Active workstations
– a NEAT way to prevent and treat overweight and obesity?

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To my wonderful family
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Abstract

Background Modern society is triggering sedentary behaviours in different domains. Different strategies can be used to reduce the time spent sitting and increase physical activity in the office environment, which is one domain where sedentary time is often high. One such strategy could be to install treadmill workstations. With these, the office workers can walk on a treadmill while performing their usual work tasks at the computer. However, the long-term effects of these workstations are not known.

Aim The overall aim of this thesis was to investigate the long-term effects on sedentary behaviour, physical activity and associated health factors of installing treadmill workstations in offices compared to regular office work.

Method In this randomized controlled trial, 80 sedentary, middle-aged, healthy office workers with overweight or obesity were individually randomized into either an intervention or a control group. Those in the intervention group had a treadmill workstation installed at their sit-stand desk, to use for at least one hour per day for 13 months. They further received boosting e-mails at four time-points during the study. Participants in the control group continued to work as normal at their sit-stand office desk. All participants also received a health consultation at the beginning of the study, where they got to discuss physical activity and diet recommendations. Measurements reported include physical activity and sedentary behaviour, anthropometric measurements, body composition, metabolic outcomes, stress, depression and anxiety, cognitive function, structural brain images and interview data. Linear mixed models were used for the main statistical analyses of the quantitative data. An exploratory approach was also undertaken, using orthogonal partial least squares regression on the baseline data. Finally, interview data from participants in the intervention group were analysed using a modified Grounded Theory approach.

Results The intervention group increased their daily walking time and their number of steps at all follow-ups compared to the control group. Concomitantly, a decrease in moderate-to-vigorous intensity physical activity (MVPA) was observed within both groups, mainly during weekends. No intervention effects were observed on any of the body, cognitive or brain volume measurements. Our exploratory analyses revealed a significant association between smaller hippocampal volume and percentage sitting time among participants over 51 years of age. From the interview data, we discovered a core category, “The Capacity to Benefit”. The categories were described as the ideal types the Convinced, the Competitive, the Responsible and the Vacillating, based on the principal characteristics of the participants representing their different
motivational status and strategies to reach the goal of benefitting from the intervention.

**Conclusion** It is possible to increase daily physical activity in office environments by introducing treadmill workstations. Future interventions should adapt strategies for the individuals based on their motivational level, but should also work with the social and physical environment and with factors within the organization to gain the best effects of these interventions.
# Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tbody>
<tr>
<td>ACC</td>
<td>Anterior cingulate cortex</td>
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<tr>
<td>BDNF</td>
<td>Brain-derived neurotrophic factor</td>
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<td>BMR</td>
<td>Basal metabolic rate</td>
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<td>dlPFC</td>
<td>Dorsolateral prefrontal cortex</td>
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<td>DXA</td>
<td>Dual X-ray absorptiometry</td>
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<td>EPOC</td>
<td>Excess postexercise oxygen consumption</td>
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<td>HDL</td>
<td>High-density lipoprotein</td>
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<td>ICC</td>
<td>Intraclass correlation coefficient</td>
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<tr>
<td>ICF</td>
<td>International classification of functioning, disability and health</td>
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<tr>
<td>LPA</td>
<td>Light-intensity physical activity</td>
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<td>MET</td>
<td>Metabolic equivalent</td>
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<td>MVPA</td>
<td>Moderate-to-vigorous physical activity</td>
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<td>NEAT</td>
<td>Non-exercise activity thermogenesis</td>
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<tr>
<td>NEPA</td>
<td>Non-exercise physical activity</td>
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<tr>
<td>OPLS</td>
<td>Orthogonal partial least squares</td>
</tr>
<tr>
<td>PFC</td>
<td>Prefrontal cortex</td>
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<tr>
<td>RMR</td>
<td>Resting metabolic rate</td>
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<tr>
<td>T2D</td>
<td>Type 2 diabetes mellitus</td>
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<tr>
<td>vlPFC</td>
<td>Ventrolateral prefrontal cortex</td>
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<td>VM</td>
<td>Vector magnitude</td>
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Definitions

**Metabolic equivalent (MET):** The ratio of the metabolic cost of the activity to the resting metabolic rate (1).

**Sedentary behaviour:** “All activities, performed while awake, in a sitting, lying or reclining posture, with an energy expenditure of 1.5 METs or less” (2).

**Physical activity:** “All bodily movement produced by skeletal muscles that results in energy expenditure” (Caspersen, 1985). Physical activity can be performed in different modes, frequencies, durations and intensity levels (3, 4);

*Mode:* The specific activity that is being performed.

*Frequency:* How often the physical activity is performed.

*Duration:* How long each bout of physical activity lasts.

*Intensity:* The energy cost of the physical activity. The higher the intensity, the higher the energy cost is.

**Light-intensity physical activity (LPA):** Physical activity performed at the intensity level of 1.5–2.9 METs (3).

**Moderate-to-vigorous physical activity (MVPA):** Physical activity performed at the intensity level of >3 METs (3).

**Physical inactivity:** Not meeting the recommendations for physical activity (2), which in Sweden are 150 minutes of moderate intensity physical activity per week, or 75 minutes of vigorous intensity physical activity, or a combination of both (5).

**Exercise:** “The physical activity that is planned, structured, repetitive and designed to improve or maintain physical fitness, physical performance or health” (6).

**Non-exercise physical activity (NEPA):** The physical activity that is not exercise (7).

**Non-exercise activity thermogenesis (NEAT):** The energy expended from non-exercise physical activity (7).
Enkel sammanfattning på svenska


**Syfte** Syftet med denna avhandlingen var att undersöka långtidseffekter av att installera gåband vid datorarbetsplatser jämfört med sedvanligt kontorsarbete.

**Metod** Vi har genomfört en kontrollerad studie, där 80 deltagare lottades till antingen en interventionsgrupp eller en kontrollgrupp. För att få vara med i studien skulle man vara frisk, ha ett kroppsmasseindex mellan 25 – 40 kg/m², vara mellan 40 till 67 år och ha mestadels stillasittande arbetsuppgifter. Samtliga deltagare hade höj- och sänkbara skrivbord. Deltagarna som lottades till interventionsgruppen fick ett gåband installerat vid sin arbetsplats. De skulle använda detta gåband under 13 månader, minst en timme per dag men gärna mer. Vid fyra tillfällen under studieperioden fick de dessutom ett mail med information om stillasittande och påminnelser om att använda gåbandet så mycket som möjligt. Deltagarna i kontrollgruppen fortsatte att arbeta som vanligt. Alla deltagare fick i början av studien ett hälsoamtal, där de fick diskutera allmänna rekommendationer kring fysisk aktivitet och kost och fick feedback kring några av de prover de tagit vid baslinjemätningarna. Vi mätte fysisk aktivitet, stillasittande, olika kroppsmått, metabol funktion, stress, depression, ångest, minnestester och hjärnvolyms vid två till fem tillfällen under studien. I slutet av studien utförde vi dessutom intervjuer med ett antal deltagare från interventionsgruppen, för att undersöka deras upplevelser av gåbandet och av att ha deltagit i studien.

**Resultat** Deltagarna i interventionsgruppen ökade sin tid i gående på vardagar under hela studien. Ökningen skedde under arbetstid och var störst i början av studien, men fortfarande signifikant ökad vid 13 månader. De ökade dessutom antal dagliga steg. Inom båda grupperna såg vi en minskning av deras tid i måttlig- till högintensiv fysisk aktivitet, framför allt inom interventionsgruppen.

**Slutsatser** Att installera gåband på kontor kan öka mängden fysisk aktivitet i dessa miljöer som i grunden faciliterar ett stillasittande beteende. Vidare fann vi att stillasittande kan kopplas till lägre volym av hippocampus, ett viktigt centrum för minnesbildning i hjärnan. Frånvaro av effekter av interventionen på bland annat metabola funktioner och minnestesterna kan bero på den friska och relativt aktiva gruppen, och/eller minskningen av måttlig- till högintensiv fysisk aktivitet. Det kan även vara så att den lågintensiva fysiska aktiviteten som gåbandet medför kräver en längre uppföljningstid för att effekter ska kunna ses.
Original papers

This thesis is based on the following papers.


Preface

As members of modern society, we are being taught to sit. It starts already at a young age, when we are being told to sit down and be good. This then continues throughout different stages of life, from the school years and throughout the working careers, at least for a large part of the population. Sitting is the norm, and for me and many others this norm has really not been questioned until quite recently.

As a physiotherapist, I believe that physical activity should be a natural part of life at all ages and in all different conditions. Creativity and inspiration have for me always been at their best when physical activity is part of my daily life – either as exercise or just by movement incorporated into my daily life. Taking long walks, alone or in good company, is the best way to get creative thoughts and ideas. So why not combine this also at work, where creativity and different cognitive processes are really important? The idea that we can actually re-think the norm of sitting was thus thrilling, although how breaking this norm should actually be done was not obvious. Is sitting the only way to perform daily office work, or can this be done in another and better way? This idea is what has inspired me from the start of this project and throughout this thesis work.
Introduction

“Eating alone will not keep a man well; he must also take exercise...”.

