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MOVEMENT BEHAVIORS AND COGNITIVE HEALTH  
FOR OFFICE WORKERS





# Movement Behaviors and Cognitive Health for Office Workers

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I dedicate this thesis to the  
ones I miss:  
Anders, Helge, Aage, and  
Ebbe



# Abstract

The lifetime trajectories of movement behavior and cognitive functioning depend on complex interactions between genetic and environmental factors. There is substantial evidence suggesting that physical activity benefits cognitive functions. However, how sedentary behavior and the composition of movement behaviors (i.e., sleep, physical activity, and sedentary behavior) influences cognitive functions remains to be elucidated.

Observational studies suggest that sedentary time is unfavorably related to cognitive functions in older adults, but the majority of evidence comes from self-reported estimates of movement behavior, which are rather weakly related to device-based measures. Furthermore, while evidence suggests that structured exercise can have protective effects on cognition in inactive older adults, much less is known about how midlife movement behavior is related to cognitive functions. Thus, knowledge of how midlife movement behavior relates to and possibly affects cognitive functions and its underlying mechanisms is much needed.

This thesis is part of a larger research project investigating how movement behaviors relate to and influence cognitive function, mental health, and neurophysiological mechanisms underpinning these. The project specifically targets healthy office workers and is co-produced with employers of office workers and health-promoting companies.

This thesis aimed to investigate how movement behaviors relate to and influence cognitive functions and neuroplasticity among office workers.

The first study investigated cross-sectional relationships between device-measured movement behavior and cognitive functions among 334 office workers. The results revealed no association between total time spent in moderate to vigorous physical activity or sedentary behavior and cognitive functions, suggesting that this association may not be as robust as previously suggested in older populations or as inferred from self-report.

The second study investigated the extent to which corticospinal excitability is influenced by different movement behaviors. Sixteen sedentary office workers participated in a cross-over randomized controlled trial. We contrasted 3 hours of prolonged sitting with 3 hours of interrupted sitting and 2.5 hours sitting followed by a 25-minute bout of exercise. Acute changes in corticospinal excitability and long-term potentiation-like neuroplasticity were investigated using transcranial magnetic stimulation and paired associative stimulation. Changes in corticospinal excitability over time did not differ between conditions, suggesting that in inactive middle-aged office workers, a physical activity

bout or frequently breaking up prolonged sitting does not induce immediate changes in corticospinal excitability or long-term potentiation-like neuroplasticity.

The third and fourth studies are based on a 6-month cluster-randomized intervention conducted in 263 healthy office workers. An ecological model for behavior change was used to design an intervention addressing the individual, environmental, and organizational levels to change movement behavior. The interventions were designed to reduce sedentary behavior or increase physical activity relative to a passive control group, with the ultimate aim of improving cognitive functions and mental health. The third study investigated how effective each intervention was at changing the 24-hour movement behavior, and the fourth study examined intervention effects on cognitive functions. The results showed that the interventions were ineffective in reducing sedentary behavior and increasing physical activity, respectively, with no detected beneficial effects on cardiorespiratory fitness or cognitive functions relative to the control group. Changes in cognition from baseline to follow-up were not associated with changes in the composition of movement behaviors or cardiorespiratory fitness, but some associations between changes in movement behaviors and cognition were moderated by sex, age, and cardiorespiratory fitness. Thus, the third and fourth studies of the thesis have highlighted the challenges involved in successfully achieving movement behavior change to address the possible effects on cognitive improvements in an ecological setting.

In summary, the results presented in this thesis did not provide support for an association between movement behaviors and cognitive functions in healthy physically active office workers, demonstrated no acute effect of a single session of physical activity or breaking up prolonged sitting on corticospinal excitability in sedentary office workers, and revealed no evidence for successful movement behavior change or benefits for cognition in an ecological cluster-randomized intervention in healthy physically active office workers. The findings suggest that among physically active office workers, sedentary behavior may not be as detrimental for cognition and neuroplasticity as previously suggested and shows that changing movement behavior in office workers at the workplace represents a challenging endeavor. Still, these findings do not exclude the possibility that changes in movement behaviors might benefit cognitive functions in physically inactive office workers at higher cardiovascular risk, with lower cardiorespiratory fitness and/or lower daily cognitive stimulation. Efforts into developing sustainable interventions for movement behavior change might be redesigned to better target individuals exposed to several risk factors for poor cognitive functions or unfavorable movement behaviors.

## Scientific papers

- I. **Emil Bojsen-Møller**, Carl-Johan Boraxbekk, Örjan Ekblom, Victoria Blom, Maria Ekblom – Relationships between physical activity, sedentary behaviour and cognitive functions in office workers [1].  
*International Journal of Environmental Research and Public Health*, 2019
- II. **Emil Bojsen-Møller**, Maria Ekblom, Olga Tarassova, David W. Dunstan, Örjan Ekblom – The effect of breaking up prolonged sitting on paired associative stimulation-induced plasticity [2].  
*Experimental Brain Research*, 2020
- III. Lisa-Marie Larisch\*, **Emil Bojsen-Møller\***, Carla F. J. Nooijen, Victoria Blom, Maria Ekblom, Örjan Ekblom, Daniel Arvidsson, Jonatan Fridolfsson, David M. Hallman, Svend Erik Mathiassen, Rui Wang, Lena V. Kallings – Effects of Two Randomized and Controlled Multi-Component Interventions Focusing on 24-Hour Movement Behavior among Office Workers: A Compositional Data Analysis [3].  
*International Journal of Environmental Research and Public Health*, 2021
- IV. **Emil Bojsen-Møller**, Emerald Heiland, Lena Kallings, Jonna Nilsson, Rui Wang, Carl-Johan Boraxbekk, & Maria Ekblom – Effects of two multicomponent behavior change interventions on cognitive functions.  
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## Abbreviations

APB	Abductor Pollicis Brevis
AURC	Area Under the Recruitment Curve
BCT	Behavior Change Technique
CSE	Corticospinal Excitability
EF	Executive Function
EM	Episodic Memory
LPA	Light Physical Activity
LTD	Long-Term Depression
LTP	Long-Term Potentiation
M1	Primary Motor Cortex
MET	Metabolic Equivalent
MRI	Magnetic Resonance Imaging
MPA	Moderate Physical Activity
MVPA	Moderate to Vigorous Physical Activity
PA	Physical Activity
PAS	Paired Associative Stimulation
PS	Processing Speed
RC	Recruitment Curve
RMT	Resting Motor Threshold
SB	Sedentary Behavior
TMS	Transcranial Magnetic Stimulation
TMT-A	Trail-Making Task A
TMT-B	Trail-Making Task B
VPA	Vigorous Physical Activity
WM	Working Memory



# 1. Introduction

Many jobs in high-income countries involve limited physical activity [4] but high cognitive functioning [5]. Working-age adults spend most of their time awake at work, and 81% of Swedish employees work in the tertiary sector [6], which predominantly consists of desk-based office jobs, resulting in large amounts of daily sitting time [7]. In addition, the period of life in which people are expected to work is becoming longer because of shifts in demographics and retirement age [8]. Thus, understanding how occupational physical movement behavior influences cognitive health is interesting for employees, employers, and other stakeholders to promote a healthy and sustainable working life.

In Sweden, employers must ensure that the employees work under healthy conditions [9], and focusing on a healthy work environment is essential to attract qualified labor. Therefore, both employers and employees are eager to know more about the health risks of their occupation. The research in this Ph.D. thesis was co-produced with several partners consisting of large Swedish corporations and health promotion companies, which meant that the interests of the partners partly guided the development of the research program. The partners were particularly interested in whether extensive sitting of office workers has the adverse health effect as stated in media (e.g., “*sitting is the new smoking*”) [10]. The partners also wanted to know if breaking up prolonged sitting would be a feasible and time-efficient intervention to benefit cognitive health and whether supporting changes in movement behavior in the workplace could enhance cognitive health. Therefore, the overarching goal of this thesis was to understand how movement behaviors relate to and influence the cognitive health of office workers.



## 2. Background

A general understanding of central concepts and terms is a prerequisite to comprehending the translational field of this thesis. In the following sections, I will describe movement behaviors and how to measure them (2.1). After that, I will introduce the concepts of cognition (2.2) and neuroplasticity (2.3). Then I review the literature regarding how cognition and neuroplasticity are related to and affected by physical activity and sedentary behavior (2.4). Then, I will describe evidence-based behavior change interventions (2.5). Lastly, I will pinpoint the research gaps addressed in the current thesis (2.6).

### 2.1 Movement behaviors

Every day we have 24 hours to engage in different movement behaviors. Researchers usually organize these movement behaviors into different categories, based on intensity, i.e., sleep, sedentary behavior, light, moderate, and vigorous-intensity physical activity, to study the health effects of such time use data.

Traditionally, the health implications of spending time in each behavior are studied in isolation [11]. For example, studies examining how a structured physical activity regimen performed at a predefined intensity level affects health outcomes have not accounted for the effects of other movement behaviors occurring throughout the 24-hour cycle. Recently, there has been an increased interest in how the combined effects of movement behaviors relate to various health outcomes. The 24-hour activity cycle [12], movement behaviors [13], and time-use behaviors [11] are some of the terms used throughout the literature.

In this thesis, I will use the term “movement behaviors.”

There exist more precise definitions of the activities constituting movement behaviors. Physical activity (PA) is any movement produced by the skeletal muscles, resulting in energy expenditure rising above resting levels [14]. Energy expenditure is expressed as metabolic equivalents (METs). When sitting still, oxygen consumption equals approximately 3.5 ml O<sub>2</sub> per kg body weight x minutes, or 1 MET [15]. Oxygen consumption increases as a function of work intensity. Thus, METs describe the metabolic demands of a given activity.

PA can be either incidental or structured and has different dimensions. Structured PA is often termed

#### Definitions

**Movement behavior:**

Physical activity, sedentary behavior, and sleep.

**Physical activity:**

Any movement produced by the skeletal muscles, resulting in energy expenditure rising above resting levels.

**Physical inactivity:**

Not fulfilling the recommendations for physical activity.

**Sedentary behavior:**

Any waking behavior with an energy expenditure of  $\leq 1.5$  METs while sitting or reclining.

exercise and is a purposeful activity performed with the specific goal to improve attributes related to health or performance, such as cardiovascular fitness [14]. Incidental PA is daily activities performed with purposes other than improving health, such as household work or transportation [14]. The PA dimensions consist of frequency (F), intensity (I), time (T), and type or mode of activity (T), known as the FITT principle [16]. The type refers to the physiological and biomechanical demands of the activity, for example, aerobic, anaerobic, or resistance activities. In comparison, activity types describe specific activities such as running, walking, or biking.

PA and sedentary behavior (SB) occur in different contexts or domains, for example, occupational (at work), domestic (at home), or during transportation or leisure time, and measuring daily movement behaviors should capture all four dimensions [17]. PA can furthermore occur once or regularly, leading to acute and long-term effects of PA, respectively.

Physical *inactivity* is sometimes used interchangeably with SB. However, while physical inactivity refers to not fulfilling the recommendations for PA (i.e., 150 to 300 min/week of moderate to vigorous PA) [18], SB is defined as any waking behavior with an energy expenditure of  $\leq 1.5$  METs while sitting or reclining [19]. Importantly, in contrast to PA, SB contains a criterion for metabolic demands and a posture.

On the other hand, sleep is neither defined by activity intensity nor posture but rather as the absence of wakefulness and refers to several stages with different electrophysiological characteristics.

### ***Measurement of movement behavior***

Movement behaviors can be investigated with either self-reports or device-based measurement methods. Self-reports (e.g., questionnaires or diaries) are historically the most common way to obtain data on free-living activities [20]. A substantial part of the observational evidence on the relationship between movement behaviors and various health outcomes stems from studies relying on self-reports of movement behaviors. Therefore, many national and international guidelines rely on data obtained from questionnaires or diaries [21]. The low cost and feasibility of collecting data in large-scale studies are advantages of self-reports. However, the validity and reliability of self-reporting are questionable [22, 23], and errors are most likely to occur due to recall and report bias [24]. Still, with self-report, valuable information can be obtained, such as separating work and leisure time, indicating cognitive involvement while sedentary (e.g., TV viewing vs. reading a book), or social behaviors. In addition, sleep or sleep-related behaviors are often self-reported as time spent in bed.

An increasing body of research examines movement behaviors using devices as an alternative to self-reported measures. Accelerometry is the most common method used in movement behavior research, and technological development has made accelerometers

affordable and available to many researchers [25]. Accelerometers measures acceleration, which is transformed into counts. Counts represent accelerations in a given time frame (i.e., epoch) and are classified into intensity categories based on cut-points equivalent to the metabolic demands of the task (i.e., energy expenditure). Thus, counts can be used to categorize behaviors into light, moderate, or vigorous PA. The metabolic demands for a given activity vary across populations, and it is, therefore, essential to apply population-specific cut-points when processing device-based data to classify movement behaviors. Activity-specific validation of cut-point is often performed using indirect calorimetry to determine the energy expenditure for activities of different intensities [26]. Double-labeled water is preferably used to validate longer periods of free-living activities [25].

Importantly, there are substantial discrepancies between self-reports and device-based measurements [24, 27]. Using self-reports, individuals tend to report more PA than the data obtained by accelerometers [23]. In addition, self-reports of SB tend to be both under-reported and over-reported [27-29], complicating the comparisons to device-based measures. In addition, device-based measures have been demonstrated to show a stronger association with health outcomes than self-reports [30].

Intensity levels	
<b>Sedentary:</b>	$\leq 1.5$ METs Sitting or reclining
<b>Light Intensity:</b>	1.5 METs to 2.9 E.g., slow walking
<b>Moderate Intensity:</b>	3.0 METs to 5.9 METs E.g., brisk walking
<b>Vigorous Intensity:</b>	6 METs $\rightarrow$ E.g., running

Until recently, the relationships between SB, PA, and health outcomes have often been studied independently using multiple linear regression models with partial adjustment for the remaining behaviors. Because of the co-dependency of movement behaviors, multi-collinearity issues may occur. For instance, increasing time in one behavior will, per definition, reduce the time spent in one or more behaviors because behaviors are part of an infinite whole (i.e., 24 hours). Because all movement behaviors occurring throughout the 24h cycle are part of a finite whole, time use data is compositional in nature.

Compositional data analysis (CoDA) is one method that can take the compositional nature of time use data into account. It can be used for analyzing the combined effects of movement behaviors. In brief, CoDA uses isometric log-ratios (ilrs) between time spent in each behavior, which can be applied to standard statistics [11, 31, 32]. Instead of using compositional data, applying multivariate latent analysis to raw accelerometer data has emerged as a promising way to analyze time use data [33, 34]. The field of device-measured movement behavior is constantly changing, and new data processing and analysis methods are evolving rapidly.

In summary, movement behaviors consist of sleep, SB, and PA performed in different domains (e.g., work, home, transport, and leisure), which can be measured via self-report or devices, such as accelerometry. As described above, device-based measures are preferable because of their higher validity and reliability relative to self-reported measures. When analyzing time-use data, the compositional nature of the data should be considered and appropriate statistical methods used, such as CoDA.

## 2.2 Cognitive functions

Cognitive functions refer to multiple mental processes that allow us to learn, remember and engage with the external environment. Constantly, we are bombarded with stimuli from the world around us, and cognitive functions help us sort, direct attention to, select and process relevant stimuli. Previous acquired knowledge and experiences can help us plan and choose the desired action. Ultimately, we can carry out the action, thus engaging with our surrounding environment. Cognitive functions are sub-divided into numerous overlapping domains that vary in names and descriptions throughout the literature [35]. Hence, the domains used in this thesis are described in the following paragraphs.

### *Attention*

Although not directly assessed in this thesis, attention is central to all cognitive domains. The brain has a limited capacity to process the information provided by the external environment. In the face of such limited capacity, attention helps us focus on and select relevant stimuli, recall relevant knowledge and choose the right action for the desired purpose [36]. Attention can be either voluntarily directed based on prior knowledge and expectations to goal-directed behavior, sometimes referred to as internal attention, or reflexive and automatically directed to moving objects or loud noises, sometimes referred to as external attention [37]. Attention is therefore not a unitary mechanism but acts on every step from stimulus detection to memory formation and later memory retrieval.

### *Processing speed*

Processing speed refers to the time it takes to prepare and execute an action in response to a stimulus [38]. Processing speed (PS) is often seen as an expression of the efficiency of cognitive processing, that is, how effective and fast a correct response is selected and executed [38]. Thus, faster, successful processing is considered an indication of better general cognitive performance. Processing speed has been shown to be associated with higher-order cognitive functions and exhibits an age-related decline from late midlife [38].

## ***Memory***

The process in which information is encoded and stored for later retrieval is called memory. Encoding is the engagement with the external environment, where the senses receive, process, and combine information for the possibility of storage in memory. Storage is the formation of a permanent record of the encoded information. When the information is stored, retrieval processes can recall that information from the memory storage [35].

A common distinction is between declarative (explicit) and non-declarative (implicit) memory [39]. Declarative memory is an effortful storage process of which we are explicitly aware. In contrast, non-declarative memory cannot be explicitly explained or described, such as performing a complex motor task. Declarative memory consists of short-term and long-term memory [39].

Short-term memory entails sensory, short-term, and working memory [40]. As the name implies, the duration of short-term memory is brief. The retention of information goes from seconds to minutes, with limited capacity. While short-term memory is simply holding information present, working memory (WM) involves actively manipulating the information. Baddeley and Hitch proposed a WM model consisting of a central executive controlling three capacity-limited memory buffers [40]. The memory buffers hold representations with different characteristics. The visuospatial sketchpad holds spatial representations and visual objects, a phonological loop holds auditory stimuli, and an episodic buffer holds multimodal representations [40]. The central executive can allocate processing capacity to the memory buffers. Each buffer can store and retain information briefly and rehearse that information to stay in WM. If rehearsed sufficiently, the information can be stored in long-term memory [41].

In opposition to short-term memory, long-term memory maintains information for days and years. Long-term memory consists of episodic and semantic memory. Both episodic and semantic memory are effortful recollections of previously consolidated information. Episodic memory (EM) stores information about past experienced events in a particular place at a given time [42]. On the other hand, semantic memory is the recollection of facts. Examples of semantic memory could be knowing a former president's name or remembering lyrics of a song from your youth.

Taken together, memory is the encoding, storage, and retrieval of information and is divided into short and long-term and subdivided into several categories. The present thesis will focus on WM and EM only.

## ***Executive function***

Executive functions (EF) are a group of higher-ordered top-down mental processes needed for tasks where you have to pay attention and concentrate on completing the task [43]. Other cognitive functions are modulated by EF in a flexible and goal-directed way

[35]. Miyake et al. (2000) have proposed a theory for EF based on Baddeley's WM model [44]. The central executive controls the three memory buffers: visuospatial sketchpad, phonological loop, and episodic buffer. In turn, the central executive has three main functions: shifting, updating, and inhibition. Shifting, also called cognitive flexibility, is when you mentally shift between tasks or mental sets. Updating is monitoring and refreshing WM representations. Inhibition is the suppression of dominant or automatic responses when necessary [44]. Indeed, EF and WM are highly correlated, suggesting that they are a part of the same underlying construct [45].

## 2.3 Probing neuroplasticity with magnetic stimulation

The central nervous system has a unique capability to modify its function and structure in response to environmental exposures. These intrinsic plastic processes underlie our ability to acquire new knowledge, which is retained throughout life [46]. Neuroplasticity encompasses persistent cellular, synaptic, and representational changes within the nervous system [47]. Early, neuroplasticity was postulated to be activity-dependent [48], supported later by experiments in anesthetized rabbits [49]. High-frequency electrical stimulation in the rabbit hippocampus induced changes in excitability via long-term potentiation (LTP) [49]. Similar LTP changes in excitability are also evident in the primary motor cortex (M1) [50]. The underlying mechanism of LTP relies on functional (e.g., neurotransmitter release [51]) and structural (e.g., formation of new synapses [52]) changes within the activated synapse. In humans, we are not able to measure LTP at the synapse level. However, brain stimulation techniques allow changes in excitability within the motor cortical systems to be assessed non-invasively.

### *Corticospinal excitability*

Transcranial magnetic stimulation (TMS) is a non-invasive brain stimulation technique used to measure the excitability of the corticospinal tract and levels of intracortical and interhemispheric facilitation and inhibition [53]. When discharging a magnetic coil, a rapid current flow elicits a short-lasting magnetic field that can penetrate the scalp with little or no pain receptors activation [53]. An electrical field is produced perpendicular to the magnetic field inside the scalp and creates an electrical current flow that will depolarize corticospinal neurons predominantly through activation of interneurons at low intensities [54]. Still, corticospinal neurons may be directly activated at higher intensities [55].

Corticospinal excitability (CSE) is quantified by measuring evoked potentials from electromyographic (EMG) signals recorded through surface electrodes positioned on the muscle belly of the stimulated muscle. Delivering a supra-threshold single-pulse TMS-stimulus to M1 produces a motor evoked potential (MEP) in the EMG. Measuring the

peak-to-peak amplitude of the signal quantifies the MEP size. However, MEP size is a highly variable measure. For this reason, a recruitment curve (RC) that consists of the mean of multiple MEPs, plotted as a function of stimulus intensity relative to the resting motor threshold (RMT), is commonly used. Calculating the average area under the RC (AURC) gives a reliable estimate of CSE [56] (See Figure 1).

