (%max)	BLa (mmol/L^{-1})	training duration (min)
1	44-65	55-75	0.8-1.5	60-360
2	66-80	75-85	1.5-2.5	60-180
3	81-87	85-90	2.5-4	50-90
4	88-93	90-95	4-6	30-60
5	94-100	95-100	6-10	15-30

Similar load in different tasks impact differently: long distance running typically contains numerous ground strikes, while same duration cycling does not have similar damaging impact on lower extremity muscles. Fatigue after prolonged running seems to originate more from central factors, while after cycling, central factors are not affecting by a similar extent (Millet

& Lepers 2004.) Endurance running exercise elicits high number of stretch-shortening cycles and repetitive use of muscle-tendon complex may induce changes in peripheral, spinal, and supraspinal sites of the body. Peripheral and central causes of fatigue occur simultaneously, but the proportion of different mechanism may vary (Millet et al. 2003.)

5.2 Acute effect of exercise on peripheral and spinal factors

Peripheral fatigue. Peripheral causes of fatigue include mechanisms on muscle or neuromuscular junction (Gandevia 2001). Reduction in energy supply and the accumulation of metabolites can cause impairment in force production, shortening velocity and a lengthening of relaxation (Allen et al. 1995). Exercise may affect not only to muscles, but also to ligaments of moving limb. Exercise may increase looseness of ligaments, which could affect to proprioception (Nawata et al. 1999.) During running, several eccentric and concentric cycles for lower limbs and continuous ground strikes stimulate foot and leg constructions (muscles, tendons, ligaments) and repetitively stimulates mechanoreceptors of lower limbs causing damage on those structures (Warhol et al. 1985).

Central fatigue on spinal level. In fatigue, firing rate of alpha-motoneurons decrease due alpha-motoneuron disfacilitation and group III and IV afferent inhibition. Presynaptic inhibition of Ia declines fusimotor activity and alters stretch reflex. These mechanisms reduce afferent feedback from spindles and thus proprioceptive feedback. **(**Hagbarth & Macefield 1994.) Group III and IV afferents may alter central processing of proprioceptive feedback **(**Taylor et al. 2000; Taylor et al. 2016). Studies of cat gastrocnemius muscle stimulations have demonstrated that local muscle fatigue decreases information from muscle spindles via projections from group III and IV afferents to γ-motoneurons, which modulates activity of muscle spindle. (Pedersen et al. 1998). For example, Racinais et al. (2007) stated 90 min running to modulate spinal loop properties, such as excitatory inputs from Ia afferences and motoneuron pool excitability. Thus, proprioception may be altered in fatigue, as muscle spindle afferents modulates these senses

(Eklund 1972). This could be the case after running also, as running repeatedly activates ankle and knee extensors and flexors.

5.3 Effects of exercise on afferent flow and brain function

Fatiguing exercise has effect on several supraspinal functions. Effect of exercise may be inhibitory or facilitative and occur in several brain areas. Physical exercise may alter activity and excitability of primary motor cortex, which directly affects to motor performance (Gandevia et al. 1996). Exercise may also affect conduction of afferent information (Bulut et al. 2003; Nakata et al. 2016), as well as on processing of afferent information in sensorimotor related brain areas (Bulut et al. 2003; Yamazaki et al. 2019), which could indirectly alter motor performances.

Acute effect of exercise on sensory and motor cortex excitability and afferent flow. Exhaustive locomotion exercise can disfacilitate or inhibit motor cortex via group III and IV afference and reduce the excitability of whole corticospinal pathway. In contrast, after non-fatiguing exercise, the effect of group III and IV afferents on motor cortex can be facilitative without effect on corticospinal excitability (Sidhu et al. 2017.) In addition to motor cortex excitability and descending drive, excitability of closely related S1 cortex has been measured after physical exercise by peripheral nerve stimulations. Bulut et al. (2003) found decreased amplitudes and increased conduction velocities of somatosensory evoked potentials (SEP) measured in S1 cortex, indicating that treadmill exercise decreased S1 cortex excitability and increased conduction of afferent flow. In contrast, Brown et al. (2020) and Nakata et al. (2016) showed unaltered SEP amplitudes in S1 after low or moderate intensity cycling exercise. Nakata et al. (2016) also found decreased tibial nerve stimulation latencies after aerobic cycling exercise. Changes in SEPs after exercise could reflect changes in somatosensory processing after physical exercise and conflicting results could be explained by differences in research designs, such as chosen components of SEPs, different limbs, fitness level of the participants and especially by intensity and type of the exercise.

Acute effect of exercise on inhibitory control. Several studies support the idea of acute aerobic or whole-body exercise affecting especially on cortical inhibitory circuits as it has been shown to reduce cortical inhibition of even nonexercised limb without changes in corticospinal excitability (Smith et al. 2014). Moderate intensity continuous cycling exercise and high-intensity interval training has been shown to suppress cortical inhibitory circuits by modulation of GABAergic interneurons in motor areas. Aerobic cycling exercise has been shown to reduce short interval intracortical inhibition (SICI) (Singh et al. 2014; Smith et al. 2014; Lulic et al. 2017; Yamazaki et al. 2019) and long interval intracortical inhibition (LICI) (Mooney et al. 2016). However, from previously mentioned studies Singh et al. (2014) showed unaltered LICI and Mooney et al. (2016) found unaltered SICI. Contrast findings could be explained by differences in exercise intensity or by methodological differences, for example different interstimulus intervals. Acute aerobic exercise has also been shown to alter other cortical inhibitory circuits, like short-latency afferent inhibition (SAI) (Yamazaki et al. 2019). SAI reflects interaction of sensory afferent signal with the motor cortex, that is, sensorimotor integration. Yamazaki et al. (2019) studied changes in sensorimotor integration after low intensity cycling exercise and found reduction in SAI without changes in corticospinal or spinal excitability.

Connectivity and activation areas. Effect of exercise on connectivity of cortical sensorimotor related areas has been studied with functional magnetic resonance imaging (fMRI). Increased connectivity in resting state brain activity has been found in precentral and/or postcentral gyri and S2 cortex (Rajab et al. 2014; Raichlen et al. 2016). However, opposite findings of exercise effect on brain functional connectivity have also been noted. Schmitt et al. (2019) found decreased functional connectivity in S1, M1 and supplementary motor area after high intensity exercise, and supposed that to reflect motor fatigue. Another interesting finding from fMRI studies was made by Benwell et al. (2005). They found fatiguing exercise to increase the variability in the activation of cortical motor networks. They found reduced number of significantly activated voxels in SM1 area due to increased variance in fMRI signal and supposed it to be explained by disruptive effect of fatigue.

Long term effect of exercise on brain activity. Ludyga et al. (2016) found that compared to less trained cyclist, more trained cyclist had increased alpha/beta ratio in frontal, central, and parietal sites of brain. The authors proposed enhanced neural efficiency due to the inhibition of task-irrelevant cognitive processes of more trained group. Decreased activation was noticeable during cycling task, which authors suggested to be due to inhibition of task-irrelevant cognitive processes, but also at rest. (Ludyga et al. 2016.) Regular exercise has also been shown to alter conduction time of afferent information and S1 cortex excitability, as regularly trained individuals seem to have shorter latencies and decreased amplitude of SEP, compared to sedentary group (Bulut et al. 2003). The idea of aerobic exercise enhancing neural efficiency is also supported by Flodin et al. (2017), who found decreased connectivity between S1 and M1 cortex and right thalamus after 6 months aerobic exercise intervention.

5.4 Acute effect of prolonged running on neuromuscular performance

As described, endurance exercise may have several effects on central and peripheral sites of human body and the proportion of different mechanism may vary. During prolonged running, numerous stretch-shortening cycles affect to capacity of neuromuscular system and can be detected as impaired motor performances (Nicol et al. 1991). Measurements of maximal isometric force (MVC) is easy, safe, and well reproducible method for evaluating impaired motor performance as strength loss in certain muscle group (Ahtiainen & Häkkinen 2004, 138–139). Continuous (~1.5–2 h) running has been shown to induce isometric strength loss in knee extensors (Millet et al. 2003; Ross et al. 2010) and plantar flexor muscles (Racinais et al. 2007; Saldanha et al. 2008). Phenomena at central, neuromuscular propagation and muscular levels all have an influence on strength loss of MVC after prolonged running (e.g. Millet et al. 2003; Ross et al. 2010). For example, group III and IV afferents can impair motor performance at spinal level by disfacilitating motoneurons, but they can also impair voluntary drive by disfacilitating or inhibiting motor cortex output after locomotion exercise (Blain et al. 2016; Sidhu et al. 2017).

Besides MVC, plyometric jumps can be used for measuring changes in neuromuscular system after running exercise. Elastic properties and stretch-reflex component of muscle-tendon unit are important in stretch-shortening cycle movements, such as running and hopping. Muscle spindle disfacilitation and inhibition by group III and IV afferents alters stiffness and reduces stretch reflex sensitivity. (Komi 2000). Repeated stretch shortening cycles during running may cause fatigue in these elements and alter lower leg stiffness. Changes in stiffness can be seen in altered plyometric performance. Straight-leg jumps has been used to measure plyometric performance and compared to running performance (Saunders et al. 2006; Nagahara et al. 2014). Reduction in muscle stiffness and reflex sensitivity after repeated stretch-shortening cycles deteriorate the benefit of elastic energy (Avela & Komi 1998). Thus, long duration running can be expected to have negative effect on jumping performance.

5.5 Acute effect of exercise on proprioceptive processing and postural stability

In addition to force production, fatigue can alter postural stability, and it has been suggested, that changes in proprioception may cause this alteration (Paillard 2012). However, as different mechanisms of fatigue are overlapping, it is difficult to determine if proprioceptive information flow, its cortical processing or any other fatigue related change is the main reason for impaired postural stability after exercise. Especially, immediately after exercise the respiratory movement have large effect on postural sway (Bouisset & Duchêne 1994), while after breathing has stabilized, other mechanisms may play a bigger role.

Effect of fatigue on central processing of proprioception. As spindle afferents are primary sources for proprioception (Goodwin et al. 1972), spindle activity may alter proprioception measures. Afferent input from muscle receptors is altered in fatigue, which further affects to neuromuscular control of limb. Exercise may not affect to proprioception only by dysfunction of muscle mechanoreceptors or by amount of afferent feedback from muscle receptors. Proprioception may be impaired in local muscle fatigue by dysfunction proprioceptors, but also by impaired central processing of proprioceptive signals (Miura et al. 2004). Miura et al. (2004)

found impaired knee joint angle matching (absolute angular error in joint position matching task) after 5 min treadmill running, which did not induce weakening in peak torque of knee flexors and extensors. However, local muscle fatigue, induced by maximal isokinetic knee flexions and extensions on the isokinetic dynamometer did not affect angular matching. Authors suggested, that as running exercise did not induce local muscle fatigue, increased angular error was caused by impaired central processing of proprioceptive information. However, even though muscle spindles are thought to modulate both static sense of limb position and dynamic sense of limb movement proprioception (Goodwin et al. 1972), it seems that static position sense and dynamic movement sense may react differently on local fatigue. In the study by Allen & Proske (2006), local muscle fatigue impaired only the sense of position, while dynamic sense of movement was not affected.

Effect of local muscle fatigue on postural stability. Ability to maintain postural balance in one or two leg standing has been shown to decrease after local lower extremity muscle fatigue (strength loss 50 %) (Johnston et al. 1998; Gribble, & Hertel 2004). According to Paillard (2012), local fatigue impairs postural stability when strength loss is higher than 25–30 % of maximal voluntary contraction. It has been argued that muscle strategies for postural balance are altered depending on surface and task difficulty. Horak (2006) explained that when balancing on firm surface, ankle muscles are used for maintaining postural stability, while balancing on compliant surface or on smaller area (e.g. narrow feet placement) muscle strategy becomes more utilizing of hip muscles. As an effect of impaired use of certain muscle due to local muscle fatigue, these muscle strategies may be altered. For example, local ankle muscle fatigue may impair use of ankle muscles in balancing and shift balancing strategy to rely more on hip muscles.

Effect of general fatigue on postural stability. As Miura et al. (2004) showed with angular matching task, exercise may have fatiguing effect on sensorimotor system and central processing of proprioception without significant strength loss. Such general fatigue has also been shown to increase postural sway (Paillard 2012). Both running and cycling has been shown

to induce general fatigue and alter postural stability (Lepers et al. 1997; Nardone et al. 1997). Lepers et al. (1997) argued that repetitive stimulation of proprioceptive, vestibular, and visual system during exercise alters the central integration of these sensory cues. According to Paillard (2012), short duration general exercise increases postural sway if intensity is high enough to exceed the lactate accumulation threshold. If exercise intensity is low, it can alter sensory and motor activity and disturb postural stability, if the duration is long enough. (Paillard 2012.)

Particular effect of running type of exercise. Because of differences in pattern of active muscles and the type of contraction, running seems to have larger effect on balance control than cycling. Lepers et al. (1997) compared postural stability after average of 1 h 44 min running and after cycling and found running to impair postural stability more than cycling. They argued that stronger stimulation of joint, tendon and cutaneous mechanoreceptors during running alters proprioceptive information and information processing. They also argued, that running stimulates vestibular and visual system more than cycling does. Nardone et al. (1997) had similar results about different effects of running and cycling. Because of differences in pattern of active muscles and the type of contraction, running seems to have larger effect on balance control (Lepers et al. 1997; Nardone et al. 1997).

Role of proprioception in impaired balance control. Romberg quotient (RQ), defined as a ratio between eyes closed (EC) and eyes open (EO) sway demonstrates use of proprioceptive clues by eliminating visual clues (Nardone et al. 1997). Romberg quotient (Nardone et al. 1997), as well as difference in absolute COP velocities of EC and EO sway (Vuillerme et al. 2001) has been used for evaluating effect of exercise on proprioception. Both local plantar flexor fatigue (Vuillerme et al. 2001) and fatiguing treadmill exercise (Nardone et al. 1997) has been shown to impair particularly proprioception, rather than any other sensory cues. It has been shown that difference between eyes closed sway and eyes open sway is larger when the difficulty of the task is increased (Horak 2006). Similarly, fatiguing treadmill walking (Nardone et al. 1997), as well as local plantar flexors muscle fatigue (Vuillerme et al. 2001) disturb eyes closed balancing more than eyes open balancing. However, the opposite observation has also been made: for

example Corbeil et al. (2003) did not find change in EC-EO-difference after local plantar flexors muscle fatigue.

Recovery of balance control. Exercise effect on postural instability is strongest immediately after exercise. Duration of disturbing effect of exercise is relatively short. Effect of 30 min running on anaerobic threshold was vanished in 5 minutes and the effect of 30 min running on ventilatory threshold disappeared in 10 minutes. (Guidetti, et al. 2011.) In the study by Nardone et al. (1997), fatiguing treadmill walking, with RPE 6.5 ± 0.2 (Borg's 0 – 10 scale) sway area and path during upright standing eyes closed and eyes open was settled back to normal values within 15 minutes after the end of exercise. Recovery of postural sway in unilateral standing test after local ankle plantar flexors and dorsiflexors fatigue occurred within in 20 minutes (Yaggie & McGregor 2002). In summary, the detrimental effect of the exercise is often disappeared after 20 minutes at the latest.

6 PURPOSE OF THE STUDY

CKC is known to be altered by ageing, but currently it is unknown whether changes in physiological states, such as fatigue, have an effect on CKC strength, i.e. cortical proprioceptive processing. This study aims to investigate effect of single bout aerobic running exercise on the strength of CKC and thus cortical proprioceptive processing. Differences in strength of CKC between before and after physical exercise, could provide us information about how afferent somatosensory information processing is altered due to acute change in physiological state. As the neural adaptation processes of CKC are still not fully understood, this study may also provide information about the nature of CKC and how it is altered acutely, such as by acute aerobic exercise.

Given that aerobic exercise may have effect on peripheral receptors and spinal circuits (Hagbarth & Macefield 1994; Pedersen et al. 1998; Taylor et al. 2000; Taylor et al. 2016), S1 and M1 activity, and other sensorimotor related networks (Bulut et al. 2003; Rajab et al. 2014; Singh et al. 2014; Smith et al. 2014; Nakata et al. 2016; Schmitt et al. 2019; Yamazaki et al. 2019; Brown et al. 2020), hypothesis is that running exercise would have effect on proprioceptive processing and thus strength of CKC would be altered. Given that stronger CKC could reflect impaired proprioceptive processing (Piitulainen et al. 2018b), which could be the case after aerobic running exercise, it is expected that running would increase the strength of CKC. Fatigue markers (BLa, HR and RPE) and physical performance tests are used for determining fatiguing effect of running exercise and for clarifying physiological effects behind possible changes in CKC.

Secondary aim of this study is to examine if the strength of CKC is associated with postural balance and use of proprioception in balance control. Some evidence about positive correlation between strength of CKC and balance control has been found previously (Piitulainen et al. 2018b). It has also been shown that aerobic exercise alters postural stability (Lepers et al. 1997;

Nardone et al. 1997), and it has been argued that changes in proprioception may cause this alteration (Paillard 2012). Correlation is evaluated between changes in CKC and changes in postural balance, between strength of CKC and postural balance before running and between CKC before running and change in postural balance. Role of proprioception in alteration of balance control is evaluated with Romberg quotient. Hypothesis is that running exercise would increase postural sway and Romberg quotient and that impaired postural balance would be associated with stronger CKC.

7 METHODS

Study was organized in University of Jyväskylä in three separate study sessions. First study session took place in laboratory facilities at the University of Jyväskylä's Faculty of Sport and Health Sciences. Second and third sessions were conducted at MEG laboratory at the University of Jyväskylä's Centre for Interdisciplinary Brain Research (CIBR). The study had a prior approval by the ethics committee of the University of Jyväskylä, and written informed consent was given by the subjects before participation.

7.1 Study subjects

Ten (6 males, 4 females) healthy volunteer adults who were exercising regularly in running and without any history of neuropsychiatric disease or movement disorders participated in the study. Mean age of 39.1 ± SD 4.7 years and mean height of 175.5 ± SD 11.6 cm was reported at the time of first MEG session. From the 10 participants 9 was using right leg as a dominant leg and one was using left leg. Dominant leg was determined by three questions: Preferred leg to 1. kick a football, 2. stepping on chair, 3. one leg jumping.

7.2 Study protocol

Subjects were invited for three separate study sessions. First lactate thresholds were determined for all subjects in maximal oxygen consumption ($VO_{2max)}$ tests during the first visit. Incremental treadmill running tests until volitional exhaustion were performed in the laboratory of the University of Jyväskylä's Faculty of Sport and Health Sciences. Lactate threshold was determined as described in Nummela (2004, 64–78I) to the point where blood lactate level rose 0.3 mmol/l from the lowest level. Velocity at first lactate threshold (10.9 ± 1.5 km/h) was used in 90 min running intervention. During the first visit, subjects signed agreements for

participating in the study and filled preliminary information sheets for MEG measurements (appendix 1 - 3).

After VO_{2max} test, subjects were invited to MEG laboratory twice. In randomized and counterbalanced order, subjects started with control or running session. Running session was set within two months after VO_{2max} tests. Both control and running sessions were identical with the exception of 90 min magazine reading or treadmill running, respectively. Each visit included subject preparation and warm-up, pre-measurement block, 90 min treadmill running or magazine reading, post-measurement block and post2-measurement block in mentioned order. Participants were guided to always move to next step as fast as possible. Time at the beginning of each block was registered. Participants were informed that they were allowed to stop the experiment at any point for any reason.

The following tests were included in this thesis and are described in more detailed in section "7.3 Measurements and data acquisition": CKC before and after reading/running, balance test (Bal) just before and straight after reading/running as well as after second MEG-measurements, and physical performance tests before and after reading/running, including straight-legged jumping test (Hop) and maximal voluntary contractions (MVC). Physiological markers were measured during reading/running and included blood lactate samples (BLa), rating of perceived exertion (RPE, appendix 4) and heart rate (HR). Protocol included total of four balance tests, from which only the last three are discussed in this thesis, as well as three Hop and MVC tests, from which only the first two are discussed. The protocol included also two additional MEG-measurements, which are not reported in this thesis: resting state (RS) MEG-measurements, where subjects sat still eight minutes eyes open and four minutes eyes closed, movement evoked fields (MEF) MEG-measurements, where passive dorsiflexions were produced every third second following slow return to ankle's lowest position. These tests are not used in this thesis but are mentioned here for better understanding of stress of the measurements for subjects and intervals between tests. Figure 6 represents the whole MEG session study protocol and time points for BLa and RPE samples.