These words were written by the Greek philosopher Hippocrates around 400 BC, and throughout history, dating as far back as the 600 BC, physical inactivity has been connected with disease development (8). And during evolution, physical activity has naturally been a part of the daily life of humans. However, in modern societies, physical activity has been “built away” from our daily lives. Instead, sedentary behaviour has been built in to the way of living and could in many ways be considered the new norm.

Overweight and obesity

Throughout history, obesity has also always existed. Artefacts dating back to the Stone Age portray obese individuals, and already in ancient civilizations, physicians all gave descriptions of obesity and medical problems related to it (9).

However, the prevalence of overweight and obesity in our societies has increased tremendously in recent decades. According to the World Health Organization, obesity is one of the greatest public health challenges today. Since the 1980s, the prevalence of obesity has doubled worldwide (10) and the global age-standardized mean body mass index (BMI; weight divided by the squared height) has steadily increased in recent decades. In 2014 a large proportion (18.4 %) of the obese population in the world lived in high-income English-speaking countries, that further also contributed to the largest number of severely obese people (27.1 %) (11). The obesity “epidemic” is a public health issue also in the Scandinavian countries. In Sweden, 48.5 % of the population aged 16 and over was overweight or obese in the years 2016–2017, of which 13.1 % was obese (12).

In Västerbotten, a county in northern Sweden, the BMI levels have steadily increased, as observed in data from 1994 and onwards, despite a population-based intervention programme implemented in the region (13).

One common way of measuring and classifying overweight and obesity is to use BMI, which is defined as body weight divided by squared body height (kg/m²). A BMI over 25 kg/ m² is classified as overweight, while a BMI over 30 kg/m² is classified as obesity. In general, with higher BMI, larger risks of e.g. diabetes incidence occur. However, some ethnic groups have a greater health-risk already at BMI levels below 25, while other populations have the same risk at levels above 25, and there might thus be a need for more specific population-based cut-off values (14). BMI is useful since it is an easy measurement to use and provides a good estimation of risks on the populational level. However, BMI cannot
distinguish how the body fat is distributed in the body. Anthropometric measurements other than BMI, such as the waist circumference, might thus be a better predictor of adiposity, especially of visceral adipose tissue (9). The waist-to-hip ratio has also proven to provide a good estimate of the risk of myocardial infarction. A high ratio might, however, be caused by a low hip circumference, which might indicate the protective role of having fat distributed around the hips rather than around the waist, or it can indicate a loss of muscle mass around the hips and the lower limbs, which might be a risk factor for cardiovascular disease in itself (15).

**Health risks of overweight and obesity**

Overweight and obesity is associated with a higher risk of the development of different morbidities, such as hypertension, obstructive sleep apnoea, non-alcoholic fatty liver disease, some cancer, osteoarthritis, gall bladder disease and cardiovascular disease such as stroke or myocardial infarction. Furthermore, overweight and obesity, with excess body fat, is one of the greatest predictors of future development of type 2 diabetes mellitus (T2D) (9). Being overweight in midlife has also shown to increase the risk of developing dementia, such as Alzheimer’s disease (16).

The manner in which fat is accumulated in the body, i.e. the fat distribution, is more closely associated with the risk of metabolic impairment than total fat mass per se (9). When the subcutaneous fat reaches its maximum capacity to store excess free fatty acids, these are stored as ectopic fat, e.g. in the visceral adipose tissue, liver, muscles and heart. Visceral adipose tissue is more metabolically active than subcutaneous adipose tissue, and is closely related to dyslipidaemia and insulin resistance, i.e. a decreased sensitivity to endogenous insulin. Hence, visceral adipose tissue is strongly linked to the development of T2D and cardiovascular diseases (9).

Even though insulin resistance increases with increasing BMI at a population-based level, insulin resistance can still be present also in normal weight individuals, and not all individuals with overweight or obesity develop insulin resistance (17). The metabolically healthy obese people are individuals with BMI-classified obesity, but with, for example, a low amount of visceral fat mass. However, many of the individuals with this metabolically healthy phenotype may be at risk of later morbidity, such as cardiovascular disease, and these individuals might, therefore, still need to be closely followed (9).

**Obesity, brain structure and cognitive functions**

Cognitive function is an umbrella term for our ability to learn, think, and process information and is a prerequisite for our daily life. Some of the most important
cognitive functions for our possibility to be able to function at work or in other
daily life situations include executive functions, working memory and episodic
memory. These different cognitive functions are related to different areas of the
brain.

Executive functions are cognitive functions of higher order that control our ability
of an efficient goal-oriented behaviour and include the abilities to organize, to
plan, initiate, adjust and complete a task, to update and manipulate information,
to inhibit inappropriate behaviours and those inappropriate to the task and to
adapt to the surrounding environment (18, 19). During learning processes, work
situations and other cognitively demanding processes, executive functions are of
the utmost importance to be able to concentrate, initiate and plan the behaviour
(18). Executive functions can be divided into three related, though distinct
cognitive processes. These include response inhibition, mental set shifting
between tasks and working memory content updating (20). Executive functions
are mainly regulated by the prefrontal cortex (PFC), and a greater volume and
thickness of the PFC has been related to a better performance (21). Other areas
also involved in the executive function control regulation are the basal ganglia,
parietal cortex, thalamus and cerebellum (19).

Working memory is regulated by different regions of the brain, including the PFC,
basal ganglia and parietal cortex (22). This cognitive function refers to the
capacity-limited system by which we can consciously process and store
information in the short term, e.g. holding no longer perceptually present
information in mind and manipulating it in some way (22, 23). This system makes
it possible for us to have an effective executive function, since the different
executive functions rely on working memory processes keeping important
current information available and inhibiting unimportant information (24).

Episodic memory is a long-term memory function that is used in our daily life to
store and recall past experiences and episodes. Episodic memory constitutes the
three stages encoding, consolidation and retrieval. Encoding refers to the
processing of the information received, consolidation to the storage of the
information, and retrieval to the process of remembering the stored information
(25). For episodic memory functions, structures in the medial temporal lobe,
mainly the hippocampus, are mostly involved (26).

Obesity has been suggested to be connected with the brain and cognitive
functions, but the association appears to be rather complex. Epidemiological
studies show that overweight and obesity are associated with cognitive functions
in different ways across the life-span. Dahl and Hassing (27), for example,
concluded that while obesity in mid-life was associated with an increased risk of
lower cognitive function later in life, overweight and obesity in later life might
have a protective role against cognitive decline. This connection in later life might, however, be due to a weight-loss occurring during the long pre-clinical phase of dementia, and the causality between these factors are not fully determined (27). Negative effects on working memory and different executive functions e.g. inhibition, cognitive flexibility, decision-making, fluency and planning, have been observed in obesity compared to normal weight (28). It is, however, of importance that most studies investigating the effects on executive function of overweight and obesity are of cross-sectional design, making causal inferences impossible (28). It might thus be that being overweight or obese affect executive functions, or that executive functions affect the weight status. There could also be a bidirectional relationship between these factors (29), although longitudinal and larger studies are needed on this area. Moreover, obesity has also been shown to negatively affect episodic memory, even though more prospective studies are needed, taking into account factors other than obesity itself, such as physical activity and dietary patterns (30). Since the brain is particularly vulnerable at mid-life to effects caused by obesity, with obese individuals showing an increased “brain age” (31), finding strategies to prevent overweight and obesity already in mid-life is therefore of importance for a healthy aging. Lifestyle interventions, including physical activity and healthy dietary habits, thereby avoiding excess fat mass accumulation and the development of e.g. T2D, is recommended in order to reduce the dementia risk (32). Indeed, weight-loss, in combination with improved insulin sensitivity and fitness level, observed after a diet intervention either with or without physical exercise has shown to increase hippocampal volume and improved functional response in the hippocampus among people with T2D (33) and post-menopausal overweight women (34).

One way to better understand how and why obesity may influence cognitive functions in different ways is to examine the association to underlying neural structures. In this line of research, it has been suggested that obesity may be related to a smaller whole brain volume and total grey matter volume among adults in all phases of the life span (35). However, Taki et al. observed a relationship between BMI and global and regional grey matter volume among men, but not among women, which was speculated to be related to the differences in the accumulation of fat mass between women and men, inducing different metabolic risk factors (36). However, cross-sectional analyses make it difficult to assess whether obesity is causing the reduced grey matter volume, or whether a reduced grey matter volume is causing the obesity. In longitudinal research, a higher BMI has been related to a greater decrease of grey matter volume and/or thickness in different parts of the brain, including the temporal, occipital and prefrontal regions, in healthy individuals throughout the lifespan (37-39). Findings from cross-sectional studies have implied a negative association between a smaller hippocampal volume and higher adiposity, but longitudinal
studies have not been able to show this connection (40). Thus, obesity appears to be connected to different regions of the brain, including the hippocampus and the PFC, which in turn has a strong connection to different cognitive functions. This association is however not fully determined yet, and more longitudinal studies are needed to explore this.