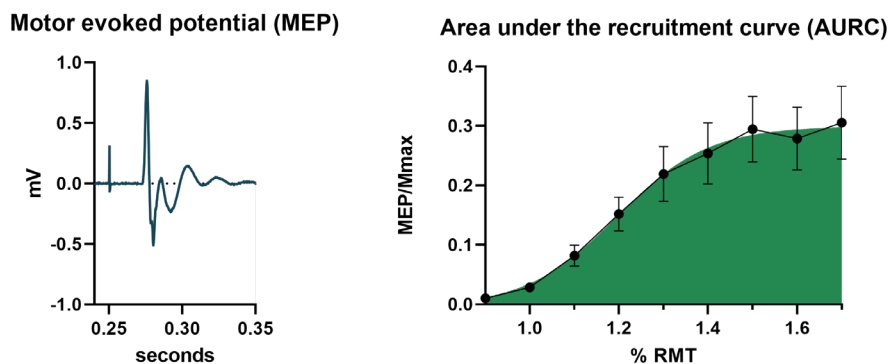


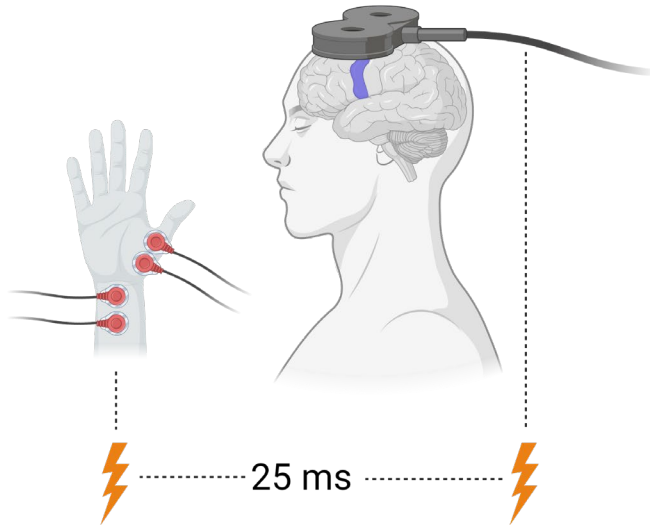
Figure 1. A single raw motor evoked potential (left) and area under the recruitment curve (right) normalized to maximal compound muscle action potential ( $M_{max}$ ). mV = millivolt, % RMT = resting motor threshold

### ***Paired Associative Stimulation***

Associative LTP is persistent increases in synaptic efficacy and can be induced experimentally in humans with paired associative stimulation (PAS) by pairing a peripheral electrical nerve stimulation with a single supra-threshold TMS stimulation applied to M1 (See Figure 2) [57, 58]. It is “associative” when stimulation of cortical afferents is near synchronous with depolarization of the postsynaptic cell [57]. Repeating this pattern for a period (e.g., 30 min) will result in changes in the excitability of the corticospinal system. The interstimulus interval (ISI) is vital for the neuroplastic outcome of the protocol, suggesting spike-timing-dependent plasticity as seen in animal models [59]. If the input from the peripheral electrical afferent nerve stimulation reaches M1 synchronously with the magnetic stimulation induced by TMS, LTP-like increases in CSE occur [58]. However, if the TMS stimulus precedes the volleys from the peripheral nerve stimulation, long-term depression-like (LTD-like) reductions in CSE arise [59].

Associative LTP-like neuroplasticity induced by PAS is comparable with CSE-increases after motor practice. It yields the same properties as LTP explored in animal models; it is rapidly evolving (<30min), long-lasting (30 to 60 min), yet reversible [58, 59].

Therefore, the magnitude of PAS-induced CSE can be evaluated to examine how movement behaviors affect corticospinal neuroplasticity. I will elaborate on this in section 2.4, Movement behaviors for cognitive health.



*Figure 2 – Paired Associative Stimulation*

## 2.4 Movement behaviors for cognitive health

A growing body of evidence shows that PA is essential for maintaining overall health throughout the lifespan. PA reduces the risk for all-cause mortality [60] and certain cancer types [61]. Interestingly, PA is a lifestyle factor that may improve neuroplastic processes and related cognitive functions in old age [62]. For instance, PA has been associated with a reduced risk for dementia [63] and attenuated age-related cognitive decline [64]. The fundamental principle thought to underlie this is that PA engages multiple cellular and molecular processes that facilitate neuroplastic modifications of the nervous system and, as part of this, the brain and cognition [65]. In this section, I will elaborate on the complexity of this field by first reviewing the evidence on associations between PA and SB and cognition and how PA and SB may causally impact cognitive functions. After that, I will address how PA affects neuroplasticity (i.e., CSE) in the healthy adult population.

### ***Physical activity, sedentary behavior, and cognitive functions***

#### *The association between physical activity and cognitive function*

The greatest amount of cross-sectional evidence on the association between PA and cognitive functions stems from children (5–18 years) and older adults (>50 years) [66, 67]. In a systematic review of preadolescent children (6–13 years), Donnelly et al. (2016) found that PA was generally favorably associated with cognitive function in the 11 cross-sectional studies included [66]. In addition, Donnelly et al. (2016) report that cardiorespiratory fitness was most often used as a PA measure, while only a single study applied device-measured PA. Moreover, several cognitive functions have been examined, including PS, EF, memory, and attention [66].

Relative to the children, the body of cross-sectional evidence for older adults (>50 years) is greater. Investigations primarily focus on individuals with mild cognitive impairment, dementia, Alzheimer's disease, or healthy older adults. In a recent systematic review, Rojer et al. (2021) included 38 studies (n = 8695) investigating the association between device-measured PA and cognitive functions [67]. Generally, device-based measures of PA (i.e., steps, total PA, activity counts, LPA, and MVPA) were associated with better global cognitive function. Across outcomes, the effect sizes were relatively small, but the largest effect sizes were found for MVPA and total PA. Cognitive outcomes were assessed using several different tools, the most common being Mini-Mental State Examination and Montreal Cognitive Assessment [67].

Compared to children and older adults, much less is known about PA and cognitive function in the working-age population [68]. In a systematic review of 14 studies with a total of 1803 participants, Cox et al. (2016) concluded that a limited body of evidence supported the relationship between PA and cognitive functions in young to middle-aged adults (18–50 years) [69]. PA levels were associated with EF in some studies, whereas others showed no association. In general, the association between different types of memory and PS was absent [69]. The studies in the meta-analysis by Cox et al. (2016) consist predominantly of studies using self-reported measures of PA, which is known to have poor validity [24]. A growing body of evidence on the cross-sectional relationship between device-measured PA and cognition among middle-aged adults has emerged since the systematic review by Cox et al. (2016). While some studies show that more time in device-measured MVPA is related to better cognition [70, 71], others found no association [72, 73]. These inconsistent findings may depend on differences in study population demographics (e.g., age, sex, education, or socioeconomic factors) or in cognitive tests delivered. Nevertheless, evidence investigating the association between PA and cognitive function and middle-aged adults is clearly lacking.

### *The association between sedentary behavior and cognitive functions*

Limited evidence exists on how SB is related to cognitive function. In a systematic review including only eight cross-sectional studies, Falck et al. (2016) reported that higher amounts of SB tended to be related to worse cognitive function [74]. Nevertheless, many of the included studies relied on self-reported measures of SB, with poor validity [27-29]. The only study included in the systematic review, Rosenberg et al. (2015), investigated the relationship between SB and cognitive functions in older adults. They found no association between device-measured SB and cognitive functions. However, self-reported TV-time was associated with poorer performance on a processing speed task (TMT-A) [75]. Although still few, since the systematic review by Falck et al. (2016), an increasing number of studies have used device-based measures to assess SB, to investigate the associations with cognitive functions [70, 71, 73, 75-77], which have elucidated a more complex association.

In line with Rosenberg et al. (2015), the absence of association was also evident in a cohort of older adults [76]. Zu et al. (2017) found that the percentage of time spent in SB was not associated with changes in cognitive functions at 3-years follow-up [76]. This non-association is further supported in a recent study of older adults [77]. Interestingly, some studies report a positive relationship between device-measured sedentary time and cognitive function [70, 71]. Additionally, Vasquez et al. (2017) found a tendency toward a significant association between sedentary time and processing speed in a large sample of middle-aged to older adults. However, the tendency was attenuated in models adjusted for confounders such as socioeconomic status and self-reported health [73].

A limitation for device-measured SB is the inability to capture the context in which SB occurs. For example, Bakrania et al. (2018) showed that computer-use time was associated with better cognitive functions in a large sample of 502,643 individuals, while TV-viewing and driving time were associated with worse cognitive functions [78]. These findings suggest that SB's adverse effect on cognitive ability is likely to be context-specific. Bakrania et al. (2018) speculate that computer use may be cognitively challenging, serving as an enriching activity, thus compensating for the negative effect of SB [77]. Thus, the findings of a positive relationship between device-measured SB and cognitive function in some studies, as previously mentioned [70, 71], could maybe be explained by context-specific associations. These context-specific effects need to be investigated more deeply to understand the impact of occupational SB on cognitive functions.

High levels of PA may also counteract the adverse effect of SB. The negative health effect of extensive SB has been shown to be eliminated by high levels of PA in a large epidemiological study of 36,383 participants across 39 studies [60]. Although less studied, this may also be evident for cognitive function.

The evidence on the association between device-measured SB and cognitive function is sparse and limited to older adults. However, the association between the extensive occupational SB and cognitive functions among the working-age population needs to be investigated further.

#### *Acute effect of exercise on cognitive functions*

Acute aerobic exercise increases arousal transiently [79] and engages a wide range of neurotransmitters and neurotrophins [80], suggesting that cognitive functions may be enhanced. There is evidence that a single bout of aerobic exercise transiently improves cognitive abilities through an interplay between psychological and neurobiological factors. In general, studies show a favorable effect of acute exercise on cognitive function with effect sizes ranging from small to moderate [81-83]. Most evidence on the acute effect of exercise stems from investigations containing aerobic exercise regimens. However, emerging evidence suggests that resistance training can induce comparable positive acute effects on cognitive functions as aerobic exercise [84].

The intensity of the exercise bout impacts cognitive benefits. Numerous studies have investigated the effect of moderate- and high-intensity aerobic exercise. In a meta-analysis, Chang et al. (2012) showed that exercise intensity and duration were significant moderators of cognition. Studies with larger effect sizes contained higher intensity and longer duration [81]. However, some evidence suggests that too high an intensity may be detrimental. For example, Wang et al. (2013) showed that high-intensity aerobic exercise was disadvantageous for EF [85]. In addition, Roig et al. (2013) showed in their meta-analysis that short bouts (< 20 min) of light intensity were most favorable for memory performance [83]. Moreover, Moreau and Chou (2019) recently showed in a meta-analysis that high-intensity aerobic exercise significantly facilitated EF compared to rest, but high-intensity was not more favorable than moderate-intensity aerobic exercise [86].

Most investigations of exercise's acute effects on cognition have focused on young, somewhat fit individuals, and only limited evidence exists on the impact in middle-aged adults [68, 82]. Therefore, it is not possible to say how fitness and age moderate the acute effects of exercise intensity on cognitive function. Indeed, meta-analytic evidence suggests that the impact of acute aerobic exercise on cognitive functions is moderated by age [82, 83, 87]. A meta-analysis by Ludyga et al. (2016) found that exercise enhanced executive function for older adults compared to younger adults [82], but studies in middle-aged individuals were not included. Another recent meta-analysis by Loprinzi et al. (2019) found that exercise had a favorable effect on memory tasks in young adults [87]. However, again no study investigating the impact of acute exercise in middle-aged adults was identified.

Taken together, the evidence on the acute effect of exercise in young adults shows a small but positive effect, but studies in a middle-aged population are greatly warranted.

### *Acute effects of breaking up sedentary behavior on cognitive functions*

Research on the effects of lower-intensity PA levels is minimal compared to the evidence on the effect of moderate- and high-intensity exercise on cognitive abilities. Breaking up prolonged sitting by frequent short activity breaks has been reported to improve working memory and EF in older overweight/obese adults ( $67\pm 7$  years) [88] and reduce fatigue in overweight/obese middle-aged to old adults (45–75 years) [89]. In a randomized cross-over design including 65 overweight/obese older adults, Wheeler et al. (2019) simulated 8-hour workdays with different experimental movement behavior conditions. Findings revealed that an exercise bout combined with activity breaks significantly improved working memory and EF compared to sitting for 8 hours [88]. In addition, Mullane et al. (2016) found that frequent bouts of standing, cycling, and walking enhanced performance on psychomotor, working memory, and attention compared to prolonged sitting in a population of overweight middle-aged adults ( $30\pm 15$  years) [90]. In a recent study containing 13 middle-aged subjects, Heiland et al. (2021) found that frequent 3-min walking breaks during three hours of sitting improved performance on an EF task and increased alertness compared to a resting condition [91]. On the contrary, Russell et al. (2016) showed that standing was not associated with improved processing speed, working memory, or work efficiency compared to sitting in office workers [92]. Additionally, standing did not improve cognitive functions in students [93].

These results collectively imply that posture transition may not be sufficient to enhance cognitive functions but that more intense PA breaks might. Therefore, changes in behaviors of greater intensity than just posture transitions seem beneficial for cognitive functions.

However, a systematic review by Magnon et al. (2018) of 9 acute interventions in the workplace found no overall effect of breaking up PA [94]. Nevertheless, the evidence is sparse, and more studies are needed to investigate further the impact of breaking up prolonged sitting with light-intensity exercises.

Taken together, while a few studies have shown that breaking up SB affects some cognitive functions, the evidence base is still small, and it is unknown whether these effects extend to other populations and whether the effects are general or domain-specific.

### *Long-term effects of physical activity on cognitive functions*

Extensive research has focused on the effect of long-term structured exercise interventions on cognitive functions. The most considerable wealth of evidence stems from investigations in older adults, and several systematic reviews and meta-analyses have been conducted in this age group [95-98]. In a meta-analysis containing 48 studies, Falck et al. (2019) showed that exercise interventions generally demonstrated a small but positive effect on cognitive function in older adults. A wider age range was included in a recent meta-analysis by Ludyga et al. (2020) of 30 randomized control trials [99]. Ludyga et al.

(2020) also found small but positive effects on cognition [99]. Results were consistent across cognitive domains, exercise modalities, and intensities, with longer interventions combined with longer session duration resulting in greater effects.

Investigating potential moderators is essential because it allows us to identify specific populations that may benefit from changing a particular movement behavior or engaging in exercise interventions [68, 100]. Moderation is present if the effect of an intervention or the association between two variables varies across the moderating variable. A moderating variable can either attenuate or augment the effect of exercise interventions on cognitive functions.

Both the effect of structured exercise interventions on cognitive functions and the association between PA and cognition have been suggested to be moderated by several variables, such as age, gender, cardiorespiratory fitness, education, and baseline PA [68, 100, 101]. For example, in their meta-analysis, Ludyga et al. (2020) showed that sex moderated the intervention effect, such that studies including more female participants observed less cognitive improvement after the intervention period [99]. These findings are conflicting with two previous meta-analyses, which found that studies with a larger proportion of female participants showed bigger effects [102, 103].

Colcombe and Kramer (2003) found in a meta-analysis of aerobic exercise interventions that age moderated the effect on cognitive functions [102]. Young-old (55 to 65 years) had significantly less impact of aerobic exercise interventions on cognitive functions compared to mid-old (66 to 70 years) and old-old (71 to 80) years. However, mid-old benefitted significantly more than old-old [102]. In a recent randomized controlled trial, Stern et al. (2019) showed that as age increased, the effect of a 24-week aerobic exercise intervention on executive functions was greater [104].

In summary, there exists little knowledge about midlife PA levels and cognitive functions. Sex, age, and participants' fitness level appear to moderate the intervention effects. There is limited knowledge on how daily movement behaviors should be distributed to support healthy cognitive functions in the most favorable way for middle-aged adults. In addition, clear evidence is lacking on how changes in cardiorespiratory fitness can enhance cognitive functions during midlife.

#### *Long-term effects of breaking sedentary behavior on cognitive functions*

Only a few intervention studies have investigated the effect of changing SB for improving cognition. In a systematic review of interventions aiming at reducing SB at work, Magnon et al. (2018) found no impact on cognitive function in the three studies included in the synthesis of studies lasting days to weeks [94]. However, the only long-term study Magnon et al. (2018) identified was not an intervention. Instead, it was a statistical real-

location of time between movement behavior categories [105]. There is a dearth of evidence on the long-term effect of breaking up long periods of SB, and more evidence is needed to inform employers and employees on how to structure their workday in the office.

### ***Neuroplasticity and physical activity***

The underlying neural mechanisms by which PA influences cognitive function have been studied on several levels in rodents and humans [80]. At the micro-level, investigations in rodents have focused on cellular and molecular processes, demonstrating influences of PA on, for example, growth factors [106, 107], formation of new blood vessels (i.e., angiogenesis) [108, 109], and the formation of new neurons (i.e., neurogenesis) [110]. In humans, macro-level studies have reported PA to affect brain volume, particularly the hippocampus [62], gray matter and white matter tissue [111], functional connectivity measures [112, 113], cerebral blood flow [114], and indices of neuroplasticity [115, 116]. It has been proposed that such neuroplastic effects of PA may underpin the beneficial effects reported for cognition. In the next section, I will review the literature on neurophysiological studies in humans using non-invasive brain stimulation techniques to assess the effects of PA on neuroplastic processes.

Exercise-induced improvements in animal learning and memory experiments are associated with how pre and post-synaptic neurotransmission is modulated, called activity-dependent plasticity [110, 117]. This form of plasticity relies on processes fundamental to different forms of learning and memory, such as long-term potentiation (LTP) [49]. In their pioneering study, Van Praag et al. (1999) demonstrated that access to a running wheel during one month improved neurogenesis, altered LTP, and enhanced learning on a spatial memory task in adult mice [110]. Similar alterations in LTP have been reported since [118, 119]. Even a single bout of exercise has been found to cause significant potentiation of the synaptic response in slices of the adult rat hippocampus, indicating an acute improvement of communication between synapses [120]. Initiation of LTP arises from both functional and structural changes related to synaptic transmission [121]. Functional changes are dependent on synapse characteristics, such as translocation of receptors to the synapse [122] and increased neurotransmitter release [51], which will modify synaptic communication. On the other hand, structural changes depend on protein synthesis [47], causing increased dendritic spine density [123] and neurogenesis [124]. Pastalkova et al. (2002) supported this by demonstrating that blocking protein synthesis impaired spatial memory retrieval in rats, most likely by reversing LTP [125].

We are unable to measure the synaptic transmission at the level of the synapse in humans. Instead, non-invasive methods, such as PAS, indirectly assess the propensity to induce neuroplastic changes in the corticospinal tract [58]. Cirillo et al. (2009) showed

considerably larger MEPs in m. abductor pollicis brevis (APB) following PAS in physically active compared to inactive subjects [126]. Furthermore, Sing et al. (2014) revealed that an acute bout of moderate exercise preceding PAS significantly increased MEPs in APB [115], which Mang et al. (2016) confirmed [127]. In addition, Mang et al. (2014) showed that aerobic exercise improved learning on a motor task and increased the response to PAS [116]. Such evidence demonstrates that acute PA can improve LTP-like plasticity, which may be mechanistically related to the beneficial effects of PA on cognition.

Alterations in corticospinal excitability are suggested to be regulated by excitatory and inhibitory neural networks. Reduction in intercortical inhibition is an essential precursor of neuroplasticity in the motor cortex [128]. Short-interval intracortical inhibition (SICI) is modulated using a paired-pulse protocol to investigate inhibitory mechanisms within M1. SICI has been shown to be reduced following an acute bout of aerobic exercise [129, 130] and after aerobic exercise combined with PAS [115].

Plasticity-inducing protocols such as theta-burst stimulation (TBS) have also been used to examine the mechanism of PA on synaptic transmission. In TBS paradigms, TMS is used to deliver bursts of high-frequency stimuli to the cortex, altering cortical excitability [131]. For example, a high-intensity interval aerobic exercise bout resulted in greater MEP amplitudes after exposure to an LTP-like inducing intermittent TBS protocol than a rest condition [132]. McDonnell et al. (2013) applied an LTD-like inducing continuous TBS protocol and revealed that only low-intensity exercise resulted in increased LTD-like effects [133]. Thus, exercise-induced effects seem to elicit different outcomes in LTP and LTD mechanisms and depend on exercise intensity. Still, the evidence is sparse, and a recent systematic review by Mellow et al. (2019) identified only 12 experiments using non-invasive brain stimulation techniques, and a considerable variation in methods applied and study design exists [131].

There is a dearth of evidence concerning how SB influences indices of neuroplasticity. In a recent study, Smith et al. (2021) showed that older adults with more sedentary time and sleep at the expense of PA showed less LTD-like corticospinal excitability compared to active older individuals [134]. However, there is lacking knowledge about how prolonged SB influences the measure of neuroplasticity both acutely and long-term.

The results reviewed above suggest that exercise and PA can result in acute and long-term neuroplastic changes within the human brain. However, elucidation of a detailed description of the different signaling pathways in humans remains. With most studies focusing on exercise and PA, not many have addressed the role of SB on neuroplasticity. Therefore, the literature lacks well-controlled studies addressing reducing SB as a potential means of enhancing neuroplasticity and cognitive function.

## 2.5 Changing movement behavior

Substantial evidence suggests that changing people's movement behavior could have major public health benefits, such as reducing the risk of all-cause mortality, cancer, dementia, and attenuating age-related cognitive decline [60, 61, 63, 64]. Achieving sustainable changes to habitual behaviors can, however, be very challenging. Movement behaviors are complex and notoriously difficult to change and sustain in the long term [135]. While evidence suggests that increasing PA or breaking up SB in the context of a research study can benefit cognitive functions acutely, achieving such behavioral changes in an ecological setting can be very challenging. Therefore, well-designed behavior change interventions are needed to implement promising, sustainable, and feasible real-life interventions.

Michie et al. (2011) define behavior change interventions as coordinated activities designed to change specified behavior patterns [136], such as reducing smoking, SB, or unhealthy eating habits. Theoretical frameworks and models can help coordinate these activities systematically to compare and evaluate interventions and extract successful components to move the research field forward. Sallis et al. (2000) propose five phases to systematically guide research studies on promoting health-related behaviors leading to evidence-based effective and feasible interventions in an epidemiological, behavioral framework [137]. The first two phases include 1) establishing a link between health and behavior 2) and developing reasonable measures of the behavior. The subsequent three phases concern 3) identifying influences of behavior, 4) evaluating behavior change interventions, and 5) translating evidence into practice. Extensive research has established the link between movement behaviors and various health outcomes, including cognitive function [60, 61, 63, 64, 138]. Moreover, an increasing body of evidence supports device-measured PA and SB to be of high validity and reliability [25, 139-141]. Thus, in PA and cognitive health research, much progress has been made regarding phases 1 and 2 of the framework. However, the remaining phases, which are critical if the empirical findings are to benefit public health, have received considerably less attention.