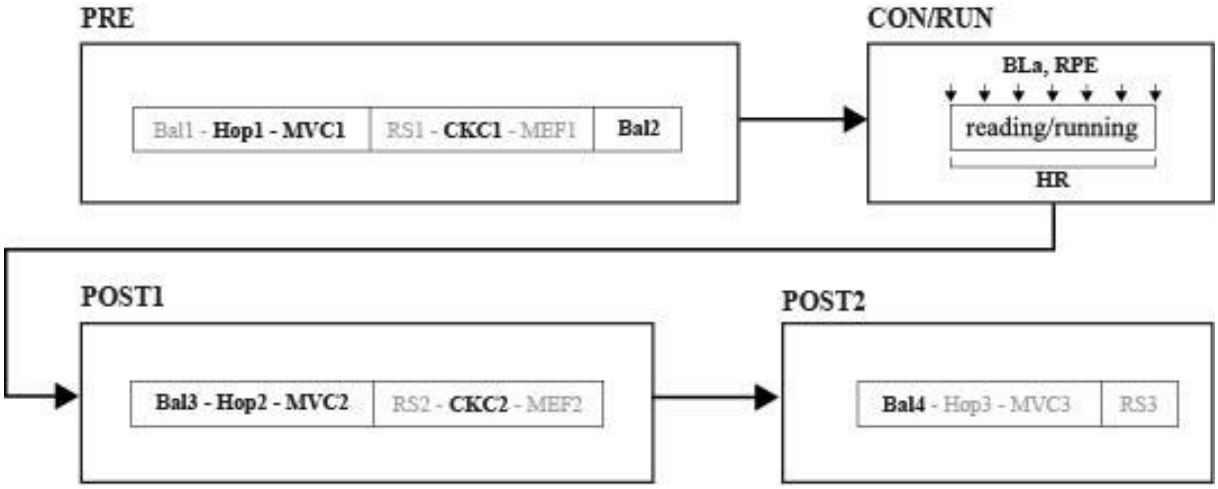

FIGURE 6. Variables reported in this work are in black. Control (CON) and running condition (RUN) included balance (Bal), straight-legged jumps (Hop), maximal voluntary contractions (MVC), resting state MEG-measurements (RS), corticokinematic coherence (CKC), movement evoked fields (MEF), heart rate (HR), blood lactate level (BLa) and rate of perceived exertion (RPE). The number after the abbreviation refers sequence number of the test.

Subject preparation. At the beginning of each visit in MEG laboratory, upcoming protocol was explained to the subjects while they were prepared for measurements. Electrooculography (EOG) and electrocardiography (ECG) electrodes, as well as a reference electrode were attached for monitoring eye movement and heart beats during MEG-measurements. Five constant head position indicator (cHPI) coils were placed on participant's head for monitoring head position during MEG-measurements. In the magnetically shielded room, placement of ankle actuator was set to fit for each individual and volume of brown noise track was set to cover noises from ankle actuator.

Warm-up. Warm-up protocol was similar in both conditions. Warm-up started with 5 minutes treadmill run at a speed of subject's choice (not higher than the speed of their individual first lactate thresholds). After running, 30 sec eyes open and 30 sec eyes closed balancing on balance board, at least two sets of straight-legged jumps at submaximal intensity and at least two sets of submaximal isometric contractions were performed. Subjects were allowed to try the tests

until they felt familiar with the tests. Safety harness for treadmill run and leg dynamometer were adjusted for each participant during warm-up on the first lab visit.

Pre-measurement block. Pre-measurement block consisted of balance test and physical performance tests, following by MEG measurements immediately after that. To ensure similar intervals from CKC measurement to balance test in pre-measurement and post-measurement blocks and for evaluating immediate effect of running on balance control, an additional balance test (Bal2 in figure 6) was performed at the end of pre-measurement block, just before 90 min reading/running.

90 minutes treadmill running or magazine reading. After first MEG measurements, subjects ran in running condition or sat on chair in control condition for 90 minutes. In running condition, subjects ran 90 min on treadmill inside the lab at the velocity of their first lactate threshold. 1% angle was set on treadmill for simulating air resistance. For safety reasons, subjects were wearing harness which was attached to sealing. When any subject strongly felt not being able to finish the run, they were allowed to reduce the velocity. 5 % velocity reduction was suggested, but subjects were instructed to reduce the velocity as much as they estimated to be necessary for finishing the run. Velocity reductions were registered. All but one subject succeeded to run 90 min at their first lactate threshold. One subject had to drop running speed from 9.4 km/h after 55 min 10 sec to 9 km/h and after 61 min 38 sec to 8.8 km/h resulting mean speed of 10.9 ± 1.5 km/h across all subjects. Subjects were allowed to listen music they have chosen with earphones or with speaker. In control condition, subjects sat 90 min on the chair inside the lab while reading magazines and listening to the same music as in running condition from speaker.

Post-measurement block. Post-measurement block was exactly similar with the pre-measurements, except there were no additional balance test after MEG-session. Post-measurements consisted of physical performance tests (for determining fatiguing effect of running on neuromuscular system) and MEG measurements (Fig. 6).

Post2-measurement block. Post2-measurement block began immediately after post-measurement block. It was similar as post-measurement block, except in MEG-session, only resting state measures were taken. Post2-measurement block consisted of physical performance tests and MEG measurements without ankle actuator tests (Fig. 6). In Figure 7 is represented how much time was used for each test or set of tests (e.g. physical performance tests) and transition times between tests.

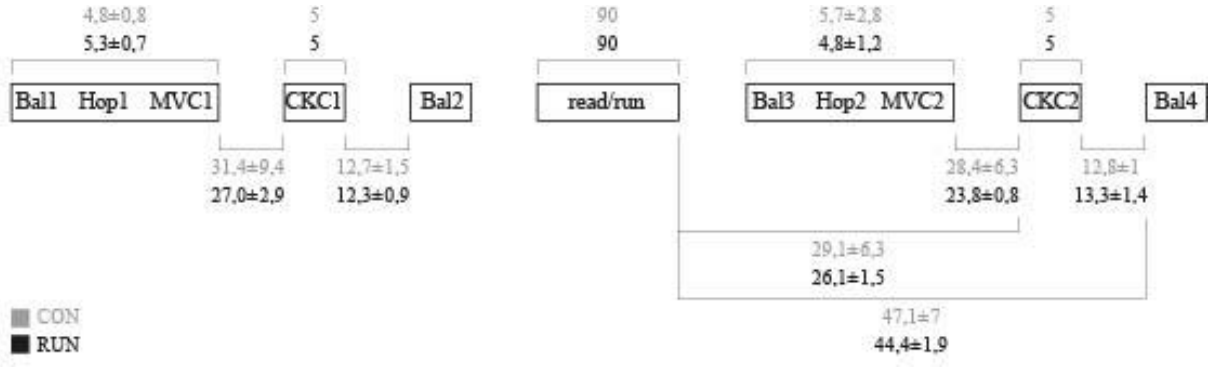

FIGURE 7. Mean durations with standard deviations are represented in minutes. Control condition (CON) in light grey and running condition (RUN) in black included balance tests (Bal), straight-legged jumping tests (Hop), maximal voluntary contractions (MVC), resting state MEG-measurements (RS), corticokinematic coherence (CKC), movement evoked fields (MEF), blood lactate levels (BLa) and rate of perceived exertions (RPE). The number after the abbreviation refers sequence number of the test.

7.3 Measurements and data acquisition

Measurements for evaluating effect of running on CKC, balance, physical performance tests and physiological markers are described in following sections. Instrumentations and methods for data acquisition are described in the beginning of each section.

7.3.1 MEG-measurements

Magnetoencephalography. MEG-measurements were conducted in a magnetically shielded room (Magnetic Shielding Cabin, VACOSHIELD, Vacuumschmelze GmbH & Co.KG, Hanau, Germany). Brain activity was measured with 306-channel (one magnetometer and two gradiometers in each of 102 sensor units) whole-head magnetometer (Elekta Neuromag® TRIUX™, Elekta Oy, Helsinki, Finland). Bandpass filter of 0.1–330 Hz and sampling frequency 1000 Hz was used. Constant head position indicator (cHPI) coils were used for monitoring head position during recording.

Electrooculography and electrocardiography. During MEG-recordings, EOG and ECG were measured with Ambu Neuroline 720 Neurology Surface Electrodes and attached to the skin with tape. Horizontal and vertical eye movements were monitored with two electrodes placed on upper corner of right eye and lower corner of left eye. Heart beats were recorded with two similar electrodes, one placed near to the right shoulder under right clavicula and second on the lower edge of left rib cage. Reference electrode was attached on right clavicula.

Ankle actuator. Non-magnetic ankle actuator movement was computer triggered and foot plate was moved with three pneumatic artificial muscles (DMSP-10-100 AM-CM, diameter 10 mm, length of the contracting part 100 mm; Festo AG & Co. Esslingen, Germany) (Fig. 8). Vertical movement was generated by changes in artificial muscles' internal air pressure (max 5 bar). Continuous 2 Hz movement (trial duration 500 ms, pulse width 200 ms, jitter 0 ms) was produced in CKC measurements. Operating principle of ankle actuator is explained in more detailed manner in the study by Piitulainen et al. (2018b).

Foot kinematics. Acceleration of ankle joint movement was measured with a MEG-compatible 3-axis accelerometer (ADXL335 iMEMS Accelerometer, Analog Devices Inc. Norwood, MA, USA). Sensor was attached with the tape on the distal site of subject's metatarsophalangeal joint.

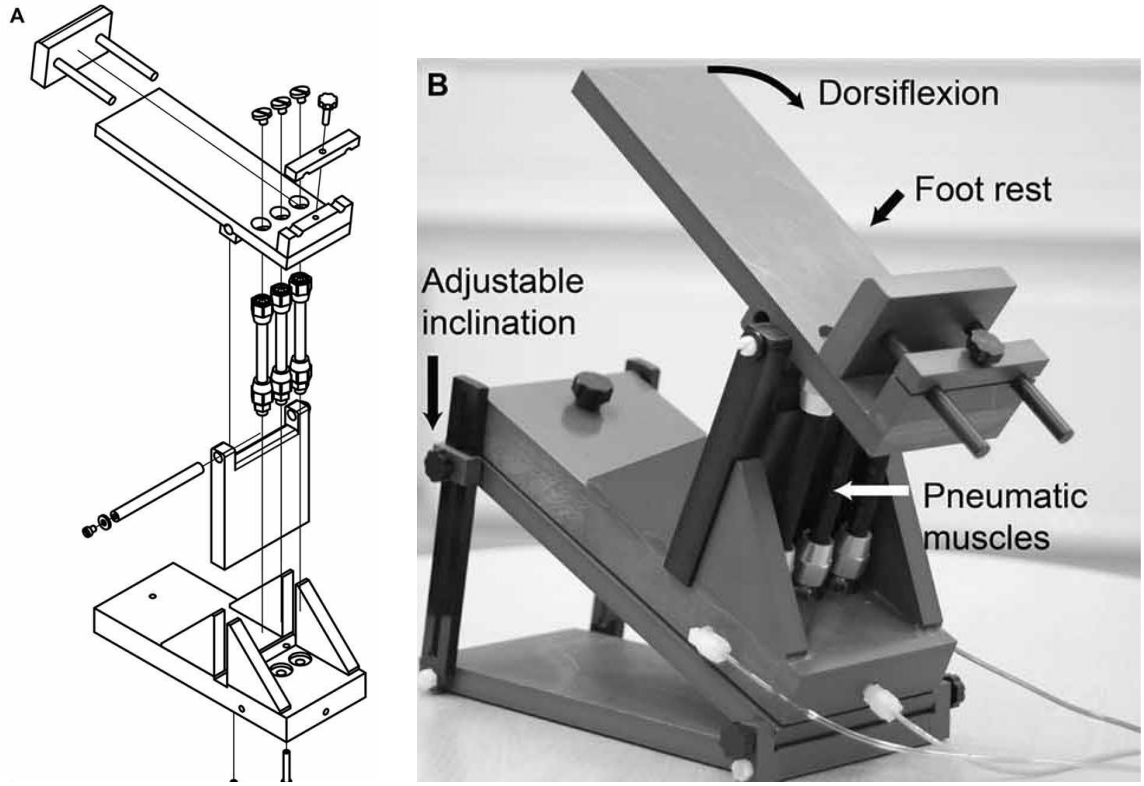

FIGURE 8. (A) Technical drawing of the non-magnetic ankle actuator. (B) Dominant foot was placed on top plate and pneumatic muscles moved the top plate to induce extension-flexion movement of the ankle. (Modified from Piitulainen et al. 2018b.)

MEG-recordings. During MEG-recordings, participants were instructed to sit immobile on the chair. MEG session started with 12 minutes resting state measurements, following by 5 minutes of cortickinematic coherence measurement and ending with 8 minutes passive movement evoked potential measurement. Only CKC is described here. For the CKC measurement, ankle actuator was placed under the subject's dominant leg and adjusted so that the rotation axis of the movement actuator corresponded with ankle's axis of rotation as closely as possible. Ankle and knee angles were set on 100 degree. Eyes were kept open and field of view was limited with paper covering the foot and actuator, leaving only fixation point visible. Participants wore ear plugs and brownian noise audio track was played from flat panels speakers to cover the noises from ankle actuator. Participants sat on relaxed sitting position, arms resting on a pillow

on lap in a way that the pillow or arms were not touching the dominant leg. During recordings with ankle actuator, participants wore ear plugs for minimizing auditory cues from the device. Figure 9 shows the setup of MEG measurements with ankle actuator. During the 5 minutes CKC recording ankle actuator was producing passive ankle joint movement with 2 Hz pace (two plantar- and dorsiflexions in one second).

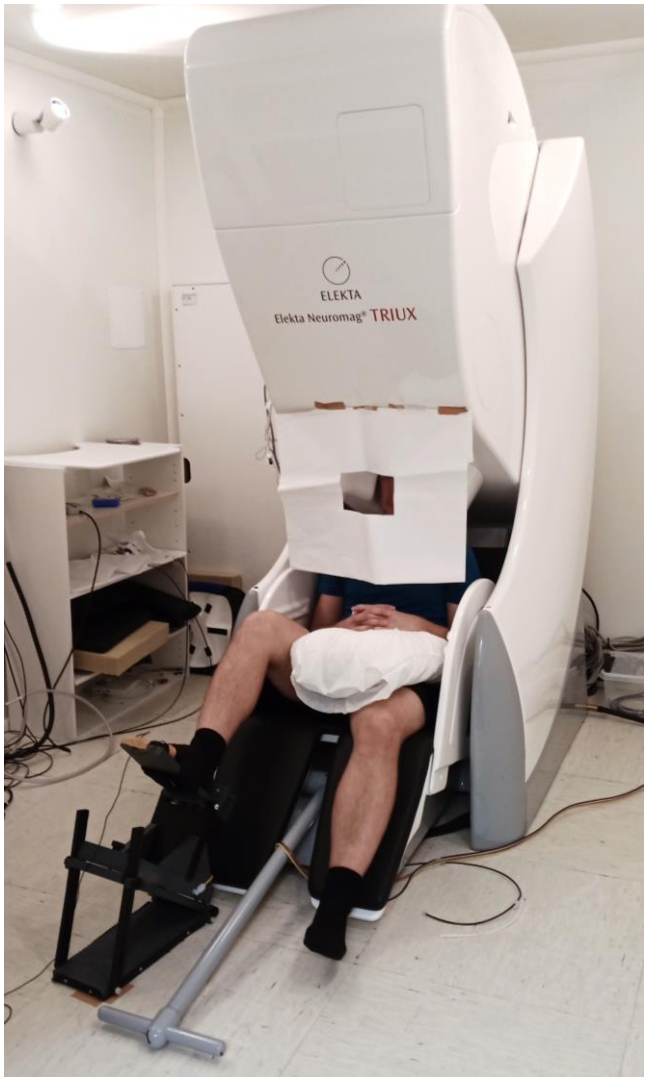

FIGURE 9. Setup of CKC protocol in magnetically shield room. Subject's dominant leg is attached to ankle actuator. Auditory interferences are blocked with ear plugs and brown noise auditory track and visual interferences of leg movement are covered with white paper.

7.3.2 Balance tests

Metitur Good balance system (Metitur Oy, Jyväskylä, Finland), including balance board and Good balance software was used for balance tests. Balance board was calibrated before every subject with Good balance manual (2003) instructions. Movement and velocity of center of pressure (COP) was collected with Good balance software. Balance test was performed legs together to minimize support surface. Subjects performed the balance test eyes open (EO) and eyes closed (EC). Starting condition was randomized and counterbalanced between individuals. Subjects were informed to stand on balance board without shoes, adjust their feet as close to each other as possible and to cross their arms on the opposite shoulders. In eyes open condition, subjects focused their eyes on the mark in the opposite wall (distance 3 m) and stood as stable as possible for 30 sec period. Immediately after or before EO, subjects closed their eyes and stood as stable as possible for another 30 sec period.

7.3.3 Physical performance tests

Straight-legged jumping test. Custom-built 80 * 80 cm contact mat (University of Jyväskylä, Faculty of Sport and Health Sciences, Jyväskylä, Finland) was used for measuring performance of continued straight-legged jumps. The mat was connected to stop-watch which collected flight times and contact times. After balance test, subjects were informed to put shoes on and step on contact mat. Subjects were informed to hold their hands at their hips and after permission to jump at least six as high jumps as possible, with as fast floor contact as possible while keeping knee ankle as straight and immutable as possible. At the first jump they were allowed to bend their knees, and a small knee bending was allowed at all jumps for avoiding any knee injuries. Flight time was measured for flight high calculations.

Maximal voluntary contraction. Force production of maximal isometric single leg contractions was measured with leg dynamometer which was connected to computer with A/D-converter. Data were collected with Spike 2, version 8.11 (CED, Cambdridge, UK) software with

sampling rate 1000 Hz. Maximal isometric single leg contractions were performed at leg dynamometer in seating position for dominant leg. Toes were placed on the top of the force platform, back was 90 degree to floor, and the distance of force platform was adjusted so that the knee ankle was 107 degrees (Ahtiainen & Häkkinen 2004, 140). Hands were held with handles on the sides of the dynamometer. After permission, subjects produced maximal force against to force plate as fast as possible and hold it until permission to relax was given (three seconds). Strong verbal encouragement was given. After 60 sec rest period by sitting on dynamometer, MVC was repeated for assure that the first attempt was maximal.

7.3.4 Physiological markers during reading and running

During reading and running, heart rate was monitored continuously with Garmin HR belt and watch (Garmin Forerunner 245M, Garmin Ltd, Schaffhausen, Switzerland) and checked manually every 15 min. At the beginning of running and after every 15 minutes, mat was paused, and blood lactate samples was taken. Just before every lactate samples, printed RPE scale (Appendix 4) was shown and RPE was asked verbally. RPE scale 0 - 10 (from rest to maximal exertion) was used. The scale is adapted from original Borg CR10 scale (Borg 1998). During reading, RPE was asked every 15 min in similar manner as in running condition and blood lactate samples were taken after RPE. Figure 10. shows how physiological markers were collected during of 90 min reading/running.

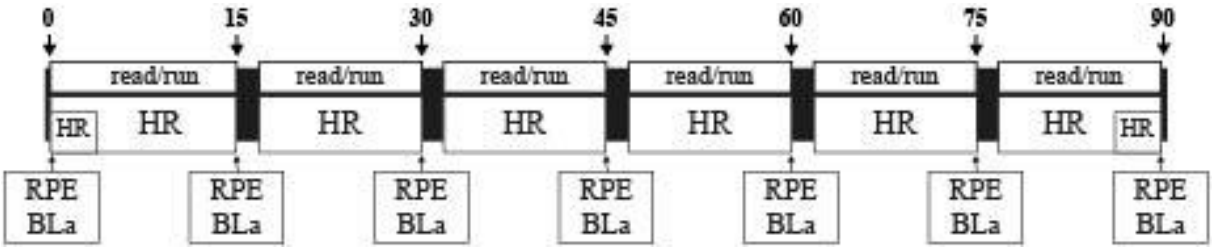

FIGURE 10. Every 15 minutes, after rating of perceived exertion (RPE) was asked the treadmill was paused for lactate samples (BLa). Heart rate (HR) was measured continuously and checked manually every 15 min.

7.4 Data analysis

Data analysis is divided into three sections. First section is for MEG data analysis, second is for data processing of physical performance and physiological measures, and third section is for statistical analyses.

7.4.1 MEG data analysis

Pre-processing. The quality of MEG data from CKC measurements was first visually checked, and noisy channels were given as argument to MaxFilter (MaxFilter 2.2 software, Elekta Neuromag Oy, Helsinki, Finland). MaxFilter temporal signal-space-separation (SSS) was used for noise reduction and head movement compensation (Taulu & Kajola 2005). Each subject's head position coordinates from their pre and post CKC measurements was aligned to same positions. Further processing steps for eye blinks and heart beats removal was applied using MNE Python. For Independent component analysis, the data was band-pass filtered 1–40 Hz. 30 independent components were extracted from the data using fast independent component analysis (FastICA algorithm). Components related to eye movements and heart beats were visually identified and subtracted.

Coherence analysis. Matlab R2018a was used for further analyses. Prior to coherence analysis, 1–195 Hz band-pass filtering was used for MEG signals and 0.5–195 Hz band-pass filtering was applied for acceleration signals. For the coherence analyses between the foot acceleration and MEG signals, continuous data were split into 2 sec epochs with 1.6 sec overlap, leading to a frequency resolution of 0.5 Hz (Bortel and Sovka, 2007). To avoid contamination by artifacts from other sources than brain activity, epochs were excluded, if magnetometer signals exceeded 3 pT or if gradiometer signals exceeded 0.7 pT/cm. Euclidian norm of the three orthogonal accelerometer signals was used for epochs of acceleration signal (Bourguignon et al. 2011). Coherence analysis with cross-, power- and coherence-spectra, along with crosscorrelograms was then applied for normalized foot acceleration and MEG signals (Halliday et al. 1995).

Peak CKC strength was quantified as the single optimized coherence value across MEG gradiometer pairs as done by Bourguignon et al. (2015) at the movement frequency (F0: 2 Hz) and its first harmonic (F1: 4 Hz) separately. Region of interest (chosen gradiometer pairs) was around the expected foot area of the SM1 cortex. Fieldtrip software was used for visualizing topographic distribution at sensor level (Oostenveld et al. 2011).