The mechanisms behind the increased risk of reduced brain function from overweight and obesity at mid-life are not fully understood. Some studies suggest that the metabolic risk factors that often accompany overweight and obesity, such as hypertension, insulin resistance or dyslipidaemia, can have negative effects on their own, or additively in combination with obesity (41, 42). Indeed, the fastest decrease in global cognitive function has been observed longitudinally in those with obesity and metabolically unhealthy profiles in midlife (41). Other studies imply that non-vascular risk factors, such as genetic factors and environmental factors during early-life might also play an important role in the association between mid-life adiposity and risk of future dementia (43), and confounding factors such as education level, socioeconomical factors or depressive status need to be taken into account in future studies (44). It is, however, not always possible to distinguish the risks of overweight and obesity alone from those of different metabolic risk factors that are often connected to obesity, and the evidence today is insufficient to say that the cognitive impairments of mid-life obesity are independent of comorbidities related to obesity (44).

**Causes of overweight and obesity**

The development of obesity is multifactorial. Genetic components are one major factor for overweight and obesity, and might influence both the development of obesity and the response to treatment (9). However, the highly increased prevalence of obesity has occurred in only a few decades, a time period too short to change genetic components. Something else must therefore be the major cause of the obesity epidemic observed globally.

Simply explained, the main underlying factor in the development of overweight and obesity around the world during recent decades is a long-lasting imbalance between energy intake and energy expenditure. If the energy intake exceeds the energy expenditure over a long period of time, a person will gain weight.

**Energy intake**

How has the trend in energy intake developed in recent decades? Some epidemiologic data implies that the energy intake has increased in the USA from 1970 to 2002, and that this increase likely explains the increase in obesity observed (45). Another study also observed an increase in energy intake in the USA from 1971 to early 2000, with a peak in energy intake during 2003–2004.
However, in this study, a decline in energy intake was observed in the years after the peak up until 2010 (46). Church et al. concluded that the weight gain observed in recent decades is not only dependent on an increase in energy intake, but that a large part is caused by occupational-related decreases in energy expenditure (47). However, a further investigation of the change in energy intake lies beyond the scope of this thesis.

**Energy expenditure**

In humans, total daily energy expenditure consists of three different parts: the basal or resting metabolic rate (BMR/RMR), the thermic effect of food, and the activity thermogenesis (Figure 1).

**Figure 1.** Components of the total daily energy expenditure. BMR = basal metabolic rate. RMR = resting metabolic rate. NEAT = non-exercise activity thermogenesis.

**Basal metabolic rate**

The BMR is the energy required to keep the body going at rest (48). BMR is measured with the individual in a fasting state for 9 hours prior to the measurements, being fully rested sleeping on the site for the testing. Closely related to the BMR is the RMR, which is a similar measure measured under less strict conditions, with the individual in a fasting state for 6 hours prior to the measurement, fully rested and being supine for at least 60 minutes prior to the testing (48). The variation in BMR or RMR between individuals largely depend on age, gender, body size and composition, where differences in fat-free mass
explain most of the difference in BMR or RMR between individuals (49). This factor of the total daily energy expenditure can thus not be altered from day to day.

**Thermic effect of food**

After a meal, energy is needed to digest, absorb and store the nutrients. Seen over 24 hours, the total thermic effect of food accounts for approximately 10% of the total daily energy expenditure in a sedentary person (48) and is therefore not a large part of the total daily energy expenditure.

**Activity thermogenesis**

Physical activity is defined as “all bodily movement produced by skeletal muscles that results in energy expenditure” (6). The energy expended in physical activity, i.e. the activity thermogenesis, is the major cause of variance in total daily energy expenditure between people, regardless of their body size. It thus plays a major role in the total daily energy expenditure (50). Activity thermogenesis is often divided into two different parts, i.e. exercise and non-exercise activity thermogenesis (NEAT).

Exercise has been defined as "the subset of physical activity that is planned, structured, repetitive, and designed to improve or maintain physical fitness, physical performance, or health" (6). NEAT however is the energy expended from non-exercise physical activity (NEPA), i.e. physical activity that is not exercise, but rather activities of daily living (7). Exercise and NEPA can both be performed at different intensity levels. While exercise in general has often been used to describe moderate-to-vigorous physical activity (MVPA), exercise can also be performed at lower intensity levels and still be defined as exercise. Likewise, NEPA, since it involves the activity of our daily lives, is most often performed at lower intensity levels. There, is however, an overlap also for these activities, where some daily activities might be performed at moderate, or perhaps also vigorous, intensity levels.

NEPA activities could include, for example, cleaning the house, working in the garden, playing with your children, taking the stairs at work, walking over to a colleague to ask for advice, carpentry, chopping wood, or walking to the coffee room to get a cup of coffee. Levine et al. showed that, during overfeeding, those individuals who effectively activated their NEAT also resisted fat gain, in comparison to those who did not activate their NEAT (7). In a later study, they concluded that the energy expended from fidgeting-like and non-exercise activities increased the energy expenditure significantly compared to either sitting or standing motionless behaviours (51). This indicates the importance that an active daily life might have on the total activity energy expenditure, where NEAT can, at least theoretically, vary by as much as 2,000 kilocalories per day,
and could thus contribute by a substantial amount to the energy balance, compared to a daily life that mainly consists of sedentary behaviour (52).

**Modern society**

Changes that have occurred in our societies during recent decades, providing a base for the obesity epidemic to grow, can be exemplified by comparing physical activity levels of today with that of societies as they were earlier in history. In an Old Order Amish society, which is a traditional farming community with a lifestyle similar to that in western countries about 150 years ago, the mean daily number of steps was measured to be 18,425 for men and 14,196 for women (53). This could be compared to modern society, where studies from different western societies show a mean number of steps per day ranging between about 5,000 to 10,000 (54). Office workers have been shown to accumulate as few as 3,700 steps during work hours and around 5,000 steps during non-work hours on weekdays (55). Furthermore, the prevalence of overweight and obesity was low in the Old Order Amish society, with 0% of the men and 9% of the women being obese (53). This could be representative of the change that has occurred in western societies in the last decade where NEPA is no longer a natural part of people's everyday lives as much as before. In fact, since the 1960s the occupation-related energy expenditure has steadily decreased due to a shift from occupations requiring MVPA to sedentary occupations (47).

**Sedentary behaviour and health**

Sedentary behaviour is defined as “all waking activities performed in a sitting, lying or reclining posture, with an energy expenditure of 1.5 Metabolic Equivalents (METs) or less”. A MET is the ratio of the metabolic cost of activity to the RMR. The energy expended while sitting at rest is defined as 1 MET. This is based on the assumption of a resting oxygen consumption of 3.5 ml/kg/min as a reference value for adults (1), even though RMR is not a fixed value but rather varies with age, sex and BMI (56). The term sedentary behaviour should not be used interchangeably with the term “physical inactivity”, which refers to a person not meeting the physical activity recommendations (2), which in Sweden includes having 150 minutes of moderate-intensity physical activity per week or 75 minutes of vigorous-intensity physical activity per week, or a combination of both (5).

Already in the 1950s, the harmful exposure to large amounts of sedentary behaviour was reported by Morris et al., who observed a higher incidence of coronary heart disease among bus drivers, who spent most of the working day sitting, compared to bus conductors, who spent most of the day running around collecting bus fares from the passengers (57). Since then, but mainly during the
last decade, a number of meta-analyses have suggested that a large amount of sedentary behaviour is detrimental to health and that it increases the risk of all-cause and cardiovascular mortality, and to a lesser extent also cancer mortality. However, large amounts of MVPA (at least 60 minutes per day) seems to erase the risks of sedentary behaviour (58, 59). Furthermore, sedentary behaviour has also been associated with the risk of developing T2D and cardiovascular diseases (60). TV-viewing is a behaviour that in itself is related to greater health risks, with the highest risk of cardiovascular mortality and/or T2D-development observed among people with the largest amount of TV-viewing (59, 60). Patterson et al. reported that above 6–8 hours per day of total sitting time, or above 3–4 hours per day of TV-time, increases the different mortality and morbidity risks, such as increased risk of cardiovascular disease mortality or T2D incidence (60). However, most or all of the studies included in the meta-analyses have used self-reported measurements of physical activity and sedentary behaviour, including TV-viewing time, measured at one time-point (58-60). Self-reported measurements of sedentary behaviour have a poor validity (61), and TV-viewing itself may not be a good representative measurement of sedentary behaviour per se, since other risk factors, such as snacking or other unhealthy eating behaviours, might be especially associated with TV-viewing (62). It is thus difficult to draw too strong conclusions from these data and to form e.g. public health recommendations about how much sitting is actually harmful and whether and how MVPA actually can erase the harms of sitting.