There exist numerous theoretical frameworks to guide designing behavior change interventions. Ecological models have been widely used as meta-models to combine several specific theoretical frameworks and incorporate them when designing holistic interventions [142]. The backbone of ecological models is the assumption that behavior can be influenced on several intervenable levels (e.g., the public policy, community, organizational, environmental, and individual) that interact and are interdependent. The model must be behavior-and context-specific [142], promoting the behavior of interest in the context identified as central. For example, promoting leisure-time PA may not translate to biking to work. This thesis's core theoretical frameworks include a behavior-specific

ecological model for SB [143] and the ecological model of health behaviors [142]. Owen et al. (2011) identify four different behavioral contexts with high SB prevalence: occupation (at work), household (at home), transport, and leisure-time [143]. At work, individuals have lower autonomy than other domains, highlighting the importance of holistic intervention at multiple levels to increase personal agency so that behavior change is more likely to occur and be sustained in the workplace.

Behavior change techniques should translate the theoretical mechanism of actions into intervention strategies. Numerous behavior change techniques (BCT) exist, and several components overlap. Michie et al.'s (2013) taxonomy of behavior techniques supports extracting essential components from several BCT [144]. This taxonomy extracts the active ingredients in different BCT and structures them into a hierarchy that helps guide interventions to be effective [144].

BCT is the active intervention component, such as self-monitoring, reinforcement, goal-setting, or acceptance techniques [144]. The BCT can be communicated to participants in different ways by counselors. In the present thesis, cognitive-behavioral therapy was combined with motivational interviewing to provide a person-centered delivery approach for enhancing autonomous and intrinsic motivation to change behavior.

In summary, there is extensive evidence that structured exercise interventions enhance various health outcomes, but there is currently limited real-life evidence of how we can change movement behavior in the long term. Therefore, behavior change interventions that target different populations at high risk for unhealthy behavior are needed. For example, office workers are at high risk for accumulating extensive SB [7], and effective intervention is needed to support behavior change. Ecological models and theoretical frameworks can guide the design of evidence-based behavior change intervention for thereafter implementing and assessing the effectiveness of these. Furthermore, BCT delivers the active intervention component to the participants. This systematic, theory-driven approach should facilitate designing, implementing, and evaluating interventions that can change behavior in a way that persists in the long term.

## 2.6 Summary of research gaps

PA has been associated with reduced risk for all-cause mortality [60], certain cancer types [61], dementia [63], attenuated age-related cognitive decline [64], and better cognitive performance [138]. SB has also been related to worse cognitive functions, although evidence is scarce [74]. However, most observational studies rely on self-reported measures of movement behavior, which have questionable validity and reliability [24], and the majority of studies focused on older adults. Thus, a research gap exists regarding the association between device-measured movement behavior and cognitive function among middle-aged individuals in general and in office workers specifically. Study I addressed this research gap.

Experimental evidence has established that acute PA can have neuroplastic effects, which in turn may underpin the beneficial effects on cognition [131]. However, much less is known about how SB may influence similar neuroplastic mechanisms in the acute phase. Study II addressed this research gap in the context of corticospinal LTP-like plasticity.

Several meta-analyses of randomized controlled trials have demonstrated that regular PA has a small but positive effect on cognition [95-99]. However, behavior is challenging to change and sustain in the long term in more ecological settings [145]. Addressing movement behavior via workplace interventions may represent a feasible context to modify movement behavior, but previous workplace interventions aiming at reducing SB or increasing PA or both have shown mixed results [146-149]. Interventions grounded in ecological models of health behavior, targeting both the individual and the environments in which they work and live, have been suggested to be more effective than interventions that target only the individual [147, 150]. However, there is a lack of scientific evaluation of workplace interventions aiming to improve movement behaviors to enhance cognitive functions and mental health. Study III and IV addressed these research gaps.

### 3. Aims

This thesis's overall aim was to address how device-measured physical activity and sedentary behaviors relate to and influence cognitive functions among office workers and how such behaviors may induce corticospinal neuroplasticity in the acute phase. The specific aims of the thesis were as follows.

- i. Investigate the cross-sectional associations between device-measured physical activity, sedentary behavior, and cognitive functions in office workers.
- ii. Examine the acute effect of breaking up prolonged sitting and a single bout aerobic exercise on LTP-like corticospinal neuroplasticity, compared to prolonged sitting in middle-aged sedentary office workers.
- iii. Investigate the effect of two 6-month multi-component behavior change interventions targeting reduced sedentary behavior or increased physical activity, respectively, on office workers' 24-hour composition of device-measured movement behaviors.
- iv. Examine the effects of the two multi-component behavior change interventions on cognition and explore whether such changes are associated with parallel changes in device-measured movement behaviors or cardiorespiratory fitness and how age, sex, and cardiorespiratory fitness may moderate such associations.

## 4. Materials & Methods

### 4.1 Populations, data collection, & study design

#### *Study I*

Study I was a cross-sectional study. Out of 1940 invited office-working employees at two collaborating companies, 369 participants at three different worksites accepted the invitation and completed activity measurements and cognitive testing. Finally, 334 participants with valid accelerometer and cognitive data were included in the study. Participants attended a test session at their workplace during working hours. After receiving verbal and written information about the study, participants signed informed consent. At first, participants received instruction on wearing an accelerometer and filling in an activity and sleep diary for eight days. Then, participants completed a thorough battery of cognitive tests, including nine validated computerized or paper-based tests. After that, participants completed a submaximal fitness test on a bike-ergometer to estimate maximal oxygen consumption ( $VO_2$  max). Associations between device-measured movement behaviors and cognitive functions were studied using multiple linear regression.

*Table 1—Characteristics of participants in the studies*

	Study I	Study II	Study III	Study IV
Age (mean, years)	42	53	43	43
Education (mean, years)	14	-	15	15
Sex (female, %)	68	50	77	75
$VO_2$ max ( $mL \cdot kg^{-1} \cdot min^{-1}$ )	40	31	37	37
N	334	16	158	139

#### *Study II*

Study II was a randomized cross-over study including sixteen inactive participants recruited through collaborating companies and advertisements. Participants attended the laboratory, one screening session, and three experimental sessions on four occasions. Anthropometrics, a TMS-familiarization, and a submaximal bike-ergometer test to estimate maximal oxygen consumption were performed on the screening session. Participants were then randomly assigned to one out of six test orders. On the day of the experimental condition, participants attended the laboratory fasting, prepared for TMS, and obtained baseline measures. Then, a standardized breakfast was served, and the experimental period began. One condition was 3-hours of uninterrupted sitting (SIT); another 3-hours of

sitting was interrupted every 30<sup>th</sup> minute by a 3-minute bout of PA (FPA). The third condition consisted of uninterrupted sitting for 2.5 hours followed by a 25-minute bout of moderate-intensity aerobic exercise on a cycle ergometer (EXE). See Figure 3 for a flow chart of the study design. Immediately after each condition, TMS measurements were obtained. After that, a paired associative stimulation (PAS) intervention was carried out. Five and 30 min after the PAS protocol, TMS measurements were obtained. Each three-minute FPA bout consisted of three rounds of three separate simple resistance exercises performed for 20 seconds each (3 minutes in total). Participants followed a video to keep the correct pace. The effect of the different conditions on PAS-induced corticospinal excitability was investigated using linear mixed models.

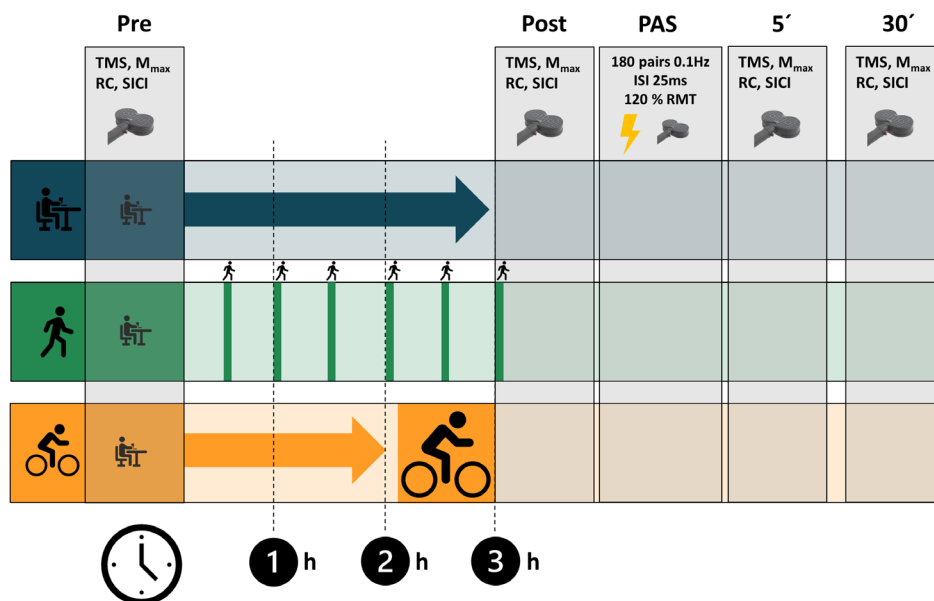


Figure 3. Flow chart of the Study II design. Maximal compound muscle action potential ( $M_{max}$ ) and transcranial magnetic stimulation (TMS) measurements (i.e., RC: recruitment curve and SICI: short-interval intracortical inhibition) were carried out prior (Pre) and after the experimental condition (Post) as well as 5 and 30 minutes after a paired associative stimulation (PAS) protocol. SIT: Sitting. FPA: Frequent Physical Activity. EXE: Exercise.

### Studies III and IV

Studies III and IV contain data from cluster-randomized ecological multi-component workplace intervention. Employees at two Swedish companies were invited to participate in a 6-month intervention to change movement behavior to improve brain health and function. Meetings presenting the project aim were held to facilitate interest in the study. Managers, researchers, and employees participated in those meetings. In total, 2033 office workers were invited through email. Due to the high PA level registered in Study I, we excluded persons performing more than 30 minutes per day in bouts of 10 minutes from participating. Although not described very well in the protocol paper [151] or the effectiveness study [152], senior researchers of the research project put much effort into instructing team leaders about their tasks. Several HR and management meetings were held throughout the recruitment process to reach the target population, less physically active office workers, and the calculated minimum of participants needed for the randomized control trial [151]. Power calculations preceding the intervention indicated a sample size of 330 [151], but only 298 volunteered, and 263 fulfilled the inclusion criteria. Participants were assigned to either an intervention aiming to reduce SB, an intervention aiming to increase PA, or a waiting list control arm, resulting in 22 clusters. Data on movement behavior, cognitive function, and VO<sub>2</sub> max were obtained at baseline and after 6-months. Motivational counseling was the main component in the two interventions. The counseling sessions consisted of a combination of motivational interviewing and cognitive-behavioral therapy. During the intervention period, participants could partake in five sessions. All intervention components are described in detail in the study protocol [151] and Study III. The theoretical basis and the intervention development are described in section 4.6 Workplace Intervention. The effect of the two interventions in changing movement behavior and cognitive function was investigated using linear mixed models.

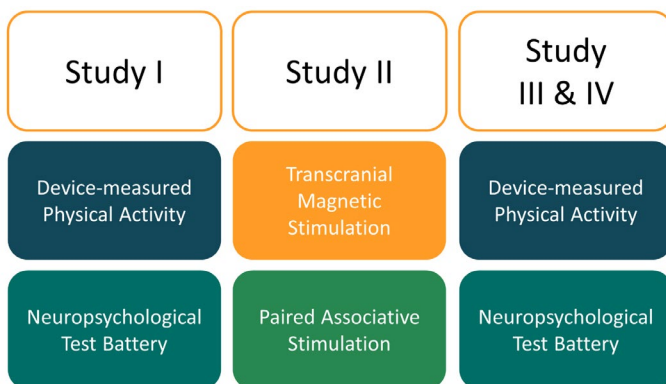


Figure 4. Overview of methods used in the thesis

## 4.2 Measuring movement behaviors with devices and diary

All four studies examined movement behaviors using an ActiGraph™ GT3X tri-axial accelerometer (ActiGraph LLC, Pensacola, FL, USA). Participants wore the accelerometer on the right hip during waking hours and on the right wrist during bedtimes. Participants should wear the accelerometer for eight days in Study I, four days in Study II, and seven days in Studies III and IV. We used self-reported in and out of bedtimes in all studies to separate wake time from sleep time. In Studies III and IV, self-reported work-times allowed separating work time and leisure time.

The standard ActiGraph software, ActiLife, was used to initialize sampling at 30 Hz and download the data after collecting data. In Studies I and II, the accelerometer data was downloaded and stored in 60-second epochs using the standard filtering of ActiGraph. In Studies III and IV, we processed raw accelerometer data based on a 10 Hz low-pass filter in opposition to the standard 1.6 Hz ActiGraph low-pass filter, using three-second epochs. Detecting higher intensity PA is more valid [140], and data is more strongly related to health outcomes, using the 10 Hz method [141]. In all studies, we combined the tri-axial accelerations into a vector magnitude and defined non-wear time as zero counts for at least 60 consecutive minutes with allowance for two minutes accelerations above zero but below the sedentary cut-point.

In Studies I and II, different intensity levels were defined according to Sasaki et al. (2011) [153] with a 200 counts per minutes cut-off for the sedentary intensity using ActiLife software [154]. At least 20 unbroken minutes of less than 199 counts per minute defined sedentary bouts. Ten unbroken minutes with at least 2690 cpm with allowance for up to two minutes of non-MVPA counts, defined MVPA bouts.

In Study III and IV, we defined intensity levels as described by Fridolfsson et al. (2019) [140] and processed accelerometer data with MATLAB R2020a (MathWorks, Natick, MA, USA). Energy expenditure levels defined the different categories; SED (<1.5 METs), LPA (1.5–3 METs), MPA (3–6 METs), VPA (>6 METs). Using compositional data analysis, we calculated compositional means and scaled all behaviors linearly, to sum up to 1440 minutes, creating each participant's composition. Then we transformed the compositions into five (i.e., one for each behavior) sets of four isometric log-ratios (ilr). We used the first ilr ( $ilr_1$ ) for each behavior to describe the behavior in relation to all other behaviors in the composition. See Study III for a detailed description of the procedure.

## 4.3 Neuropsychological test battery measuring cognitive function

In Studies I and IV, we applied a neuropsychological test battery to measure cognitive function. The battery was adapted from Jonasson et al. (2017) and consisted of multiple tests [155]. In Study I, single test outcomes were used as dependent variables and related to device-measured movement behaviors. In Study IV, we formed in three domains: executive functions (EF), episodic memory (EM), and processing speed (PS). For an overview of the cognitive tests used in Studies I and IV, please see Figure 5.



Figure 5. Overview of the cognitive test order used in Studies I and IV

In Study IV, Digit symbol [156], 1-back reaction time, and Trail-Making Task A (TMT-A) tested PS. Free recall [157] and word recognition [158] were to test EM. EF was tested using Trail-Making Task B (TMT-B), n-back [159], Stroop color and word test [160], backward digit span, and automated operation span [156].

In Studies I and IV, each cognitive test was unified, and standardized scores (z-scores) were calculated by subtracting the population mean at baseline from the score and dividing it by the population standard deviation at baseline.

### ***Processing speed***

*Digit symbol:* One line containing nine digit-symbol combinations was presented ascending from left to right on the upper half of the screen. A single digit-symbol combination was shown on the lower part of the screen. The task was to identify, as quickly as possible, if the digit-symbol combination on the lower part of the screen was present on the upper screen. If the combination were present, the subject was supposed to press the left arrow on the keyboard, and if the combination could not be found, the subject should press the left keyboard arrow. In each trial, all digit-symbol combinations were randomly changed [156]. The dependent measures were the number of correct answers and the response time on correctly answered trials expressed in seconds.

*Trail-making task A (TMT-A):* The objective was to connect circles containing numbers from 1 to 25 as fast as possible without lifting the pen from the paper [161]. Subjects should connect the numbers as quickly as possible without making mistakes. The dependent measure was the time it took to complete the task expressed in seconds.

### ***Episodic memory***

*Free recall:* A list of 16 nouns was presented to the subject visually [157]. Each word was shown for 3 seconds with an interstimulus interval (ISI) of 1 second. Immediately after the word presentation, subjects were asked to recall as many words as possible and write them on a blank paper in any order. The number of correctly recalled words was the dependent outcome.

*Word recognition:* A list of 30 nouns was visually presented to the subject. The subject was required to encode the words and approximately 25 minutes later recall as many words as possible [158]. During encoding, words were presented for 3 seconds with an ISI of 1 second. During recollection, the subject should indicate if the word was a part of the list originally presented or not with a keypress. The dependent outcome was the number of correctly recalled words.

### ***Executive functions***

*n-back (Updating)*: Subjects performed a computerized version of the n-back task proposed by Kirchner (1958) [159]. The objective was to indicate with a keypress and within 2 seconds from stimulus onset whether the number shown is the one that was presented one stimulus (1-back), two stimuli (2-back), or three (3-back) earlier. Before each trial, all subjects performed a practice trial. Each trial contained a sequence of 20 digits. Each digit was presented for 1.5 seconds with an ISI of 500 milliseconds. The test measures updating, and the dependent outcome is 2-back accuracy and response time on correct answers.

*Trail making B (TMT-B) (Task switching)*: The task was to connect the circles as fast as possible without lifting the pen from the paper [161]. Every other circle contained a number, and every other contained a letter. Subjects should connect all circles alternating between numbers and letters. For example, combine 1 with A, A with 2, 2 with B until all connections are made. Subjects were instructed to do it as fast as possible without making mistakes. The dependent measure was the time it took to complete the task expressed in seconds.

*Stroop color and word test (Inhibition)*: To test interference resistance (inhibition), a modified version of the Stroop color and word test was used [160]. The participants were instructed to say the printed color of the written word and not read the word. This was to be done as fast as possible without making any mistakes. The dependent outcome was the time it took to complete the task expressed in seconds.

*Backward digit span*: A sequence of numbers was presented to be memorized in reverse order. The correct answer to the sequence 3–5–9 is 9–5–3. Numbers were presented one at a time and displayed for 1 s with an ISI of 250 milliseconds. Participants answered by pressing the number panel on the keyboard. Two practice sequences with feedback were given prior to testing. After practice, sequences began at three numbers, and if a correct answer was provided, a number was added to the next sequence, thus increasing the difficulty of the task. Two incorrect answers at the same level of difficulty will stop the test. If a wrong answer was given, the same sequence length was displayed again. If a subject answered incorrectly two times on a sequence length, the test was ended. The dependent outcome was the length of the longest correctly completed sequence. The test is a digitalized version of the backward digit span task in the Wechsler Adult Intelligence Scale (WAIS-R) [156].

*Automated operation span (AOS)*: The objective of this task was to remember a sequence of letters while answering simple mathematical equations with true or false [162]. Four practice rounds on the letter part of the task were performed. Series of two or three letters were shown for 1 second with an ISI of 250 milliseconds. After each sequence, a response screen was presented with 12 boxes containing letters. Participants were supposed to choose the letters that had appeared in the sequence in the correct order. After

practicing the letter task, 15 simple mathematical tasks had to be judged as true or false. When the equations were solved, an answer appeared on the screen. Participants should answer by pressing either true or false. After practicing the math part, a practice session of a combination of letter and math tasks was completed. After each mathematical judgment, a letter was presented for 1 second, followed by a new mathematical equation. This was repeated until all letters in the sequence had been displayed. Then, the answer screen was shown, and the subject had to click the boxes to the corresponding numbers. After selecting the letters on the answer screen, a new block started. Participants were instructed to maintain a rate of at least 85% correct answers on the math tasks to ensure that participants did not skip performing the math tasks. This rate was indicated at the upper right-hand corner of the screen. The dependent measure was the sum of correctly remembered sets multiplied by the respective set size.

## 4.4 Transcranial magnetic stimulation

In Study II, transcranial magnetic stimulation (TMS) was used to assess corticospinal excitability (CSE) and the paired associative stimulation protocol (PAS). For both these purposes, the TMS coil was placed on the contralateral M1 to the dominant hand at a 45° angle to the mid-sagittal plane. We used a four-camera motion system (Qqus 7, Qualisys AB, Gothenburg, Sweden) to standardize the position of the coil. The camera system located reflective markers on the participant's head and the coil in the three-dimensional space. Continuous kinematic data was sampled and transferred to MATLAB (The MathWorks, Inc., USA). The relative distance between the participant's head and the coil were calculated in a MATLAB script. The position of the coil eliciting the most prominent and most consistent MEP was defined as the hotspot, and the position of the coil relative to the head position was saved as a reference point. The minimum TMS stimulator output that resulted in an MEP above 50 $\mu$ V in 5 of 10 stimulations defined the RMT.

### *Assessment of corticospinal excitability (CSE)*

The peak-to-peak amplitude of the MEP as a function of stimulus intensity was used to create a RC consisting of 80 stimulations using intensities in 10% steps from 80% to 170% of RMT. AURC was calculated to assess the CSE. In the present study, we obtained EMG from the APB. All MEPs were normalized to maximal compound muscle action potential ( $M_{\max}$ ) of the APB. Peripheral electrical stimulation was applied to the median nerve through a bipolar electrode montage. The intensity was increased until the maximal M-wave, measured as peak-to-peak, was obtained. When an increase in stimulus intensity did not result in further increases in  $M_{\max}$  an additional 10% increase in intensity was

applied to ensure the maximal M-wave was obtained. SICI was measured using a conditioning stimulation at 80% of RMT and a test stimulation at 140% of RMT with a 3-ms interval between the paired pulses. In random order, ten conditioned pairs of stimulation and ten test stimulations were applied. SICI was calculated as MEP-size of the conditioned paired-pulse relative to the test stimulation.

### ***Paired associative stimulation (PAS)***

The PAS protocol consisted of 180 pairs of peripheral electric and single-pulse TMS stimulations delivered with a frequency of 0.1 Hz. The sensory threshold was defined as the lowest intensity of the peripheral electric stimulus participants could feel. The intensity of the peripheral electric stimulation in PAS was defined as three times above the sensory threshold, and the intensity of the TMS stimulations was 120% of RMT.