7.4.2 Data processing of physical performance and physiological measures

Postural balance test. Good Balance2.64 software calculated mean velocity of the displacement of the COP (mm/s) in the anteroposterior (AP) and mediolateral (ML) directions. The effect of vision and proprioception was defined as Romberg quotient (RQ). RQ was calculated by dividing COP displacement velocity of eyes closed test by COP displacement velocity of eyes open test. Similar method used for example in study by Nardone et al. (2007).

Maximal voluntary contractions. All force data from maximal isometric contractions were processed in Spike 2, version 8.11 (CED, Cambdridge, UK) software. Data was measured in kilograms and converted into newtons (N) for further analysis. Peak force of both attempts was analysed in case of unsuccessful test performance and force values of the first attempt was used in statistical analysis.

Straight-legged jumps. Jump height was calculated from flight times with following formula: $h = g * t^2 * 8^{-1}$ (h = jump height (m), g = gravitational constant (9.81 m/s^2) and t = flight time (s) (Bosco et al. 1983). Results of first jump was excluded, as it was allowed bent knees on first take-off and test was focusing only to straight-legged jumps. Mean value of the rest of the five jumps was calculated for each subject.

Heart rate during reading and running. Heart rate during running and reading was recorded continuously second by second. Treadmill was paused every 15 minutes, and mean heart rate was calculated for each set. Because of the drops in heart rate during the breaks, only the last

13 min was used in averaging mean HR of each set. In control condition, some HR data was damaged due to poor conduction between HR belt and skin. If there was no HR data in some of the 13 min sets, mean HR was calculated from the values at two minutes before and two minutes after that 13 min time window. HR values of each 13 min reading sets was compared to manually filled transcript to ensure that poor conduction was not affecting on HR results. For studying the difference between HR in the beginning and at the end of running/reading, mean HR of the first and last 30 sec were calculated. Each set is represented in Figure 10.

7.4.3 Statistical analysis

CKC alpha level. The statistical significance of coherence and alpha level was assessed as described in study by Piitulainen et al. (2018a). Hypothesis of linear independence of fourier coefficients was used in assessing statistical significance (Halliday et al. 1995) and alpha level was set to 0.05/(Nf x Ns), where Nf = 1 (number of tested frequency bins (F0 and F1)) and Ns = 20 (number of gradiometer pairs included in the analysis).

Stability of acceleration signal. Stability of the peak acceleration magnitude of dorsiflexions was quantified as the coefficient of variation (CV) for the peak value of the Euclidian norm of the three orthogonal accelerometer signals. CV was defined separately for each individual at each time point and condition.

Effect of time, condition, and interaction. IBM SPSS Statistics 25 software was used for statistical analysis. All data is reported as mean ± standard deviation (SD). Alpha level less than 0.05 were considered statistically significant. Effect of time, condition and interaction was computed for fatigue markers, physical performance tests, CKC values, peak acceleration magnitudes and balance tests. Effect of condition was tested between control (CON) and running (RUN) condition for all parameters. For RPE and BLa, time effect was tested between seven time points corresponding samples taken every 15 minutes during reading/running. For HR during reading and running, time effect weas tested between six time points (mean HR of

each 15 min set) and for HR at the beginning and end of reading/running time effect was tested between two time points (mean 30 sec HR). Time effect of MVC, Hop and CKC at F0 and at F1, as well as peak accelerations were tested between two time points: before and after reading/running. Postural sway and Romberg quotient were compared between three time points: just before and straight after reading/running and after second MEG measurements.

The Shapiro-Wilk test was applied to ensure the data to have normal distribution. If data was normally distributed, two-way repeated measures ANOVA was used (HR, Hop, MVC, Bal, CKC and acceleration). Greenhouse-Geisser correction was used if Mauchly's test of sphericity showed non-equal variance of differences. In case of statistically significant main effects, 1-way repeated measures ANOVA with pairwise comparison (if several time points) or paired samples t-test (if two time points or condition difference) was conducted with Bonferroni adjustment. Time points were compared to first time point as well as subsequent time points after first statistically significant change. Condition difference was tested between every time point.

In the case of non-normal distribution, a logarithmic transformation (lg10) was computed and if data distribution was corrected, parametric tests was used for transformed data. In case of only few outliers, parametric tests were used if removing outliers did not significantly affect to the results. Nonparametric Friedman test was used for RPE and BLa, as the data was non-normally distributed after logarithmic transformation and/or parametric tests was violated by outliers. In case of significant results in time, pairwise comparisons with Bonferroni's correction were applied for every time point similarly as with parametric tests. In case of significant results in condition, pairwise comparison with Bonferroni's correction was applied for results at the beginning and at the end. Wilcoxon signed rank test was also applied for total changes between conditions.

Correlations. Correlation was calculated between two variables of CKC (F0 and F1) and six variables of postural balance (COP velocity eyes open, COP velocity eyes closed and Romberg

quotient respectively in mediolateral and antero-posterior directions). All calculations were conducted in three combinations of time points: CKC before running (CKC1) and balance scores before running (Bal2); CKC before running (CKC1) and changes in balance scores (difference between Bal2 and Bal3); changes in CKC (difference between CKC1 and CKC2) and changes in balance scores (difference between Bal2 and Bal3). Pearson correlation coefficient was used in all except one variable pair: correlation between CKC at F1 before running and RQ in mediolateral sway before running was calculated with Spearman's correlation as there were significant outliers. Strength of correlation is verbally described "very high", when correlation is 0.80–1.0, "high" when 0.60–0.80 and "moderate" when correlation is 0.40–0.6 and due to small sample size, results below 0.40 is seen as no statistically significant correlation (Metsämuuronen, J. 2011).

8 RESULTS

Fatiguing effect of 90 min running was evaluated during running with blood lactate, heart rate and RPE. Physical performance tests (jumps and isometric contractions) and CKC were conducted before and after running. Postural stability was evaluated before and after running and after second MEG-measurements.

8.1 Heart rate (HR)

HR of 15 min sets. Statistically significant effect of condition ($F(1.9) = 938.651$, $p < 0.001$, $\eta_p^2 = 0.991$), time ($F(1.518, 13.662) = 17.116$, $p < 0.001$, $\eta_p^2 = 0.655$) and interaction between condition and time was found ($F(1.442, 12.981) = 12.981$, $p = 0.002$, $\eta_p^2 = 0.575$) in the heart rate during reading/running.

Running HR was statistically significantly higher in every 15 min sets than reading HR ($p < 0.001$). Effect of time was not found in control condition ($F(1.245, 11.207) = 0.772$, $p = 0.575$, $\eta_p^2 = 0.079$). In running condition, effect of time was found ($F(1.380, 12.423) = 51.125$, $p < 0.001$, $\eta_p^2 = 0.850$). Mean HR of second 15 min running set was 6 ± 3 BPM (4% ± 2) higher than first set ($p = 0.004$), and elevated 5 ± 2 BPM (3% ± 2) to third set ($p = 0.001$) and 3 ± 1 BPM (2% ± 1) from third to fourth set ($p = 0.005$) (Fig. 11A). After 60 min running the elevation was not statistically significant.

HR of the first and last 30 sec. Heart rate of one subject at the end of the 90 min reading was not recorded due to poor conduction between HR belt and skin, resulting n = 10 in running condition and n = 9 in control condition. Statistically significant effect of condition ($F(1.8) = 493.511$, $p < 0.001$, $\eta_p^2 = 0.984$), time ($F(1.8) = 29.716$, $p = 0.001$, $\eta_p^2 = 0.788$) and interaction between condition and time was found ($F(1.8) = 85.529$, $p < 0.001$, $\eta_p^2 = 0.914$) in the first and last 30 secs.

Hr was 44 ± 5 BPM (72% ± 34) higher in running than reading condition at first 30 seconds ($t(8) = -8.392$, $p < 0.001$) and 102 ± 4 BPM (174% ± 49) higher at last 30 seconds ($t(8) = -28.483$, $p < 0.001$). Running HR increased 55 ± 17 BPM (55% ± 26) from first 30 seconds ($t(9) = 10.250$, $p < 0.001$) and reached 163 ± 8 BPM at the end of running . HR did not change in control condition ($t(8) = -0.816$, $p = 0.438$). Mean heart rates during first and last 30 seconds of reading and running are illustrated in Figure 11B.

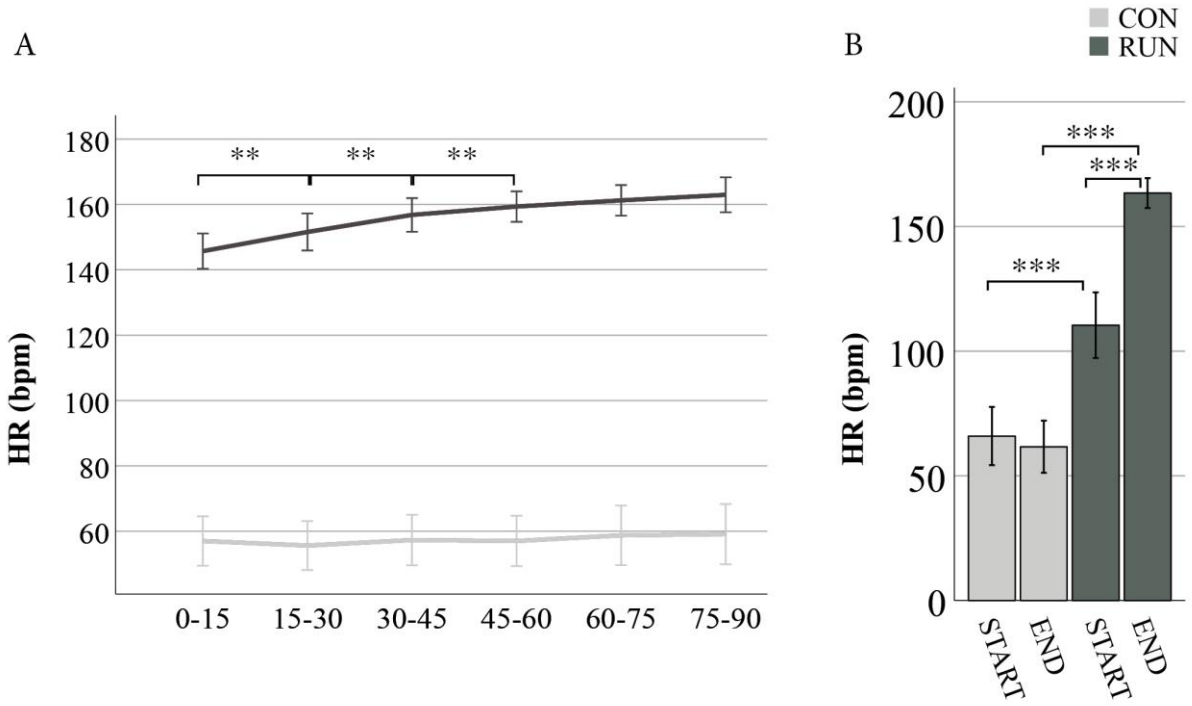

FIGURE 11. (A) Heart rate (HR) at every 15 min sets during reading (CON) and running (RUN) and statistically significant elevations (first elevation from 0–15 min and subsequent elevations). (B) Mean HR at first (START) and last (END) 30 seconds of reading (CON) and running (RUN) and statistical significances between times and conditions. Error bars: 95 CL. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

8.2 Rate of perceived exertion (RPE)

Statistically significant effect of time was found in control condition ($\chi2(6) = 17.294$, $p = 0.008$), but pairwise comparison with Bonferroni adjustment did not show any significant differences between time points. Statistically significant effect of time was found in running condition ($\chi2(6) = 49.881$, $p < 0.001$). First statistically significant elevation (3,6 ± 2,3) of mean RPE was seen after 60 min running ($p = 0.006$). No subsequent elevation was found after time point 60. Mean RPEs are illustrated in Figure 12A.

During the whole 90 min running, RPE increased 4.7 ± 2.7 ($p < 0.001$), while in control condition RPE decreased, but not statistically significantly. Changes in RPE were statistically significantly different between conditions ($Z = -2.842$, $p = 0.004$). Pairwise comparison with Bonferroni adjustment showed that RPE at 0 was not different between conditions ($p = 0.234$), but at 90 RPE was higher in running condition ($p = 0.005$). (Figure 12B.)

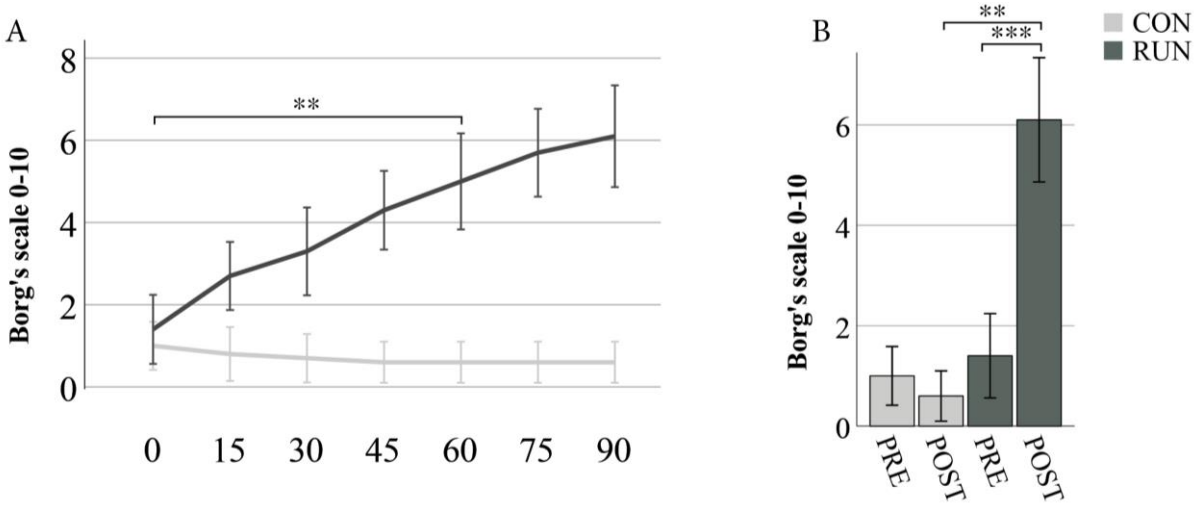

FIGURE 12. (A) Rating of perceived exertion (RPE) at every time point during reading (CON) and running (RUN) and statistically significant elevations (first elevation from 0 min and subsequent elevations). (B) RPE before (PRE) and after (POST) reading/running in control (CON) and running (RUN) conditions. Statistical significances between times and conditions. Error bars: 95 CL. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

8.3 Blood lactate level (BLa)

Friedman test did not find statistically significant effect of time in control ($\chi2(6) = 3.660$, $p = 0.723$) or running blood lactate levels ($\chi2(6) = 8.183$, $p = 0.225$) (Fig. 13A). During 90 min reading, BLa declined 0.06 ± 0.34 mmol/l, while during running, BLa increased 1.19 ± 1.41 mmol/l, reaching 2.58 ± 1.31 mmol/l. Changes in BLa values during 90 min reading/running were statistically significantly different between conditions ($Z = -2.701$, $p = 0.007$). Pairwise comparison with Bonferroni adjustment found no differences in BLa levels between conditions at 0 ($p = 1.000$), or at 90 ($p= 0.072$) (Fig. 13B).

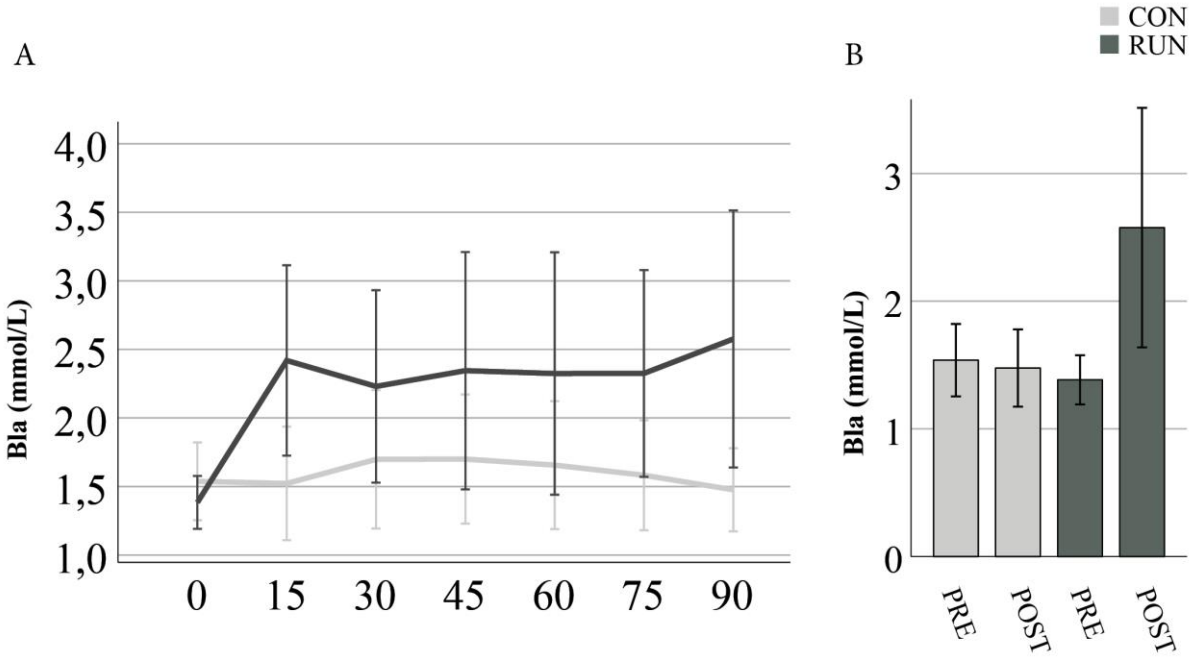

FIGURE 13. (A) Blood lactate (BLa) at every time point during reading (CON) and running (RUN). (B) BLa before (PRE) and after (POST) reading/running in control (CON) and running (RUN) conditions. No differences between time points or conditions. Error bars: 95 CL.

8.4 Physical performance test

Straight-legged jumps (Hop). There was no statistically significant effect of condition ($F(1.9) = 2.626$, $p = 0.140$, $\eta_p^2 = 0.226$), time ($F(1.9) = 0.178$, $p = 0.683$, $\eta_p^2 = 0.019$) or interaction between condition and time ($F(1.9) = 4.003$, $p = 0.076$, $\eta_p^2 = 0.308$) in jump height. Results are illustrated in Figure 14A.

Maximal voluntary contraction (MVC). There was no statistically significant effect of condition ($F(1.9) = 0.431$, $p = 0.528$, $\eta_p^2 = 0.046$) in MVC, but main effect of time ($F(1.9) = 21.352$, $p = 0.001$, $\eta_p^2 = 0.703$) and interaction between condition and time ($F(1.9) = 7.661$, $p = 0.022$, $\eta_p^2 = 0.460$) was found. 90 min reading declined MVC 31 ± 15 N (11% ± 6) and running declined it 10 ± 18 N (4% ± 7), but the change was significant only in control condition ($t(9) = 5.397$, $p < 0.001$). Results are illustrated in Figure 14B.

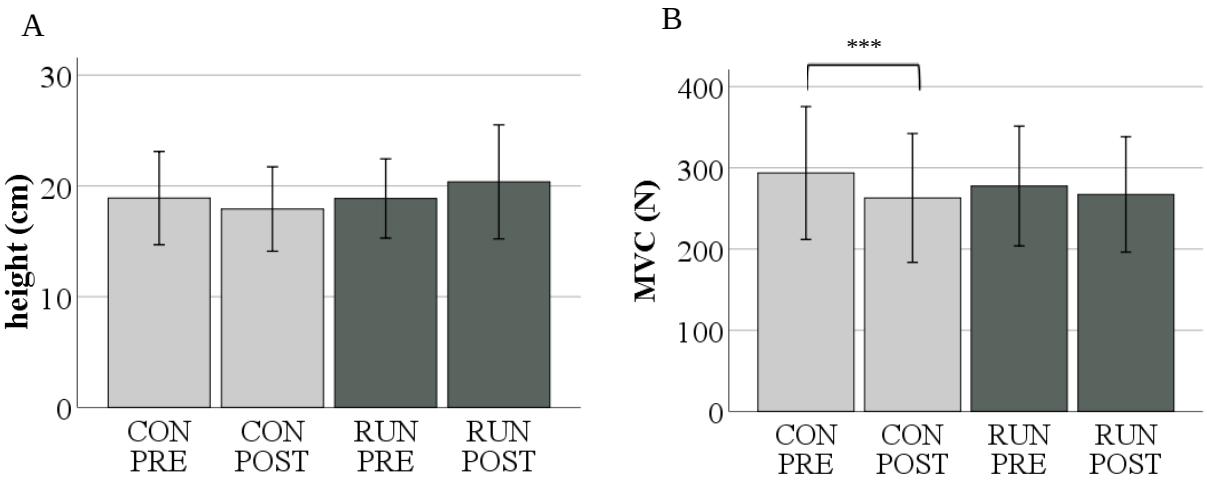

FIGURE 14. (A) Mean jump height and (B) mean maximal voluntary contraction (MVC) before (PRE) and after (POST) reading (CON) and running (RUN). Statistical significances between times and conditions. Error bars: 95 CL. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

8.5 Corticokinematic coherence (CKC)

Due to poor data quality and one subject having left dominant leg, CKC was analysed for four subjects at F0 and for eight subjects at F1. Data quality and exclusions are discussed in section "9.4.1 CKC data quality and exclusions". Coherence of each analysed subject exceeded the statistical threshold in both conditions and time points at F0 and F1 (Fig. 16 - 17).