Observational studies measuring sedentary behaviour using objective measurements however show similar risks of total and prolonged sitting, with cross-sectional associations between, for instance, a large amount of sedentary behaviour and negative effects on different metabolic risk factors such as waist circumference, fasting glucose and insulin, high-density lipoprotein (HDL) cholesterol and triglyceride levels (63), psychological distress (64), and also, at least among individuals with overweight or obesity, with depression (65). Longitudinal studies using objective measurements have also observed associations between a large amount of sedentary behaviour with increases in metabolic risk factors, at least in those who simultaneously increased their BMI levels (66). Observational studies also imply that it is not only the total amount of sedentary behaviour that is a health risk, but also the way that it is accumulated. A large amount of prolonged uninterrupted sitting has been shown to have negative effects on different cardiometabolic risk factors, such as waist circumference, BMI, triglycerides, 2-hour plasma glucose and blood pressure (67, 68), and both the total volume and the accumulation of uninterrupted prolonged objectively measured sedentary behaviour has also been associated with all-cause mortality (69).
Regarding the effects of a large amount of sedentary behaviour on the brain, not much is known. It is most likely a complex relationship between multiple factors, including e.g. MVPA, dietary patterns, fitness levels and sedentary behaviour, and the brain. This is indicated by the longitudinal study by Kesse-Guyot et al. (70), in which a large amount of TV-viewing in midlife was associated with a lower performance regarding verbal memory and global cognitive function 13 years later, although these and other individual associations disappeared when adjusting the models for other lifestyle behaviours, such as physical inactivity, low fruit and vegetable consumption or alcohol abstinence. This suggests that multiple lifestyle factors in combination act on the association with future cognitive decline, and perhaps not only sedentary time alone (70). Cross-sectional analyses have also revealed a relationship between a larger amount of TV-viewing and poorer cognitive function and higher depressive symptoms. Interestingly however, internet use showed the opposite associations to that of TV time, where a higher time using the computer was associated with better cognitive functions (71, 72). The type of task that you do while sitting seems thus to affect the cognitive outcomes differentially. This was also reported in a longitudinal study, where those who had more of a cognitively “active” sedentary behaviour had a smaller hazard risk of major depressive disorder 13 years later compared with those who had more of the cognitively “passive” sedentary behaviour (73). What is more, the previously mentioned health risks that TV-viewing seem to have on its own need to be considered when drawing conclusions based on these studies. Other longitudinal analyses have shown that computer use is associated with a better cognitive function over a six-year follow-up (72), while other studies have not shown any longitudinal associations between sedentary behaviour and cognitive outcomes (71). A recent review of observational studies concluded that the evidence suggests a negative association between sedentary behaviour and cognitive function, but the measurements of sedentary behaviour and cognitive function need to be objective, valid and more standardized before stronger conclusions can be drawn (74).

The ecological model of sedentary behaviour

One of the theoretical frameworks that has guided this thesis work is the “ecological model of sedentary behaviour” (75). In an ecological model, it is assumed that human behaviour is influenced by factors on multiple levels, namely on the intra- and interpersonal, environmental, organizational, community and public policy levels. These factors do not work separately but rather act together on an individual to influence their behaviour (76). This model can be of help in the understanding of the interaction between individuals and their environment, and can be of guidance when constructing interventions aiming to change a behaviour, such as physical activity or sedentary behaviour. For best guidance, the ecological model needs to be directed specifically towards
a certain behaviour. For example, strategies used for increasing active commuting to work might be different from those used when trying to promote physical activity at the office. Thus, different factors at each level of influence need to be identified and targeted for the behaviour of interest to gain the most effect (77).

In 2006, Sallis et al. described an ecological model of four domains of active living. This model was further adapted in 2011 by Owen et al. for use as a guidance for sedentary behaviour research (Figure 2). This model shows that sedentary behaviour takes place in different behaviour settings – which is defined as the physical and social context where sitting takes place – within the four domains of transport, occupation, household and leisure-time (75). Different determinants of sitting exist in each of these behavioural settings, affected by the physical environment and the social frame that are surrounding it. Multiple factors on and across each level act together in a complex interaction to influence the amount of sedentary behaviour taking place. Interventions that aim to reduce sitting can work with factors on one or more of these different levels. If interventions only use strategies to change separate factors on separate levels, the effects may, however, not be large enough to produce a change that is sustained in the long term (76). Thus, the best effect is most likely gained by targeting multiple factors on multiple levels of influence (75, 76, 78).
Figure 2. The ecological model of sedentary behaviour. Reprinted from American Journal of Preventive Medicine, volume 41 number 2, Owen N, Sugiyama T, Eakin E.E, Gardiner P.A, Tremblay M.S, Sallis J.F, Adults´ Sedentary Behaviour –Determinants and Interventions, p189-196 (75), with permission from Elsevier.
Our sedentary working life

An important domain to work with in sedentary behaviour interventions is the occupational domain. One group that is particularly exposed to a large amount of sitting in the occupational domain is office workers. Studies show that office workers in different sectors spend up to 70–80 % of the work day sitting (55, 79-81). The office setting is thus one of the most important to intervene in to reduce sedentary behaviour. Office workers have shown large amounts of sitting during both weekdays and weekends (55, 79, 82). Some studies indicate that office workers spend more time in sedentary behaviour and less time in light-intensity physical activity (LPA) on working days compared to non-working days, and during working hours compared to non-working hours on working days (55, 79, 81). This group also tends to have a sedentary pattern that is of a greater health risk, with fewer breaks from sitting and a higher dose of uninterrupted prolonged sitting, during work time compared to non-work time (79). It has also been observed that individuals who have the most sitting time at work also tend to have the most sitting time and least time in LPA on weekends and on non-working hours on weekdays (55), although Tigbe et al. could not observe any differences in leisure-time physical activity between those with active compared to sedentary occupations (83). Patterns of sitting may differ based on the type of office, and also depend on which country and sociodemographic background the participants come from, but based on the previously reported deleterious health effects that comes from a large amount of sitting, it is of a major importance to facilitate an increased physical activity level in this group.

Measurement techniques

Physical activity is a complex, multifactorial behaviour, which includes the four dimensions of mode, frequency, duration and intensity. The mode, or type, of activity refers to the specific activity being performed, and can also be defined by the physiological demands of the specific activity, such as aerobic or resistance physical activity. Frequency refers to the number of activity sessions performed per day or week, while duration refers to how long a time each bout of activity lasts. Intensity levels is an indicator of the energy cost and metabolic demand of the activity (3, 4). As previously mentioned, physical activity can be performed in different domains, namely the occupational, transportation, domestic and leisure-time domains (3, 4, 84). When measuring total physical activity, all of these domains need to be taken into consideration, so that potential compensatory effects of physical activity in one domain caused by an increase or decrease of physical activity in another domain, can be captured to gain a picture of the total physical activity performed (3). Physical activity results in increased
energy expenditure, which is closely related to the intensity of the physical activity (3), and these two thus represent different constructs (49).

When measuring physical activity and/or sedentary behaviour, it is possible to use either subjective or objective measurement techniques. The choice of measurement depends on the study outcome, the resources available, the feasibility/practicality and the administration of the measurement method (3).

**Subjective measurements**

With subjective measurements, the individual is asked about their physical activity and/or sedentary behaviour that is currently ongoing or that has occurred in the past, either by recording it in log books or by using questionnaires. Global physical activity questionnaires aim to give a quick overview of the total physical activity level, they are short with about 2–4 questions, and aim to guide whether a person meets the physical activity recommendations or not. Short recall physical activity questionnaires consist of a few more items, usually between 7–20 items, and can give a quick assessment of the total physical activity in different intensity levels or domains. Quantitative history physical activity questionnaires can in greater detail capture physical activity over a previous time-period, e.g. the last month, year or over the course of a life. These questionnaires need a little more administration, since they consist of more items (usually 20–60 items) which often, due to the details of the items, need to be administered by an interviewer (3, 84).

With subjective measurements, all four dimensions and domains of physical activity can be captured, including mode, frequency, duration and intensity. Similarly, when using subjective measurements of sedentary behaviour, the frequency and duration in the different domains can be captured (4). However, questionnaires are often prone to different bias, such as recall bias, or social desirability bias (3), and log books are rather time-consuming for the participants (3). Furthermore, the digitalization of the subjective measurement takes time for the personnel. Compared to the objective measurement device activPAL, subjective measurements of sedentary time have showed poor precision and wide limits of agreement, where most of the evaluated subjective measurements underestimated total sitting time. Furthermore, the correlation coefficient was low (0.02 to 0.36) for all evaluated subjective measurements (61). The commonly used “international physical activity questionnaire” has shown poor general agreement with objective data from the Actigraph, with correlation coefficients ranging between 0.23 and 0.46 (85). Participants in that study underreported their sedentary time and time in moderate physical activity, and overestimated their time in vigorous physical activity. However, age, gender and educational level affected the relationship between the questionnaire and the objective
Actigraph, where e.g. a larger overestimation of vigorous physical activity was reported among those with lower compared to higher educational level and among men compared to women (85). Advantages of using subjective measurements include the fact that they are easy and relatively cheap to use, they are easy to administer to a lot of people, and they can capture the domain and context in which physical activity or sedentary behaviour is taking place (3).