## **4.5 Cardiorespiratory fitness**

In all studies, a submaximal bike ergometer test, the Ekblom-Bak test, was used to estimate cardiorespiratory fitness [163, 164]. Participants biked on a cycle ergometer with a pedaling rate of 60 rounds per minute. For the first four minutes, participants biked on a low standardized workload (0.5 kiloponds). For the additional four minutes, participants biked on an individual workload. The workload was based on the exercising history of the participant. The difference in heart rate divided by the difference in workload between the first four minutes and the last four minutes was inserted in the formula presented by Björkman et al. (2016) [163] to estimate relative  $\text{VO}_2 \text{ max}$  ( $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ) in Studies I and II, and both relative and absolute  $\text{VO}_2 \text{ max}$  (L/min) in Studies III and IV.

## **4.6 Workplace intervention**

### ***Theoretical basis and intervention development***

The intervention development in Studies III and IV was guided by an ecological framework of health behavior [142] and an ecological model for SB [143]. The taxonomy of behavior changes was used [144] to translate theoretical components into practical strategies for the interventions. In close dialog with the companies and with experiences and results from the first study in this project, the active components of the different levels were developed. It is advised to investigate needs and possibilities at the different levels for a successful intervention. Our group conducted a study addressing facilitating factors and barriers for reducing SB at work [165]. The most-reported barrier was that sitting is a habit and that standing is uncomfortable and tiring were frequently reported. Office workers proposed walking and standing meetings and possibilities and reminders for

breaks as facilitators [165]. These findings guided the theoretical formation of the intervention, and we incorporated these findings as components.

### ***The ecological model for interventions aiming at changing sedentary behavior***

As previously described, an ecological approach to behavior changes suggests that behavior should be influenced on multiple levels, including individual, social, organizational, environmental, and policy [142], to be effective. The modified ecological model of SB specifies that the behavior setting, which is the physical and social context where the SB occurs, is central in detecting determinants of SB. The environment influences this behavior setting (e.g., the office, where the possibility for not sitting is low) and the social context (e.g., meetings where standing is uncommon and therefore not socially accepted) [143].

### ***Taxonomy of behavior change techniques***

Multiple behavior change techniques have been used to change behavior (e.g., increasing PA or reducing SB). The taxonomy of behavior change techniques consensually by Michie et al. (2013) extracts the active components in different behavior change techniques and structures them into a hierarchy that helps guide interventions to be effective. We will use this taxonomy to extract effective intervention components from other behavior change techniques [144].

### ***Intervention design***

Both interventions consisted of motivational counseling based on cognitive-behavioral therapy and feedback on the specific behavior at the individual level. At the environmental level, participants in the PA intervention got access to a commercial gym and could attend exercise sessions and lunch walks organized by team leaders. Participants in the SB intervention were exposed to the implementation of standing and walking meetings arranged by team leaders. At the organizational level, team leaders encouraged participants to increase PA or reduce SB and were accountable for implementing the identified facilitators (i.e., walking and standing meetings) [151].

Studies have shown that individuals may compensate when changing behavior in one context by increasing unwanted behavior in other contexts. Therefore, this intervention aimed at changing both leisure time and work time behavior [166].

## 4.7 Statistical analyses

In Study I, associations between measures of PA and SB were tested using multiple linear regression analysis performed with IBM SPSS statistics version 24 (IBM, Armonk, NY, USA). Standardized beta values and 99% confidence intervals, adjusting all models for age, gender, and education, were used. Analysis of movement behavior measurements was done with and without adjustment for VO<sub>2</sub> max. Models containing bout measures of PA and SB were additionally adjusted for wear time.

In addition, regression analyses were performed on the median split of VO<sub>2</sub> max in the two cognitive tests, Stroop and Word Recognition. Separate models for participants below or above and the median VO<sub>2</sub> max were carried out. The threshold for statistical significance was set at  $p < 0.01$  to adjust for multiple testing.

All statistical analyses in Studies II, III, and IV were conducted in R studio (version 4.0.2) [167]. In Study II, linear mixed models were used to compare changes in CSE over the course of the experiment between each of the three experimental conditions. We fitted models using the lme4 package [168], and preplanned pair-wise comparisons were calculated using the Multcomp package [169]. AURC was the outcome variable. Time (4 levels) and condition (3 levels) were entered into the linear mixed models as fixed effects and subject as a random effect. Bivariate correlations were performed to explore the relationship between changes in AURC and SICI. The threshold for statistical significance was set at  $p < 0.05$ .

In Study III, linear mixed models were used to test the effect of the two workplace interventions in changing movement behavior and cardiorespiratory fitness. Moreover, we investigated domain-specific changes in movement behavior during work and leisure time separately. The first *ilr* (*ilr*<sub>1</sub>) in each behavior category, representing the time spent in that specific behavior in relation to time spent in all other behavior categories, was used as the outcome variable in linear mixed models. Both relative ( $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ) and absolute (L/min) VO<sub>2</sub> max for cardiorespiratory fitness were used as outcome variables. Time and group and the interaction were entered as fixed effects. In addition, subject and cluster were entered as random effects.

In Study IV, we defined four latent constructs, PS, EM, and EF. We first tried to fit a latent change score model for each identified latent cognitive construct as suggested by Kievit et al. (2018), using the Lavaan package in R Studio. We tested measurement invariance across time and group [170-172] stepwise by constraining factor loadings (metric), intercepts (scalar), and residuals (strict) to be equal between time points, comparing

the models using chi-square tests. We found some level of invariance. Metric level measurement invariance was identified for time and strict level for the group. However, we identified severe Heywood cases for EF, and models for EM and PS failed to converge. Because of these problems, we applied conventional cognitive composite scores of t-scores as dependent variables to the models. We calculated t-scores by multiplying the z-score from each test by ten and adding 50. Each cognitive domain score consisted of the sum of all tests in that domain divided by the number of tests. We constructed linear mixed models containing intervention groups, time, and interaction between group and time to test the RCT effect as fixed effects. In addition, subject and cluster were entered as random effects. Moreover, all models included age, sex, and education as covariates.

To investigate whether changes in movement behaviors were related to cognitive function changes, we added a two-way interaction between changes in behavior (i.e., cardiorespiratory fitness or movement behavior) and time to the linear mixed model.

Examination of how cardiorespiratory fitness, age, and sex moderated the association between movement behavior changes and cognitive function changes, we added a three-way interaction between time, change in movement behavior, and the moderators to the linear mixed model.

## 5. Results

### 5.1 Study I

Multiple linear regressions based on 334 participants revealed that the percentage of time spent in MVPA or SB was not related to any assessed cognitive functions. See Figure 6 for standardized beta values from the multiple linear regressions adjusted for relative  $\text{VO}_2$  max, age, sex, and education.

When analyzing the bouts measures of MVPA and SB, total time in both MVPA and SB bouts were not associated with any cognitive test. However, the average length of MVPA bouts was associated with better performance on the Stroop test. However, this association was turned into a tendency when the models were adjusted for fitness.

Additionally, we divided the sample into high and low cardiorespiratory fitness based on relative  $\text{VO}_2$  max. Figure 7 shows the standardized beta values for the models for bout measures. The average length of MVPA bouts was associated with better Stroop and worse Word recognition performance among the low-fit and high-fit participants, respectively. The percentage of time spent in MVPA or SB was not associated with any cognitive outcome in either fitness group.

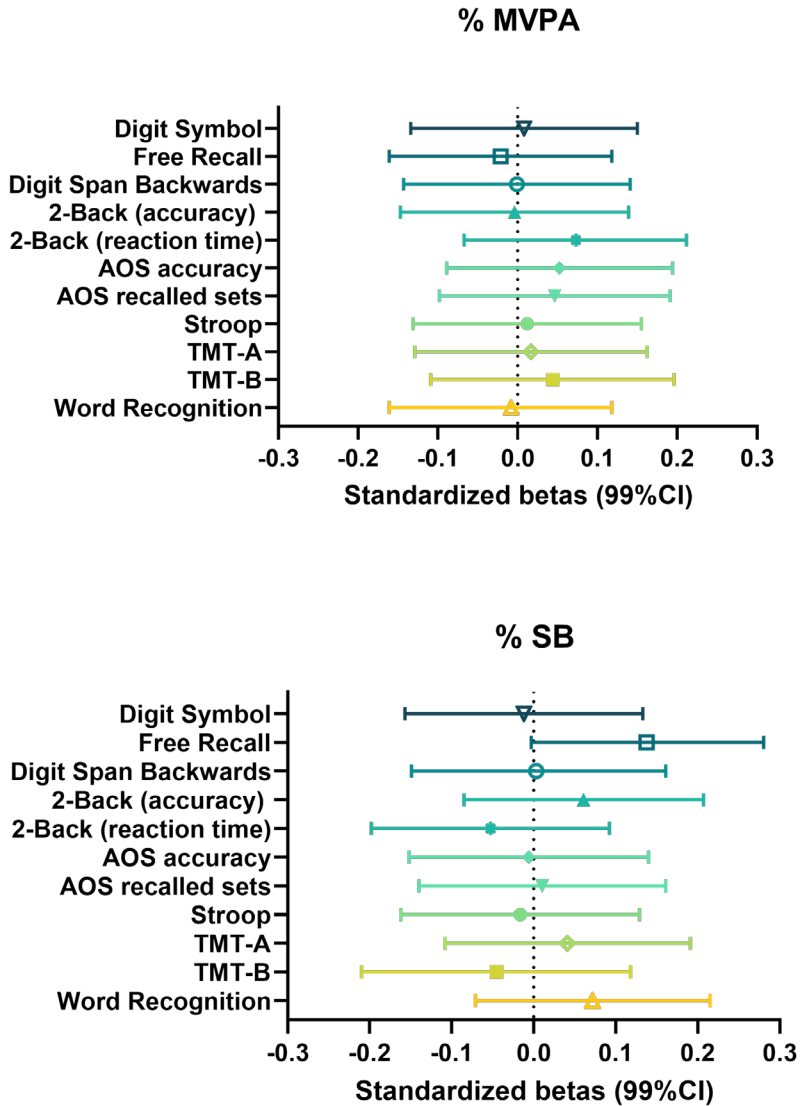


Figure 6. Multiple linear regression models with cognition as dependent variable and % moderate to vigorous physical activity (%MVPA) and sedentary behavior (%SB) as predictors. Models are adjusted for age, gender, and education and  $VO_2$  max. Standardized beta coefficients ( $\beta$ ) and 99% confidence intervals (99% CI) are given for every cognitive test. TMT-B = trail making task B. TMT-A = trail making task A. AOS = automated operation span.

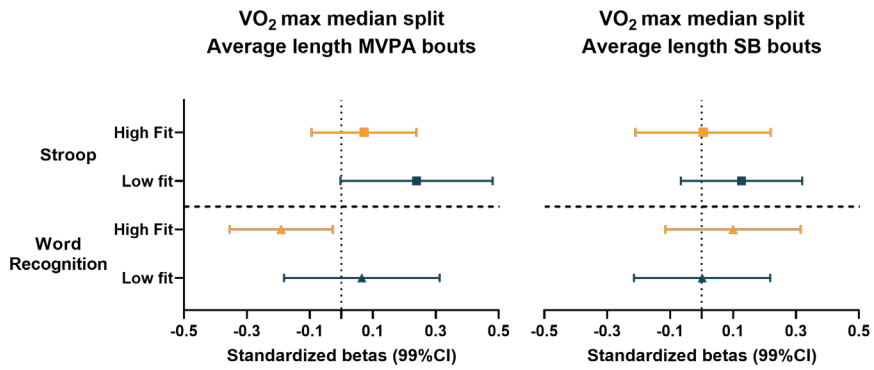


Figure 7. Multiple linear regression models with Stroop and Word recognition as dependent variables and the average bout length of moderate to vigorous physical activity (MVPA) and sedentary behavior (SB) as predictors. Models are adjusted for age, gender, education, and wear time. Standardized beta coefficients ( $\beta$ ) and 99% confidence interval (99% CI).

## 5.2 Study II

The linear mixed model showed that changes in AURC did not differ between conditions. Pre-planned pairwise comparisons showed that CSE increased from Pre to Post PAS 30' within the breaking up sitting condition (FPA) only. Figure 8 displays changes in AURC for each of the experimental conditions.

There was a main effect of time, but not condition or interaction between time and condition for SICI. Multiple comparisons on time significantly decreased from baseline to 5-min post-PAS. However, no significant changes within any condition were seen (See Figure 9). Baseline values or changes in AURC and SICI were not associated.

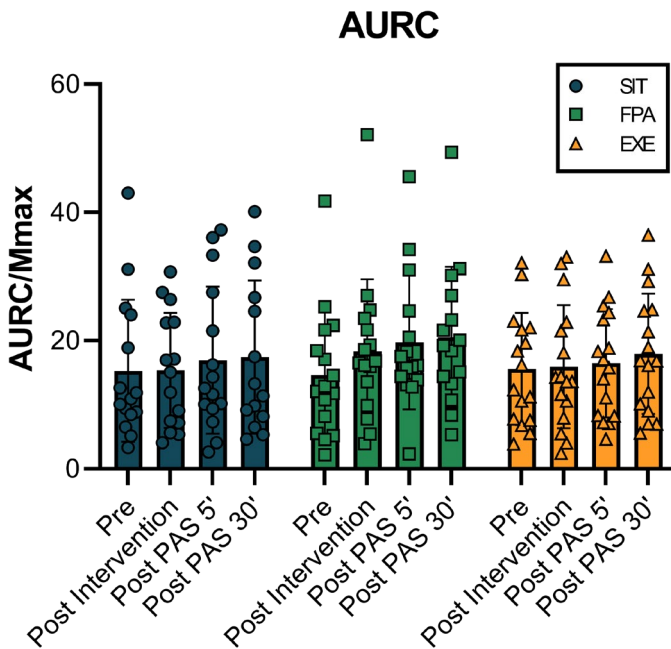


Figure 8—Area under the recruitment curve (AURC) for each condition. SIT (blue) = sitting condition marked with  $\circ$ . FPA (green) = frequent short bout of physical activity condition marked with  $\square$ . EXE (orange) = exercise condition marked with  $\Delta$ . Each symbol illustrates the value of one subject. Error bars represent the standard deviation.

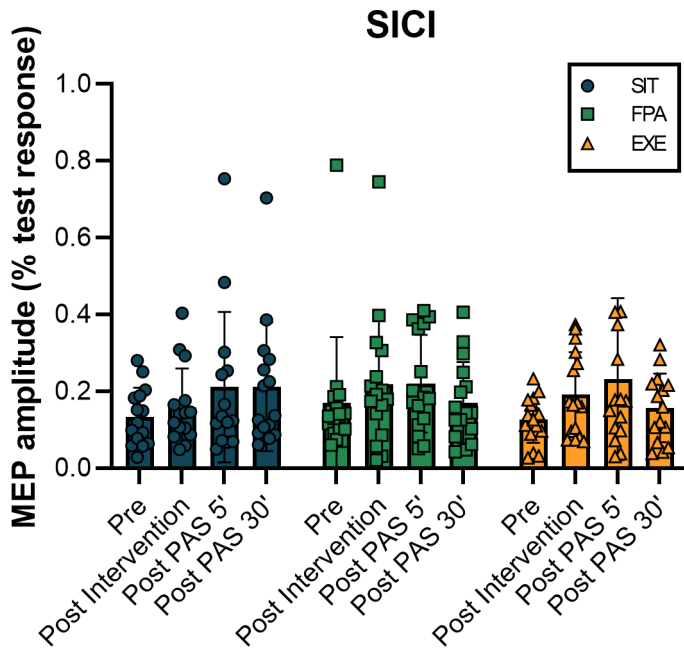


Figure 9. Short interval intracortical inhibition (SICI) for each condition. SIT (blue) = sitting condition marked with  $\circ$ . FPA (green) = frequent short bout of physical activity condition marked with  $\square$ . EXE (orange) = exercise condition marked with  $\Delta$ . Each symbol illustrates the value of one subject. Error bars represents the mean standard deviation

## 5.3 Study III

In Study III, all three analytic samples were very similar. Participants were on average 43 ( $\pm 8$ ) years old, approximately one-quarter were male, with 15 ( $\pm 2$ ) years of education, and had a BMI of 25.2 ( $\pm 4.2$ ), as displayed in Table 2.

*Table 2. Participants' baseline characteristics for the three analytic samples*

	<b>Demographic Characteristics</b>	<b>All Participants n = 158</b>	<b>iPA n = 62</b>	<b>iSED n = 39</b>	<b>Control Group n = 57</b>
Complete cases for movement behavior analysis	Age, years (mean (SD))	43 (8)	41 (9)	42 (8)	45 (7) <sup>a</sup>
	Sex, men (n (%))	36 (23)	13 (21)	10 (26)	13 (23)
	Education, years (mean (SD))	15 (2)	15 (2)	15 (2)	15 (2)
	BMI, kg/m <sup>2</sup> (mean (SD))	25.2 (4.2)	24.9 (4.0)	24.7 (3.7)	26.2 (4.5) <sup>b</sup>
		<b>All Participants n = 150</b>	<b>iPA n = 57</b>	<b>iSED n = 37</b>	<b>Control Group n = 56</b>
Complete cases for domain-specific movement behavior analysis	Age, years (mean (SD))	43 (8)	41 (9)	41 (8)	45 (7) <sup>a</sup>
	Sex, men (n (%))	37 (25)	13 (23)	10 (27)	10 (25)
	Education, years (mean (SD))	15 (2)	15 (2)	15 (2)	15 (2)
	BMI, kg/m <sup>2</sup> (mean (SD))	25.2 (4.2)	24.9 (4.1)	24.0 (2.7)	26.2 (4.5) <sup>b</sup>
		<b>All Participants n = 151</b>	<b>iPA n = 60</b>	<b>iSED n = 34</b>	<b>Control Group n = 57</b>
Complete cases for cardiorespiratory fitness analysis	Age, years (mean (SD))	43 (8)	42 (9)	42 (8)	45 (8)
	Sex, men (n (%))	39 (26)	13 (22)	11 (32)	15 (26)
	Education, years (mean (SD))	15 (2)	15 (2)	15 (2)	15 (2)
	BMI, kg/m <sup>2</sup> (mean (SD))	25.2 (4.1)	24.7 (3.6)	24.2 (3.9)	26.3 (4.5) <sup>a,b</sup>

There were no baseline differences for movement behavior in total time or irrespective of the domain (i.e., work vs. leisure). In addition, we found no intervention effect for any of the movement behavior for both total time and domain-specific analyses as visualized in Figure 10. Domain-specific movement behaviors are reported in Table 3.

*Table 3. Baseline and 6-month follow-up values for minutes spent in domain-specific 24-h movement behaviors (compositional mean and % of 24-h in parentheses)*

	<b>All Participants n = 150</b>		<b>iPA n = 57</b>		<b>iSED n = 37</b>		<b>Control Group n = 56</b>	
	<b>Baseline</b>	<b>Follow-up</b>	<b>Baseline</b>	<b>Follow-up</b>	<b>Baseline</b>	<b>Follow-up</b>	<b>Baseline</b>	<b>Follow-up</b>
Leisure VPA	6 (0.4)	5 (0.4)	6 (0.4)	5 (0.4)	7 (0.5)	6 (0.4)	6 (0.4)	5 (0.4)
Leisure MPA	61 (4.2)	60 (4.2)	63 (4.3)	58 (4.0)	61 (4.2)	65 (4.5)	60 (4.2)	59 (4.1)
Leisure LPA	70 (4.8)	68 (4.8)	71 (4.9)	68 (4.7)	69 (4.8)	69 (4.8)	70 (4.9)	69 (4.8)
Leisure SED	421 (29.2)	418 (29.0)	419 (29.1)	415 (28.8)	430 (29.8)	420 (29.2)	417 (29.0)	421 (29.2)
Work VPA	1 (0.05)	1 (0.07)	1 (0.06)	1 (0.09)	1 (0.06)	1 (0.04)	1 (0.04)	1 (0.04)
Work MPA	33 (2.3)	34 (2.4)	33 (2.3)	36 (2.5)	33 (2.3)	34 (2.4)	32 (2.2)	33 (2.3)
Work LPA	33 (2.3)	34 (2.4)	31 (2.1)	33 (2.3)	34 (2.4)	35 (2.4)	33 (2.3)	35 (2.4)
Work SED	399 (27.7)	399 (27.7)	400 (27.8)	397 (27.6)	401 (27.8)	406 (28.2)	398 (27.7)	399 (28.9)
Time in bed	417 (28.9)	420 (29.2)	422 (29.3)	423 (29.4)	414 (28.7)	417 (28.9)	414 (28.7)	418 (29.0)