Corticokinematic coherence at movement frequency (F0). Pre reading CKC at F0 ranged from 0.114 to 0.307 and post reading from 0.207 to 0.426. Pre running CKC ranged from 0.208 to 0.483 and post running from 0.128 to 0.342. Statistically significant interaction of time and condition was found at F0 ($F(1.3) = 10.329$, $p = 0.049$, $\eta p2 = 0.775$). Main effect of time ($F(1.3) = 0.066$, $p = 0.813$, $\eta p2 = 0.022$) or condition ($F(1.3) = 0.767$, $p = 0.446$, $\eta p2 = 0.204$) was not found. Pairwise comparisons did not found differences in pre values ($p = 0.330$) or post values ($p = 1.000$) between conditions, or between control pre and run post ($p = 1.000$) or between control post and run pre ($p = 1.000$). Group averages in both conditions and time points are illustrated in Figure 15A, while individual F0 values are illustrated in Figure 15B. Combined group averages of CKC spectra and topographical representation of CKC strength at movement frequency are represented in Figures 16A-D.

Corticokinematic coherence at first harmonic (F1). Pre reading CKC at F1 ranged from 0.191 to 0.613 and post reading from 0.153 to 0.580. Pre running CKC ranged from 0.2189 to 0.7055 and post running from 0.1570 to 0.6570. Statistically significant effect of time ($F(1.7) = 1.357$, $p = 0.282$, $\eta p2 = 0.162$), condition ($F(1.7) = 2.527$, $p = 0.156$, $\eta p2 = 0.265$) or interaction between time and condition ($F(1.7) = 0.409$, $p = 0.543$, $\eta p2 = 0.055$) was not found at F1. Group averages in both conditions and time points are illustrated in Figure 15C, while individual F1 values are illustrated in Figure 15D. Combined group averages of CKC spectra and topographical representation of CKC strength at F1 are represented in Figures 17A-D.

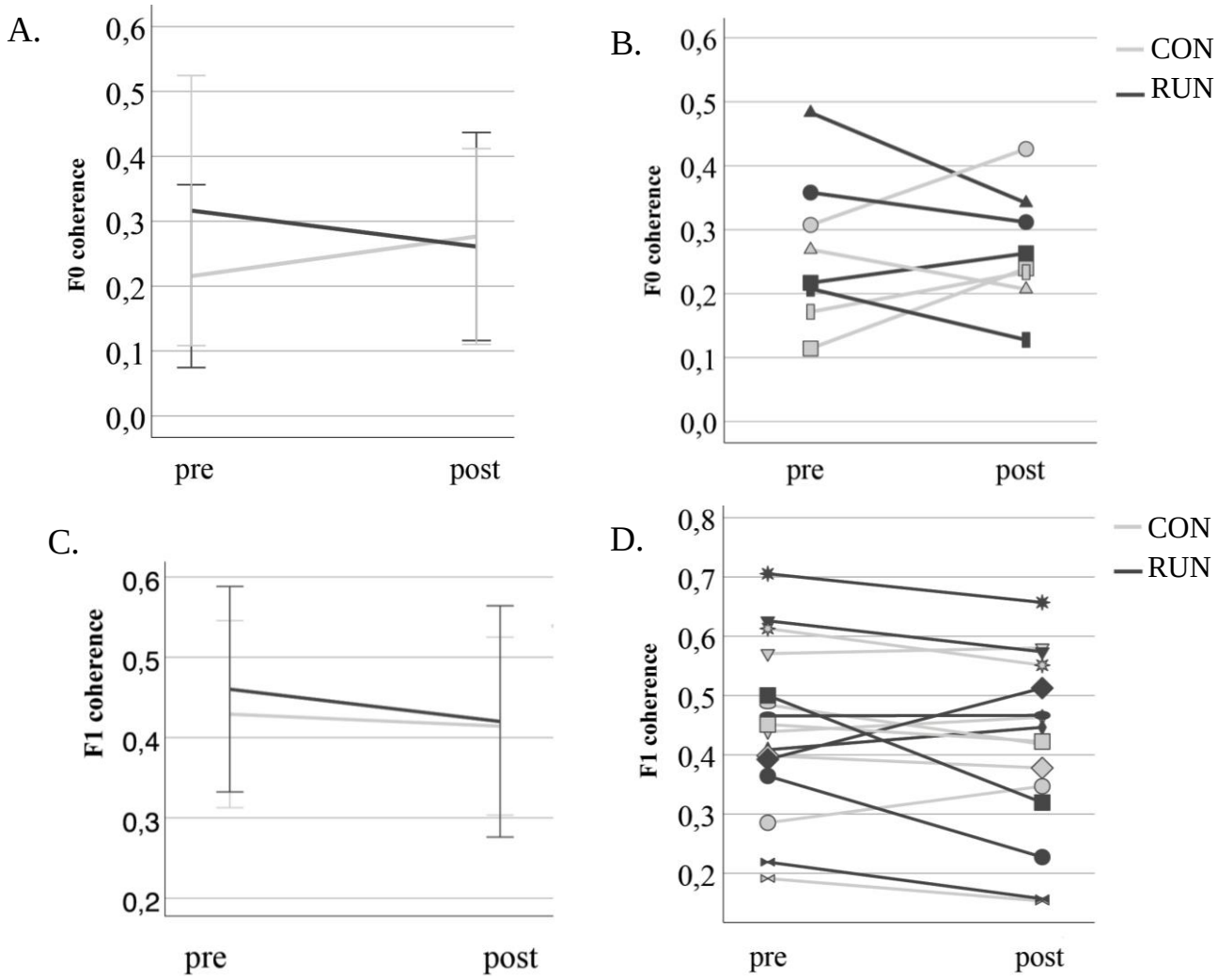

FIGURE 15. (A) Mean CKC and (B) individual CKC values at F0. (C) Mean CKC and (D) individual CKC values at F1. Control (CON) in grey and running (RUN) in black before (pre) and after (post) reading/running.

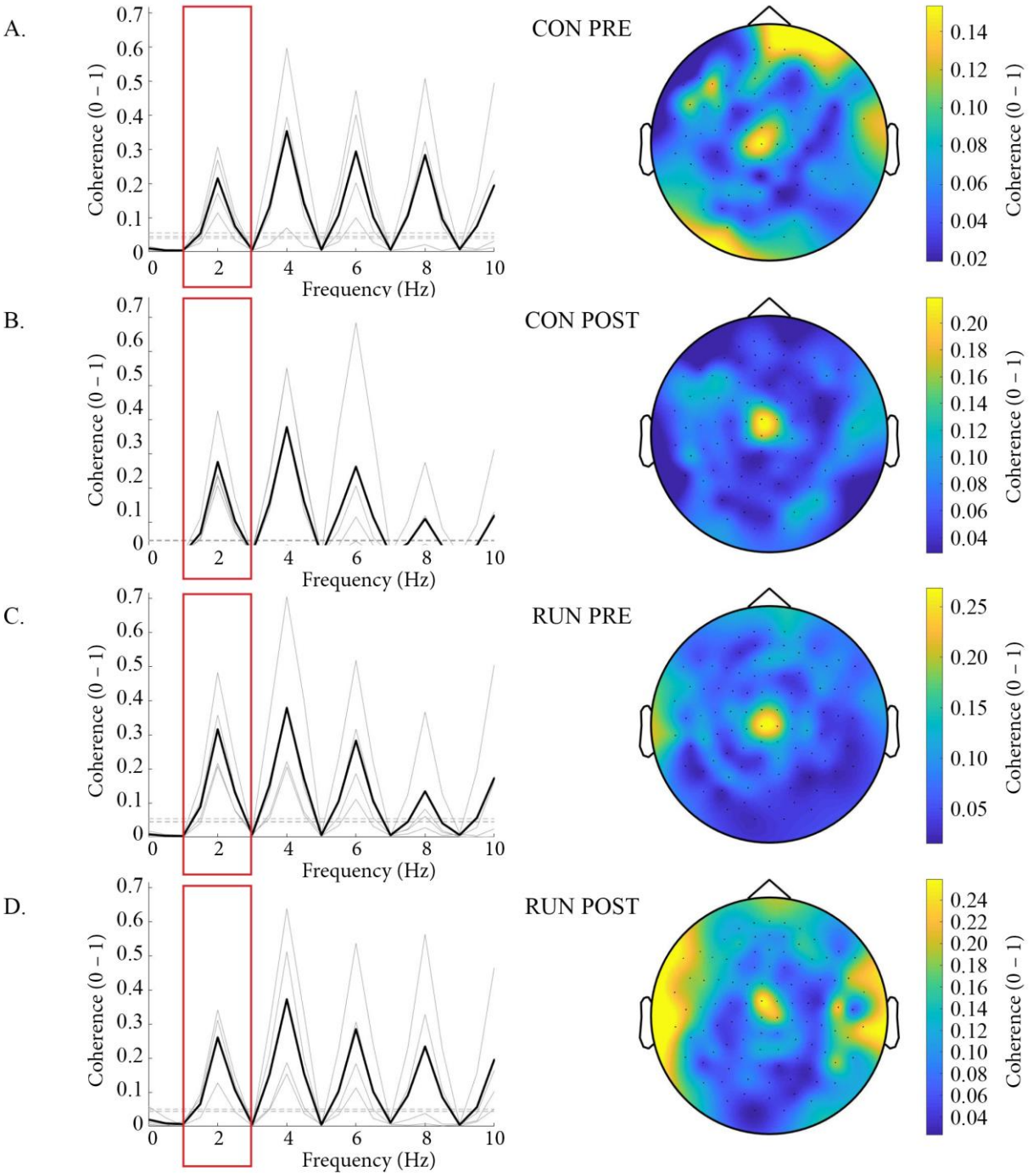

FIGURE 16. Combined group averages of CKC spectra (black) and for individuals (grey) with horizontal line representing statistical threshold (left). Topographical representation of CKC strength (from blue to yellow = from weakest coherence to strongest) at F0 (right). (A) before reading; (B) after reading; (C) before running; (D) after running. (N = 4).

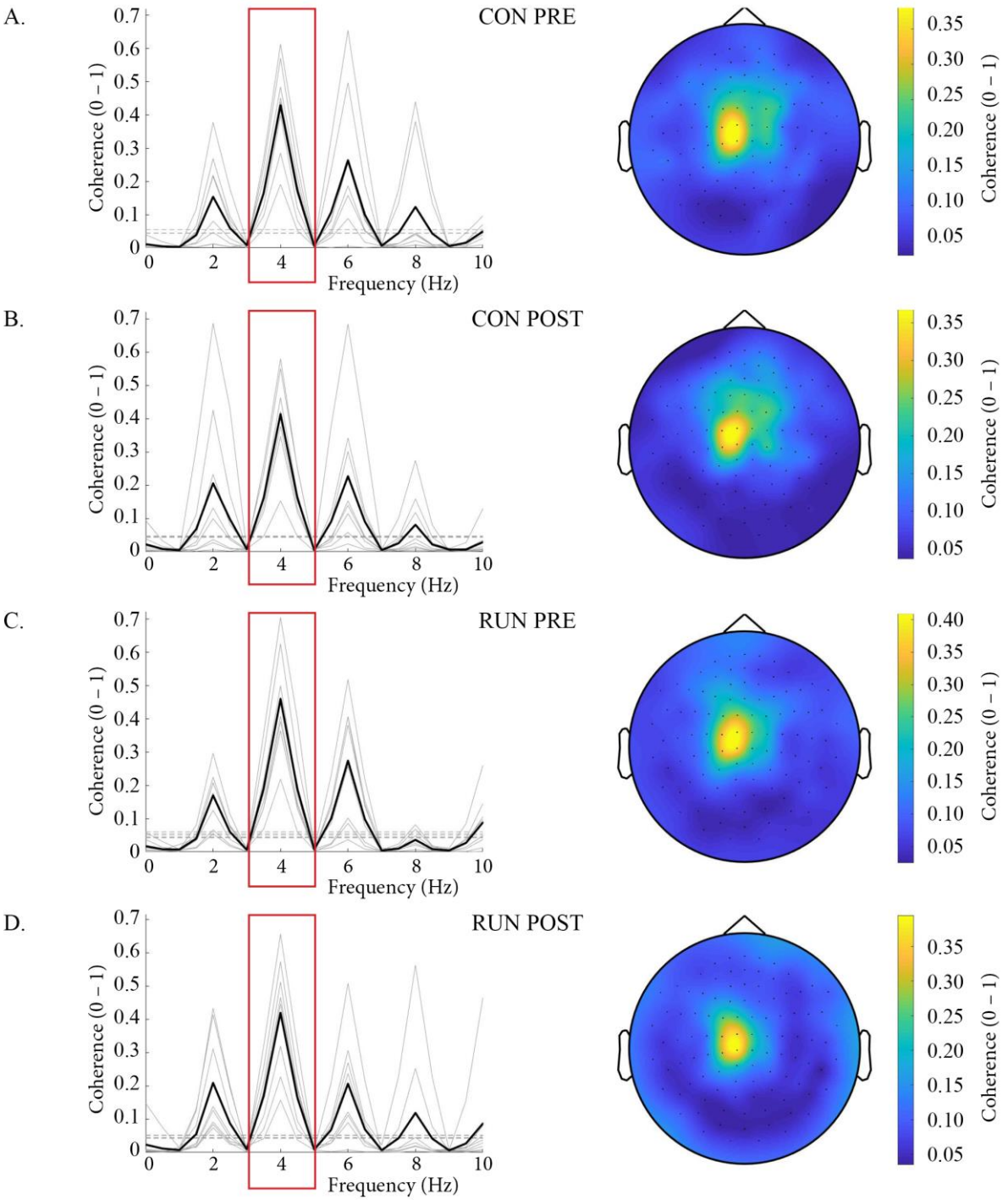

FIGURE 17. Combined group averages of CKC spectra (black) and for individuals (grey) with horizontal line representing statistical threshold (left). Topographical representation of CKC strength (from blue to yellow = from weakest coherence to strongest) at F1 (right). (A) before reading; (B) after reading; (C) before running; (D) after running. (N = 8).

Stability of acceleration signal. Peak acceleration magnitude was at similar level across conditions and time points as shown in Table 2. No statistically significant variation in peak acceleration magnitude was found between condition ($F(1.8) = 0.050$, $p = 0.828$, $\eta p2 = 0.006$) or time ($F(1.8) = 1.122$, $p = 0.320$, $\eta p2 = 0.123$), or interaction between time and condition ($F(1.7) = 0.008$, $p = 0.932$, $\eta p2 = 0.001$). Averaged peak acceleration magnitudes and coefficient of variations (CV) for the peak magnitudes across all dorsiflexions in both conditions and time points are represented in Table 2.

TABLE 2. Peak acceleration magnitudes (peak acc.) (m/s^2) and coefficient of variation (CV) in control (CON) and running (RUN) conditions before (pre) and after (post) reading/running.

	CON pre	CON post	RUN pre	RUN post
peak acc.	5.419 ± 0.457	5.318 ± 0.388	5.394 ± 0.658	5.261 ± 0.664
CV	2.21 ± 0.87 %	2.01 ± 0.74 %	1.69 ± 0.74 %	2.19 ± 0.68 %

8.6 Postural balance

Mediolateral sway eyes open. There was no statistically significant effect of condition ($F(1.9) = 0.002$, $p = 0.969$, $\eta p2 = 0.000$), time ($F(2.18) = 1.656$, $p = 0.219$, $\eta p2 = 0.155$) or interaction ($F(2.18) = 0.029$, $p = 0.971$, $\eta p2 = 0.003$) in mediolateral sway during eyes open.

Antero-posterior sway eyes open. There was no statistically significant effect of condition ($F(1.9) = 3.119$, $p = 0.111$, $\eta p2 = 0, 257$), but effect of time ($F(2.18) = 13.566$, $p < 0.001$, $\eta p2 = 0.601$) and interaction between condition and time ($F(2.18) = 8.979$, $p = 0.002$, $\eta p2 = 0.499$) was found in antero-posterior sway during eyes open test. Time effect was found in control condition ($F(2.18) = 4.045$ $p = 0.035$, $\eta p2 = 0.310$), but Bonferroni's post hoc test did not show difference between time points. Time effect in running condition ($F(1.289, 11.604) = 13.656$, $p = 0.002$, $\eta p2 = 0.603$) was found between tests before (Bal2) and after (Bal3) running (-3.0 mm/s, $p = 0.014$) and between after running (Bal3) and after second MEG-measurement (3.0 mm/s, $p = 0.009$).

Mediolateral sway eyes closed. There was no statistically significant effect of condition ($F(1.9) = 3.434$, $p = 0.097$, $\eta p2 = 0, 276$) or interaction between condition and time ($F(2.18) = 3.267$, $p = 0.062$, $\eta p2 = 0.266$) in mediolateral sway during eyes closed, but effect of time ($F(2.18) = 18.311$, $p < 0.001$, $\eta p2 = 0.670$) was found. Time effect was found in control condition ($F(2.18) = 4.076$, $p = 0.035$, $\eta p2 = 0.312$) but pairwise comparison with Bonferroni adjustment did not show differences between time points. Effect of time was also found in running condition ($F(2.18) = 16.673$, $p < 0.001$, $\eta p2 = 0.649$), and post hoc test showed statistically significant difference between tests before (Bal2) and after (Bal3) running (-5.5 mm/s, $p = 0.005$) and between after running (Bal3) and after second MEG-measurement (Bal4) (6.2 mm/s, $p = 0.003$).

Antero-posterior sway eyes closed. Statistically significant effect of condition ($F(1.9) = 6.306$, $p = 0.033$, $\eta p2 = 0, 412$), time ($F(2.18) = 17.713$, $p < 0.001$, $\eta p2 = 0.663$) and interaction between time and condition ($F(2.18) = 8.368$, $p = 0.003$, $\eta p2 = 0.482$) was found in antero-posterior sway during eyes closed task. Only difference between conditions was found in after reading/running test (Bal3), where sway was 4 ± 3.6 mm/s higher in running condition ($t(9) = 0.692$, $p = 0.006$). Time effect was found in running condition ($F(2.18) = 20.574$, $p < 0.001$, $\eta p2 = 0.696$), where -6.1 mm/s difference was found between before (Bal2) and after (Bal3) running ($p = 0.001$) and 6.5 mm/s between after running (Bal3) and after second MEG-measurement (Bal4) ($p = 0.001$). Postural sway did not change in time in control condition $F(2.18) = 2.046$, $p = 0.158$, $\eta p2 = 0.185$).

Romberg quotient. There was no statistically significant effect of condition ($F(1.9) = 1.432$, $p = 0.262$, $\eta p2 = 0.137$), time ($F(2.18) = 3.201$, $p = 0.065$, $\eta p2 = 0.262$) or interaction between condition and time ($F(2.18) = 1.571$, $p = 0.235$, $\eta p2 = 0.149$) in RQ in mediolateral direction. Effect of condition ($F(1.9) = 0.011$, $p = 0.918$, $\eta p2 = 0.001$), time ($F(2.18) = 1.544$, $p = 0.241$, $\eta p2 = 0.146$) or interaction between condition and time ($F(2.18) = 0.430$, $p = 0.657$, $\eta p2 = 0.046$) in antero-posterior RQ was not found. Figure 18 shows COP velocities and Romberg quotients in all conditions.