**Objective measurements**
The use of objective measurements of physical activity and/or sedentary behaviour has rapidly increased during the last decade. In 2006, the proportion of published papers measuring physical activity that used objective measurements was around 4 % – in 2016, the same number was about 71 % (86). Multiple techniques are available to objectively measure the constructs of energy expenditure, physical activity and/or sedentary behaviour.

**Measurements of energy expenditure**
Energy expenditure can be measured using doubly labelled water or indirect calorimetry.

**Doubly labelled water**
In this method, the hydrogen and oxygen of the water molecule is “tagged” with stable isotopes in order to estimate the production of carbon dioxide and thus total energy expenditure over one to three weeks. This method is often considered the golden standard of measurements of total energy expenditure. By drinking known amounts of the two stable isotopes deuterium and oxygen–18 as water, the different elimination rates of these two isotopes can be quantified. While deuterium is eliminated as water, oxygen–18 is eliminated as water and carbon dioxide. The difference in how much of these isotopes that has been eliminated from the body thus represents the carbon dioxide production over that measured time period (3, 48). The elimination rate is calculated from urine, blood or saliva samples taken daily during the measurement period. The methodology has a small error rate (6–8 %) (48), but is rather expensive.

To estimate the average activity thermogenesis of the measurement period, the BMR or RMR also needs to be measured. Assuming that the thermic effect of food is 10 % of the total energy expenditure, the activity thermogenesis is calculated as 0.9 * total energy expenditure – BMR (or RMR) (kcal/day). Using this method, you can however not acquire detailed information regarding, for example, the mode, intensity, duration or variability in physical activity between days during the measurement period (49, 87).
**Indirect calorimetry**
With indirect calorimetry, the amount of oxygen that is consumed and/or the carbon dioxide that is produced is measured, making it possible to determine how much energy that is required during different physical activities (49). This method is highly accurate and is considered to be the golden standard measurement during more strict measurement conditions, such as when measuring energy expenditure in a laboratory (3), but is also commonly used during more free-living conditions (49). It is however rather expensive and demanding regarding equipment, and trained personnel is needed (3).

**Motion sensors**
To measure sedentary behaviour and/or physical activity using motion sensors, pedometers and accelerometers can be used. These can then be used to estimate the energy expenditure levels.

**Pedometers**
A pedometer is most often worn on the belt or with a waistband, and as it counts the number of steps taken it is a measure of total physical activity. Pedometers are relatively easy to use, cheap and of low burden for both participants and researchers with easy processing of the data. For this reason, they are a popular tool to use when aiming to motivate and encourage physical activity (49). The newer models of pedometers include microelectromechanical systems, with processing of the data using algorithms of the system signals to calculate the number of steps taken. This has improved the accuracy of the devices, but the measurement of energy expenditure is not adequate from these devices (84). Some of these more advanced pedometers are also capable of measuring distance, cadence and time spent at different intensity levels (3, 84).

The downsides of pedometer are that they cannot register body position or static activities (84) and nor are they valid when measuring lower walking speeds (<3.2km/h), thus making them less suitable when measuring physical activity in certain populations (49, 84). There are also questions about their accuracy when measuring in different sub-populations, where, for example, central obesity might affect the number of steps taken due to the device being “rotated” by the larger waist circumference. Further, false steps can relatively easily be recorded in the device by, for example, shaking it (3, 49).

**Accelerometers**
The accelerations, i.e. the change in velocity over a given time period, of the body during movement can be captured by accelerometers. These accelerations can then be used to estimate the intensity, frequency and duration of the physical activity. This technology has rapidly increased in recent years when the accelerometers have become more readily available on the market (3, 49). Since
Sedentary behaviour has started to be highlighted as an important factor for health, inclinometers have also been developed that also measure the posture to better distinguish sitting and standing postures (84).

When processing the data, the accelerations are summarized in the software throughout a pre-defined time period (called an epoch). The accelerations then need to be converted to another unit, most commonly to “counts”, which can be expressed, for example, as counts per minute or counts per day. Based on different thresholds for these counts, the duration and frequency of time spent at different intensity levels, such as sedentary behaviour, LPA or MVPA, can be calculated. Based on different algorithms, the energy expenditure can be estimated from the accelerometer data (3, 49, 84). In general, however, the ability of these algorithms in estimating energy expenditure compared to, for example, indirect calorimetry, is rather low (88).

The more days you measure using an accelerometer, the more likely you are to capture the habitual pattern of activity. Intraclass correlation coefficient (ICC) has often been used to try to calculate the reliability of these devices. With this method, both the intra- and interindividual variability are accounted for. To reach an ICC-value of 0.80 for measurements of total time, three to five days of monitoring is needed (89). The higher the variability of a behaviour, the more days of measurement are needed to capture the habitual patterns. Pedersen et al. thus observed that when measuring MVPA during work and leisure-time hours, 4.2 and 5.8 days were needed, respectively, to reach an ICC of 0.80. When measuring sedentary behaviour during work and leisure-time, at least 4.7 and 5.5 days were needed to reach an ICC of 0.80, implying domain specific variability in behaviour with a greater variability in MVPA and sedentary behaviour during leisure-time (90).

Advantages of using accelerometers include the detail of the data regarding intensity, frequency and duration that can be received, the low burden of the participants, and that they can store data for a relatively long time period. Disadvantages include the time-consuming data processing, the inability to measure certain activities such as cycling or weight-lifting, and the fact that, if the device is used on the thigh or waist, activities that mainly involve the upper body are missed (3).

**Physiological measures**

Common ways of estimating physical activity based on physiological measurements is to measure the heart rate. This can also be combined with, for example, accelerometer data in order to obtain a better estimate of the physical activity.
Heart rate
As heart rate has a strong linear connection to the intensity of the physical activity, thus oxygen consumption, devices that measure heart rate can be used to estimate time spent in different physical activity intensity levels and energy expenditure (3, 49). With these devices, electrodes measuring heart rate can be fastened to the chest, sending wireless signals to a wrist-born monitor receiver (3). Before the start of measuring an individual calibration should be performed, in which a submaximal test is carried out after the assessment of RMR (49).

However, since heart rate can be influenced by other factors (such as caffeine, body temperature or stress) bias exist, especially for physical activity performed at lower intensity levels. For physical activity performed at MVPA levels, the method is more precise. Another bias is, however, that activities that involve the upper extremity have a higher heart rate per second compared to activities involving the lower extremity. Another issue is the time-lag between the start or stop of the physical activity and the increase and decrease in heart rate, respectively. Advantages of the method include the relatively low burden of the participants and the fact that it is a relatively inexpensive method (3).

Multisensor systems
By combining physiological measures with accelerometry, the measures of physical activity and energy expenditure can be more precise and capture more aspects of physical activity. When using devices that combine, for example, physical activity and heart rate monitoring, the increase in heart rate can more easily be applied to an actual increase in physical activity based on the accelerometer data, and not to other factors that might also increase the heart rate, such as caffeine or stress. Other devices record other physiological measures, such as skin temperature and heat flux, and combine this with accelerometer data. In combination with other factors, such as age, gender, weight and height, the energy expenditure can be calculated more accurately from these multisensory systems. However, the method is often more expensive and, depending on which device used, the burden of the participants is often higher (3, 84).

Other approaches
Physical activity can also be captured using other methodologies than described above, such as direct observation.

Direct observation
With this method, an observer watches and records the physical activity and/or sedentary behaviour that a person is performing. This can be done by either observing directly or by video recording the person, capturing the amount of physical activity or sedentary behaviour being performed and also the context in
which the physical activity/ sedentary behaviour takes place. Usually, small time intervals are being registered, with different coding systems for intensity level, type of activity and location of the physical activity or sedentary behaviour. The method is time-consuming for the researchers and it is important to provide essential training before the assessments (3), especially if many observers are involved.

**Physical activity intensity levels**

The higher the intensity of the activity, the more energy is needed during the actual performance, and oxygen uptake is thus increased to meet the demand of the higher energy need. After the activity session is completed, the oxygen consumption is still elevated for a period of time, called the “excess postexercise oxygen consumption” (EPOC) (91). Evidence suggests that one factor influencing EPOC is the intensity of exercise, where a higher intensity physical activity has a larger EPOC compared to moderate intensity physical activity. However, in order to provide a significant effect on weight loss over a year, at least one hour of vigorous intensity physical activity (70 % of VO₂max) three times per week is needed in order to lose about three kilograms of fat. In response to moderate intensity physical activity sessions (about 50 % of VO₂max) three times per week, the annual reduction in fat would be approximately 311 g from EPOC. This amount of fat loss could be relevant for some people struggling with overweight or obesity, but would, however, be difficult for many overweight or obese people to achieve (91). Diabetes and obesity have been shown to be the major determinants of non-adherence to a cardiac rehabilitation programme including aerobic and resistance training, with waist circumference and body fat percentage acting as important moderating factors to the adherence rate (92). Thus, since the adherence to moderate- or high-intensity programmes is most likely low among the general population, and among overweight and obese individuals in particular, simply relying on exercise to lose weight may be difficult. Even though MVPA compared to LPA has a higher energy expenditure per time unit and a higher EPOC, LPA may still contribute to a greater extent to the total daily energy expenditure, since the total volume of these light-intensity activities can be higher compared to MVPA.