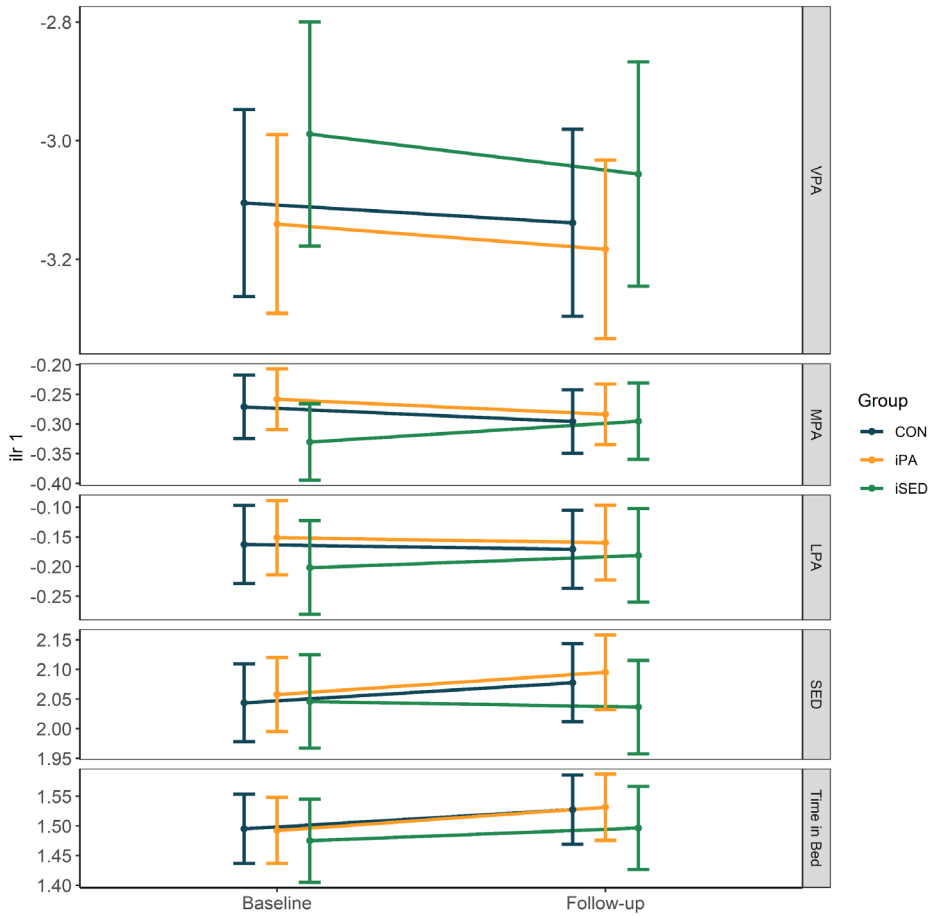
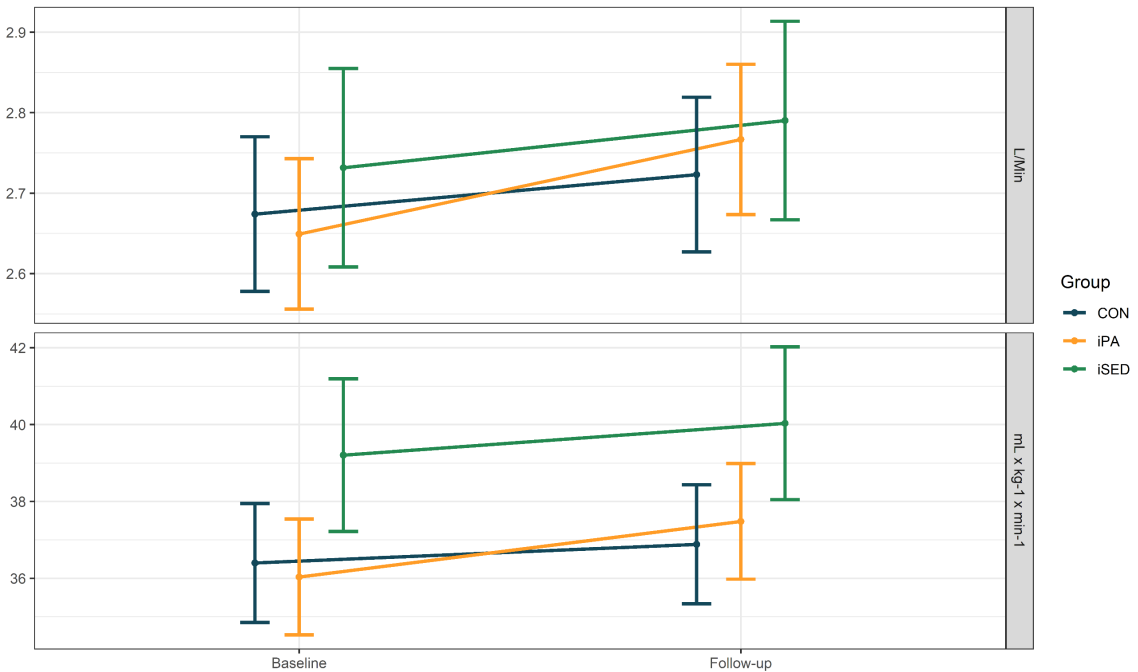


Figure 10. Marginal means (with 95% CI) for each movement behavior, expressed in terms of  $ilr_1$  (time spent in that behavior relative to time spent in all other behaviors) at baseline and 6-month follow-up. Values were estimated based on the results in the linear mixed models. VPA: vigorous-intensity physical activity, MPA: moderate-intensity physical activity, LPA: light-intensity physical activity, SED: sedentary behavior. iPA: Intervention group focused on increasing physical activity, iSED: Intervention group focused on reducing sedentary behavior, CON: Control group.

In the subsequent analysis, the effect of the intervention on cardiorespiratory fitness was considered. At baseline, cardiorespiratory fitness was higher for participants in the iSED group as visualized in Figure 11, there were no significant intervention effects on cardiorespiratory fitness. However, cardiorespiratory fitness increased significantly only within the iPA group. Table 4 shows values at baseline and follow-up.

*Table 4. Baseline and 6-month follow-up values for cardiorespiratory fitness (mean (SD)).*

Cardiorespiratory Fitness	All Participants <i>n</i> = 151		iPA <i>n</i> = 60		iSED <i>n</i> = 34		Control Group <i>n</i> = 57	
	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up
	mL·kg <sup>-1</sup> ·min <sup>-1</sup>	36.9 (7.4)	37.8 (7.4)	36.6 (7.0)	37.8 (7.2)	39.8 (7.5)	40.7 (7.2)	35.5 (7.5)
L/min	2.7 (0.60)	2.8 (0.6)	2.6 (0.6)	2.8 (0.6)	2.8 (0.6)	2.9 (0.6)	2.6 (0.6)	2.7 (0.6)



*Figure 11—Marginal means (with 95% CI) for cardiorespiratory fitness, expressed as mL·kg<sup>-1</sup>·min<sup>-1</sup> (bottom) and as L/min (top), at baseline and 6-month follow-up. Values were estimated based on the linear mixed models.*

## 5.4 Study IV

In Study IV, the potential effects of the intervention on cognitive performance were investigated. Linear mixed models showed that neither workplace intervention changed cognitive performance in any domains relative to the control intervention, see Table 5.

In the subsequent analysis, the effect of time on cognitive performance was considered in each intervention group separately, see Table 6. All groups improved their performance in all cognitive domains from pre-test to post-test.

Figure 12 shows changes in cognitive performance from baseline to follow-up.

Table 5. Differences in change from baseline to 6-month follow-up between groups for the cognitive domains

<i>Between-group differences</i>	<b>iPA vs. control</b> <i>Estimate (95%CI)</i>	<b>iSED vs. control</b> <i>Estimate (95%CI)</i>	<b>iPA vs. iSED</b> <i>Estimate (95%CI)</i>
Executive function	-0.811 (-2.83 – 1.20)	-0.959 (-3.33 – 1.41)	0.148 (-2.19 – 2.49)
Episodic memory	-1.205 (-4.86 – 2.45)	0.693 (-3.59 – 4.98)	-1.897 (-6.14 – 2.35)
Processing speed	1.506 (-0.40 – 3.41)	1.819 (-0.45 – 4.09)	-0.313 (-2.55 – 1.93)
Global Cognition	-0.349 (-1.80 – 1.10)	-0.015 (-1.74 – 1.71)	-0.334 (-2.03 – 1.36)

*Estimates for the time x group interaction with 95% confidence intervals from the linear mixed models. Models contained fixed effects of time, group, age, sex, and education. Cluster and subject were entered as random effects. Cognitive domains consisted of t-composite scores. iPA =intervention group to increase moderate to vigorous physical activity; iSED=intervention group to reduce sedentary behavior.*

Table 6. Differences in change from baseline to 6-month follow-up within each group for the cognitive domains

<i>Change within the intervention groups</i>	<b>iPA</b> <i>Estimate (95%CI)</i>	<b>iSED</b> <i>Estimate (95%CI)</i>	<b>Control</b> <i>Estimate (95%CI)</i>
Executive function	1.892 (0.47 – 3.32)*	1.743 (-0.17 – 3.66)	2.703 (1.22 – 4.18)*
Episodic memory	4.460 (1.86 – 7.06)*	6.358 (2.89 – 9.82)*	5.665 (2.99 – 8.34)*
Processing speed	3.284 (1.93 – 4.63)*	3.597 (1.75 – 5.44)*	1.778 (0.38 – 3.18)*
Global Cognition	2.776 (1.75 – 3.80)*	3.110 (1.71 – 4.51)*	3.125 (2.06 – 4.19)*

*Estimates with 95% confidence intervals from the linear mixed models. Models contained time, age, sex, and education as fixed effects. Models considered random effects of subject and cluster. Cognitive domains consisted of t-composite scores. \* Significantly changed from baseline to 6-months follow-up. iPA =intervention group to increase moderate to vigorous physical activity; iSED=intervention group to reduce sedentary behavior.*

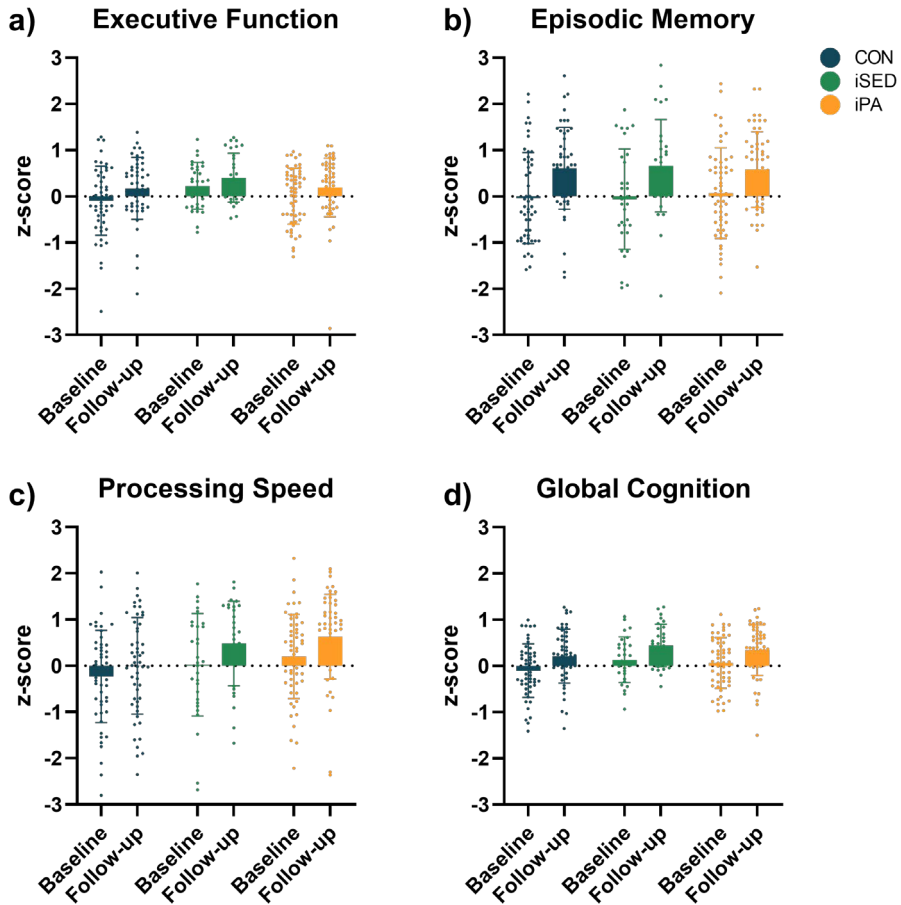


Figure 12. Cognitive performance (z-scores) from baseline to 6-month follow-up for the three groups, including individual data. iPA =intervention group to increase moderate to vigorous physical activity; iSED=intervention group to reduce sedentary behavior. CON = wait-list control. a) Executive Function, b) Episodic Memory, c) Processing Speed, and d) Global Cognition. Error bars are displayed as standard deviation.

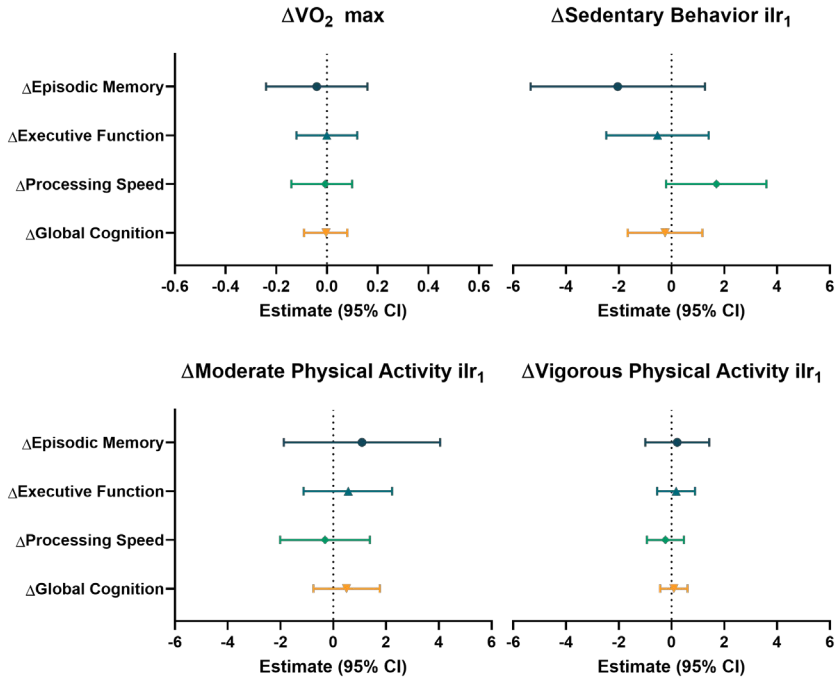


Figure 13. Linear mixed model estimates of the two-way interactions between changes in  $VO_2$  max or  $ilr_1$  movement behavior (i.e.,  $VO_2$  max, sedentary behavior, moderate, and vigorous physical activity) and changes in cognitive domain (i.e., Episodic memory, Executive function and Processing speed and global cognition) with 95% confidence interval.

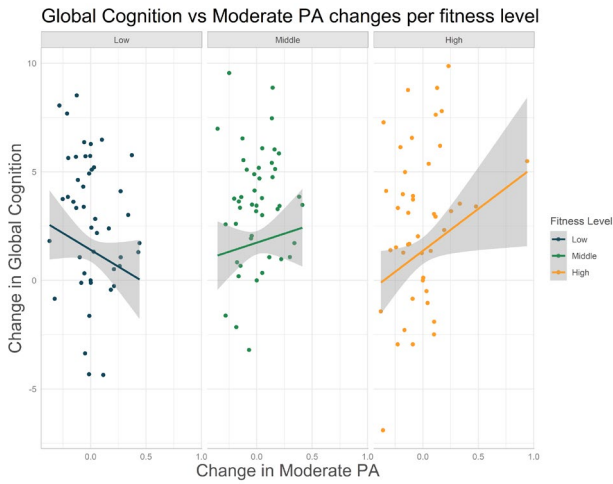
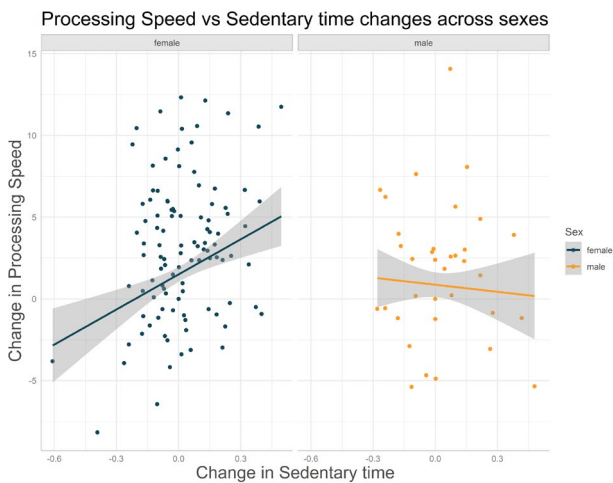
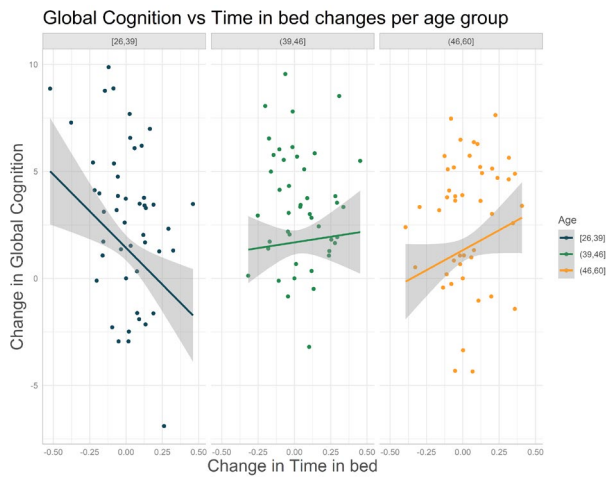


Figure 14. Visualization of the significant moderators (i.e., fitness, age, and sex) of the association between changes in movement behavior  $ilr_1$  and changes in cognitive domain. For visualization purposes cardiorespiratory fitness and age are divided into tertials.



Changes in fitness or any movement behavior did not predict changes in cognitive functions across groups. Estimates from the change-change model are visualized in Figure 13.

Our explorative moderation analysis found that sex, age, and cardiorespiratory fitness significantly moderated some relations between movement behaviors and cognition changes (see Figure 14). Baseline cardiorespiratory fitness moderated the association between changes in  $ilr_1$  MPA and changes in Global cognition, such as having higher cardiorespiratory fitness was associated with a more positive association between changes in  $ilr_1$  MPA and changes in Global cognition. Age moderated the association between changes in  $ilr_1$  Time in bed and changes in EF and Global cognition, such as increasing age was associated with a more positive association between changes in  $ilr_1$  Time in bed and EF and Global cognition changes. Age did not moderate any other change on change association. Sex moderated the relationship between changes in  $ilr_1$  SED and changes in PS, such as being male versus female was associated with a less positive relation between  $ilr_1$  SED and PS changes.

## 6. Discussion

This thesis investigated how movement behaviors relate to and influences office workers' cognitive functions and corticospinal neuroplasticity. Data from three sub-projects within a larger research project formed the basis for this thesis: a cross-sectional study (Study I), an acute experimental intervention (Study II), and an ecological cluster-randomized multi-component workplace intervention (Studies III and IV).

The main findings of the thesis are:

- I. Study I found no cross-sectional relationship between performance at cognitive tests and the percentage of time spent in MVPA or SB. However, in a follow-up analysis, average daily minutes in prolonged MVPA bouts were found to be related to better EF performance for low-fit participants. In contrast, prolonged MVPA bouts related to worse performance on EM for high-fit participants.
- II. Study II showed that neither a single 25 min bout of moderate-intensity aerobic exercise nor frequent breaks of simple resistance activities altered the potential for inducing long-term potentiation-like plasticity in the primary motor cortex using paired associative stimulation relative to prolonged sitting. However, exploratory analyses showed that frequent breaks of simple resistance exercises increased corticospinal excitability from baseline to 30 min after paired associative stimulation, whereas aerobic exercise and uninterrupted sitting did not.
- III. Study III found no intervention effects of the two ecological multi-level cluster-randomized workplace interventions aiming to reduce SB and increase PA, respectively, on cardiorespiratory fitness or any movement behaviors in total or when work and leisure time were investigated separately.
- IV. Study VI found no evidence for differential cognitive change following the experimental interventions relative to the control intervention in any investigated domains. Changes in cardiorespiratory fitness and any movement behavior did not predict changes in cognitive functions. Follow-up analyses revealed that higher cardiorespiratory fitness was related to a more positive association between changes in MPA and global cognition. The relationship between changes in time in bed and changes in both EF and global cognition was moderated by age, such that a more positive relation was seen with increasing age, whereas a less positive association was seen between changes in SB and PS for men vs. women.

## 6.1 Physical activity, sedentary behavior, and cognitive functions in healthy office workers

Based on the findings in Study I, the device-measured daily percentage of time spent in MVPA or SB was not associated with performance in any of the cognitive tests. Studies III and IV found that the two workplace interventions were ineffective in changing either movement behavior or cognitive functions on a group level and that there was no association between changes in daily movement behavior and change in cognitive functions in Study IV.

These results imply that cross-sectional associations and longitudinal change-change associations between PA and SB and cognitive functions may be weak or non-existing in a physically active middle-aged office worker population.

Thus, this thesis adds to the sparse and conflicting evidence on device-based movement behavior and cognitive functions in middle-aged adults. More time in device-measured MVPA has been associated with cognition in some studies [70, 71], while others support our findings and fail to find associations [72, 73]. Likewise, studies examining the association between device-measured SB and cognitive functions have shown mixed results. While some studies support our findings and show no association [73, 75-77], others reveal a positive association [70, 71], suggesting that more SB is favorable for cognitive functions. Collectively, these results indicate a highly complex relationship between movement behaviors and cognitive functions.

One reason for the conflicting findings and the null finding in this thesis could be that device-measured PA and SB do not capture parameters of relevance to cognitive health. Cardiorespiratory fitness has been more consistently associated with better cognitive functions in children [173, 174], adolescents [175], young adults [176], and older adults [177]. Although PA is related to cardiorespiratory fitness [178], PA reflects a more complex behavior pattern that may have a different relationship to cognitive functions. Cardiorespiratory fitness level partly depends on genetics [179], long-term PA, and exercise habits [178] and is, therefore, a more stable measure. In comparison, device-based measures of PA performed over a week give only a snapshot of an individual's PA behavior and can be modified to enhance cardiorespiratory fitness. Our research group showed that in an almost identical sample drawn from the same population, cardiorespiratory fitness up to 44 and 43 mL·kg<sup>-1</sup>·min<sup>-1</sup> was positively related to performance on tests examining EF and EM, respectively [180], indicating a non-linear relationship. Still, we failed to find such a linear association between device-measured % in MVPA and cognitive function in Study I, indicating that PA and cardiorespiratory fitness have distinct associations to cognition. Moreover, changes in cardiorespiratory fitness or movement

behaviors did not relate to change in cognitive function at an interindividual level in Study IV. However, as I will discuss in section 6.3, the two workplace interventions were ineffective in changing movement behavior and therefore no change in cardiorespiratory fitness was found on a group level.

A protective factor for the potentially adverse effect of SB could be the high level of PA of participants in Studies I and IV. When we first started the larger research project, epidemiological evidence suggested that SB increased the risk for all-cause mortality and cardiovascular diseases [181]. Since then, epidemiological evidence has shown that a high PA level may counteract the adverse health effects of extensive SB [60]. Although less studied, this may also be evident for cognitive functions. Almost all Studies I and IV participants adhered to the PA guidelines' lowest bound, recommending more than 150 min/week of PA for overall health [182]. In Studies I and IV, participants spent on average approximately 7% per day in MVPA, which is high compared to other Swedish populations. In examining PA levels in a Swedish cohort of 851 individuals, Dohrn et al. (2018) reported 3.6% of MVPA per day among the included participants [183]. Thus, our participants' high PA level may counteract the adverse effect of extensive sitting, weakening the expected association between SB and cognitive function to undetectable levels. Our participants' high PA may also have influenced the expected association between MVPA and cognitive function. Lower variability in PA or a generally weaker association at the higher end of the PA continuum could both have hindered an association from emerging in our study. We cannot infer causality from this finding because of the cross-sectional design of Study I and the ineffectiveness of Study IV in experimentally modulating movement behavior. However, the results indicate that an association, cross-sectional or longitudinal, of SB and MVPA with cognitive functions among office workers with high PA levels is not very likely or at least minimal.