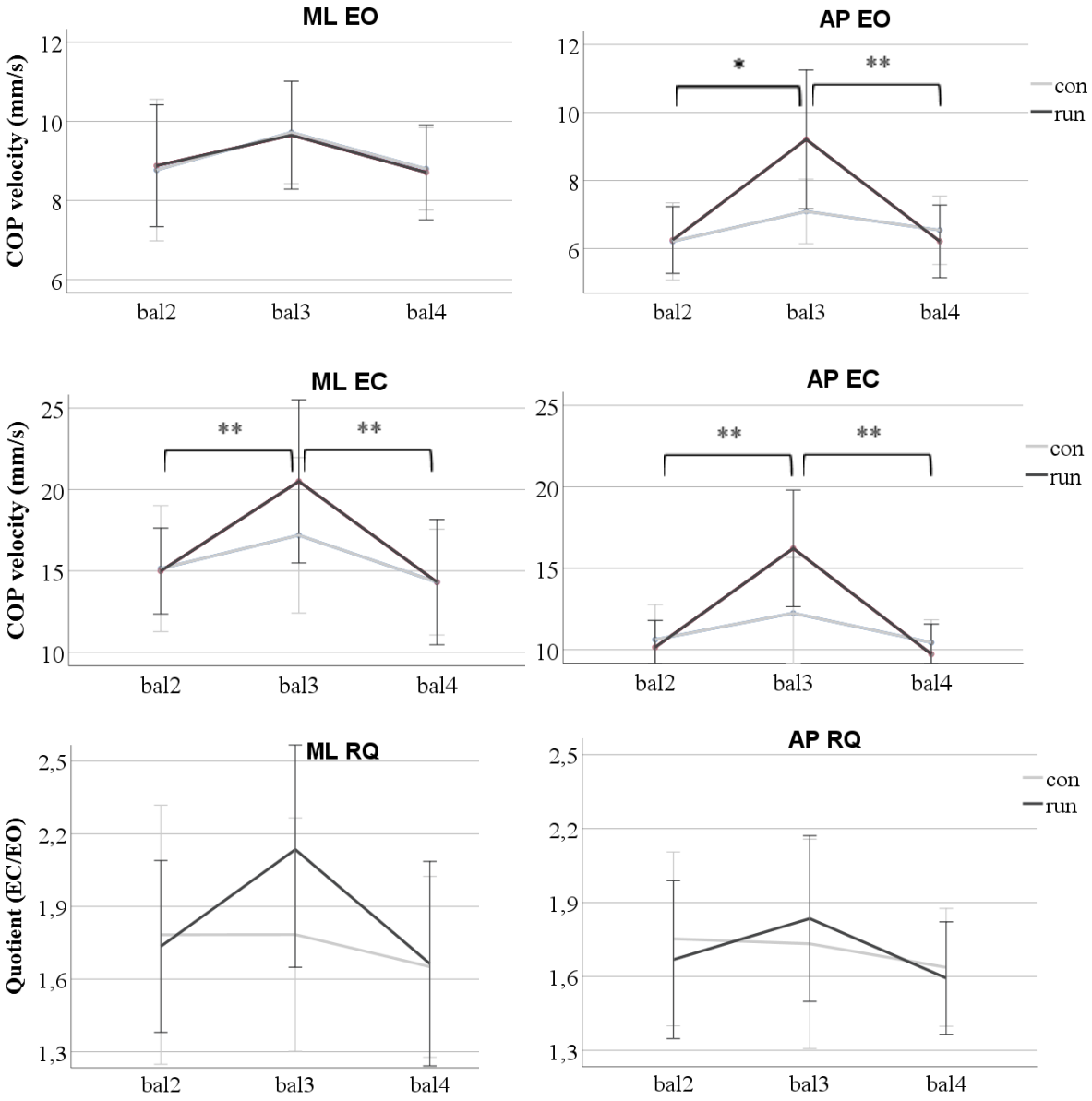

FIGURE 18. Mean COP velocity (mm/s) and Romberg quotients just before running (bal2), straight after running (bal3) and after second MEG measurements (bal4) in control (con) and running (run) conditions. EO = eyes open, EC = eyes closed, ML = mediolateral direction, AP = anteroposterior direction. Statistically significant effects of time are marked. Error bars: 95 CL. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

8.7 Correlation between CKC and postural stability

Correlation between pre CKC and Balance. Statistically significant correlation was found in pre-values between F0 strength and anteroposterior COP velocity in eyes closed condition (-0.988, p = 0.012, n = 4). Correlation represented in Figure 19. No correlation was found in pre values between F0 and any other balance scores or in pre values between F1 and any of the balance scores (Table 3).

Correlation between pre CKC and change in balance. There was no correlation between pre values of F0 or F1 (CKC1) and change in any of the balance scores (Bal3 - Bal2).

Correlation between change in CKC and change in balance. There was no correlation between change at F0 or F1 (CKC2 - CKC1) and change in any of the balance scores (Bal3 - Bal2).

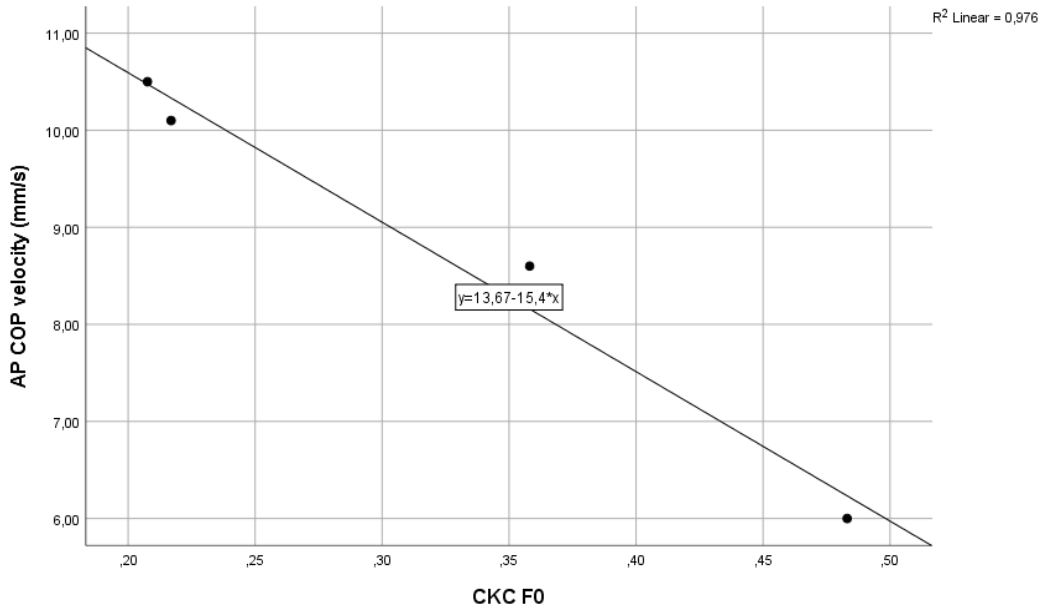

FIGURE 19. Correlation between centre of pressure's (COP) anteroposterior (AP) displacement velocity during eyes closed balance test (vertical axis) and CKC at movement frequency (horizontal axis) before running.

TABLE 3. Correlation coefficients between CKC and balance values before (pre) running and between differences of pre and post running (change).

	F0 pre		F1 pre		F0 change		F1 change	
	r(2)	p-value	r(6)	p-value	r(2)	p-value	r(6)	p-value
ML EO pre	-0.603	0.397	-0.421	0.299				
ML EC pre	-0.779	0.221	-0.143	0.735				
ML RQ pre	-0.166	0.834	0.381	0.352				
AP EO pre	-0.689	0.311	-0.146	0.730				
AP EC pre	-0.988	0.012**	-0.176	0.677				
AP RQ pre	-0.430	0.570	-0.002	0.996				
ML EO change	0.571	0.429	0.073	0.864	-0.598	0.402	-0.037	0.930
ML EC change	-0.381	0.619	-0.157	0.711	0.358	0.642	0.046	0.913
ML RQ change	-0.493	0.507	-0.028	0.948	0.457	0.543	-0.065	0.878
AP EO change	0.343	0.657	-0.302	0.468	-0.058	0.942	0.073	0.863
AP EC change	-0.325	0.675	-0.200	0.635	0.616	0.384	0.296	0.477
AP RQ change	-0.285	0.715	0.111	0.793	0.462	0.538	0.199	0.637

9 DISCUSSION

Effect of 90 minutes treadmill running on cortical proprioceptive processing was evaluated by comparing strength of corticokinematic coherence during passive ankle movement before and after 90 min treadmill running. As it was expected, CKC peaked at SM1 cortex, but contrary to hypothesis, this study did not show statistically significant change in CKC strength at F0 or at F1 induced by running. Moreover, opposite to expectations CKC showed tendency to decrease more than increase. Running effect on balance control was evaluated by COP displacement velocities during eyes closed and eyes open upright standing. The role of proprioception during balancing was evaluated by quotient of eyes closed and eyes open velocities (Romberg quotient). In line with expectations, COP velocity was increased immediately after running exercise, but the role of proprioception in balance control, defined as Romberg quotient seemed to remain unchanged. Association between CKC strength and balance control was found only between pre values of F0 strength and anteroposterior COP velocity in eyes closed test and against expectations, this correlation was negative. No association found between CKC and the role of proprioception during balance control. However, due to extremely small sample size in CKC at F0 (n = 4), reliable conclusions about the strength of CKC or its association with balance control cannot be made. Fatiguing effect of running exercise was tested with physiological markers during running and with physical performance tests before and after running. Although there was some variation in the exertion of the running between individuals, exercise seemed to cause some cardiovascular stress without being maximal or disturbing force production of lower limbs.

9.1 Evaluation of the fatiguing effect of running exercise

It was expected that 90 min treadmill running would induce fatigue in peripheral and central sites of neuromuscular system and thus affect to proprioceptive feedback and its central processing. Possible reasons for strengthened CKC due to 90 min running was expected to be

caused by altered afferent feedback or altered activation of cerebral cortex during passive ankle movement. Altered afferent feedback by fatigue induced deficit in muscle receptors and spinal level and changes in cortical circuits and activation areas could have cause alteration in cortical activity and thus in the strength of coherence. Fatigue markers (BLa, HR and RPE) and physical performance tests (MVC and Hop) was used for evaluating fatiguing effect of running. Fatiguing effect of running was seen in elevated HR, RPE and BLa, of which the results of only HR and RPE reached statistical significance. MVC and Hop did not show statistically significant changes in running condition.

HR. As expected, HR at the last 30 seconds was 55% ± 26 higher than first 30 seconds in running condition. During running, HR was increased already in second 15 min set compared to first 15 min set and continued increasing to third and from third to fourth set, after which the increase of HR was no more statistically significant. Elevation in HR indicated that running was causing stress to cardiovascular system from the very beginning of the exercise. Based on heart rate, running exercise was fatiguing but not near maximal, as HR of the last 30 sec was only 163 ± 8 BPM, while subjects age estimated maximum heart rate would have been 181 (Tanaka et al. 2001). Reading did not elevate mean 30 sec HR or mean HR of 15 min sets and it was statistically significantly lower than running HR at every time point. Despite the daily variation in HR, difference between last 30 second heart rates between conditions was clear: running HR was 174% ± 49 higher than reading HR at the end of the 90 min. Clear difference between conditions indicate that changes in running HR was due to running and not randomly due to time. Increased HR during running together with slight decrease in reading HR most likely caused interaction effect.

RPE. At the beginning of reading/running, RPEs were at similar levels between conditions, indicating equal baseline. RPE increased quite linearly from the beginning of the running, but because of the variation between individuals, first statistically significant elevation in RPE was not seen before 60 min running, after which the elevation of RPE was not statistically significant. The total increase during 90 min running was 4.7 ± 2.1 units, mean subjective load

increasing from very easy or easy to hard or very hard. Only one subject in our study had to lower the running speed and reached RPE value of 10, while the rest of the subjects reported RPE 4–7 at the end of the running, indicating variation in perceived exertion. Although all subjects had similar relative load (speed of individual first lactate threshold), heterogeneous training and individual differences in running economy and other properties, caused variation in the total neuromuscular and cardiovascular load. However, in line with HR elevation, RPE indicated that the exercise was strenuous but not maximal. After all mean RPE at the end of the running was higher than in the study by Nardone et al. (1997), where fatiguing treadmill walking had disturbing effect on balance control. Effect of time was found also in control condition, but the change in perceived exertion was on opposite direction than during running. Slight decline in RPE was expected, as participants had 90 minutes to sit and relax after pre session measurements.

BLa. Expectedly, blood lactates were at similar level at the beginning of reading/running. Based on Seiler & Tønnessen's (2009) intensity scale, it was expected that 90 min running would increase blood lactate levels somewhere close to 2.5 mmol/l, which would correspond training on first lactate threshold (Table 1). Blood lactate rose to expected 2.58 ± 1.31 mmol/l during 90 min running, but the effect of time was not statistically significant, as the sample size was small and there was some variation in the BLa levels. Reading BLa did not elevate either and there were no statistically significant differences in BLa levels at the end of the running. Even though the elevation in blood lactate during running did not reach statistically significance, the total change in BLa levels were significantly different between conditions, giving a guide to different effects of reading and running.

MVC. Running exercise was expected to show impaired performances in MVC and straight-legged jumps as fatigue was developed in neuromuscular system. Maximal isometric contraction of knee extensors was used to evaluate combination of central and peripheral fatigue of lower limbs, as impaired voluntary activation, reduced efferent neural drive and attenuated contractile properties of knee extensors are reasons for loss in MVC force after prolonged

running exercise (e.g. Millet et al. 2003; Ross et al. 2010). However, statistically significant, 11% ± 6 reduction in MVC appeared only after 90 min reading, while running exercise did not reduce MVC statistically significantly. Results indicate that only 90 min passive reading impaired neuromuscular system and maximal force production capability. Impaired MVC after reading was most likely caused by unequal activity prior physical performance tests before and after reading: slightly before the first tests, subjects had warm-up session, which included jogging and submaximal attempts of physical performance test pattern, while after reading test were performed straight after 90 min passive sitting. Pre reading MVC was most likely higher due to increased nerve conduction and other muscle temperature related advantages (Bishop 2003).

MVC was chosen to physical performance test pattern, as it has been previously used for evaluating fatigue in lower extremities after running exercise (e.g. Millet et al. 2003; Ross et all. 2010). In the study by Ross et al. (2010) subjects ran similar time (91.4 ± 6.4 min) as in our study (90 min) and began to run at or just above their lactate threshold, but they were running a self-paced 20 km running trial and were allowed to modulate their running speed for achieving the fastest time possible. In the study by Millet et al. (2003) subjects were running in 30 km race (duration was 188.7 ± 27.0 min). Contrary to our study, previously mentioned studies had self-paced maximal running exercise and longer duration and/or distance. It is possible, that intensity of our running exercise was not high enough to induce strength loss in knee extensor muscles and voluntary activation. This view is strengthened by results in Ross et al. (2010) study, as the reduction in MVC was not seen until after 15 km running. Subjects in current study were recreational endurance runners, who are typically not specialized training maximal strength and has smaller portion of fast twitching muscle fibers (Saltin et al. 1977). It has been previously shown that greater maximal isometric strength is correlated with greater strength loss after continuous running exercise (Millet et al. 2003), which would support the idea of the effects of the neuromuscular characteristics of our study subjects. In conclusion, it is possible, that our protocol was not intense or long enough to induce loss in endurance runners' MVC.

Despite the fact, that MVC test failed to show fatiguing effect of exercise, it must be noted, that possible fatiguing effect may have been recovered before the MVC test. According to Ross et all. (2010), long distance running declines MVC due to central factors, and not contractile properties of running. Studies, including the study by Millet et al. (2003) supports the idea of more important role of central than peripheral properties causing loss MVC force after long duration (+30 km) running, as they found attenuated MVC together with decreased voluntary activation and only minor reduction in M-wave. Portion of which of these central and peripheral properties are causing loss in MVC is altered by intensity and duration of exercise (Thomas et al. 2015), and in current study, these properties were not measured. If we suppose that 90 min running induced some central fatigue, it could have been recovered before MVC test, as the mean recovery time between end of the running and MVC test was at least 3 minutes: the whole physical performance protocol after running took 4.8 ± 1.2 min, and test of MVC was the last task of the set. First attempt of the two MVCs was used in analyses, and the recovery time between attempts were 60 seconds, meaning that before the first attempt, at least 3 minutes plus the transition time from treadmill to balancing task was gone after running. Central fatigue may recover in first few minutes after long duration endurance exercise (Carroll et al. 2017). As the intensity of running was not maximal and MVC was measured several minutes after running has ended, it is possible that evoked central fatigue was recovered before MVC task. Altogether, with measures used in this study, it is impossible to conclude or rule out central changes in efferent, and especially in afferent pathways.

Straight-legged jumps. Straight-legged jumps was used to evaluate changes in structures in muscle-tendon units of ankles due to repeated stretch shortening cycles. Jump height was very slightly lower after reading and higher after running, but the time effect was not statistically significant, nor was the difference between conditions. Thus, 90 min reading or running had no effect on jump height, indicating that reflex circuits or mechanical properties of plantar flexors was not altered. As with unaltered MVC, type I fibers, which are less sensitive to mechanical stress and typically seen in high portion with long distance runners, could explain why 90 min running had no effect on straight-legged jumps (Saltin et al. 1977). It should also be noted that

participants practiced jumping performance only few times during the warm-up of each session and they may not have been familiar with straight-legged jumps. Although each participant succeeded to perform jumps as it was instructed, challenge of the task must be considered.

To conclude, physical performance tests failed to show fatigue, possibly because of intensity and duration of the exercise was not high enough to impair isometric force production or plyometric ankle jumps or due to long recovery time between the end of running and test protocol. Characteristics of endurance runners were probably partly explaining why chosen neuromuscular tests did not show any evidence about fatigue. Interindividual variation in fatigue markers had an influence on nonsignificant results. Altogether, results of RPE and HR, and partly BLa indicated that 90 min running exercise was not near maximal but caused physiological stress in cardiovascular system which was not reflected in neuromuscular performance tests.

9.2 Effect of running exercise on corticokinematic coherence

In line with previous studies, where clear CKC during passive movement was visible with all subjects (Piitulainen et al 2013b; 2015), coherence values of each analysed subject in each condition and time point at F0 and at F1 exceeded the statistical threshold in current study (Fig. 16 and 17). However, CKC analyses were conducted only for four (F0) and eight (F8) subjects due to contaminated data and one subject having left dominant leg. Data quality and exclusion criteria are discussed in section “9.4.1 CKC data quality and exclusions”. Individuals’ anatomical magnetic resonance images (MRIs) were not available and topographical representations were used for localising and illustrating source in sensor level. As expected, CKC peaked around the expected foot area of the SM1 cortex (Fig. 16 and 17).

9.2.1 Adaptation of CKC

Hypothesis was, that 90 min treadmill running would alter afferent feedback and/or activation of cortical neural circuits during passive ankle movement, which would have been seen as altered strength of CKC. Impaired proprioception, measured with angle matching task has been shown to occur after general, whole body exercise without local muscle fatigue (Miura et al. 2004), which led us to expect 90 min running exercise to disturb proprioceptive processing and strengthen CKC. Contrary to hypothesis, this study did not show that 90 min treadmill run at velocity of first lactate threshold alters the strength of CKC.

Time window for measuring changes in CKC. Differences in the strength of CKC has been previously observed between age groups. Less precise activation of cortex seems to cause stronger coherence, as Piitulainen et al. (2018b) found older individuals to have stronger CKC, while cortical activation and amplitudes of sustained movement evoked fields were not stronger. Fatiguing exercise has been shown to increase the variability in the activation of cortical motor networks (Benwell et al. 2005). Variability in activation of cerebral cortex could affect the strength of coherence, but our study did not show evidence about increased coherence. Although precision of SM1 activation seems to operate the strength of CKC, the exact neural mechanism behind CKC strength is not known, and thus, it is not known which mechanisms would have caused changes in CKC after running. With age groups, one possible explanation for appeared differences in CKC levels could be found in SM1 inhibitory circuits. Age related deprivation in inhibitory synapses and the resulting alteration in inhibitory circuits (Poe et al. 2001) as well as loss of grey matter thickness (Magnotta et al. 1999) could cause deficits in sensory processing and change activity in sensorimotor cortex. Even though acute exercise may increase (Rajab et al. 2014; Raichlen et al. 2016) or decrease (Schmitt et al. 2019) connectivity in sensorimotor related areas and reduce cortical inhibition (Singh et al. 2014; Smith et al. 2014; Yamazaki et al. 2019) and inhibition of sensorimotor integration (Yamazaki et al. 2019), these changes are not necessarily related to processing of proprioceptive input. Thus, it is possible that these acute changes in SM1 cortex are not operating corticokinematic coherence, i.e.

cortical proprioceptive processing. On the other hand, activity of SM1 cortex may have been altered acutely, but have been recovered by the time of CKC measurement, as CKC was measured 26.1 ± 1.5 minutes after running. It has been shown that postural balance, which among other sensory systems relies on proprioception, could be recovered within 5 - 15 minutes after physical exercise (Nardone et al. 1997; Guidetti, et al. 2011). As cortical proprioceptive processing may also recover in relatively short time window, CKC should be measured sooner after exercise in the future.

Long term adaptation and the type of exercise. Alternatively, it is possible that CKC is not altered by single bout of moderate intensity endurance exercise, but rather requires regular exercising. It is possible, that differences in CKC strength may be caused by the kind of anatomical and structural differences, which cannot be modulated acutely. Evidence about regular aerobic exercise enhancing inhibition of task-irrelevant cognitive processes have been observed previously (Ludyga et al. 2016; Flodin et al. 2017). It would be beneficial to see if months or years long aerobic exercise would enhance proprioceptive processing. Another possible explanation for unaltered CKC due to aerobic running exercise is that it was not loading sensory-motor system enough. Treadmill running is quite simple locomotion task and thus co-operation of sensory and motor system is not as skill demanding than tasks which require constant, awareness adjustment of body positions. Perhaps treadmill running is not straining proprioceptive system in a manner that will cause major acute or long-term changes in proprioceptive processing. Skill training on the other hand would potentially enhance sensory-motor integration in a way that can be seen in altered CKC: it seems that more precise activation of the SM1 neuron population would supress CKC (Piitulainen et al. 2018b) and motor-skilled subjects has been shown to activate lesser neurons in sensorimotor areas (Jäncke et al. 2000; Krings et al. 2010). For future, it would be interesting to see weather skill trained individuals (skilled in specific joint movement that requires high sensorimotor integration) would appear to have weaker CKC in passive joint movement.

Changes in periphery. Another age-related explanation for differences in CKC strength would be changes in spindle morphology (Swash & Fox 1972) and sensory nerve endings (Kim et al. 2007), which may result in loss of proprioception and thus altered higher order processing. Similarly, repeated stretch shortening cycles and ground strikes during numerous plantar and dorsiflexions in 90 min running exercise was expected to cause mechanical changes in muscle spindles, reduce spindle sensitivity and alter spinal loop properties (Horita et al. 1996; Avela et al. 1999; Racinais et al. 2007), which could modulate afferent proprioceptive information. As coherence is dependent on amplitude and phase of the signals (Pitkänen et al. 2019), decreased afferent input could have potentially decreased CKC. Alternatively, strength of afferent feedback may be modulating cortical processing of proprioception and decreased proprioceptive information could lead to overcompensation of proprioceptive processing by activation of wider neuronal populations. Specific measure about the afferent feedback would have been amplitudes of movement evoked fields (MEF), which was not analysed for this thesis. As MEFs are thought to reflect similar proprioceptive feedback as CKC (Cheyne et al. 1997; Hoshiyama et al. 1997) and to offer information about sensory feedback and/or sensorimotor modulation of movement (Kristeva et al. 1991), it would have been interesting to know, were the MEF amplitudes or latencies altered without change in CKC.