To define different intensity levels, either absolute or relative intensities can be used. Absolute intensity is the energy required to perform an activity, and is not related to the individual’s maximum capacity (3). One common way of quantifying absolute intensity is to use METs. The energy expended during activity is then reported as multiples of the energy demand of sitting quietly at rest. For example, walking slowly (less than 3.2 km/h) on a level surface demands twice as much energy as when sitting quietly at rest, i.e. it has a MET-value of 2, while walking at 4 km/h on a firm level surface demands three times as much
energy as when sitting quietly at rest, i.e. it has a MET-value of 3 (1). LPA is often classified as activities between 1.5 and 2.9 METs, and MVPA is classified as activities over 3 METs (3). Relative intensity on the other hand is related to the individuals maximum capacity, for example to the maximal oxygen uptake (VO₂max) (3). A more detailed description of this measurement lies beyond the scope of this thesis.

**Light-intensity physical activity**

MVPA and exercise in different modes is known to have good effects on several obesity-related diseases, such as T2D (93), and brain health (94, 95). Whether similar effects observed by a large amount of MVPA can also be found by a large amount of NEPA, or LPA, is largely unknown, since the physiological and health effects of LPA have not been as well studied as those of MVPA. Before the introduction of accelerometers, the most commonly used method to capture physical activity was self-reported measurements. However, due to LPA activities often being more closely incorporated into the activities of daily life compared to MVPA and exercise activities, that are planned and structured, the LPA activities are more difficult to capture using self-reported measurements. Thus, questionnaires have more commonly been better at capturing vigorous than light- or moderate-intensity physical activity (96). Furthermore, not all questionnaires have been developed to capture these types of daily activities, with the biggest focus in research throughout history being on MVPA. However, with objective measurements becoming more available, it is also now possible to measure LPA more easily and with a better accuracy. Thus, LPA and the putative health effects emerging from it now have a better potential to be further examined.

From prospective epidemiological studies, it has been reported that there is an association between higher amount of LPA and a reduced all-cause mortality risk (97). The same conclusion was drawn from longitudinal studies measuring LPA objectively where MVPA was adjusted for (98), and it has been observed that for every 60-minute increase in LPA, the all-cause mortality hazard was reduced by 16 % (99). Furthermore, as observed in isotemporal substitution models based on longitudinal data, sedentary time that is replaced by LPA is observed to reduce the all-cause mortality risk (100, 101). This has also been observed in cross-sectional data, where replacing sedentary time with LPA has been shown to reduce the odds of having the metabolic syndrome (102). Mixed results have been reported from prospective studies on the relationships between LPA and different cardiometabolic diseases and risk markers (97). Although cross-sectional studies have shown associations between a larger amount of LPA and better outcomes on, for example, inflammatory markers, adiposity, triglyceride and insulin levels, the cross-sectional evidence for associations between LPA and other metabolic markers, such as glycaemia, is, however, low or inconsistent (97, 98).
Associations have also been observed between higher levels of LPA and a lower risk of psychological distress (64).

Perhaps the strongest evidence base today on the effects of increased LPA comes from acute experimental studies. The systematic review and meta-analysis by Chastin et al. (97) concluded that, based on experimental studies, breaking up sitting has a positive effect on postprandial glucose and insulin levels, with effects on glucose perhaps being greater among people with obesity or metabolic impairments (97). Dempsey et al. have also shown persisting nocturnal effects on glucose when interrupting sitting with either LPA walking or simple resistance exercises in overweight and obese individuals with T2D (103), suggesting that the effects of breaking up sitting on glucose lasts longer than just during the acute phase. However, another study did not observe any differences in night-time mean glucose levels when interrupting sitting every 15 or 30 minutes compared to when breaking sitting every hour in people with T2D. An improvement in fasting glucose, night-time glycemic variability and nocturnal glucose increment (the dawn phenomenon) was however observed when interrupting sitting every 15 minutes, but not when interrupting it every 30 minutes, indicating a dose-response relationship (104). This however needs to be further investigated in larger long-term studies. Effects on triglycerides of acutely breaking up sitting with LPA breaks are less clear (97). Notably, lipid levels may be more affected by the timing of the measurements and might need to be measured at a later stage than glucose or insulin, since the effect on lipid metabolism may not come immediately after the intervention (105).

Acute effects on different cognitive functions, such as inhibition, cognitive flexibility or episodic memory, brain-derived neurotrophic factor (BDNF) or cortisol levels of breaking up sitting with light- or moderate-intensity physical activities have also been investigated. While Mullane et al. did observe positive effects on cognitive functions, including working memory and executive functions, of regularly breaking up sitting with either walking or cycling activity breaks (106), others have not been able to show any effects on cognition in the acute phase (107, 108). Further, improvements in self-reported fatigue, energy, vigour and/or mood have been reported when breaking up sitting with light- or moderate-intensity physical activities, or when performing one bout of moderate-intensity physical activity in the morning (107, 108). These results imply that regularly breaking up sitting might have important effects on reduced fatigue and mood levels, and perhaps also on cognitive functions, but this needs to be studied in the longer term.

Whether one bout of MVPA can “eliminate” the negative health effects of prolonged sitting and whether regular breaks from sitting has the same or better effects than one bout of MVPA is yet to be established. Holmstrup et al. observed
that an exercise session of one hour in the morning resulted in higher glucose levels throughout a large part of the day in young obese individuals with impaired glucose tolerance compared both to a day of uninterrupted sitting and to a day of breaking up sitting once an hour for five minutes. While the regular activity breaks reduced insulin levels throughout the entire day of testing compared to uninterrupted sitting, the one-hour exercise session lowered the insulin levels early in the day in the hours close to the exercise bout, but increased the insulin concentrations later in the day compared to uninterrupted sitting and to the regular breaks condition (109). However, Maylor et al, did not observe any differences in glucose and insulin when performing either one 30-minute bout of continuous moderate intensity physical activity in the morning or when breaking up sitting every 60 minutes with 2 minutes of long vigorous intensity physical activity bouts in healthy subjects. The vigorous intensity physical activity breaks did improve the triglyceride and HDL levels compared to uninterrupted sitting (110). Duvivier et al. pooled results from three different studies performed on individuals with normal weight and with overweight and obesity with and without T2D. Interestingly, they observed that, when replacing 5–6 hours per day of sitting with 2–3 hours of standing and 2–4 hours of LPA walking for four days, positive effects were observed on lipids and insulin resistance. These effects were not observed when performing 60 minutes of MVPA cycling in the morning over the four days. However, the MVPA cycling had positive effects on markers for endothelial dysfunctions, which was not observed when replacing sitting time with standing or LPA walking. It thus seems, based on this study, that LPA and MVPA might have different effects on vascular and metabolic markers, suggesting the importance of performing both behaviours (111), but, again, more research is needed.

In summary, emerging evidence from both acute and epidemiological studies implies that increasing LPA in substitution of sedentary behaviour has a great potential in improving health, but more long-term studies using objective measurements are needed. It is important to measure and investigate all these different behaviours, i.e. sedentary behaviour, LPA and MVPA, in the population, since they all may contribute to health in different ways. Among people with overweight and obesity, physical inactivity and sedentary behaviour has been shown to be more common compared to among people with normal-weight (112, 113). Overweight and obese people also tend to self-report a lower amount of physical activity and higher amount of TV-viewing compared to normal weight individuals (114). Furthermore, healthy obese people tend to have a higher total physical activity level compared to unhealthy obese people (113), indicating the importance of physical activity in this population. Some evidence further states that obese individuals may have greater health-risks from a sedentary lifestyle (115), although this needs to be further established. Overweight and obese populations are important target groups for interventions aiming to increase
physical activity and reducing sedentary behaviour. Importantly, overweight or obese individuals may face more barriers than normal weight subjects when starting an exercise or MVPA-programme. Since lack of time and lack of enjoyment are important barriers for lifestyle changes among obese individuals (116), introducing interventions that increases people’s LPA, integrating it into their daily lives, might be more feasible and be as important for public health compared to only focusing on structured exercise or MVPA interventions alone.