### ***Moderation of cardiorespiratory fitness, age, and sex***

The effect of movement behaviors on cognitive functions is suggested to be moderated, for example, by cardiorespiratory fitness level, age, and sex [68]. Using a median split, Study I investigated if the cross-sectional association between MVPA, SB, and cognitive functions depended on cardiorespiratory fitness level. Study IV examined the moderating effect of cardiorespiratory fitness (as a continuous variable), age, and sex on the association between changes in movement behaviors and changes in cognitive functions.

When we examined the association between % of time in MVPA or SB and cognitive functions in Study I, no relationship was found regardless of fitness level. However, in the subsequent analyses with measures including prolonged time in MVPA or SB (i.e., bout measures), we found some weak support for that the association is moderated by

fitness level. Longer MVPA bouts were favorably associated with one EF test for low-fit individuals and unfavorably associated with an EM test for high-fit individuals. These findings, therefore, suggest that the relationship between device-measured PA and cognitive functions may be different for individuals with high and low cardiorespiratory fitness.

Longer bouts of MVPA have previously been associated with successful aging, defined as good cognitive, motor, respiratory function, and the absence of mental health problems and major chronic diseases in older adults [184]. The physiological demands of spending more time in MVPA bouts may be relatively higher in low fit compared to high fit individuals, inducing more favorable cardiovascular and cognitive effects. Thus, the positive association of MVPA and EF performance for low-fit individuals demonstrated in Study I might reflect the increased physiological demand of spending more time in MVPA in this group. The finding that longer MVPA bouts in high-fit individuals were associated with worse EM performance was unexpected but may reflect an inverted U-shaped relationship, where the physiological demand of spending more time in MVPA for individuals who already have high fitness may be negative for EM performance. Considering these results, further elucidation of the influence of fitness on the association between MVPA and cognitive functions, using individual fitness levels derived cut-points, could be interesting.

It is important to state that we cannot infer causality from these findings of Study I, and the explorative nature of these analyses should lead to careful interpretation. In Study I, we conducted a total of 44 linear regression models, not including the subgroup analyses. Models for the 11 cognitive outcomes were carried out for all four movement behavior outcomes. Although a stricter level for statistical significance ( $\alpha=0.01$ ) was used to account for multiple testing, there is still a possibility that the significant associations represent Type I errors.

In addition, there are known limitations with the median split. First and foremost, when dichotomizing a continuous variable, the information contained in the variable is drastically reduced, as it now only contains two possible values. Second, since the median split is entirely data-driven, it is not a dichotomization method that is grounded in the theory of previous findings. Whilst the median split is often used for communicating public health messages in epidemiology, treating cardiorespiratory fitness as a continuous moderator for the analyses in Study I would have been preferable.

In Study IV, the association between MPA and global cognition changes was moderated by fitness level at baseline, as reflected in a more positive association between MPA and global cognition for higher levels of cardiorespiratory fitness. These findings may suggest that individuals with higher baseline fitness who managed to increase their daily time spent in MPA, independent of the intervention, exhibited greater improvements in

overall cognitive function relative to individuals with lower fitness. Cardiovascular risk factors may be relevant for the interpretation of these findings. In a recent 6-month randomized controlled trial, a cardiovascular risk score moderated the effect of aerobic exercise on EF in a 6-month randomized controlled trial, with individuals with low cardiovascular risk scores showing enhanced EF in response to exercise compared to individuals with high-risk scores [185]. Thus, good cardiovascular health may be a prerequisite for assimilating PA's effect on cognitive health. It should be noted, however, that the moderator analyses in Study I were not consistent with the account, suggesting that the role of fitness as a moderator of the association between PA and cognition may differ for cross-sectional and longitudinal change-change associations.

In Study IV, we also found that age moderated the association between changes in time in bed and changes in EF and global cognition. A more positive association between time in bed and EF and global cognition was seen at higher ages. These findings suggest that increases in time in bed were more closely associated with improvement in EF and global cognition for older compared to younger participants in our middle-aged study sample. Interestingly, age did not moderate any other association between movement behavior and changes in cognitive functions in Study IV. It, therefore, appears that for older active office workers, achievable changes in time spent in bed are more critical for global cognition than achievable changes in PA and SB measures.

It is well established that sleep is essential for memory encoding and consolidation processes [186], and cross-sectional evidence suggests that there is a U-shape between sleep duration and mental health, general health [187], and cognitive functions [188], with both short and long sleep durations are related to worse outcomes. In addition, the probability of being a poor sleeper increases with age [187]. Thus, an interpretation of the findings could be that as individuals get older, increasing time in bed, and presumably sleep duration is becoming increasingly important for cognitive functions. However, it should be noted that our sample was relatively young and with time spent in bed within the recommended range. Furthermore, we used self-reported time in bed as a proxy for sleep, which complicates the interpretation of the results. It is possible that people engaged in cognitively stimulating activities while spending time in bed, such as reading or listening to audiobooks.

Age was not found to moderate any other association between movement behavior changes and cognitive changes in Study IV.

Effects of structured aerobic exercise interventions on cognitive functions have been shown to differ between sexes, but with conflicting results [99, 102, 103]. We did find a moderating effect of sex on the association between SB and PS. We found that the association between SB and PS was less positive for males than for females, meaning that

males who increased SB had smaller PS improvements than women who increased SB. More SB has previously been associated with better cognitive functions [70, 71], with a proposed dependence on the context in which SB takes place [77]. Namely, increasing SB in a cognitive stimulating context (e.g., reading) relative to a non-stimulating context (e.g., watching TV) has been reasoned to benefit some cognitive functions [78]. However, the reason for the moderating effect of age in this context remains unclear.

Taken together, the moderation analyses in Study I and Study IV indicates that fitness, age, and sex may influence associations between movement behavior and cognitive function in middle-aged office workers. However, the moderating effects in Study I and Study IV were not consistent and resulted from exploratory analyses, which calls for caution in their interpretation. Future research should continue to investigate the role of these and other moderators to identify for whom movement behavior interventions may be particularly effective.

## 6.2 Aerobic exercise and breaking up sitting for improved neuroplasticity

In Study II, we found that neither breaks in sitting nor a bout of aerobic exercise altered the potential to induce LTP-like neuroplasticity in the primary motor cortex using a paired associative stimulation (PAS) protocol compared to prolonged sitting. However, our pre-planned pairwise comparisons revealed that only in the condition with breaks in sitting did excitability increase significantly from baseline (Pre) to 30 minutes after the PAS protocol. This provides some indication that breaking up prolonged sitting is indeed associated with increased corticospinal excitability but also emphasizes that this increase in excitability did not differ sufficiently from the increase in the other interventions to be detected as an interaction effect.

Breaking up sitting has previously been shown to enhance cognitive performance [88, 89], and changes in neuroplastic processes have been proposed as a possible mechanism. Whilst Study II did not involve any cognitive measures, the findings provide some weak support for that breaking up prolonged sitting is associated with increases in corticospinal neuroplasticity.

However, the increased excitability within the interrupted sitting condition may also be explained by an indirect effect, such as alterations in attentional resources. For example, the response to PAS has been shown to be modulated by attention [189], and intermittent bouts of PA in a simulated workplace can improve working memory measures that depend on attentional resources [36]. Thus, enhanced attention could account for the

increase in PAS-response in the interrupted sitting condition. Participants were instructed to count stimulations and focus on the hand and the stimulus during the protocol, but we did not obtain any measure of attention. It would be interesting to see whether the attentional focus could account for some of the variances between conditions. Nevertheless, changes in excitability may not be due to PAS alone because the significant increases were only seen from baseline (Pre) to 30 minutes after PAS.

Contrary to previous research, a single bout of aerobic exercise did not alter CSE. Both acute [115, 116, 127] and long-term [126] PA have been found to increase CSE in response to PAS in young populations. The older age group investigated in this study may partly explain this discrepancy with previous research in young adults. PAS-induced excitability is furthermore shown to be reduced as a function of age [190, 191]. Nevertheless, we found an effect of time that might indicate that the PAS protocol could induce changes in excitability in this population. However, our comparisons between time points revealed only a difference from baseline to 30 min after PAS, suggesting that PAS-induced changes in CSE may have been limited. Still, the exercise bout did not enhance the effects of PAS compared to the rest condition, which contrasts previous work [115, 116, 127].

Furthermore, interindividual and intraindividual variability in response to the PAS protocol may also account for the lack of robust findings. It is well-known that PAS-induced CSE varies both between subjects and between sessions [138]. One study found that PAS induced increases in CSE in only half of their young participants [90]. Differences in neurophysiology and neuroanatomy may explain some of the variances [192]. For example, a low MEP threshold for eliciting an MEP of 1mV and a low resting motor threshold has been found to predict PAS responders [90]. We found a relatively low resting motor threshold was on average 34.9% ( $\pm 8.2SD$ ) of stimulator output with no difference between conditions, indicating responding subjects and good coil positioning. Unfortunately, in the present study, we did not account for neuroanatomic differences by using magnetic resonance imaging (MRI) guided coil positioning. To ensure that the correct position of the TMS-coil was consistent, we used a four-camera navigation system. It is possible that applying individual MRI scans of each participant to ensure stimulation of the hand-knob of the primary motor cortex could have further improved stimulation precision. However, previous studies showing a potentiating effect of PA or exercise on PAS-induced CSE did not apply MRI scans to their protocol [115, 116]. Thus, while MRI-guided positioning of the coil may have improved precision, it is unlikely to explain the lack of effects in Study II entirely.

Genetics [193] and time of day [194] may also impact the LTP-like induced effects of PAS. However, the randomized cross-over design should account for these differential effects. We tested the same subjects at the same time of day, but the order of conditions was randomized, with at least one week between sessions. However, the reproducibility of PAS-induced increases in CSE has been questioned [195], which may complicate the interpretation of the results in our cross-over designed study.

It is important to note that although we did not find greater PAS-induced CSE in the interrupted sitting and exercise condition compared to rest, this does not exclude the possibility that other measures of neuroplasticity may be more sensitive to the investigated interventions. For example, functional MRI or near-infrared spectroscopy can be applied to assess oxygenation of regional blood flow to give indices of alterations in neural activity, which is of more immediate relevance for cognitive processing. However, such measures are at best proxies of neuroplastic processes, leaving PAS-induced CSE as one of the few methodologies for investigating neuroplasticity more directly in humans.

In summary, Study II showed that the propensity to induce increases in corticospinal excitability in the primary motor cortex did not change by either breaking up prolonged sitting frequently or performing a moderate-intensity exercise bout compared to uninterrupted sitting. This suggests that prolonged sitting for three hours may not be detrimental for PAS-induced LTP-like neuroplasticity.

## 6.3 Workplace interventions for movement behaviors and cognitive health

Ineffectiveness of the intervention components at each of the different levels (i.e., organizational, environmental, and individual) may partly explain the lack of effect of the two ecological workplace interventions.

At the organizational and environmental level, the team leaders had an essential role in implementing facilitating factors identified prior to the intervention. The interventions were designed with common barriers to SB in mind, and team leaders were responsible for implementing identified facilitators based on instructions from the research team. However, we did not measure how effective team leaders were in implementing these strategies. Process and fidelity evaluations, including qualitative analyses, would have helped us identify how effective the team leaders were in implementing the intervention component, but this was beyond the scope of this thesis.

The main active component was designed to be the counseling sessions based on cognitive-behavioral therapy combined with motivational interviewing at the individual level. Cognitive-behavioral therapy has previously been successful in changing several behaviors [196], such as eating habits [197] and improving mental health outcomes [198]. However, limited evidence exists on how cognitive-behavioral therapy can effectively change PA and SB. In a recent study involving the same participants as Study III and IV, our research group showed that the intervention successfully increased self-efficacy in both intervention groups [199]. Self-efficacy is a person's belief in their capability in executing actions required to change a given behavior and is a central component in behavior change [200]. Thus, even though we could not detect any differences in movement behavior, primary psychological measures changed. This might be reflected in the movement behavior data with a longer follow-up.

Another explanation for the lack of effect can be the baseline PA level of participants included in the study. Extensive effort was put into recruiting inactive participants. We held several information meetings for the employees at the two participating companies. In addition, we provided written information about the study to all employees. To include the least active participants, we excluded persons who spent more than 30 min/day in sustained bouts of MVPA. Still, we failed to recruit the least active participants. Indeed, participants were more physically active compared to another Swedish population who spent 31 min/day in MVPA [183]. Across all groups, participants in our study spent on average 34 minutes/day at work alone and 77 minutes/day during leisure in MVPA. Thus, it is not surprising that the intervention aiming to increase PA could not raise the behavior further.

A growing body of research has recently focused on reducing SB in the workplace [147, 149]. Multi-component interventions seem to be effective in reducing sitting time at work. However, only a few low-quality studies exist, while high-quality evidence is lacking [147].

We found no intervention effect on SB. These results conflict with findings from two multi-component cluster-randomized interventions in office workplaces [201, 202]. Edwardson et al. (2018) and Healy et al. (2013) showed a reduction of 64 and 125 min/work-day in sitting time, respectively, compared to the control group [201, 202].

Variations in the intervention components between studies could explain the conflicting results. For example, the installation of height-adjustable desks was a central environmental component in Edwardson et al. (2018) and Healy et al. (2013). However, in contrast, office workers in the present study already had height-adjustable desks available

when the study began. The primary environmental component in reducing SB intervention in the present study was the organization of walking and standing meetings by each cluster's team leader.

Another discrepancy is apparent at the individual level. Five counseling sessions during the six months were the primary individual component in the present study. Counseling was less frequent in Edwardson et al. (2018), who provided one counseling the first month to give one session every three months, during the 12 months the intervention lasted [201]. Healy et al. (2013) delivered an initial face-to-face counseling session to give telephone counseling one time per week during the four-week intervention. Thus, counseling frequency but also delivery quality could explain the conflicting results.

Both the companies and the participants are a biased selection. The larger project was a co-production of research concerning office workers' brain health, and both companies were already active in their health promotion strategies. Thus, the employees may not reflect the broader office worker population. Furthermore, the recruited participants may volunteer because they were interested in these questions and, therefore, exercised regularly. Still, co-production is critical to provide strong evidence for a particular population that are feasible and implementable in a specific context. Including companies with no health promotion initiatives in place could be a target for future studies.

## 6.4 Methodological discussion

### *Measuring sedentary behavior and physical activity with accelerometry*

SB is defined as any waking behavior with an energy expenditure of  $\leq 1.5$  METs while sitting or reclining [19]. It is essential to acknowledge that by using hip-worn accelerometers in Studies I and III, we could not obtain data on the posture component of SB and could have misclassified SB. In addition, bicycling may also be hard to detect [203]. By adding thigh-worn inclinometers to the analyses, we would be able to differentiate between sitting and standing, detect bicycling, and thus improve our measure on SB and bicycling.

In Study I, we used 200 counts per minute as the cut-point for SB to minimize light-intensity PA misclassification as SB [154]. This cut-point was initially validated in older individuals, and there is a possibility that we have overestimated time spent sedentary in this younger population [204].

The high activity level of the participants forced us to rethink the data processing of the ActiGraph accelerometer. The standard low-pass filter has been shown to attenuate some of the higher intensity accelerations, resulting in validity issues [140]. Therefore,

we analyzed the accelerometer data in a new way in Studies III and IV. In collaboration with researchers in Gothenburg, we analyzed the raw accelerometer data using a 30 Hz low-pass filter instead of the standard 1.6 Hz low-pass filter [139, 140]. Increasing the intensity range has been shown to correlate better with cardiometabolic health outcomes than traditional processing [99]. In addition, we chose to separate moderate and vigorous PA instead of the conventional combination into MVPA. We did that to get a better resolution at the higher intensity spectrum. The results showed that participants spend less than 10 min/day in vigorous-intensity compared to more than 90 minutes in moderate-intensity PA. The high volume of moderate-intensity PA might account for most health benefits. However, the dose-response relationship to cognitive functions and neuroplasticity remains to be elucidated.

Measuring movement behaviors with accelerometers is cheap and feasible to measure habitual PA and SB in large populations. However, limitations exist with regards to measuring both SB and PA. For example, weight-bearing activities could be misclassified as SB or light-intensity PA despite substantially greater physiological demands. Thus, we could not detect changes in weight-bearing exercises, which is, of course, a limitation. Advancements in the processing and analysis of accelerometer data were made constantly, and we adapted the analysis along the way to obtain data that was as valid as possible.

Accelerometer cut-points used to classify different intensities of behavior do not take fitness levels into account. Methods obtaining relative intensities rather than absolute intensities may be more precise [205] and help clarify the cross-sectional relationship between PA and cognitive functions. Still, the accelerometer cut points are validated in a population that should reflect the population studied here [153].

### ***Neuropsychological test battery***

A strength of the present thesis is the inclusion of multiple tests to assess cognitive function. This gives a measure of the cognitive domain that is less sensitive to a single test but instead reflects the underlying construct of interest. In Study IV, we took advantage of the multiple tests and created composite scores to reflect ability in the different cognitive domains of interest. Here it would have been optimal to include the same number of tests for each domain, but unfortunately, we also had to consider the total duration of the cognitive testing procedure. In Studies I and IV, all cognitive testing happened at the two companies, and participants were permitted to partake during work hours, which meant that a lengthier testing procedure would have put feasibility at risk. Thus, we did not have unlimited time, and more lengthy testing procedures could result in problems regarding fatigue.

Ceiling effects in several tests might have limited our ability to obtain sufficient cognitive function variation. The battery is adapted from Jonasson et al. (2017) [155], who measured cognitive functions in an older population, whereas our population is middle-aged. Indeed, we experienced that almost all participants in our studies performed well on specific tasks. For example, in Study I, 222 participants (66%) had more than 90% correct trials on 2-back, and the median performance score was 93% correct trials, indicating a ceiling effect. Thus, the battery may not have been sensitive enough for getting sufficient variation in this sample of middle-aged office workers.

### ***Power issues***

The null finding in this thesis should be interpreted carefully since some of the studies may not be sufficiently powered to detect small differences.

Before the data collection in Study II, we examined studies investigating the effect of exercise on paired associative stimulation (PAS) [115, 116] to estimate the number of subjects needed to detect a difference. The power calculation revealed that a sample size of 12 subjects would be sufficient to detect a difference of similar size as in Singh et al. (2014) [115] (i.e., 2000 AURC calculated as MEP-amplitude relative to % RMT) between resting and the exercise condition with 80% statistical power and a significance level of  $\leq 0.05$ . We included 16 subjects in total, four more than the power calculation estimated, to ensure sufficient statistical power. Retrospectively, with the large inter- and intra-individual variability changes in excitability in response to PAS observed in our and several other studies [190, 195], the sample size should have been bigger to ensure sufficient statistical power.

In the study protocol of Studies III and IV, a detailed power calculation was carried out [151]. This estimated a sample of approximately 330 for three groups for detecting a mean difference of 1 hour/day ( $\pm 1.4$  hour/day) of SB and 7 seconds ( $\pm 9.85$  SD) at the Stroop test. However, we managed to recruit only 298 employees, and only 263 were enrolled in the study. At follow-up, only 194 participants remained. In the complete analysis, maximally 158 and 139 participants were analyzed in Studies III and IV. This is only approximately half of the participants we expected before the data collection. Thus, the study was probably not sufficiently powered to detect a small difference between the groups.

### ***Study population***

The study population in this thesis was mainly employees of two Swedish companies. They were characterized by high education and cardiorespiratory fitness, similar to other high-skilled Swedish office workers [206]. Notably, in Studies I, III, and IV, office workers were highly physically active. Participants spent on average approximately 7% of the

day in MVPA, which is high compared to another Swedish population who showed approximately 2% [207]. Although highly physically active, participants spent more than half of the day sedentary (59% in Study I and 53% in Studies III and IV). Still, we do not know if office workers' extensive SB influences cognitive abilities despite high PA levels. Investigations in other populations at larger risk for impaired cognitive functions later in life would help illuminate the effect of sedentary work life on cognitive functions for healthy aging. Individuals with lower PA levels, overweight, Type-2 diabetes, or mental ill-health could be of particular interest.

## 7. Conclusions

This thesis investigated how movement behavior relates to and influences office workers' cognitive functions and corticospinal neuroplasticity.

The findings from the first study did not provide support for cross-sectional associations between movement behaviors and cognitive functions in healthy physically active office workers, suggesting that this association may not be as robust as previously demonstrated in other populations or as inferred from self-report. The results from the second study question if the previously shown exercise-induced improvements in corticospinal neuroplasticity in fit young men are transferable to middle-aged inactive office workers. We provided weak support that frequent short activity breaks might increase corticospinal excitability during prolonged sitting in this population.

Lastly, the third and fourth studies demonstrated the challenges involved in designing a workplace intervention that successfully changes movement behaviors, cardiorespiratory fitness, and, ultimately, cognitive functions.

In conclusion, the findings presented in this thesis suggest that the role of movement behavior for cognitive function may not be as all-encompassing as previously thought. The findings indicate that extensive sedentary behavior may not be detrimental to cognitive functions and neuroplasticity in a healthy and physically active population. While adhering to the WHO physical activity recommendations appears essential for many health outcomes, specifically targeting increased physical activity or decreased sedentary time through individual, environmental and organizational components was not effective for promoting changes in movement behaviors or cognitive functions in this sample of physically active office workers. Thus, changing movement behavior in the workplace remains a challenging endeavor. Future investigations may consider targeting more vulnerable populations with less physical activity, cognitive health problems, or cardiometabolic diseases to provide employers and health-promoting companies with valuable information.

## 8. Svensk sammanfattning

Utvecklingen genom livet av såväl kognitiv förmåga som fysiskt aktivitetsmönster beror på en komplex interaktion mellan arv och miljö. Det finns stark evidens för att fysisk aktivitet kan förbättra kognitiv förmåga, men vi saknar kunskap om hur stillasittande och det sammansatta fysiska aktivitetsmönstret (omfattande sömn, fysiskt aktivitet och stillasittande) påverkar kognition.