Consequence of the intensity of running exercise. As mentioned, reliable outcomes about the effect of running exercise on the strength of corticokinematic coherence cannot be made as the sample size was not large enough. Although CKC strength did not change statistically significantly, contrary to hypothesis, CKC at F0 and F1 showed tendency to decrease more than increase after exercise. Intensity and duration of the exercise is crucial in determining what kind of effect it has on neural and muscular sites of the body. It was hypothesized, that 90 min running would impair proprioception in peripheral, spinal and/or supraspinal sites and thus increase strength of CKC. Possibility of the intensity being too low to disturb proprioceptive processing must be noted. In fact, possibility of enhanced proprioceptive processing after low intensity exercise cannot be ruled out, as intensity of exercise can determine if there is an effect and weather it is positive or negative. Intensity has been shown to determine whether exercise

have positive or negative effect at least on cognitive functions (e.g. Tomporowski 2003; Chang et al. 2012). Athletes has shown more selective involvement of task related cortical networks during standing (Del Percio et al. 2009) and reduced cortical activity during cycling and at rest (Ludyga et al. 2016), which supports the hypothesis of regular exercise enhancing cortical processes and thus potentially decreasing CKC. Moreover, if CKC can be altered by acute exercise, it cannot be ruled out that exercise in certain intensity could actually enhance cortical proprioceptive processing and activate cortical neurons in more specific manner, which would in turn decline coherence.

Inter session variability. Previously, Piitulainen et al. (2018a) showed good group level reproducibility of CKC during passive finger movement, but reproducibility of lower limbs has not been studied. In current study, there was no statistically significant difference in CKC before reading/running at F0 or at F1 indicating that baseline levels were similar between sessions. However, even though baseline values were not statistically significantly different, CKC at F0 appeared to be stronger in running conditions (0.316 ± 0.131) compared to reading condition (0.216 ± 0.089), which together with decreased CKC during running and increased CKC during reading led to statistically significant interaction. Figure 15 represents clearly, that there was intra-individual variation in baseline values between conditions. Although Piitulainen et al. (2018a) showed good reproducibility in group level, they also found that some individuals had clear inter-session variation in CKC levels, which was case in our study. With this small sample size, inter-session variation of individuals has significant effect on statistics. When considering effect of time at individual level (Fig. 15), running decreased CKC in most cases, but with this small sample size, even one opposite effect shifts mean values radically. If running had some effect on CKC levels, large intra-individual variation between sessions could have been overridden the effect.

9.3 Alteration in postural balance and connection to CKC

Running effect on balance control was evaluated by COP displacement velocities and Romberg quotient (RQ). 90 min running increased postural sway straight after running, but the role of proprioception (RQ) in balance control did not change statistically significantly. Strength of CKC at F0 before running correlated negatively with eyes closed anteroposterior COP velocity before running. Sample size (n = 10) must be noted in results of balance tests, as it was relatively small for counterbalancing order of eyes open and eyes closed tests (five subjects began with eyes closed, while five started with eyes open).

9.3.1 Effect of exercise on postural balance

Mean velocity of COP displacement was chosen for measure postural stability, as it has been shown to be the most reliable measure of COP in balance tests, compared to sway area, COP range etc. (Lafond et al. 2004). Statistically significant difference in COP velocity between before and after running was found in three out of four conditions. According to Paillard (2012), postural stability is impaired if local muscle fatigue induces over 25–30 % strength loss of MVC or if the duration of low intensity exercise is long enough. Our running exercise did not alter MVC but may have been long enough to induce general fatigue which affect sensory and motor activity and disturb postural stability. Postural stability was impaired in all condition and direction except mediolateral sway during eyes open. Results are in line with previous studies, where fatigue has been shown to have effect only anteroposterior sway or having effect on mediolateral sway only in most difficult tasks (e.g. unipedal standing) (Winter et al. 1996; Horak 2006). Horak (2006) argued smaller range of motion (ROM) in mediolateral direction to be reason for slighter effect of fatigue.

Chances on COP velocity between time points. Velocity of COP displacement was highest straight after 90 min running. As the balance test was conducted immediately after running, respiratory movement have potentially had large effect on disturbed postural balance (Bouisset

& Duchêne 1994). Although altered information flow from muscle receptors and changes in cortical neural circuits cannot be ruled out, respiratory movement is more likely reason for increased postural sway straight after running exercise. There was no difference between balance tests before running and after second MEG-measurements, indicating that running increased postural sway, but it was recovered till the time of the last balance test, which was measured 44.4 ± 1.9 min after running. This recovery is in line with previous studies that have shown that impaired postural control after aerobic running or walking exercise has returned to baseline within 15 min. (Nardone et al. 1998; Fox et al. 2008) and after local ankle plantar flexors and dorsiflexors fatigue within 20 minutes (Yaggie & McGregor 2002).

Condition differences. Even though COP velocity was increased after running in three out of four conditions, effect of time was also seen in two conditions of reading session and only statistically significant difference between conditions was found straight after running in the most challenging task: anteroposterior sway during eyes closed condition (largest ROM and least sensory cues). Most likely increased postural sway after 90 min reading was caused by opposite effect than after running: similarly, as physical performance tests were better after warm-up than after 90 min sitting, passive sitting did not prepare neuromuscular system to balancing task. Subasi et al. (2008) showed, that even five minutes warmups improved proprioception (joint position sense) and unilateral eyes closed standing test compared to no warmup situation. However, time effects in control condition were relatively small, and despite statistically significant main effect, pairwise comparisons did not find differences between time points, indicating that 90 min passive sitting did not have large, significant effect on balance control. Based on these results it can be conducted, that balancing task was most difficult straight after running exercise, and that also long duration passive sitting has small effect on balancing ability. It seems that 90 min running had clearly negative effect on balance control straight after exercise, but the balance control was returned to baseline within 44.4 ± 1.9 min after running. It also seems, that subjects performed balancing task better after small warm-up than after 90 min passive sitting.

Romberg quotient. Contrary to expectations, current study did not show statistically significant differences in Romberg quotient (ratio between eyes closed and eyes open sway) between any time point or between conditions in any direction. Although RQ tend to increase straight after running in mediolateral direction but did not reach statistical significance. Contrast findings with previous studies may be explained by different fatiguing effect (general or local), different intensities of fatiguing tasks or by different balancing tasks. More challenging balance task, as for example unipedal stance would have highlighted difficulties in eyes closed task and maybe revealed possible disturbance of proprioception better. On the other hand, too difficult task straight after running would have increased the risk of total failure of the task (falling or stepping). Besides Romberg quotient as in our study and for example in the study by Nardone et al. (1997), some studies have used difference of the absolute values of EC and EO sway (Vuillerme et al. 2001; Corbeil et al. 2003), which may show larger differences than quotient of two values. As explained previously, respiratory movement may have been the main reason for increased postural sway after exercise, which would explain unaltered use of proprioception. Additionally, small sample size may have influenced why altered use of proprioception was not visible or statistically significant. As there was no change in Romberg quotient, these results did not provide support to possible changes in proprioceptive processing during balance control.

9.3.2 Association between CKC and postural balance

Proprioception is in essential role in balance control (Lord et al. 1999) and some evidence about connection between poorer balance control and stronger CKC at F1 has been found previously (Piitulainen et al. 2018b). Thus, secondary aim of this study was to investigate if postural balance or alteration in postural balance after exercise is connected to the strength of CKC or changes in CKC due to 90 min running. However, sample size (n = 4 at F0 and n = 8 at F1) was not large enough for making reliable conclusions about correlations, especially because there seemed to be some intraindividual variation in CKC strength between days and between time points in control condition.

Several correlation coefficients were calculated between CKC and balance tests (Table 3). Values before running and changes in these parameters between before and after running was used, but only connection was found between baseline values of F0 strength and anteroposterior COP velocity in eyes closed condition. Changes in COP velocity or in CKC due to running did not show any correlations. COP velocity increased only immediately after exercise, and was returned to baseline after second MEG session, indicating that postural control could have been recovered already when CKC was measured 26 minutes after running and explain why there was no connection. Thus, correlation between the strength of CKC and COP velocity was seen only in the most difficult balancing task (eyes closed and largest ROM). It is possible that other tasks were not difficult enough to express differences between subjects.

Furthermore, this correlation was very strong, but was expected to be positive (the stronger the CKC, the higher the COP velocity) instead of negative, which is not supported by the idea of stronger CKC reflecting impaired proprioceptive processing. Expected positive correlation between RQ and CKC parameters would have provided information about stronger CKC predicting attenuated use of proprioception in postural balance, as RQ and CKC are both supposed to reflect proprioception. It is possible that balancing on two feet was not challenging enough to express difference in postural balance between EO and EC conditions. Furthermore, lack of association between RQ and CKC suggests that mechanisms which alter postural sway between EO and EC standing could be different from mechanisms that alter the strength of CKC. Changes in postural sway could have been because of increased ventilation or local muscle fatigue without effect of proprioception. Based on these results and by taking into account the small sample size, strong conclusion about association between CKC and balance or evidence about CKC predicting effect of exercise on balance control cannot be made.

9.4 Study limitations

Quality of CKC data is discussed in detail, as the contaminated CKC data led to exclusion of several subjects and extremely small sample size of the study. Special caution must be followed

when making any assumptions concerning CKC results. Some general limitations of this study have been discussed in previous sections and are concluded in final paragraph of this section.

9.4.1 CKC data quality and exclusions

Acceleration stability. Dorsiflexion movement regularity was successful in all conditions and time points. Coefficient of variation for the peak value of acceleration signal during each CKC measurement separately was only 1.69 ± 0.74 % - 2.21 ± 0.87 %. Nor was there difference between conditions or time points.

CKC data exclusions. Corticokinematic coherence values were analysed for four subjects at F0 and eight subjects at F1. One subject was excluded from all coherence analyses, as the dominant leg was left, while the dominant leg of the other nine subjects was right. Challenges in averaging across group when region of interest (ROI) of one subject is on the opposite hemisphere was removed by ruling out this one subject. It is known, that CKC with dominant leg may differ from CKC with non-dominant leg at F1, (Piitulainen et al. 2018b), but because the knowledge about the mechanism of how leg dominance is affecting to the strength of CKC is minimal, it was decided to exclude the deviant subject and to have more homogenous group overall.

From analyses of F0, five additional subjects were excluded because of possible contamination of the signal, resulting four subjects in F0 analyses. As it can be seen in Figure 16, strong coherent between MEG and acceleration signals (marked as yellow) was visible in several additional regions than expected leg area of SM1. All cases, where it was possible that MEG signals from non-brain sources would have contaminated signal in the SM1, was excluded. Analyses was conducted for the cases in which possible artefacts were clearly on the distinct area from ROI. Similar exclusion criteria were used for F1, where one additional subject was excluded, resulting eight subjects in F1 analyses. As CKC measures coherence of two ongoing signals, it is very sensitive for frequent inferences in signal, which can be caused by for even very small magnetism. Possible sources for artefacts can be found in subjects, as even small

magnetism in e.g. their skin or hair products would cause coherent non-brain source MEG signal with movement rhythmicity. The limb actuator can also contain magnetic elements, which coherence analyses pick up from MEG signal. Further investigations revealed some magnetism in artificial muscles of the ankle actuator in current study. Furthermore, especially with larger limb movements as ankle joint (compared to finger movement), any additional movement will affect to data quality and easily cause artifacts in signal. To conclude, unwanted movement and small magnetism in ankle actuator and/or subjects most likely caused contamination of the CKC data which led to several subject exclusions. The remining data contained some artifacts which resulted in coherent signals, but it was located apart from SM1, mostly on the outer edges of the head (Fig. 16).

In our study, data was violated especially at F0. 6 out of 10 subjects had to be removed from analyses. Possible reason for more contaminated data at F0 than at F1 is that observed coherence was covered by coherent signals from other than acceleration and brain sources, while at F1, observed coherence was strengthened in relation to artefact signals. The movement regularity, or in other words the stability of frequency strengthens the coherence, and at F1, frequency is twofold, and thus affects to coherence level twice as much as at F0. Previous studies of CKC in passive movement has also shown strengthened CKC at F1 compared to F0 (Piitulainen et al. 2013b; Bourguignon et al. 2015).

9.4.2 General limitations

Small sample size. Sample size of this study (n = 10) was somewhat small and set limitations for statistical analyses and averaging of findings. With small sample size, varying exercise load between subjects is highlighted and makes it difficult to draw reliable conclusions about exercise effect, as the total load of exercise and physiological changes caused by running, may alter the effect it has on CKC and postural balance. With CKC data, where only four subjects at F0 and eight subjects at F1 were selected for further analyses, special caution must be taken when making any conclusions. As Piitulainen et al (2018a) stated, CKC as a measure of cortical

proprioceptive processing seems to be promising in group level, but not necessary with single individuals, which can be problematic in studies with very few subjects. Because correlation analyses were conducted with CKC data, sample size was only four at F0 and eight at F1.

Time periods between tests. Long time frame between the end of the running and physical performance test may have caused recovery of especially central fatigue before test onset. Lack of warmup before post reading tests had negative effect on physical performance tests (Bishop 2003). Similarly, time between end of the running and last balance test was long enough for full recovery, while time between end of the running and post running balance test was so short, that increased ventilation has probably override possible other effects. With CKC, exercise effect has not been studied before, meaning that time for full recovery is not known and possible changes in CKC may have been recovered before post running CKC measurements.

Test protocol. As described in earlier sections, some tests patterns failed to show expected fatiguing effect of exercise. Because of typical endurance runners power characteristics and muscle fiber type, as well as lack of experience in straight-legged jumps, knee extensors MVC and Hop failed to show fatigue in lower limb force production. Besides physical performance tests, straight indicators of changes in peripheral, spinal and cortical levels, for example amplitude and latency of movement evoked fields and measures of cortical excitability, connectivity in sensorimotor related areas and shifting in activation areas would have provided more detailed information.

9.5 Conclusion

As a conclusion, these results suggest that 90 minutes moderate intensity aerobic running exercise has no effect on corticokinematic coherence at F0 or at F1. However, if the 90 min treadmill run at velocity of first lactate threshold modulates CKC strength, the effect is recovered within 26 minutes. Moreover, contrary to hypothesis, CKC showed tendency to

decrease more than increase. In line with hypothesis, running exercise disturbed postural balance when standing on two feet eyes closed and eyes open. However, running did not have statistically significant effect on Romberg quotient, which represents use of proprioception in postural balance. Only anteroposterior sway during eyes closed standing correlated with the strength of CKC, but further evidence about association between the strength of CKC and postural balance, or connection between the effect of exercise on the strength of CKC and postural balance, or evidence about CKC predicting change in postural balance due to running exercise was not found.

Because of extremely small sample size of the study (n = 4 at F0 and n = 8 at F1), these results must be considered only preliminary. Long intervals between individual measurements must be noted when making assumptions about possible effects of running exercise. Because the large amount of contaminated CKC data, caution must be taken when making any conclusions about effect of running on CKC. However, as the nature of corticokinematic coherence is still poorly understood, this study provided at least directional new information about how CKC is acting after acute endurance exercise.

Future studies should continue clarifying neural processes behind coherent signals between limb kinematics and SM1 activity and to reveal which neural activities are responsible of the strength of CKC. As the results about correlation between balance and CKC were somewhat inconsistent with previous findings, connection between CKC and balance, especially quotient of eyes closed and eyes open should be studied more. Although this study suggests that single bout of aerobic running exercise has no effect on corticokinematic coherence, effect of acute exercise should be studied with larger sample size, with higher exercise intensity and with a smaller time window after the exercise as well as with more sensory system-loading and more sensorimotor integration demanding exercises. Furthermore, long term effect of aerobic exercise, as well as long term effect of skill training that requires sensorimotor integration should be studied.

10 REFERENCES

Adamo, D. E., Martin, B. J., & Brown, S. H. 2007. Age-related differences in upper limb proprioceptive acuity. Perceptual and motor skills, 104(3_suppl), 1297–1309.

Ahtiainen, J. & Häkkinen, K. 2004. Hermo-lihasjärjestelmän toiminnan mittaaminen. In Keskinen, K., Häkkinen, K., & Kallinen, M. (eds.). Kuntotestauksen käsikirja. Helsinki: Liikuntatieteellinen Seura ry, 125–141.

Allen, D. G., Lannergren, J., & Westerblad, H. 1995. Muscle cell function during prolonged activity: cellular mechanisms of fatigue. Experimental Physiology: Translation and Integration, 80(4), 497–527.

Allen, T. J. & Proske, U. 2006. Effect of muscle fatigue on the sense of limb position and movement. Experimental Brain Research, 170(1), 30–38.

Anthony J. & Kellogg, D. 2005. Homunculus: Somatosensory and Somatomotor Cortex. Referred 8.10.2020. https://www.ebmconsult.com/articles/homunculus-sensory-motor-cortex.

Avela, J. & Komi, P. V. 1998. Reduced stretch reflex sensitivity and muscle stiffness after long-lasting stretch-shortening cycle exercise in humans. European journal of applied physiology and occupational physiology, 78(5), 403–410.

Avela, J., Kyrolainen, H., & Komi, P. V. 1999. Altered reflex sensitivity after repeated and prolonged passive muscle stretching. Journal of Applied Physiology, 86(4), 1283–1291.

Baillet, S. 2017. Magnetoencephalography for brain electrophysiology and imaging. Nature neuroscience, 20(3), 327–339.

Baker, S. N. 2007. Oscillatory interactions between sensorimotor cortex and the periphery. Current opinion in neurobiology, 17(6), 649–655.

Bardouille, T., Bailey, L., & Group, C. 2019. Evidence for age-related changes in sensorimotor neuromagnetic responses during cued button pressing in a large open-access dataset. NeuroImage, 193, 25–34.

Benwell, N. M., Byrnes, M. L., Mastaglia, F. L., & Thickbroom, G. W. 2005. Primary sensorimotor cortex activation with task-performance after fatiguing hand exercise. Experimental brain research, 167(2), 160-164.

Bishop, D. 2003. Warm up II. Sports medicine, 33(7), 483–498.

Bizzi, E., Accornero, N., Chapple, W., & Hogan, N. 1984. Posture control and trajectory formation during arm movement. Journal of Neuroscience, 4(11), 2738–2744.

Blain, G. M., Mangum, T. S., Sidhu, S. K., Weavil, J. C., Hureau, T. J., Jessop, J. E., & Amann, M. 2016. Group III/IV muscle afferents limit the intramuscular metabolic perturbation during whole body exercise in humans. The Journal of physiology, 594(18), 5303–5315.

Borg, G. 1998. Borg's perceived exertion and pain scales. Human kinetics.

Bortel, R. & Sovka, P. 2007. Approximation of statistical distribution of magnitude squared coherence estimated with segment overlapping. Signal Processing, 87(5), 1100–1117.

Bosco, C., Luhtanen, P., & Komi, P. V. 1983. A simple method for measurement of mechanical power in jumping. European journal of applied physiology and occupational physiology, 50(2), 273–282.

Bouisset, S. & Duchêne, J. L. 1994. Is body balance more perturbed by respiration in seating than in standing posture? Neuroreport, 5(8), 957–960.

Bourguignon, M. De Tiège, X. de Beeck, M. O. Pirotte, B. Van Bogaert, P. Goldman, S., & Jousmäki, V. 2011. Functional motor-cortex mapping using corticokinematic coherence. Neuroimage, 55(4), 1475–1479.

Bourguignon, M., De Tiège, X., de Beeck, M. O., Van Bogaert, P., Goldman, S. Jousmäki, V., & Hari, R. 2013(a). Primary motor cortex and cerebellum are coupled with the kinematics of observed hand movements. Neuroimage, 66, 500–507.

Bourguignon, M., Jousmäki, V., de Beeck, M. O., Van Bogaert, P., Goldman, S., & De Tiège, X. 2012. Neuronal network coherent with hand kinematics during fast repetitive hand movements. Neuroimage, 59(2), 1684–1691.

Bourguignon, M., Jousmäki, V., Dalal, S. S., Jerbi, K., & De Tiège, X. 2019. Coupling between human brain activity and body movements: Insights from non-invasive electromagnetic recordings. Neuroimage, 203, 116177.

Bourguignon, M., Jousmäki, V., Marty, B., Wens, V., De Beeck, M., O. Van Bogaert, P., ... & Bruneau, M. 2013(b). Comprehensive functional mapping scheme for non-invasive primary sensorimotor cortex mapping. Brain topography, 26(3), 511–523

Bourguignon, M., Piitulainen, H., Smeds, E., Zhou, G., Jousmäki, V., & Hari, R. 2017. MEG insight into the spectral dynamics underlying steady isometric muscle contraction. Journal of Neuroscience, 37(43), 10421–10437.

Bourguignon, M., Piitulainen, H., De Tiège, X., Jousmäki, V., & Hari, R. 2015. Corticokinematic coherence mainly reflects movement-induced proprioceptive feedback. Neuroimage, 106, 382–390.

Brown, K. E., Neva, J. L., Mang, C. S., Chau, B., Chiu, L. K., Francisco, B. A., ... & Boyd, L. A. 2020. The influence of an acute bout of moderateintensity cycling exercise on sensorimotor integration. European Journal of Neuroscience.

Bulut, S., Özmerdivenli, R., & Bayer, H. 2003. Effects of exercise on somatosensory-evoked potentials. International journal of neuroscience, 113(3), 315–322.