Increasing light-intensity physical activity in offices

One way of working with the environmental level to reduce sitting and increase LPA in the office environment is to install so-called active workstations, consisting of e.g. a treadmill or bike desk installed at the office desk. With these, the office workers might increase their NEPA level while still continuing working as usual at their computers. Treadmill workstations were invented as early as 1989 by Edelson and Danoff, who already at that time point questioned whether sitting is the best way to perform office work (117). Levine and Miller started to further investigate the effects of treadmill workstations in 2007, observing a mean increase in energy expenditure of 119 kcal/hour for walking and working compared to sitting (118). Since then, more research on treadmill and other types of active workstations has been performed. In the short-term, active workstations have shown to be feasible for, for example, radiologists interpreting computed tomography scans (119), and an increase of up to 2,000 steps per day has been observed when using a treadmill workstation for two weeks (120). What is more, the participants reported that they would continue to use it if it was available for a longer time-period (120).

Changing behaviour and maintaining the change over time is difficult. Hence, even though short-term studies may look promising, it is important to investigate the long-term effects of such interventions. A few studies exist that have investigated the long-term effects of treadmill workstations. Table 1 describes and shows the results of studies investigating the effects of individual treadmill workstations with a study period of 6 months or longer.
Table 1. Studies of 6 months or longer investigating the effects of individual treadmill workstations.

<table>
<thead>
<tr>
<th>Author, year, country</th>
<th>Study design and length</th>
<th>Study population</th>
<th>Significant results from baseline to last measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Koepp, 2013, USA (121)</strong></td>
<td>Prospective trial, no control group but a control period of 6 months before study start for 23 participants</td>
<td>Employees of all BMI-levels at a financial services company (n=36)</td>
<td>Measured with waist-worn Actical Physical activity and sedentary behaviour</td>
</tr>
<tr>
<td><strong>John, 2011, USA (122)</strong></td>
<td>Prospective trial – no control group</td>
<td>Overweight and obese university office workers (n=12)</td>
<td>Measured with thigh-worn activPAL Physical activity and sedentary behaviour</td>
</tr>
</tbody>
</table>
Ben-Ner, 2014, USA (123)  
Prospective trial; 17 participants had treadmills for 12 months; 23 participants had a control period of 6 months and then treadmills for 6 months.  
Employees at a national financial services company. BMI not reported (n=30)  
6–12 months  
Increased time in light (1-2 mph) and “active” intensity (>2 mph)  
Decreased sedentary time  
Measured with waist-worn Actical  
Not reported  
BMI = body mass index. HDL = high-density lipoprotein.

Thompson, 2014, USA (124)  
Randomized cross-over trial  
6 months (intervention for 3 months, control period for 3 months)  
Overweight and obese physicians (n=20)  
Increased daily physical activity (activity units) during treadmill desk period  
Decreased weight  
Decreased percent total fat mass  
Not reported  
Measured with waist-worn GRUVE  
Decreased weight  
Decreased percent total fat mass  
No other effects  
BMI = body mass index. HDL = high-density lipoprotein.
Regarding productivity at work while using treadmill workstations, both Koepp et al. and Ben-Ner et al. observed an initial decrease in work performance after installing the treadmill workstations, followed by an increase in work performance to levels above baseline values at the end of the study, i.e. there was an improvement over time (121, 123).

Instead of buying individual treadmill workstations, it is also possible to have shared workstations between several employees. This has also been shown to increase the daily number of steps and LPA and reduce the sedentary behaviour during working hours (125). The implementation of these shared workstations might, however, induce other difficulties than the implementation of individual workstations. One such difficulty when using shared treadmill workstations could be to find a good schedule that suits all of the employees who are supposed to use the same treadmill workstation. Hence, it can be more difficult for people to be flexible and use the shared treadmill when it suits them the most, which can affect the adherence rates (126).

Other options are to install bike desks, where the office workers use a bike installed at the office desk. This has also been shown to increase daily physical activity and reduce percent body fat when examined over a 20-week time period, but no effects on anthropometric measurements, cognitive functions, work performance or brain activity were observed (127). Furthermore, participants using a bike desk have been reported to be positive about the use of the bike desk, and almost all of the participants wanted to continue to use them (128).

According to these studies of active workstations, physical activity seems to increase when they are installed in offices. The effects on body measurements and metabolic function are, however, less clear, where some observed a positive response on some of the metabolic parameters, while others did not. Based on the promising results on work performance from these previous studies of treadmill workstations (123), and the well-known effects on cognitive function of increased levels of MVPA or fitness (95), one can suspect that an improved cognitive function can be observed also when increasing LPA levels, but this has not been evaluated in long term studies. Furthermore, effects on other parameters, such as stress or depression, have not to our knowledge been investigated either. None of these previous studies with individual workstations have had a “true” randomized controlled design, since either they were lacking a control group, included a control group that was followed for a shorter period of time compared to the intervention group, or divided the participants into groups based on the participants own preferences. Furthermore, the study samples have been relatively small, ranging between 12 and 36 participants.
As indicated by the latest Cochrane review (129), investigating the effect of workplace interventions aiming to reduce sitting time at work, the evidence for different types of interventions including sit-stand tables or active workstations, is of low quality. Also, not much is known about the effects on different body measurements or brain functions of reducing sitting and increasing walking at work. There is thus a strong need for a randomized controlled trial with a long follow-up and larger sample size, to investigate whether active workstations can influence these parameters, important for public health, and whether they are feasible in the long-term. It is also recommended to include measurement of sedentary behaviour and physical activity in other domains, to capture potential compensatory effects outside work of changes in occupational behaviour (129). Since the workplace is the biggest contributor to total sedentary time (55), interventions targeting this domain are of major importance. With emerging research showing the negative effects of prolonged, uninterrupted sitting, it is of the utmost importance to find strategies and interventions that can increase LPA levels in office environments.
**Aims**

The overall aim of this thesis was to investigate long-term effects on sedentary behaviour, physical activity and associated health factors of installing treadmill workstations in offices compared to regular office work.

Our primary hypothesis was that, compared to the control group, the intervention group would increase their daily time spent walking.

The secondary hypotheses were that, compared to the control group, the intervention group would:

- Increase their daily sitting time, increase their daily standing time, and increase their daily LPA. No changes in MVPA levels were hypothesized.
- Improve their anthropometric measurements, body composition, metabolic function, and stress, depression and anxiety levels.
- Improve their cognitive functions and brain structures.

Further, aims in paper number 3 was to explore putative baseline relationships between measurements of sedentary behaviour, physical activity, body and stress measurements, cognitive function and brain structure.

Finally, in paper number 4 we investigated the experiences of being part of the study, exploring barriers and facilitators among the treadmill workstation users, using a qualitative approach.
Materials and Methods

The theoretical model

Figure 3 shows the theoretical model behind our intervention. The Increasing physical activity (Inphact) Treadmill study can be seen as a complex intervention, in which different factors interact at different levels of complexity. Our model for the study was based on the ecological model of sedentary behaviour (75), and developed by the use of the components in the International Classification of Functioning, Disability and Health (ICF). This is a model recognizing that a disease or disability affects a person both regarding their body structures and function, as well as their activities and participation, all influenced by environmental and personal factors (130). By installing the treadmill, we induced changes at the environmental level. By anchoring the study among the company management, for example, by sending information to the managers closest to the participants, by making it possible for the participants to perform the different measurements during their work hours, and by raising awareness on the companies with information about the health risks of sedentary behaviour, changes at the social level were targeted. Finally, individual factors were targeted by an individual health consultation, by giving each participant individual feedback on some of their test values and by the boosting e-mails sent out to the participants in the intervention group.

Study design
The Inphact Treadmill study was a randomized controlled trial, in which the participants were individually randomized either to an intervention or a control group.

Participants

Recruitment
Managers at different local offices in Umeå, Sweden, were contacted with information about the research field and the planned study. Employees of companies from both the private, governmental, municipality and county work sections were recruited. If granted permission, the research team visited the workplace and gave thorough information about the study to the employees. Information about the study was also given via telephone to interested employees who could not attend the information meeting.

Inclusion and exclusion criteria
To be included, the subjects had to be between 40 and 67 years old, have a BMI between 25 and 40 kg/m² and have an office job mainly consisting of sedentary work tasks. All participants had a sit-stand office desk at their office work place. Subjects were excluded if they had diabetes mellitus or other severe diseases. Furthermore, pregnant women and people not able to walk on a treadmill were excluded. For a detailed description of the exclusion criteria, see Papers 1 and 2.

Screening procedure
A screening procedure was performed with interested employees, first via a telephone interview and then at a visit to the University Hospital of Umeå. Those who met the inclusion and none of the exclusion criteria were included in the study and followed for 13 months.

The intervention
After the baseline measurement, all participants received a health consultation with a nurse. This consultation consisted of a discussion of some of the individual screening or baseline measurements in relation to general recommendations about physical activity and diet.

Whereas the participants in the control group then continued to work as usual at their sit-stand desk, participants in the intervention group received a treadmill workstation installed at their sit-stand desk. Figure 4 shows the treadmill workstation. They were asked to use this for at least one hour per day. The installation of the treadmill workstation was performed by an experienced
physiotherapist. The participants in this group also received four boosting e-mails during the study (Figure 5), which included reminders to use the treadmill as much as possible and information about the health risks of a large amount of sitting. The participants in the control group continued to work as usual at their sit-stand office desk.