Observationsstudier på äldre har visat att mer stillasittande tid är relaterat till sämre kognitiv prestation, men de flesta av dessa studier har utgått från självskattat stillasittande. Självskattningar av fysisk aktivitet och stillasittande är ofta ganska svagt associerade till uppmätt fysiskt aktivitetsmönstret. Emedan träning har visat sig ha en skyddande effekt på äldres kognition, så vet man fortfarande väldigt lite om hur det fysiska aktivitetsmönstret i den arbetsföra befolkningen relaterar till och påverkar kognition. Därför behövs det kunskap om hur fysiskt aktivitetsmönster i medelåldern påverkar kognition och vilka mekanismer som ligger till grund för denna effekt.

Avhandlingen är en del av ett större forskningsprojekt som syftar till att undersöka hur kontorsarbetares fysiska aktivitetsmönster relaterar till och påverkar kognition, psykisk hälsa och neurofysiologiska mekanismer för dessa. Kunskapen samproduceras med arbetsgivare och friskvårdsföretag.

Syftet med denna avhandling var att belysa hur kontorsarbetares fysiska aktivitetsmönster relaterar till och påverkar kognition och neuroplasticitet.

Avhandlingens första studie undersökte sambandet mellan fysiska aktivitetsmönster och kognitiva förmågor bland 334 kontorsarbetare. Studien visade inga samband mellan total tid i medel-till-högintensiv fysisk aktivitet eller stillasittande och prestationen på kognitiva tester. Detta tyder på att sambandet som tidigare påvisats i äldre mellan fysiskt aktivitetsmönster och kognitiva funktioner inte går att generalisera till medelåldern.

Den andra studien undersökte omedelbara effekter av tre timmars stillasittande uppbrutet av tre olika rörelseinterventioner på kortikospinal neuroplasticitet. Sexton inaktiva kontorsarbetare i medelåldern deltog i tre separata interventioner, genomförda i randomiserad ordning, separerade av minst 7 dagar. Effekter av tre timmars stillasittande jämfördes med tre timmars stillasittande uppbrutet med korta rörelsepauser eller 2,5 timmars stillasittande följt av 25 minuters medelintensiv träning. Transkraniell magnetstimulation

användes för att utvärdera kortikospinal retbarhet och svaret på ett neuroplasticitetsinducerande protokoll. Studien fann inga statistiskt säkerställda skillnader mellan de tre experimentella interventionerna. Detta tyder på att ett enskilt träningspass eller uppbrutet stillasittande inte är mer fördelaktigt än långvarigt stillasittande för kortikospinal neuroplasticitet eller retbarhet bland inaktiva kontorsarbetare.

Vi genomförde sedan en sex månaders ekologisk klusterrandomiserad multikomponent intervention med stöd till mer fysisk aktivitet eller minskat stillasittande bland 263 friska kontorsarbetare i syfte att främja hälsosamma hjärnfunktioner. Stödet gavs på individ, miljö och organisationsnivå. Den tredje studien undersökte hur effektiva interventionerna var på att ändra sammansättningen av det fysiska aktivitetsmönstret från studiens start till sex-månaders-uppföljningen. Den fjärde studien undersökte hur interventionerna påverkade kognition. Varken fysiska aktivitetsmönster, kondition eller kognitiva funktioner påverkades av interventionerna. Ändringar i fysiska aktivitetsmönster och kondition var inte relaterade till ändringar i kognition. Relationen mellan förändringar i sammansättningen av fysiskt aktivitetsmönster och kognition modererades till viss del av kön, ålder och kondition.

Denna avhandling fann sammanfattningsvis inga stöd för samband mellan fysiskt aktivitetsmönster och kognition bland friska kontorsarbetare, inga omedelbara effekter av ett träningspass eller uppbrutet stillasittande på kortikospinal neuroplasticitet bland inaktiva kontorsarbetare och inget stöd för att de utvärderade ekologiska klusterrandomiserade interventionerna med stöd på individ, miljö och organisationsnivå hade effekter på fysiskt aktivitetsmönster eller kognition bland friska kontorsarbetare. Sammantaget tyder fynden på att stillasittande nog inte är så negativt för kognitionen och neuroplasticiteten bland friska, fysiskt aktiva kontorsarbetare som tidigare föreslagits. Dessutom belyser resultaten svårigheten med att stödja hållbara förändringar i fysiskt aktivitetsmönster via arbetsplatsen.

Vi kan inte utesluta möjligheten att ändringar i fysiskt aktivitetsmönster kan leda till förbättringar i kognition för fysiskt inaktiva kontorsarbetare med risk för kardiovaskulär sjukdom, lägre kondition och/eller lägre daglig kognitiv stimulation. Framtida interventioner skulle kunna utformas med en mer avgränsad målgrupp i fokus.

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## 10. References

1. Bojsen-Moller, E., et al., *Relationships between Physical Activity, Sedentary Behaviour and Cognitive Functions in Office Workers*. Int J Environ Res Public Health, 2019. 16(23).
2. Bojsen-Moller, E., et al., *The effect of breaking up prolonged sitting on paired associative stimulation-induced plasticity*. Exp Brain Res, 2020. 238(11): p. 2497-2506.
3. Larisch, L.M., et al., *Effects of Two Randomized and Controlled Multi-Component Interventions Focusing On 24-Hour Movement Behavior among Office Workers: A Compositional Data Analysis*. Int J Environ Res Public Health, 2021. 18(8).
4. Steeves, J.A., et al., *Classification of occupational activity categories using accelerometry: NHANES 2003-2004*. Int J Behav Nutr Phys Act, 2015. 12: p. 89.
5. Kubicek, B., M. Paškvan, and C. Korunka, *Development and validation of an instrument for assessing job demands arising from accelerated change: The intensification of job demands scale (IDS)*. European Journal of Work and Organizational Psychology, 2014. 24(6): p. 898-913.
6. OECD, *Labor Force Statistics*. 2020.
7. Prince, S.A., et al., *Device-measured physical activity, sedentary behaviour and cardiometabolic health and fitness across occupational groups: a systematic review and meta-analysis*. Int J Behav Nutr Phys Act, 2019. 16(1): p. 30.
8. Andersen, T.M., N. Määtänen, and T. Valkonen, *Pension reforms: Longevity and retirement*. In: *The Nordic model - challenged but capable of reform*. Nordic Council of Ministers. 2014: Copenhagen. p. 113-144.
9. Arbetsmiljöverket, *Arbetsmiljölagen*. 2018.
10. Vallance, J.K., et al., *Evaluating the Evidence on Sitting, Smoking, and Health: Is Sitting Really the New Smoking?* Am J Public Health, 2018. 108(11): p. 1478-1482.
11. Pedišić, Ž., D. Dumuid, and T. Olds, *Integrating sleep, sedentary behaviour and physical activity research in emergign field of time-use epidemiology: Definitions, Concepts, Statistical Methods, Theoretical Framework, and Future Directions*. Kinesiology, 2017. 49.
12. Rosenberger, M.E., et al., *The 24-Hour Activity Cycle: A New Paradigm for Physical Activity*. Med Sci Sports Exerc, 2019. 51(3): p. 454-464.
13. Ross, R., et al., *Canadian 24-Hour Movement Guidelines for Adults aged 18-64 years and Adults aged 65 years or older: an integration of physical activity, sedentary behaviour, and sleep*. Appl Physiol Nutr Metab, 2020. 45(10 (Suppl. 2)): p. S57-S102.
14. Caspersen, C.J., K.E. Powell, and G.M. Christenson, *Physical activity, Exercise, and physical fitness - Definitions and distinctions for health-related research*. Public Health Reports, 1985. 100(2): p. 126-131.

15. Jetté, M., K. Sidney, and G. Blümchen, *Metabolic Equivalents (METs) in Exercise Testing, Exercise Prescription, and Evaluation of Functional Capacity*. Clinical Cardiology, 1990. 13.
16. Medicine, A.C.o.S., *ACSM's guidelines for exercise testing and prescription*. 2013: Lippincott Williams & Wilkins.
17. Strath, S.J., et al., *Guide to the assessment of physical activity: Clinical and research applications: a scientific statement from the American Heart Association*. Circulation, 2013. 128(20): p. 2259-79.
18. Tremblay, M.S., et al., *Sedentary Behavior Research Network (SBRN) – Terminology Consensus Project process and outcome*. International Journal of Behavioral Nutrition and Physical Activity, 2017. 14(1).
19. Sedentary Behaviour Research, N., *Letter to the editor: standardized use of the terms "sedentary" and "sedentary behaviours"*. Appl Physiol Nutr Metab, 2012. 37(3): p. 540-2.
20. Haskell, W.L., *Physical activity by self-report: a brief history and future issues*. J Phys Act Health, 2012. 9 Suppl 1: p. S5-10.
21. WHO, *Global recommendations on physical activity for health*. 2010: Switzerland.
22. Chastin, S.F.M., et al., *Systematic comparative validation of self-report measures of sedentary time against an objective measure of postural sitting (activPAL)*. Int J Behav Nutr Phys Act, 2018. 15(1): p. 21.
23. Dyrstad, S.M., et al., *Comparison of self-reported versus accelerometer-measured physical activity*. Med Sci Sports Exerc, 2014. 46(1): p. 99-106.
24. Prince, S.A., et al., *A comparison of direct versus self-report measures for assessing physical activity in adults: a systematic review*. Int J Behav Nutr Phys Act, 2008. 5: p. 56.
25. Arvidsson, D., J. Fridolfsson, and M. Borjesson, *Measurement of physical activity in clinical practice using accelerometers*. J Intern Med, 2019. 286(2): p. 137-153.
26. de Almeida Mendes, M., et al., *Calibration of raw accelerometer data to measure physical activity: A systematic review*. Gait Posture, 2018. 61: p. 98-110.
27. Prince, S.A., et al., *A comparison of self-reported and device measured sedentary behaviour in adults: a systematic review and meta-analysis*. Int J Behav Nutr Phys Act, 2020. 17(1): p. 31.
28. Larsson, K., et al., *Criterion validity and test-retest reliability of SED-GIH, a single item question for assessment of daily sitting time*. BMC Public Health, 2019. 19(1): p. 17.
29. Lagersted-Olsen, J., et al., *Comparison of objectively measured and self-reported time spent sitting*. Int J Sports Med, 2014. 35(6): p. 534-40.
30. Atienza, A.A., et al., *Self-reported and objectively measured activity related to biomarkers using NHANES*. Med Sci Sports Exerc, 2011. 43(5): p. 815-21.
31. Gupta, N., et al., *Time-Based Data in Occupational Studies: The Whys, the Hows, and Some Remaining Challenges in Compositional Data Analysis (CoDA)*. Ann Work Expo Health, 2020. 64(8): p. 778-785.
32. Gupta, N., et al., *A comparison of standard and compositional data analysis in studies addressing group differences in sedentary behavior and physical activity*. Int J Behav Nutr Phys Act, 2018. 15(1): p. 53.

33. Aadland, E., et al., *Multicollinear physical activity accelerometry data and associations to cardiometabolic health: challenges, pitfalls, and potential solutions*. Int J Behav Nutr Phys Act, 2019. 16(1): p. 74.
34. Aadland, E., et al., *The multivariate physical activity signature associated with metabolic health in children*. Int J Behav Nutr Phys Act, 2018. 15(1): p. 77.
35. Purves, D., et al., *Principles of Cognitive Neuroscience, 2nd Edition*. 2007: Sinaur Associates, Inc. .
36. Driver, J., *A selective review of selective attention research from the past century*. The British Psychological Society, 2001. 92.
37. Chun, M.M., J.D. Golomb, and N.B. Turk-Browne, *A taxonomy of external and internal attention*. Annu Rev Psychol, 2011. 62: p. 73-101.
38. Kail, R. and T.A. Salthouse, *Processing speed as mental capacity*. Acta Psychologica, 1994. 86.
39. Squire, L.R., *Memory systems of the brain: a brief history and current perspective*. Neurobiol Learn Mem, 2004. 82(3): p. 171-7.
40. D'Esposito, M. and B.R. Postle, *The cognitive neuroscience of working memory*. Annu Rev Psychol, 2015. 66: p. 115-42.
41. Baddeley, A., *Working memory: theories, models, and controversies*. Annu Rev Psychol, 2012. 63: p. 1-29.
42. Tulving, E., *Episodic memory: From mind to brain*. Annu. Rev. Psychol., 2002. 53.
43. Diamond, A., *Executive functions*. Annu Rev Psychol, 2013. 64: p. 135-68.
44. Miyake, A., et al., *The unity and diversity of executive functions and their contributions to complex "Frontal Lobe" tasks: a latent variable analysis*. Cogn Psychol, 2000. 41(1): p. 49-100.
45. McCabe, D.P., et al., *The relationship between working memory capacity and executive functioning: evidence for a common executive attention construct*. Neuropsychology, 2010. 24(2): p. 222-243.
46. Pascual-Leone, A., et al., *The plastic human brain cortex*. Annu Rev Neurosci, 2005. 28: p. 377-401.
47. Kandel, E.R., Y. Dudai, and M.R. Mayford, *The molecular and systems biology of memory*. Cell, 2014. 157(1): p. 163-86.
48. Hebb, D.O., *The organization of behavior*. 1949, New York: Wiley.
49. Bliss, T.V. and T. Lomo, *LONG-LASTING POTENTIATION OF SYNAPTIC TRANSMISSION IN THE DENTATE AREA OF THE ANAESTHETIZED RABBIT FOLLOWING STIMULATION OF THE PERFORANT PATH*. J Physiol, 1973. 232: p. 331-356.
50. Hess, G. and J.P. Donoghue, *Long-term potentiation of horizontal connections provides a mechanism to reorganize cortical motor maps*. J Neurophysiol, 1994. 71(6): p. 2543-7.
51. Bliss, T.V., et al., *CORRELATION BETWEEN LONG-TERM POTENTIATION AND RELEASE OF ENDOGENOUS AMINO ACIDS FROM DENTATE GYRUS OF ANAESTHETIZED RATS*. J Pysiol, 1986. 377.
52. Kleim, J.A., et al., *Motor learning-dependent synaptogenesis is localized to functionally reorganized motor cortex*. Neurobiol Learn Mem, 2002. 77(1): p. 63-77.
53. Rossini, P.M., et al., *Non-invasive electrical and magnetic stimulation of the brain, spinal cord, roots and peripheral nerves: Basic principles and*

- procedures for routine clinical and research application. An updated report from an I.F.C.N. Committee.* Clin Neurophysiol, 2015. 126(6): p. 1071-107.
54. Hallett, M., *Transcranial magnetic stimulation and the human brain.* Nature, 2000. 406.
  55. Rothwell, J., et al., *Transcranial electrical stimulation of the motor cortex in man: further evidence for the site of activation.* J Physiol, 1994. 481 ( Pt 1): p. 243-50.
  56. Carson, R.G., et al., *Characterizing changes in the excitability of corticospinal projections to proximal muscles of the upper limb.* Brain Stimul, 2013. 6(5): p. 760-8.
  57. Stefan, K., et al., *Mechanisms of enhancement of human motor cortex excitability induced by interventional paired associative stimulation.* J Physiol, 2002. 543(Pt 2): p. 699-708.
  58. Stefan, K., et al., *Induction of plasticity in the human motor cortex by paired associative stimulation.* Brain, 2000. 123 Pt 3: p. 572-84.
  59. Carson, R.G. and N.C. Kennedy, *Modulation of human corticospinal excitability by paired associative stimulation.* Front Hum Neurosci, 2013. 7: p. 823.
  60. Ekelund, U., et al., *Dose-response associations between accelerometry measured physical activity and sedentary time and all cause mortality: systematic review and harmonised meta-analysis.* BMJ, 2019. 366: p. 14570.
  61. Lynch, B.M. and M.F. Leitzmann, *An Evaluation of the Evidence Relating to Physical Inactivity, Sedentary Behavior, and Cancer Incidence and Mortality.* Current Epidemiology Reports, 2017. 4(3): p. 221-231.
  62. Erickson, K.I., et al., *Exercise training increases size of hippocampus and improves memory.* Proc Natl Acad Sci U S A, 2011. 108(7): p. 3017-22.
  63. Xu, W., et al., *Leisure time physical activity and dementia risk: a dose-response meta-analysis of prospective studies.* BMJ Open, 2017. 7(10): p. e014706.
  64. Blondell, S.J., R. Hammersley-Mather, and J.L. Veerman, *Does physical activity prevent cognitive decline and dementia?: A systematic review and meta-analysis of longitudinal studies.* BMC Public Health, 2014. 14: p. 510.
  65. Stillman, C.M., et al., *Mediators of Physical Activity on Neurocognitive Function: A Review at Multiple Levels of Analysis.* Front Hum Neurosci, 2016. 10: p. 626.
  66. Donnelly, J.E., et al., *Physical Activity, Fitness, Cognitive Function, and Academic Achievement in Children: A Systematic Review.* Med Sci Sports Exerc, 2016. 48(6): p. 1197-222.
  67. Rojer, A.G.M., et al., *Objectively assessed physical activity and sedentary behavior and global cognitive function in older adults: a systematic review.* Mech Ageing Dev, 2021. 198: p. 111524.
  68. Erickson, K.I., et al., *Physical Activity, Cognition, and Brain Outcomes: A Review of the 2018 Physical Activity Guidelines.* Medicine & Science in Sports & Exercise, 2019. 51(6): p. 1242-1251.
  69. Cox, E.P., et al., *Relationship between physical activity and cognitive function in apparently healthy young to middle-aged adults: A systematic review.* J Sci Med Sport, 2016. 19(8): p. 616-28.
  70. Ekblom, M.M., et al., *Device-Measured Sedentary Behavior, Physical Activity and Aerobic Fitness Are Independent Correlates of Cognitive Performance in*

- Healthy Middle-Aged Adults-Results from the SCAPIS Pilot Study*. Int J Environ Res Public Health, 2019. 16(24).
71. Spartano, N.L., et al., *Accelerometer-determined physical activity and cognitive function in middle-aged and older adults from two generations of the Framingham Heart Study*. Alzheimer's & Dementia: Translational Research & Clinical Interventions, 2019. 5(1): p. 618-626.
  72. Boucard, G.K., et al., *Impact of Physical Activity on Executive Functions in Aging: A Selective Effect on Inhibition Among Old Adults*. Journal of Sport & Exercise Psychology, 2012. 34(6): p. 808-827.
  73. Vasquez, E., et al., *Is there a relationship between accelerometer-assessed physical activity and sedentary behavior and cognitive function in US Hispanic/Latino adults? The Hispanic Community Health Study/Study of Latinos (HCHS/SOL)*. Prev Med, 2017. 103: p. 43-48.
  74. Falck, R.S., J.C. Davis, and T. Liu-Ambrose, *What is the association between sedentary behaviour and cognitive function? A systematic review*. Br J Sports Med, 2016. 51(10): p. 800-811.
  75. Rosenberg, D.E., et al., *Independent Associations Between Sedentary Behaviors and Mental, Cognitive, Physical, and Functional Health Among Older Adults in Retirement Communities*. J Gerontol A Biol Sci Med Sci, 2016. 71(1): p. 78-83.
  76. Zhu, W., et al., *Objectively Measured Physical Activity and Cognitive Function in Older Adults*. Med Sci Sports Exerc, 2017. 49(1): p. 47-53.
  77. Wu, Z.J., et al., *Relationships of accelerometer-based measured objective physical activity and sedentary behaviour with cognitive function: a comparative cross-sectional study of China's elderly population*. BMC Geriatr, 2020. 20(1): p. 149.
  78. Bakrania, K., et al., *Associations Between Sedentary Behaviors and Cognitive Function: Cross-Sectional and Prospective Findings From the UK Biobank*. Am J Epidemiol, 2018. 187(3): p. 441-454.
  79. Audiffren, M., P.D. Tomporowski, and J. Zagrodnik, *Acute aerobic exercise and information processing: energizing motor processes during a choice reaction time task*. Acta Psychol (Amst), 2008. 129(3): p. 410-9.
  80. Voss, M.W., et al., *Bridging animal and human models of exercise-induced brain plasticity*. Trends Cogn Sci, 2013. 17(10): p. 525-44.
  81. Chang, Y.K., et al., *The effects of acute exercise on cognitive performance: a meta-analysis*. Brain Res, 2012. 1453: p. 87-101.
  82. Ludyga, S., et al., *Acute effects of moderate aerobic exercise on specific aspects of executive function in different age and fitness groups: A meta-analysis*. Psychophysiology, 2016. 53(11): p. 1611-1626.
  83. Roig, M., et al., *The effects of cardiovascular exercise on human memory: a review with meta-analysis*. Neurosci Biobehav Rev, 2013. 37(8): p. 1645-66.
  84. Wilke, J., et al., *Acute Effects of Resistance Exercise on Cognitive Function in Healthy Adults: A Systematic Review with Multilevel Meta-Analysis*. Sports Med, 2019. 49(6): p. 905-916.
  85. Wang, C.C., et al., *Executive function during acute exercise: the role of exercise intensity*. J Sport Exerc Psychol, 2013. 35(4): p. 358-67.
  86. Moreau, D. and E. Chou, *The Acute Effect of High-Intensity Exercise on Executive Function: A Meta-Analysis*. Perspect Psychol Sci, 2019. 14(5): p. 734-764.