Carroll, T. J., Taylor, J. L., & Gandevia, S. C. 2017. Recovery of central and peripheral neuromuscular fatigue after exercise. Journal of Applied Physiology, 122(5), 1068–1076.

Capaday, C. & Cooke, J. D. 1981. The effects of muscle vibration on the attainment of intended final position during voluntary human arm movements. Experimental Brain Research, 42(2), 228–230.

Chambers, D., Huang, C., & Matthews, G. 2019. Basic physiology for anaesthetists. Cambridge University Press.

Chang, Y. K., Chi, L., Etnier, J. L., Wang, C. C., Chu, C. H., & Zhou, C. 2014. Effect of acute aerobic exercise on cognitive performance: Role of cardiovascular fitness. Psychology of Sport and Exercise, 15(5), 464–470.

Chang, Y. K., Labban, J. D., Gapin, J. I., & Etnier, J. L. 2012. The effects of acute exercise on cognitive performance: a meta-analysis. Brain research, 1453, 87–101.

Cheyne, D., Endo, H., Takeda, T., & Weinberg, H. 1997. Sensory feedback contributes to early movement-evoked fields during voluntary finger movements in humans. Brain research, 771(2), 196–202.

Ciccarelli, O., Toosy, A. T., Marsden, J. F., Wheeler-Kingshott, C. M., Sahyoun, C., Matthews, P. M., ... & Thompson, A. J. 2005. Identifying brain regions for integrative sensorimotor processing with ankle movements. Experimental brain research, 166(1), 31–42.

Cohen, D. 1968. Magnetoencephalography: evidence of magnetic fields produced by alpha-rhythm currents. Science, 1613843, 784–786.

Conway, B. A., Halliday, D. M. Farmer, S. F. Shahani, U., Maas, P., Weir, A. I., & Rosenberg, J. R. 1995. Synchronization between motor cortex and spinal motoneuronal pool during the performance of a maintained motor task in man. The Journal of physiology, 489(3), 917–924.

Corbeil, P., Blouin, J. S., Bégin, F., Nougier, V., & Teasdale, N. 2003. Perturbation of the postural control system induced by muscular fatigue. Gait & posture, 18(2), 92–100.

Da Silva, F. L. 2010. Electrophysiological basis of MEG signals. In Hansen, P., Kringelbach, M., & Salmelin, R. (eds.). MEG: an introduction to methods. New York: Oxford university press, 1–23.

Del Percio, C., Brancucci, A., Bergami, F., Marzano, N., Fiore, A., Di Ciolo, E., & Gallamini, M. 2007. Cortical alpha rhythms are correlated with body sway during quiet open-eyes standing in athletes: a high-resolution EEG study. Neuroimage, 36(3), 822–829.

Del Percio, C., Babiloni, C., Marzano, N., Iacoboni, M., Infarinato, F., Vecchio, F., & Gallamini, M. 2009. “Neural efficiency” of athletes’ brain for upright standing: A high-resolution EEG study. Brain research bulletin, 79(3–4), 193–200.

Eklund, G. 1972. Position sense and state of contraction; the effects of vibration. Journal of Neurology, Neurosurgery & Psychiatry, 35(5), 606–611.

Fitzpatrick, R. & McCloskey, D. I. 1994. Proprioceptive, visual and vestibular thresholds for the perception of sway during standing in humans. The Journal of physiology, 478(1), 173–186.

Fitzpatrick, D. & Mooney, R. D. Sensation and Sensory processing. 2012. In Purves, D. Augustine, G. J. Fitzpatrick, D. Hall, W. C. LaMantia, A-S., & White, L. E. (eds.). Neuroscience. Fifth edition. Sunderland: Sinauer Associates, 189–350.

Fitzpatrick, D. & Mooney, R. D. The Somatosensory System: Touch and Proprioception. 2019. In Purves, D., Augustine, G. J., Fitzpatrick, D., Hall, W. C., LaMantia, A., Mooney, R. D., White, L. E. (eds.). Neuroscience. Sixth edition. New York: Sinauer Associates, an imprint of Oxford University Press, 181–200.

Fitzpatrick, R. Rogers, D. K., & McCloskey, D. I. 1994. Stable human standing with lower-limb muscle afferents providing the only sensory input. The Journal of physiology, 480(2), 395–403.

Flanders, M. & Soechting, J. F. 1990. Parcellation of sensorimotor transformations for arm movements. Journal of Neuroscience, 10(7), 2420–2427.

Flodin, P., Jonasson, L. S., Riklund, K., Nyberg, L., & Boraxbekk, C. J. 2017. Does aerobic exercise influence intrinsic brain activity? An aerobic exercise intervention among healthy old adults. Frontiers in aging neuroscience, 9, 267.

Foster, C., Florhaug, J. A., Franklin, J., Gottschall, L., Hrovatin, L. A., Parker, S., ... & Dodge, C. 2001. A new approach to monitoring exercise training. The Journal of Strength & Conditioning Research, 15(1), 109–115.

Fox, Z. G., Mihalik, J. P., Blackburn, J. T., Battaglini, C. L., & Guskiewicz, K. M. 2008. Return of postural control to baseline after anaerobic and aerobic exercise protocols. Journal of athletic training, 43(5), 456–463.)

Gabernet, L., Jadhav, S. P., Feldman, D. E., Carandini, M., & Scanziani, M. 2005. Somatosensory integration controlled by dynamic thalamocortical feed-forward inhibition. Neuron, 48(2), 315–327.

Gandevia, S. C. 2001. Spinal and supraspinal factors in human muscle fatigue. Physiological reviews, 81(4), 1725–1789.

Gandevia, S. C., Allen, G. M., Butler, J. E., & Taylor, J. L. 1996. Supraspinal factors in human muscle fatigue: Evidence for suboptimal output from the motor cortex. Journal of Physiology (London), 490(2), 529–536.

Gandevia, S. C., & Burke, D. 1992. Does the nervous system depend on kinesthetic information to control natural limb movements? Behavioral and Brain Sciences, 15, 614–614.

Gandevia, S.C., Enoka, R. M. McComas, A. J., Stuart, D. G., & Thomas, C. K. 1994. Fatigue: Neural and Muscular mechanisms. Springer Science & Business Media. New York.

Gandevia, S.C., Refshauge, K.M., Collins, D.F. 2002. Proprioception: peripheral inputs and perceptual interactions. Adv. Exp. Med. Biol. 508, 61–68.

Georgopoulos, A. P., Kalaska, J. F., Caminiti, R., & Massey, J. T. 1982. On the relations between the direction of two-dimensional arm movements and cell discharge in primate motor cortex. Journal of Neuroscience, 2(11), 1527–1537.

Goble, D. J., Coxon, J. P., Van Impe, A., Geurts, M., Doumas, M., Wenderoth, N., & Swinnen, S. P. 2011. Brain activity during ankle proprioceptive stimulation predicts balance performance in young and older adults. Journal of Neuroscience, 31(45), 16344–16352.

Goble, D. J., Coxon, J. P., Van Impe, A., Geurts, M., Van Hecke, W., Sunaert, S., & Swinnen, S. P. 2012. The neural basis of central proprioceptive processing in older versus younger adults: an important sensory role for right putamen. Human brain mapping, 33(4), 895–908.

Goble, D. J., Coxon, J. P., Wenderoth, N., Van Impe, A., & Swinnen, S. P. 2009. Proprioceptive sensibility in the elderly: degeneration, functional consequences and plastic-adaptive processes. Neuroscience & Biobehavioral Reviews, 33(3), 271–278.

Goldring, S. & Ratcheson, R. 1972. Human motor cortex: sensory input data from single neuron recordings. Science, 1754029, 1493–1495.

Goodwin, G. M., McCloskey, D. I., & Matthews, P. B. 1972. The contribution of muscle afferents to kinesthesia shown by vibration induced illusions of movement and by the effects of paralysing joint afferents. Brain, 95, 705–48.

Gribble, P. A. & Hertel, J. 2004. Effect of lower-extremity muscle fatigue on postural control. Archives of physical medicine and rehabilitation, 85(4), 589–592.

Guidetti, L., Franciosi, E., Gallotta, M. C., Emerenziani, G. P., & Baldari, C. 2011. Postural control after a prolonged treadmill run at individual ventilatory and anaerobic threshold. Journal of sports science & medicine, 10(3), 515.

Hagbarth, K.-E. & Macefield, V. 1994. The fusimotor system: Its role in fatigue. In Gandevia, S. C. Enoka, M. R. McComas, A. J. Stuart, D. G. & Thomas, C. K. Fatigue: neural and muscular mechanisms (Vol. 384). Springer Science & Business Media. New York. 259 – 270.

Halliday, D. M., Rosenberg, J. R., Amjad, A. M., Breeze, P., Conway, B. A., & Farmer, S. F. 1995. A framework for the analysis of mixed time series/point process data-theory and application to the study of physiological tremor, single motor unit discharges and electromyograms. Progress in biophysics and molecular biology, 64(2), 237.

Hogervorst, E., Riedel, W., Jeukendrup, A., & Jolles, J. 1996. Cognitive performance after strenuous physical exercise. Perceptual and motor skills, 83(2), 479–488.

Horak, F. B. 2006. Postural orientation and equilibrium: what do we need to know about neural control of balance to prevent falls? Age and ageing, 35(suppl_2), ii7–ii11.

Horita, T., Komi, P. V., Nicol, C., & Kyröläinen, H. 1996. Stretch shortening cycle fatigue: interactions among joint stiness, reflex, and muscle mechanical performance in the drop jump. European journal of applied physiology and occupational physiology, 73(5), 393–403.

Hoshiyama, M., Kakigi, R., Berg, P., Koyama, S., Kitamura, Y., Shimojo, M., & Nakamura, A. 1997. Identification of motor and sensory brain activities during unilateral finger movement: spatiotemporal source analysis of movement-associated magnetic fields. Experimental brain research, 115(1), 6–14.

Hämäläinen, M., Hari, R., Ilmoniemi, R. J., Knuutila, J., & Lounasmaa, O. V. 1993. Magnetoencephalography—theory, instrumentation, and applications to noninvasive studies of the working human brain. Reviews of modern Physics, 65(2), 413.

James, T. W., Kim, S., & Fisher, J. S. 2007. The neural basis of haptic object processing. Canadian Journal of Experimental Psychology/Revue canadienne de psychologie expérimentale, 61(3), 219.

Jerbi, K., Lachaux, J. P., Karim, N., Pantazis, D., Leahy, R. M., Garnero, L., & Baillet, S. 2007. Coherent neural representation of hand speed in humans revealed by MEG imaging. Proceedings of the National Academy of Sciences, 104(18), 7676–7681.

Johnston 3rd, R. B., Howard, M. E., Cawley, P. W., & Losse, G. M. 1998. Effect of lower extremity muscular fatigue on motor control performance. Medicine and science in sports and exercise, 30(12), 1703–1707.

Jäncke, L., Shah, N. J., & Peters, M. 2000. Cortical activations in primary and secondary motor areas for complex bimanual movements in professional pianists. Cognitive Brain Research, 10(1–2), 177–183.

Kakigi, R., & Forss, N. 2010, Electrophysiological basis of MEG signals. In Hansen, P., Kringelbach, M., & Salmelin, R. (eds.). MEG: an introduction to methods. New York: Oxford university press, 300–345

Kandel, E., Schwartz, J., & Jessell, T. 2000. Principles of Neural Science. (4th edition). McGraw-Hill Medical.

Kim, G. H., Suzuki, S., & Kanda, K. 2007. Age-related physiological and morphological changes of muscle spindles in rats. The Journal of physiology, 582(2), 525–538.

Komi, P. V. 2000. Stretch-shortening cycle: a powerful model to study normal and fatigued muscle. Journal of biomechanics, 33(10), 1197–1206.

Kramer, M.A. 2014. An Introduction to Field Analysis Techniques: The Power Spectrum and Coherence.

Krings, T., Töpper, R., Foltys, H., Erberich, S., Sparing, R., Willmes, K., & Thron, A. 2000. Cortical activation patterns during complex motor tasks in piano players and control subjects. A functional magnetic resonance imaging study. Neuroscience letters, 278(3), 189–193.

Kristeva, R., Cheyne, D., & Deecke, L. 1991. Neuromagnetic fields accompanying unilateral and bilateral voluntary movements: topography and analysis of cortical sources. Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section, 81(4), 284–298.

Lafond, D., Corriveau, H., Hébert, R., & Prince, F. 2004. Intrasession reliability of center of pressure measures of postural steadiness in healthy elderly people. Archives of physical medicine and rehabilitation, 85(6), 896–901.

Lambourne, K., & Tomporowski, P. 2010. The effect of exercise-induced arousal on cognitive task performance: a meta-regression analysis. Brain research, 1341, 12–24.

Lattier, G., Millet, G. Y., Martin, A., & Martin, V. 2004. Fatigue and recovery after high-intensity exercise part I: neuromuscular fatigue. International journal of sports medicine, 25(06), 450–456.

Lefaivre, S. C. & Almeida, Q. J. 2015. Can sensory attention focused exercise facilitate the utilization of proprioception for improved balance control in PD?. Gait & posture, 41(2), 630–633.

Lepers, R., Bigard, A. X., Diard, J. P., Gouteyron, J. F., & Guezennec, C. Y. 1997. Posture control after prolonged exercise. European journal of applied physiology and occupational physiology, 76(1), 55–61.

Liu, J., Sheng, Y., & Liu, H. 2019. Corticomuscular coherence and its applications: a review. Frontiers in human neuroscience, 13, 100.

Lord, S. R., Clark, R. D., & Webster, I. W. 1991. Postural stability and associated physiological factors in a population of aged persons. Journal of gerontology, 46(3), M69–M76.

Lord, S. R., Rogers, M. W., Howland, A., & Fitzpatrick, R. 1999. Lateral stability, sensorimotor function and falls in older people. Journal of the American Geriatrics Society, 47(9), 1077–1081.

Lucier, G. E., Rüegg, D. C., & Wiesendanger, M. 1975. Responses of neurones in motor cortex and in area 3A to controlled stretches of forelimb muscles in cebus monkeys. The Journal of physiology, 251(3), 833–853.

Lulic, T., El-Sayes, J., Fassett, H. J., & Nelson, A. J. 2017. Physical activity levels determine exercise-induced changes in brain excitability. PLoS One, 12(3), e0173672.

Ludyga, S., Gronwald, T., & Hottenrott, K. 2016. The athlete's brain: Cross-sectional evidence for neural efficiency during cycling exercise. Neural Plasticity, 2016.

Magnotta, V. A., Andreasen, N. C., Schultz, S. K., Harris, G., Cizadlo, T., Heckel, D. ... & Flaum, M. 1999. Quantitative in vivo measurement of gyrification in the human brain: changes associated with aging. Cerebral Cortex, 9(2), 151–160.

Mao, T., Kusefoglu, D., Hooks, B. M., Huber, D., Petreanu, L., & Svoboda, K. 2011. Long-range neuronal circuits underlying the interaction between sensory and motor cortex. Neuron, 72(1), 111–123.

Marzetti, L., Basti, A., Chella, F. D'Andrea, A., Syrjala, J., & Pizzella, V. 2019. Brain functional connectivity through phase coupling of neuronal oscillations: a perspective from magnetoencephalography. Frontiers in Neuroscience, 13, 964.

Marty, B., Bourguignon, M., de Beeck, M. O., Wens, V., Goldman, S., Van Bogaert, P., ... & De Tiège, X. 2015. Effect of movement rate on corticokinematic coherence. Neurophysiologie Clinique/Clinical Neurophysiology, 45(6), 469–474.

Marty, B., Naeije, G., Bourguignon, M., Wens, V., Jousmäki, V., Lynch, D. R., & De Tiège, X. 2019. Evidence for genetically determined degeneration of proprioceptive tracts in Friedreich ataxia. Neurology, 93(2), 116–124.

Metsämuuronen, J. 2011. Tutkimuksen tekemisen perusteet ihmistieteissä: E-kirja opiskelijalaitos. Helsinki: International Methelp, Booky.fi

Meyer, E., Ferguson, S. S. G., Zatorre, R. J., Alivisatos, B., Marrett, S., Evans, A. C., & Hakim, A. M. 1991. Attention modulates somatosensory cerebral blood flow response to vibrotactile stimulation as measured by positron emission tomography. Annals of neurology, 29(4), 440–443.

Millet, G. Y. & Lepers, R. 2004. Alterations of neuromuscular function after prolonged running, cycling and skiing exercises. Sports medicine, 34(2), 105–116.

Millet, G. Y., Martin, V., Lattier, G., & Ballay, Y. 2003. Mechanisms contributing to knee extensor strength loss after prolonged running exercise. Journal of Applied Physiology, 94(1), 193–198

Mima, T. & Hallett, M. 1999. Corticomuscular coherence: a review. Journal of clinical neurophysiology, 16(6), 501.

Miura, K., Ishibashi, Y., Tsuda, E., Okamura, Y., Otsuka, H., & Toh, S. 2004. The effect of local and general fatigue on knee proprioception. Arthroscopy: The Journal of Arthroscopic & Related Surgery, 20(4), 414–418.

Mo, C. & Sherman, S. M. 2019. A Sensorimotor Pathway via Higher-Order Thalamus. The Journal of neuroscience: the official journal of the Society for Neuroscience, 39(4), 692–704.

Mooney, R. A., Coxon, J. P., Cirillo, J., Glenny, H., Gant, N., & Byblow, W. D. 2016. Acute aerobic exercise modulates primary motor cortex inhibition. Experimental brain research, 234(12), 3669–3676.

Moran, D. W. & Schwartz, A. B. 1999. Motor cortical representation of speed and direction during reaching. Journal of neurophysiology, 82(5), 2676–2692.

Miyashita, E., Keller, A., & Asanuma, H. 1994. Input-output organization of the rat vibrissal motor cortex. Experimental brain research, 99(2), 223–232.

Nagahara, R., Naito, H., Miyashiro, K., Morin, J. B., & Zushi, K. 2014. Traditional and ankle-specific vertical jumps as strength-power indicators for maximal sprint acceleration. J Sports Med Phys Fitness, 54(6), 691–699.

Nakata, H., Oshiro, M., Namba, M., & Shibasaki, M. 2016. Effects of aerobic exercise under different thermal conditions on human somatosensory processing. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology, 311(4), R629–R636.

Nardone, A., Tarantola, J., Giordano, A., & Schieppati, M. 1997. Fatigue effects on body balance. Electroencephalography and Clinical Neurophysiology/Electromyography and Motor Control, 105(4), 309–320.

Nawata, K., Teshima, R., Morio, Y., Hagino, H., Enokida, M., & Yamamoto, K. 1999. Anterior-posterior knee laxity increased by exercise: quantitative evaluation of physiologic changes. Acta Orthopaedica Scandinavica, 70(3), 261–264.

Nicol, C., Komi, P. V., & Marconnet, P. 1991. Fatigue effects of marathon running on neuromuscular performance: II. Changes in force, integrated electromyographic activity and endurance capacity. Scandinavian Journal of Medicine & Science in Sports, 1(1), 18–24.

Nummela, A. 2004. Aerobisen kestävyyden suorat mittausmenetelmät. In Keskinen, K. Häkkinen, K. & Kallinen, M. (eds.). Kuntotestauksen käsikirja. Helsinki: Liikuntatieteellinen Seura ry, 64–78.

Oostenveld, R., Fries, P., Maris, E., & Schoffelen, J. M. 2011. FieldTrip: open source software for advanced analysis of MEG, EEG, and invasive electrophysiological data. Computational intelligence and neuroscience, 2011.

Paillard, T. 2012. Effects of general and local fatigue on postural control: a review. Neuroscience & Biobehavioral Reviews, 36(1), 162–176.

Paillard J, Brouchon M. Active and passive movements in the calibration of position sense. In Freedman S. (eds.). The neuropsychology of spatially oriented behavior. Homewood, IL: Dorsey Press; 1968. p 37–55.

Parkkonen, L. 2010. Instrumentation and Data Preprocessing. In Hansen, P., Kringelbach, M., & Salmelin, R. (eds.). MEG: an introduction to methods. New York: Oxford university press, 24–64.

Parkkonen, L. & Salmelin, R. 2010. Measurements. In Hansen, P., Kringelbach, M., & Salmelin, R. (eds.). MEG: an introduction to methods. New York: Oxford university press, 65–82.

Pedersen, J., Ljubisavljevic, M., Bergenheim, M., & Johansson, H. 1998. Alterations in information transmission in ensembles of primary muscle spindle afferents after muscle fatigue in heteronymous muscle. Neuroscience, 84(3), 953–959

Penfield, W., & Boldrey, E. 1937. Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation. Brain, 60(4), 389–443.

Piitulainen, H., Bourguignon, M., De Tiège, X., Hari, R., & Jousmäki, V. 2013(a). Coherence between magnetoencephalography and hand-action-related acceleration, force, pressure, and electromyogram. Neuroimage, 72, 83–90.

Piitulainen, H., Bourguignon, M., De Tiege, X., Hari, R., & Jousmäki, V. 2013(b). Corticokinematic coherence during active and passive finger movements. Neuroscience, 238, 361–370.

Piitulainen, H., Bourguignon, M., Hari, R., & Jousmäki, V. 2015. MEG-compatible pneumatic stimulator to elicit passive finger and toe movements. Neuroimage, 112, 310–317.

Piitulainen, H., Illman, M. J., Jousmäki, V., & Bourguignon, M. 2020. Feasibility and reproducibility of electroencephalography-based corticokinematic coherence. Journal of Neurophysiology.

Piitulainen, H., Illman, M., Laaksonen, K., Jousmäki, V., & Forss, N. 2018(a). Reproducibility of corticokinematic coherence. Neuroimage, 179, 596–603.

Piitulainen, H., Seipäjärvi, S., Avela, J., Parviainen, T., & Walker, S. 2018(b). Cortical proprioceptive processing is altered by aging. Frontiers in aging neuroscience, 10, 147.

Pitkänen, M., Yazawa, S., Airaksinen, K., Lioumis, P., Nurminen, J., Pekkonen, E., & Mäkelä, J. P. 2019. Localization of Sensorimotor Cortex Using Navigated Transcranial Magnetic Stimulation and Magnetoencephalography. Brain topography, 32(5), 873–881.

Poe, B. H., Linville, C., & Brunso-Bechtold, J. 2001. Age-related decline of presumptive inhibitory synapses in the sensorimotor cortex as revealed by the physical disector. Journal of Comparative Neurology, 439(1), 65–72.

Poole, J. L. 1992. Age related changes in sensory system dynamics related to balance. Physical & Occupational Therapy in Geriatrics, 10(2), 55–66.

Proske, U., & Gandevia, S. C. 2012. The proprioceptive senses: their roles in signaling body shape, body position and movement, and muscle force. Physiological reviews, 92(4), 1651–1697.

Racinais, S., Girard, O., Micallef, J. P., & Perrey, S. 2007. Failed excitability of spinal motoneurons induced by prolonged running exercise. Journal of neurophysiology, 97(1), 596–603.

Raichlen, D. A., Bharadwaj, P. K., Fitzhugh, M. C., Haws, K. A., Torre, G. A., Trouard, T. P., & Alexander, G. E. 2016. Differences in resting state functional connectivity between young adult endurance athletes and healthy controls. Frontiers in human neuroscience, 10, 610.

Rajab, A. S., Crane, D. E., Middleton, L. E., Robertson, A. D., Hampson, M., & MacIntosh, B. J. 2014. A single session of exercise increases connectivity in sensorimotor-related brain networks: a resting-state fMRI study in young healthy adults. Frontiers in human neuroscience, 8, 625.

Rocco-Donovan, M., Ramos, R. L., Giraldo, S., & Brumberg, J. C. 2011. Characteristics of synaptic connections between rodent primary somatosensory and motor cortices. Somatosensory & motor research, 28(3–4), 63–72.

Ross, E. Z. Goodall, S., Stevens, A., & Harris, I. 2010. Time course of neuromuscular changes during running in well-trained subjects. Medicine and Science in Sports and Exercise, 42(6), 1184–1190.

Saldanha, A., Nordlund Ekblom, M. M., & Thorstensson, A. 2008. Central fatigue affects plantar flexor strength after prolonged running. Scandinavian journal of medicine & science in sports, 18(3), 383–388.

Saltin, B., Henriksson, J., Nygaard, E., Andersen, P., & Jansson, E. 1977. Fiber types and metabolic potentials of skeletal muscles in sedentary man and endurance runners. Annals of the New York Academy of Sciences, 301, 3–29.

Sanes, J. N., Mauritz, K. H., Dalakas, M. C., & Evarts, E. V. 1985. Motor control in humans with large-fiber sensory neuropathy. Human neurobiology, 4(2), 101–114.

Saunders, P. U., Telford, R. D., Pyne, D. B., Peltola, E. M., Cunningham, R. B., Gore, C. J., & Hawley, J. A. 2006. Short-term plyometric training improves running economy in highly trained middle and long distance runners. Journal of Strength and Conditioning Research, 20(4), 947.

Schmitt, A., Upadhyay, N., Martin, J. A., Rojas, S., Strüder, H. K., & Boecker, H. 2019. Modulation of distinct intrinsic resting state brain networks by acute exercise bouts of differing intensity. Brain Plasticity, 5(1), 39–55.

Seiler, S. & Tønnessen, E. 2009. Intervals, thresholds, and long slow distance: the role of intensity and duration in endurance training. Sportscience, 13.

Shields, R. K., Madhavan, S., Cole, K. R., Brostad, J. D., DeMeulenaere, J. L., Eggers, C. D., & Otten, P. H. 2005. Proprioceptive coordination of movement sequences in humans. Clinical neurophysiology, 116(1), 87–92.

Shumway-Cook, A. & Woollacott, M. H. 2010. Motor control. Translating research into clinical Practice. Fourth edition. Baltimore: Lippincott Williams&Wilki.

Sidhu, S. K., Weavil, J. C., Mangum, T. S., Jessop, J. E., Richardson, R. S., Morgan, D. E., & Amann, M. (2017). Group III/IV locomotor muscle afferents alter motor cortical and corticospinal excitability and promote central fatigue during cycling exercise. Clinical Neurophysiology, 128(1), 44-55.

Singh, A. M., Duncan, R. E., Neva, J. L., & Staines, W. R. 2014. Aerobic exercise modulates intracortical inhibition and facilitation in a nonexercised upper limb muscle. BMC sports science, medicine and rehabilitation, 6(1), 23.

Singer, W. 1999. Neuronal synchrony: a versatile code for the definition of relations?. Neuron, 24(1), 49–65.

Smeds, E., Vanhatalo, S., Piitulainen, H., Bourguignon, M., Jousmäki, V., & Hari, R. 2017. Corticokinematic coherence as a new marker for somatosensory afference in newborns. Clinical Neurophysiology, 128(4), 647–655.

Smith, A. E., Goldsworthy, M. R., Garside, T., Wood, F. M., & Ridding, M. C. 2014. The influence of a single bout of aerobic exercise on short-interval intracortical excitability. Experimental brain research, 232(6), 1875–1882.

Soechting, J. F. 1982. Does position sense at the elbow reflect a sense of elbow joint angle or one of limb orientation? Brain Res. 248:392–95

Stark, E., Drori, R., Asher, I., Ben-Shaul, Y., & Abeles, M. 2007. Distinct movement parameters are represented by different neurons in the motor cortex. European Journal of Neuroscience, 26(4), 1055–1066.

Subasi, S. S., Gelecek, N., & Aksakoglu, G. 2008. Effects of different warm-up periods on knee proprioception and balance in healthy young individuals. Journal of Sport Rehabilitation, 17(2), 186–205.

Swash, M. & Fox, K. P. 1972. The effect of age on human skeletal muscle studies of the morphology and innervation of muscle spindles. Journal of the neurological sciences, 16(4), 417–432.

Taylor, J. L., Amann, M., Duchateau, J., Meeusen, R., & Rice, C. L. 2016. Neural contributions to muscle fatigue: from the brain to the muscle and back again. Medicine and science in sports and exercise, 48(11), 2294.

Taylor, J. L., Butler, J. E., & Gandevia, S. C. 2000. Changes in muscle afferents, motoneurons and motor drive during muscle fatigue. European journal of applied physiology, 83(2–3), 106–115.

Tanaka, H., Monahan, K. D., & Seals, D. R. 2001. Age-predicted maximal heart rate revisited. Journal of the american college of cardiology, 37(1), 153–156.

Taulu, S., Simola, J., & Kajola, M. 2005. Applications of the signal space separation method. IEEE transactions on signal processing, 53(9), 3359–3372.

Theyel, B. B., Llano, D. A., & Sherman, S. M. 2010. The corticothalamocortical circuit drives higher-order cortex in the mouse. Nature neuroscience, 13(1), 84–88.

Thomas, K., Goodall, S., Stone, M., Howatson, G., Gibson, A. S. C., & Ansley, L. 2015. Central and peripheral fatigue in male cyclists after 4-, 20-, and 40-km time trials. Medicine & Science in Sports & Exercise, 47(3), 537–546.

Tokimura, H., Di Lazzaro, V., Tokimura, Y., Oliviero, A., Profice, P., Insola, A., & Rothwell, J. C. 2000. Short latency inhibition of human hand motor cortex by somatosensory input from the hand. The Journal of Physiology, 523(2), 503–513.

Tomporowski, P. D. 2003. Effects of acute bouts of exercise on cognition. Acta psychologica, 112(3), 297–324.

Vannucci, L., Falotico, E., & Laschi, C. 2017. Proprioceptive feedback through a neuromorphic muscle spindle model. Frontiers in Neuroscience, 11, 341.

Vaugoyeau, M., Viel, S., Assaiante, C., Amblard, B., & Azulay, J. P. 2007. Impaired vertical postural control and proprioceptive integration deficits in Parkinson's disease. Neuroscience, 146(2), 852–863.

Vaugoyeau, M., Hakam, H., & Azulay, J. P. 2011. Proprioceptive impairment and postural orientation control in Parkinson's disease. Human movement science, 30(2), 405–414.

Vuillerme, N., Nougier, V., & Prieur, J. M. 2001. Can vision compensate for a lower limbs muscular fatigue for controlling posture in humans?.Neuroscience letters, 308(2), 103–106.

Warhol, M. J, Siegel, A. J, Evans, W. J., & Silverman, L. M. 1985. Skeletal muscle injury and repair in marathon runners after competition. The American journal of pathology, 118(2), 331.

Wardman, D. L., Gandevia, S. C., & Colebatch, J. G. 2014. Cerebral, subcortical, and cerebellar activation evoked by selective stimulation of muscle and cutaneous afferents: an f MRI study. Physiological Reports, 2(4), e00270.

Weiller, C., Jüptner, M., Fellows, S., Rijntjes, M., Leonhardt, G., Kiebel, S., & Thilmann, A. F. 1996. Brain representation of active and passive movements. Neuroimage, 4(2), 105–110.

Wiesmeier, I. K., Dalin, D., & Maurer, C. 2015. Elderly use proprioception rather than visual and vestibular cues for postural motor control. Frontiers in aging neuroscience, 7, 97.

Winter, D. A., Prince, F., Frank, J. S., Powell, C., & Zabjek, K. F. 1996. Unified theory regarding A/P and M/L balance in quiet stance. Journal of neurophysiology, 75(6), 2334–2343.

Womelsdorf, T., Schoffelen, J. M., Oostenveld, R., Singer, W., Desimone, R., Engel, A. K., & Fries, P. 2007. Modulation of neuronal interactions through neuronal synchronization. science, 3165831, 1609–1612.

Yaggie, J. A. & McGregor, S. J. 2002. Effects of isokinetic ankle fatigue on the maintenance of balance and postural limits. Archives of physical Medicine and Rehabilitation, 83(2), 224–228.

Yamazaki, Y., Sato, D., Yamashiro, K., Nakano, S., Onishi, H., & Maruyama, A. 2019. Acute low-intensity aerobic exercise modulates intracortical inhibitory and excitatory circuits in an exercised and a non-exercised muscle in the primary motor cortex. Frontiers in physiology, 10, 1361.

APPENDIX 1.1

SUOSTUMUS TIETEELLISEEN TUTKIMUKSEEN

Minua on pyydetty osallistumaan tutkimukseen "Palautumisen seuranta syke- ja suorituskykymittauksilla – yhteydet harjoituskuormitukseen ja koettuun kuormittuneisuuteen". Olen perehtynyt tutkimusta koskevaan tiedotteeseen (tietosuojailmoitus) ja saanut riittävästi tietoa tutkimuksesta ja sen toteuttamisesta. Tutkimuksen sisältö on kerrottu minulle myös suullisesti ja olen saanut riittävän vastauksen kaikkiin tutkimusta koskeviin kysymyksiini. Minulla on ollut riittävästi aikaa harkita tutkimukseen osallistumista. Ymmärrän, että tähän tutkimukseen osallistuminen on vapaaehtoista. En osallistu veri- ym. kokeita tai fyysistä rasitusta sisältäviin tutkimuksiin flunssaisena, kuumeisena, toipilaana tai muuten huonovointisena. Minulla on oikeus, milloin tahansa tutkimuksen aikana ja syytä ilmoittamatta keskeyttää tutkimukseen osallistuminen tai peruuttaa suostumukseni tutkimukseen. Tutkimuksen keskeyttämisestä tai suostumuksen peruuttamisesta ei aiheudu minulle kielteisiä seuraamuksia. Tutkimustuloksiani ja kerättyä aineistoa saa käyttää ja hyödyntää sellaisessa muodossa, jossa yksittäistä tutkittavaa ei voi tunnistaa.

	Kyllä	Ei
Olen tutustunut tiedotteessa tietosuojailmoituksessa kerrottuihin rekisteröidyn oikeusiin ja rajoituksiin		
Suostun yllämainitun projektin mittauksiin annettujen ohjeiden mukaisesti		
Annan luvan tulosteni käyttöön tutkimuksen raportoinnissa		
Suostun siihen, että tutkimuksessa käsitellään erityisiin henkilötietoryhmiin kuuluvia tietoja (terveyttä koskevat kysymykset)		
Annan luvan henkiötunnisteettomien tulosteni käyttöön tuotekehitystoiminnassa (harjoitusten syke- ja GPS-data, yösykemittaukset, suoran maksimaalisen hapenottokyvyn testin tulokset)		
Annan luvan mittausten yhteydessä otetun video/valokuvani käyttöön liikuntabiologian tieteenalaryhmän ei-kaupallisessa kirjallisessa ja suullisessa raportoinnissa. Videot/valokuvat esitetään niin, että niistä ei voi tunnistaa yksittäisiä henkilöitä. Videot/valokuvat ovat arkistoituna anonymisoituna liikuntabiologian tieteenalaryhmän salasanasuojatulla tietokoneella, ja ne hävitetään tutkimushankkeen päättymisen jälkeen 31.12.2022.		
Olen tutustunut suoritettaviin testeihin ja mittauksiin, ja olen ymmärtänyt mittausten tarkoituksen ja niihin liittyvät riski- ja hyötynäkökohdat.		

* Firstbeat Technologies hyödyntää suostumuksellanne tuotekehitystyössä mahdollisesti aineistoja, jotka pitävät sisällään harjoitusten syke- ja GPS-datan, yösykemittausten tulokset ja suoran maksimaalisen hapenottokyvyn testin tulokset. Tuotekehitystoiminta liittyy liikuntateknologisten tuotteiden kehitystyöhön.

Allekirjoituksellani vahvistan, että osallistun tutkimukseen vapaaehtoisesti ja hyväksyn tietojeni käytön tietosuojailmoituksessa kuvattuun tutkimukseen.

Päiväys

Tutkittavan allekirjoitus

Nimenselvennys

APPENDIX 1.2

Päiväys Tutkijan allekirjoitus

Nimenselvennys

SUOSTUMUS TIETEELLISEEN TUTKIMUKSEEN

Minua on pyydetty osallistumaan ”liikunnan akuutit aivovasteet” -lisätutkimukseen. Olen perehtynyt tutkimusta koskevaan tiedotteeseen (tietosuojailmoitus) ja saanut riittävästi tietoa tutkimuksesta ja sen toteuttamisesta. Tutkimuksen sisältö on kerrottu minulle myös suullisesti ja olen saanut riittävän vastauksen kaikkiin tutkimusta koskeviin kysymyksiini. Minulla on ollut riittävästi aikaa harkita tutkimukseen osallistumista. Ymmärrän, että tähän tutkimukseen osallistuminen on vapaaehtoista. En osallistu veri-ym. kokeita tai fyysistä rasitusta sisältäviin tutkimuksiin flunssaisena, kuumeisena, toipilaana tai muuten huonovointisena. Minulla on oikeus, milloin tahansa tutkimuksen aikana ja syytä ilmoittamatta keskeyttää tutkimukseen osallistuminen tai peruuttaa suostumukseni tutkimukseen. Tutkimuksen keskeyttämisestä tai suostumuksen peruuttamisesta ei aiheudu minulle kielteisiä seuraamuksia. Tutkimustuloksiani ja kerättyä aineistoa saa käyttää ja hyödyntää sellaisessa muodossa, jossa yksittäistä tutkittavaa ei voi tunnistaa.

	Kyllä	Ei
Olen tutustunut tiedotteessa tietosuojailmoituksessa kerrottuihin rekisteröidyn oikeusiin ja rajoituksiin		
Suostun yllämainitun projektin mittauksiin annettujen ohjeiden mukaisesti		
Annan luvan tulosteni käyttöön tutkimuksen raportoinnissa		
Suostun siihen, että tutkimuksessa käsitellään erityisiin henkilötietoryhmiin kuuluvia tietoja (terveyttä koskevat kysymykset)		
Annan luvan tietojeni käyttämiseen ”liikunnan akuutit aivovasteet” – ja ”lyhyen ja pitkän aikavälin palautuminen erilaisista kestävyyskuormituksista” – tutkimusten välillä tutkimuksen osalta relevanttien tietojen kohdalla		
Olen tutustunut suoritettaviin testeihin ja mittauksiin, ja olen ymmärtänyt mittausten tarkoituksen ja niihin liittyvät riski- ja hyötynäkökohdat.		

Allekirjoituksellani vahvistan, että osallistun tutkimukseen vapaaehtoisesti ja hyväksyn tietojeni käytön tietosuojailmoituksessa kuvattuun tutkimukseen.

Päiväys Tutkittavan allekirjoitus

Nimenselvennys

Päiväys Tutkijan allekirjoitus

Nimenselvennys

APPENDIX 2

ESITIETO- JA TERVEYSKYSELY

JYVÄSKYLÄN YLIOPISTO

Nimi:_____ Synt.aika:_____ Paino:_____kg Pituus:_____cm

Testauksen turvallisuuden kartoittamiseksi pyydämme sinua täyttämään oheisen terveyskyselyn. Tämä on vapaaehtoinen kysely, mutta ellemme tiedä testaamisen olevan turvallista, emme voi sitä tehdä.

Oireet viimeisen 6 kk aikana:	Kyllä	Ei	En osaa sanoa
1. Onko sinulla ollut rintakipuja?			
2. Onko sinulla ollut rasitukseen liittyvää hengenahdistusta?			
3. Onko sinulla ollut huimausoireita?			
4. Onko sinulla ollut rytmihäiriötuntemuksia?			
5. Onko sinulla ollut harjoittelua estäviä kipuja liikuntaelimissä? Missä?			
6. Oletko tuntenut ylikuormitus- tai stressioireita?			

Todetut sairaudet: Onko sinulla tai onko sinulla ollut jokin/joitakin seuraavista? (ympyröi)

01 sepelvaltimotauti	02 sydäninfarkti	03 kohonnut verenpaine	04 sydänläppävika
05 aivohalvaus	06 aivoverenkierron häiriö	07 sydämen rytmihäiriö	08 sydämentahdistin
09 sydänlihassairaus	10 syvä laskimotukos	11 muu verisuonisairaus	12 krooninen bronkiitti
13 keuhkolaajentuma	14 astma	15 muu keuhkosairaus	16 allergia
17 kilpirauhasen toimintahäiriö	18 diabetes	19 anemia	20 korkea veren kolesteroli
21 nivelreuma	22 nivelrikko, -kuluma	23 krooninen selkäsairaus	24 mahahaava
25 pallea-, nivus- tai napatyrä	26 ruokatorven tulehdus	27 kasvain tai syöpä	28 leikkaus äskettäin
29 mielenterveyden ongelma	30 tapaturma äskettäin	31 matala veren K tai Mg	32 kohonnut silmänpaine
33 näön tai kuulon heikkous	34 urheiluvamma äskettäin		

muita sairauksia tai oireita, mitä:_____

Lääkitys: Käytätkö jotain lääkitystä tai lääkeainetta säännöllisesti tai usein? 1 En 2 Kyllä, mitä:_____
_____

Jatkuu seuraavalla sivulla…

Tupakoitko 1 En 2 Kyllä

Onko Sinulla todettu synnynnäinen sydänvika? 1 Ei 2 Kyllä,

mikä:_____
_____

Onko lähisuvussasi todettu perinnöllisiä sydänsairauksia tai sydänperäisiä äkkikuolemia?
1 Ei 2 Kyllä

Kuumetta, flunssaista oloa tai muuten poikkeavaa väsymystä viimeisen viikon aikana:
1 Ei 2 Kyllä

APPENDIX 3

TAUSTATIETOLOMAKE MEG

1. Onko sinulla kehon sisällä metallia (esim. leikkauksen jälkeiset metallit, implantit, hammasraudat)	☐ ei	☐ kyllä	☐ ei tietoa
2. Oletko oikea-, vasen vai molempi-kätinen?	☐ oikea	☐ vasen	☐ molempi
3. Onko sinulla tai onko sinulla aiemmin ollut lukemisen tai kirjoittamisen vaikeutta?	☐ ei	☐ kyllä	☐ ei tietoa
Jos on, mikä? _____			
4. Onko sinulla asiantuntijan toteama tarkkaavuushäiriö (ADHD), epilepsia, neurologinen sairaus tai pysyviä pään vammojen aiheuttamia ongelmia?	☐ ei	☐ kyllä	☐ ei tietoa
Jos on, mikä? _____			
5. Käytätkö keskushermostoon vaikuttavia lääkkeitä?	☐ ei	☐ kyllä	☐ ei tietoa
Mitä lääkkeitä käytät? _____			

Olen vastannut kysymyksiin rehellisesti parhaan tietämykseni mukaan,

Päiväys

Tutkittavan allekirjoitus

Nimenselvennys

APPENDIX 4

Koetun kuormittuneisuuden asteikko

Arvo	Kuvaus
10	Maksimaalinen
9	
8	
7	Hyvin rasittava
6	
5	Rasittava
4	
3	Kohtalaisen rasittava
2	Kevyt
1	Hyvin kevyt
0	Lepo

(Rating of Perceived Exertion; Borg 1998)