87. Loprinzi, P., et al., *The Temporal Effects of Acute Exercise on Episodic Memory Function: Systematic Review with Meta-Analysis*. Brain Sciences, 2019. 9(4).
88. Wheeler, M.J., et al., *Distinct effects of acute exercise and breaks in sitting on working memory and executive function in older adults: a three-arm, randomised cross-over trial to evaluate the effects of exercise with and without breaks in sitting on cognition*. Br J Sports Med, 2019.
89. Wennberg, P., et al., *Acute effects of breaking up prolonged sitting on fatigue and cognition: a pilot study*. BMJ Open, 2016. 6(2): p. e009630.
90. Mullane, S.L., et al., *Acute effects on cognitive performance following bouts of standing and light-intensity physical activity in a simulated workplace environment*. J Sci Med Sport, 2016. 20(5): p. 489-493.
91. Heiland, E.G., et al., *Frequent, Short Physical Activity Breaks Reduce Prefrontal Cortex Activation but Preserve Working Memory in Middle-Aged Adults: ABBaH Study*. Front Hum Neurosci, 2021. 15: p. 719509.
92. Russell, B.A., et al., *A randomised control trial of the cognitive effects of working in a seated as opposed to a standing position in office workers*. Ergonomics, 2016. 59(6): p. 737-44.
93. Schwartz, B., et al., *Effect of alternating postures on cognitive performance for healthy people performing sedentary work*. Ergonomics, 2018. 61(6): p. 778-795.
94. Magnon, V., G.T. Vallet, and C. Auxiette, *Sedentary Behavior at Work and Cognitive Functioning: A Systematic Review*. Front Public Health, 2018. 6: p. 239.
95. Falck, R.S., et al., *Impact of exercise training on physical and cognitive function among older adults: a systematic review and meta-analysis*. Neurobiol Aging, 2019. 79: p. 119-130.
96. Northey, J.M., et al., *Exercise interventions for cognitive function in adults older than 50: a systematic review with meta-analysis*. Br J Sports Med, 2018. 52(3): p. 154-160.
97. Rathore, A. and B. Lom, *The effects of chronic and acute physical activity on working memory performance in healthy participants: a systematic review with meta-analysis of randomized controlled trials*. Systematic Reviews, 2017. 6(1).
98. Kelly, M.E., et al., *The impact of exercise on the cognitive functioning of healthy older adults: a systematic review and meta-analysis*. Ageing Res Rev, 2014. 16: p. 12-31.
99. Ludyga, S., et al., *Systematic review and meta-analysis investigating moderators of long-term effects of exercise on cognition in healthy individuals*. Nature Human Behaviour, 2020. 4(6): p. 603-612.
100. Stillman, C.M. and K.I. Erickson, *Physical activity as a model for health neuroscience*. Ann N Y Acad Sci, 2018. 1428(1): p. 103-111.
101. Stenling, A., et al., *Physical activity and cognitive function: between-person and within-person associations and moderators*. Neuropsychol Dev Cogn B Aging Neuropsychol Cogn, 2021. 28(3): p. 392-417.
102. Colcombe, S.J. and A.F. Kramer, *Fitness effects on the cognitive function of older adults: a meta-analytic study*. Psychological Science, 2003. 14(2): p. 125-130.

103. Barha, C.K., et al., *Sex differences in exercise efficacy to improve cognition: A systematic review and meta-analysis of randomized controlled trials in older humans*. *Front Neuroendocrinol*, 2017. 46: p. 71-85.
104. Stern, Y., et al., *Effect of aerobic exercise on cognition in younger adults*. *Neurology*, 2019.
105. Fanning, J., et al., *Replacing sedentary time with sleep, light, or moderate-to-vigorous physical activity: effects on self-regulation and executive functioning*. *J Behav Med*, 2017. 40(2): p. 332-342.
106. Uysal, N., et al., *Effects of voluntary and involuntary exercise on cognitive functions, and VEGF and BDNF levels in adolescent rats*. *Biotech Histochem*, 2015. 90(1): p. 55-68.
107. Vaynman, S., Z. Ying, and F. Gomez-Pinilla, *Hippocampal BDNF mediates the efficacy of exercise on synaptic plasticity and cognition*. *Eur J Neurosci*, 2004. 20(10): p. 2580-90.
108. Kleim, J.A., N.R. Cooper, and P.M. VandenBerg, *Exercise induces angiogenesis but does not alter movement representations within rat motor cortex*. *Brain Research*, 2001. 934.
109. Swain, R.A., et al., *Prolonged exercise induces angiogenesis and increases cerebral blood volume in primary motor cortex of the rat*. *Neuroscience*, 2003. 117(4): p. 1037-1046.
110. van Praag, H., et al., *Running enhances neurogenesis, learning, and long-term potentiation in mice*. *Proc Natl Acad Sci U S A*, 1999. 96(23): p. 13427-31.
111. Colcombe, S.J., et al., *Aerobic Exercise Training Increases Brain Volume in Aging Humans*. *Journal of Gerontology*, 2006. 61A(11): p. 1166-1170.
112. Prehn, K., et al., *Using resting-state fMRI to assess the effect of aerobic exercise on functional connectivity of the DLPFC in older overweight adults*. *Brain Cogn*, 2019. 131: p. 34-44.
113. Boraxbekk, C.J., et al., *Physical activity over a decade modifies age-related decline in perfusion, gray matter volume, and functional connectivity of the posterior default-mode network-A multimodal approach*. *Neuroimage*, 2016. 131: p. 133-41.
114. Kleinloog, J.P.D., et al., *Aerobic Exercise Training Improves Cerebral Blood Flow and Executive Function: A Randomized, Controlled Cross-Over Trial in Sedentary Older Men*. *Front Aging Neurosci*, 2019. 11: p. 333.
115. Singh, A.M., J.L. Neva, and W.R. Staines, *Acute exercise enhances the response to paired associative stimulation-induced plasticity in the primary motor cortex*. *Exp Brain Res*, 2014. 232(11): p. 3675-85.
116. Mang, C.S., et al., *A single bout of high-intensity aerobic exercise facilitates response to paired associative stimulation and promotes sequence-specific implicit motor learning*. *J Appl Physiol (1985)*, 2014. 117(11): p. 1325-36.
117. Farmer, J., et al., *Effects of voluntary exercise on synaptic plasticity and gene expression in the dentate gyrus of adult male Sprague-Dawley rats in vivo*. *Neuroscience*, 2004. 124(1): p. 71-9.
118. Miller, R.M., et al., *Running exercise mitigates the negative consequences of chronic stress on dorsal hippocampal long-term potentiation in male mice*. *Neurobiol Learn Mem*, 2018. 149: p. 28-38.
119. Tsai, S.F., et al., *Long-Term Moderate Exercise Rescues Age-Related Decline in Hippocampal Neuronal Complexity and Memory*. *Gerontology*, 2018. 64(6): p. 551-561.

120. Ahmed, T., J.U. Frey, and V. Korz, *Long-term effects of brief acute stress on cellular signaling and hippocampal LTP*. J Neurosci, 2006. 26(15): p. 3951-8.
121. Dayan, E. and L.G. Cohen, *Neuroplasticity subserving motor skill learning*. Neuron, 2011. 72(3): p. 443-54.
122. Hayashi, Y., et al., *Driving AMPA Receptors into Synapses by LTP and CaMKII: Requirement for GluR1 and PDZ Domain Interaction*. Science, 2000. 287.
123. Eadie, B.D., V.A. Redila, and B.R. Christie, *Voluntary exercise alters the cytoarchitecture of the adult dentate gyrus by increasing cellular proliferation, dendritic complexity, and spine density*. J Comp Neurol, 2005. 486(1): p. 39-47.
124. Bruel-Jungerman, E., et al., *Long-term potentiation enhances neurogenesis in the adult dentate gyrus*. J Neurosci, 2006. 26(22): p. 5888-93.
125. Pastalkova, E., et al., *Storage of spatial information by the maintenance mechanism of LTP*. Science, 2006. 313(5790): p. 1141-4.
126. Cirillo, J., et al., *Motor cortex plasticity induced by paired associative stimulation is enhanced in physically active individuals*. J Physiol, 2009. 587(Pt 24): p. 5831-42.
127. Mang, C.S., et al., *Promoting Motor Cortical Plasticity with Acute Aerobic Exercise: A Role for Cerebellar Circuits*. Neural Plast, 2016. 2016: p. 6797928.
128. Jacobs, K.M. and J.P. Donoghue, *Reshaping the cortical motor map by unmasking latent intracortical connections*. Science, 1991. 251(4996): p. 944-7.
129. Smith, A.E., et al., *The influence of a single bout of aerobic exercise on short-interval intracortical excitability*. Exp Brain Res, 2014. 232(6): p. 1875-82.
130. Singh, A.M., et al., *Aerobic exercise modulates intracortical inhibition and facilitation in a nonexercised upper limb muscle*. BMC Sports Sci Med Rehabil, 2014. 6: p. 23.
131. Mellow, M.L., et al., *Acute aerobic exercise and neuroplasticity of the motor cortex: A systematic review*. J Sci Med Sport, 2019.
132. Andrews, S.C., et al., *Intensity Matters: High-intensity Interval Exercise Enhances Motor Cortex Plasticity More Than Moderate Exercise*. Cereb Cortex, 2020. 30(1): p. 101-112.
133. McDonnell, M.N., et al., *A single bout of aerobic exercise promotes motor cortical neuroplasticity*. J Appl Physiol (1985), 2013. 114(9): p. 1174-82.
134. Smith, A.E., et al., *Daily activities are associated with non-invasive measures of neuroplasticity in older adults*. Clin Neurophysiol, 2021. 132(4): p. 984-992.
135. Howlett, N., et al., *Are physical activity interventions for healthy inactive adults effective in promoting behavior change and maintenance, and which behavior change techniques are effective? A systematic review and meta-analysis*. Transl Behav Med, 2019. 9(1): p. 147-157.
136. Michie, S., M.M. van Stralen, and R. West, *The behaviour change wheel: A new method for characterising and designing behaviour change interventions*. Implementation Science, 2011. 6(1).
137. Sallis, J.F., N. Owen, and M.J. Fotheringham, *Behavioral epidemiology: a systematic framework to classify phases of research on health promotion and disease prevention*. Ann Behav Med, 2000. 22(4): p. 294-8.

138. Engeroff, T., T. Ingmann, and W. Banzer, *Physical Activity Throughout the Adult Life Span and Domain-Specific Cognitive Function in Old Age: A Systematic Review of Cross-Sectional and Longitudinal Data*. Sports Med, 2018. 48(6): p. 1405-1436.
139. Fridolfsson, J., M. Borjesson, and D. Arvidsson, *A Biomechanical Re-Examination of Physical Activity Measurement with Accelerometers*. Sensors (Basel), 2018. 18(10).
140. Fridolfsson, J., et al., *Effects of Frequency Filtering on Intensity and Noise in Accelerometer-Based Physical Activity Measurements*. Sensors (Basel), 2019. 19(9).
141. Fridolfsson, J., et al., *Stronger Association between High Intensity Physical Activity and Cardiometabolic Health with Improved Assessment of the Full Intensity Range Using Accelerometry*. Sensors (Basel), 2020. 20(4).
142. Sallis, J.F., N. Owen, and E.B. Fischer, *Ecological models of health behavior*, in *Health Behavior*. 2008, Jossey-Bass: San Fransisco.
143. Owen, N., et al., *Adults' sedentary behavior determinants and interventions*. Am J Prev Med, 2011. 41(2): p. 189-96.
144. Michie, S., et al., *The behavior change technique taxonomy (v1) of 93 hierarchically clustered techniques: building an international consensus for the reporting of behavior change interventions*. Ann Behav Med, 2013. 46(1): p. 81-95.
145. Sperandei, S., M.C. Vieira, and A.C. Reis, *Adherence to physical activity in an unsupervised setting: Explanatory variables for high attrition rates among fitness center members*. J Sci Med Sport, 2016. 19(11): p. 916-920.
146. Conn, V.S., et al., *Meta-analysis of workplace physical activity interventions*. Am J Prev Med, 2009. 37(4): p. 330-9.
147. Shrestha, N., et al., *Workplace interventions for reducing sitting at work*. Cochrane Database Syst Rev, 2018. 12: p. CD010912.
148. Chu, A.H., et al., *A systematic review and meta-analysis of workplace intervention strategies to reduce sedentary time in white-collar workers*. Obes Rev, 2016. 17(5): p. 467-81.
149. Prince, S.A., et al., *A comparison of the effectiveness of physical activity and sedentary behaviour interventions in reducing sedentary time in adults: a systematic review and meta-analysis of controlled trials*. Obes Rev, 2014. 15(11): p. 905-19.
150. Robroek, S.J., P. Coenen, and K.M. Oude Hengel, *Decades of workplace health promotion research: marginal gains or a bright future ahead*. Scand J Work Environ Health, 2021. 47(8): p. 561-564.
151. Nooijen, C.F.J., et al., *Improving office workers' mental health and cognition: a 3-arm cluster randomized controlled trial targeting physical activity and sedentary behavior in multi-component interventions*. BMC Public Health, 2019. 19(1): p. 266.
152. Nooijen, C.F.J., et al., *The effectiveness of multi-component interventions targeting physical activity or sedentary behaviour amongst office workers: a three-arm cluster randomised controlled trial*. BMC Public Health, 2020. 20(1): p. 1329.
153. Sasaki, J.E., D. John, and P.S. Freedson, *Validation and comparison of ActiGraph activity monitors*. J Sci Med Sport, 2011. 14(5): p. 411-6.

154. Aguilar-Farias, N., W.J. Brown, and G.M. Peeters, *ActiGraph GT3X+ cut-points for identifying sedentary behaviour in older adults in free-living environments*. J Sci Med Sport, 2014. 17(3): p. 293-9.
155. Jonasson, L.S., et al., *Aerobic Exercise Intervention, Cognitive Performance, and Brain Structure: Results from the Physical Influences on Brain in Aging (PHIBRA) Study*. Front Aging Neurosci, 2017. 8: p. 336.
156. Wechsler, D., *Manual for the Wechsler Adult Intelligence Scale Revised*. 1981, New York: Psychological Cooperations
157. Murdock, B., B., *THE SERIAL POSITION EFFECT OF FREE RECALL*. Journal of Experimental Psychology, 1962. 64(5): p. 482-488.
158. Nyberg, L., et al., *General and specific brain regions involved in encoding and retrieval of events*. Proc Natl Acad Sci U S A, 1996. 93: p. 11280-11285.
159. Kirchner, W.B., *Age differences in short-term retention of rapidly changing information*. Journal of Experimental Psychology, 1958. 55(4).
160. Stroop, J.R., *Studies of interference in serial verbal reactions*. Journal of Experimental Psychology, 1935. 18(6): p. 643-662.
161. Delis, D.C., E. Kaplan, and J.H. Kramer, *Delis-Kaplan Executive Function System (D-KEFS)*. APA PsychTests, 2001.
162. Unsworth, N., et al., *An automated version of the operation span task*. Behavior research methods, 2005. 37(3): p. 498-505.
163. Bjorkman, F., et al., *Validity of the revised Ekblom Bak cycle ergometer test in adults*. Eur J Appl Physiol, 2016. 116(9): p. 1627-38.
164. Ekblom-Bak, E., et al., *A new submaximal cycle ergometer test for prediction of VO<sub>2</sub>max*. Scand J Med Sci Sports, 2014. 24(2): p. 319-26.
165. Nooijen, C.F.J., et al., *Common Perceived Barriers and Facilitators for Reducing Sedentary Behaviour among Office Workers*. Int J Environ Res Public Health, 2018. 15(4).
166. Kirk, M.A. and R.E. Rhodes, *Occupation correlates of adults' participation in leisure-time physical activity: a systematic review*. Am J Prev Med, 2011. 40(4): p. 476-85.
167. R Core Team, *A Language and Environment for Statistical Computing; R Foundation for Statistical Computing: Vienna, Austria, 2013*. Vienna 2013.
168. Bates, D., et al., *Fitting Linear Mixed-Effects Models Using lme4*. Journal of Statistical Software, 2015. 67(1).
169. Hothorn, T., F. Bretz, and P. Westfall, *Simultaneous inference in general parametric models*. Biom J, 2008. 50(3): p. 346-63.
170. Wang, S., et al., *A Call for, and Beginner's Guide to, Measurement Invariance Testing in Evolutionary Psychology*. Evolutionary Psychological Science, 2017. 4(2): p. 166-178.
171. Könen, T. and J. Karbach, *Analyzing Individual Differences in Intervention-Related Changes*. Advances in Methods and Practices in Psychological Science, 2021. 4(1).
172. Kievit, R.A., et al., *Developmental cognitive neuroscience using latent change score models: A tutorial and applications*. Dev Cogn Neurosci, 2018. 33: p. 99-117.
173. Hillman, C.H., D.M. Castelli, and S.M. Buck, *Aerobic Fitness and Neurocognitive Function in Healthy Preadolescent Children*. Medicine & Science in Sports & Exercise, 2005. 37(11): p. 1967-1974.

174. Scudder, M.R., et al., *Aerobic capacity and cognitive control in elementary school-age children*. Med Sci Sports Exerc, 2014. 46(5): p. 1025-35.
175. Westfall, D.R., et al., *Associations Between Aerobic Fitness and Cognitive Control in Adolescents*. Front Psychol, 2018. 9: p. 1298.
176. Åberg, M., et al., *Cardiovascular fitness is associated with cognition in young adulthood*. PNAS, 2009. 106(49).
177. Barnes, D.E., et al., *A Longitudinal Study of Cardiorespiratory Fitness and Cognitive Function in Healthy Older Adults*. Journal of American Geriatrics Society 2003. 51.
178. Zeiher, J., et al., *Correlates and Determinants of Cardiorespiratory Fitness in Adults: a Systematic Review*. Sports Med Open, 2019. 5(1): p. 39.
179. Bouchard, C., et al., *Aerobic performance in brothers, dizygotic and monozygotic twins*. Med Sci Sports Exerc, 1986. 18(6): p. 639-46.
180. Pantzar, A., et al., *Relationships Between Aerobic Fitness Levels and Cognitive Performance in Swedish Office Workers*. Front Psychol, 2018. 9: p. 2612.
181. Biswas, A., et al., *Sedentary time and its association with risk for disease incidence, mortality, and hospitalization in adults: a systematic review and meta-analysis*. Ann Intern Med, 2015. 162(2): p. 123-32.
182. *WHO guidelines on physical activity and sedentary behaviour*. 2020, World Health Organization: Geneva
183. Dohrn, I.M., et al., *Accelerometer-measured sedentary time and physical activity-A 15 year follow-up of mortality in a Swedish population-based cohort*. J Sci Med Sport, 2018. 21(7): p. 702-707.
184. Menai, M., et al., *Accelerometer assessed moderate-to-vigorous physical activity and successful ageing: results from the Whitehall II study*. Sci Rep, 2017. 8: p. 45772.
185. Barha, C.K., et al., *Cardiovascular risk moderates the effect of aerobic exercise on executive functions in older adults with subcortical ischemic vascular cognitive impairment*. Sci Rep, 2021. 11(1): p. 19974.
186. Stickgold, R., *Sleep-dependent memory consolidation*. Nature, 2005. 437(7063): p. 1272-8.
187. Gadie, A., et al., *How are age-related differences in sleep quality associated with health outcomes? An epidemiological investigation in a UK cohort of 2406 adults*. BMJ Open, 2017. 7(7): p. e014920.
188. Wilckens, K.A., et al., *Role of sleep continuity and total sleep time in executive function across the adult lifespan*. Psychol Aging, 2014. 29(3): p. 658-65.
189. Stefan, K., M. Wycislo, and J. Classen, *Modulation of associative human motor cortical plasticity by attention*. J Neurophysiol, 2004. 92(1): p. 66-72.
190. Müller-Dahlhaus, J.F., et al., *Interindividual variability and age-dependency of motor cortical plasticity induced by paired associative stimulation*. Exp Brain Res, 2008. 187(3): p. 467-75.
191. Fathi, D., et al., *Effects of aging on the human motor cortical plasticity studied by paired associative stimulation*. Clin Neurophysiol, 2010. 121(1): p. 90-3.
192. Conde, V., et al., *Cortical thickness in primary sensorimotor cortex influences the effectiveness of paired associative stimulation*. Neuroimage, 2012. 60(2): p. 864-70.
193. Cheeran, B., et al., *A common polymorphism in the brain-derived neurotrophic factor gene (BDNF) modulates human cortical plasticity and the response to rTMS*. J Physiol, 2008. 586(23): p. 5717-25.

194. Sale, M.V., M.C. Ridding, and M.A. Nordstrom, *Cortisol inhibits neuroplasticity induction in human motor cortex*. J Neurosci, 2008. 28(33): p. 8285-93.
195. Fratello, F., et al., *Modulation of corticospinal excitability by paired associative stimulation: reproducibility of effects and intraindividual reliability*. Clin Neurophysiol, 2006. 117(12): p. 2667-74.
196. Hofmann, S.G., et al., *The Efficacy of Cognitive Behavioral Therapy: A Review of Meta-analyses*. Cognit Ther Res, 2012. 36(5): p. 427-440.
197. Dalle Grave, R., et al., *Cognitive-behavioral strategies to increase the adherence to exercise in the management of obesity*. J Obes, 2011. 2011: p. 348293.
198. Tsiros, M.D., et al., *Cognitive behavioral therapy improves diet and body composition in overweight and obese adolescents*. Am J Clin Nutr, 2008. 87(5): p. 1134-40.
199. Blom, V., et al., *The effects on self-efficacy, motivation and perceived barriers of an intervention targeting physical activity and sedentary behaviours in office workers: a cluster randomized control trial*. BMC Public Health, 2021. 21(1): p. 1048.
200. Bandura, A., *Health promotion by social cognitive means*. Health Educ Behav, 2004. 31(2): p. 143-64.
201. Edwardson, C.L., et al., *Effectiveness of the Stand More AT (SMaRT) Work intervention: cluster randomised controlled trial*. BMJ, 2018. 363: p. k3870.
202. Healy, G.N., et al., *Reducing sitting time in office workers: short-term efficacy of a multicomponent intervention*. Prev Med, 2013. 57(1): p. 43-8.
203. Herman Hansen, B., et al., *Validity of the ActiGraph GT1M during walking and cycling*. J Sports Sci, 2014. 32(6): p. 510-6.
204. Kozey-Keadle, S., et al., *Validation of wearable monitors for assessing sedentary behavior*. Med Sci Sports Exerc, 2011. 43(8): p. 1561-7.
205. Ozemek, C., et al., *Estimating relative intensity using individualized accelerometer cutpoints: the importance of fitness level*. BMC Medical Research Methodology, 2013. 13.
206. Vaisanen, D., et al., *Cardiorespiratory Fitness in Occupational Groups-Trends over 20 Years and Future Forecasts*. Int J Environ Res Public Health, 2021. 18(16).
207. Hagstromer, M., P. Oja, and M. Sjostrom, *Physical activity and inactivity in an adult population assessed by accelerometry*. Med Sci Sports Exerc, 2007. 39(9): p. 1502-8.