**Figure 4.** The treadmill workstation. Photo: Mattias Pettersson, Inhousebyrån, Umeå University.
Figure 5. Timeline of the intervention.
Measurements

Quantitative measurements were taken at 2 to 5 times during the study period. Table 2 shows the time points for the different measurements reported in this thesis. The participants visited the University Hospital of Umeå or the University in Umeå on two different days at baseline, 6 months and 13 months, where anthropometric, body composition and metabolic functions were measured on one day, and cognitive function at another day. Those who performed magnetic resonance imaging (MRI) visited the University Hospital of Umeå on a third day at baseline and 13 months. Accelerometers, questionnaires and food diaries were handed out to the participant at their workplace. The interviews were conducted either in connection with any of the other measurements at the University or University Hospital, or at another time point, all according to what worked best for the participants.

Table 2. Main outcome variables reported in the different papers in the thesis.

<table>
<thead>
<tr>
<th>Reported in</th>
<th>Measurement</th>
<th>Baseline</th>
<th>2 m</th>
<th>6 m</th>
<th>10 m</th>
<th>13 m</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Paper 2</strong></td>
<td>Sedentary behaviour, physical activity</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td></td>
<td>Diet</td>
<td>x</td>
<td>x</td>
<td></td>
<td>x</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Anthropometry</td>
<td>x</td>
<td></td>
<td>x</td>
<td></td>
<td>x</td>
</tr>
<tr>
<td></td>
<td>Body composition</td>
<td>x</td>
<td>x</td>
<td></td>
<td>x</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Metabolic function</td>
<td>x</td>
<td></td>
<td></td>
<td>x</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Salivary cortisol</td>
<td>x</td>
<td></td>
<td></td>
<td>x</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stress and energy</td>
<td>x</td>
<td></td>
<td></td>
<td>x</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Depression and anxiety</td>
<td>x</td>
<td></td>
<td></td>
<td>x</td>
<td></td>
</tr>
<tr>
<td><strong>Paper 3</strong></td>
<td>Cognitive function</td>
<td>x</td>
<td>x</td>
<td></td>
<td>x</td>
<td></td>
</tr>
<tr>
<td></td>
<td>MRI&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>x</td>
</tr>
<tr>
<td><strong>Paper 4</strong></td>
<td>Interview</td>
<td></td>
<td></td>
<td>x</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>MRI = magnetic resonance imaging
**Sedentary behaviour and physical activity**

To be able to measure both sedentary behaviour and physical activity intensity levels in a valid way, the accelerometers activPAL and Actigraph were used. Participants were also asked to report their usual sleeping and working hours, as well as any longer removal times of any of the two accelerometers, during the measurement periods.

**activPAL**

The activPAL3 is a tri-axial accelerometer that is worn on the front middle thigh. The inclinometer in the device can register the position of the leg, and the device can thus distinguish between sitting/lying, standing or walking based on accelerometer signals and thigh position. The activPAL has, compared to the criterion measure of direct observation, shown to have good to excellent interdevice reliability for sitting, standing, upright and walking positions, and for steps and cadence (ICC ranging between 0.79 and 0.99) (131, 132), with the lowest ICC of 0.79 observed for walking during ADL-tasks, which was probably caused by a small interindividual variability lowering the ICC (131). Furthermore, the study by Grant et al. demonstrated that, compared to direct observation, the activPAL has an excellent validity for detecting sitting, upright, standing and walking behaviours, with a good level of agreement, an overall percentage of agreement of 95.9 %, and overall sensitivity and predictive values ranging between 88.1 and 99.6 % (131). The activPAL is also valid in measuring steps and cadence, with an excellent level of agreement (<1 % mean difference) and a low value of percentage error (<1.2 %) at different walking speeds or surfaces (treadmill or outdoors) (132). Further, its accuracy in measuring breaks from sitting is demonstrated to be excellent, with a small and narrow percentage bias (133), and it is also sensitive in finding changes in sitting time and in breaks from sitting between two conditions (133, 134).

However, when determining physical activity at different intensity levels, the activPAL is not as accurate. Even though it demonstrated the smallest mean absolute percent errors when estimating the energy demand of sedentary behaviour and LPA, it demonstrated large errors for moderate-intensity and vigorous-intensity physical activity when compared to indirect calorimetry (135).

Compared to subjective measurements of sedentary time or physical activity, or with different cut-points from the Actigraph, the activPAL is more accurate and precise for measuring sedentary behaviour, and it is also more sensitive in finding differences in sitting time or breaks from sitting between different conditions (133, 134). All in all, the activPAL has a good support in the literature for being a reliable and valid device for measuring different aspects of sedentary and walking behaviour in free-living and laboratory environments.
In our study, the activPAL3 and activPAL3 micro (PAL Technologies Limited, Glasgow, UK; default settings) was used to measure sitting, standing and walking time, number of steps and different aspects of sedentary patterns. The activPAL was worn on the anterior mid-line of the right thigh, fastened with a Mepore surgical dressing. The participants were instructed to wear this device for 24 hours a day for seven consecutive days when they were also wearing the ActiGraph, and only to remove it during water-based activities. Outcomes from the activPAL were processed in a custom-made Excel macro (HSC PAL analysis software v2.19s) based on different time filters. All data processing was performed by one researcher. As a quality check, 10% of the files analysed were double-checked by a student within the research group.

The Actigraph

One of the most commonly used accelerometers to estimate physical activity of different intensity levels is the Actigraph (ActiGraph, Pensacola, Florida, USA). The GT3x-model of the Actigraph is a triaxial device that registers accelerations in the vertical, antero-posterior and medio-lateral orthogonal plane. Counts, based on the frequency and intensity of the accelerations, are created and predefined cut-points can be used to categorize these counts into different intensity levels. The higher the counts, the higher the intensity of the activity is. The cut-points can be based on vertical axis accelerations alone, or on a composite vector magnitude (VM), based on two axes (VM2) or all three axes (VM3). Using VM3 has been shown to increase the correlation between the gold standard doubly labelled water-technique and different accelerometer metrics, such as daily activity counts, steps, physical activity energy expenditure and time in MVPA, compared to when using vertical axis counts alone (136). The so-far most often used VM3 activity cut-points (137) were developed by Sasaki et al (138).

In our study, the ActiGraph wGT3x-BT was used to measure LPA and MVPA. This device was worn by the participants with an elastic belt around the waist, above their right hip, for 14 consecutive days per time point. They were instructed to put the device on as soon as they got out of bed in the morning, and to remove it just before going to bed in the evening. It was also removed during water-based activities. Data was collected at 30Hz, and agd-files with a 60-second epoch length were used. To define a non-wear time period, a modified version of the Choi algorithm (139) was used, with 60 minutes of consecutive zero counts, no spike tolerance and a small window length of one minute (137), using VM3. Based on the count values created from the post-filtered files, the data was divided into different intensity levels, based on cut-points modified from the Freedson Adult VM3 (2011) algorithm (138). LPA was classified as 201–2,689 counts per minute and MVPA as ≥2,690 counts per minute. For the Actigraph, data was only calculated for total time awake during weekdays and weekends. A summary of the activPAL and Actigraph data processing is given in Table 3.
Table 3. Information about the activPAL and ActiGraph data processing.

<table>
<thead>
<tr>
<th>Device</th>
<th>Filter</th>
<th>Day of week</th>
<th>Calculations based on</th>
<th>Non-wear periods based on</th>
<th>Valid day definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>activPAL</td>
<td>Total time awake</td>
<td>Weekdays and weekends</td>
<td>Self-reported sleeping hours</td>
<td>Self-reported non-wear time</td>
<td>≥10 hours wear time, ≥500 steps, and ≤95% of the time spent sitting or standing</td>
</tr>
<tr>
<td></td>
<td>Working hours</td>
<td>Weekdays</td>
<td>Self-reported working hours</td>
<td>Self-reported non-wear time</td>
<td>≥4 hours wear time, ≥250 steps, and ≤95% of the time spent sitting or standing</td>
</tr>
<tr>
<td></td>
<td>Non-working hours</td>
<td>Weekdays</td>
<td>Total time awake – working hours</td>
<td>Self-reported non-wear time</td>
<td>≥4 hours wear time, ≥250 steps, and ≤95% of the time spent sitting or standing</td>
</tr>
<tr>
<td>ActiGraph</td>
<td>Total time awake</td>
<td>Weekdays and weekends</td>
<td>Modified Choi algorithm</td>
<td>Algorithm defined non-wear times</td>
<td>≥10 hours wear time</td>
</tr>
</tbody>
</table>
**Dietary intake**

To capture dietary intake, a food diary was used, in which the participants filled in everything they ate and drank during four consecutive days; three weekdays and one weekend day. To estimate portion sizes, a food-portion picture book was used in which portion-weights are illustrated (140). The nutritional analysis software Dietist XP version 3.2 (Kost och Näringsdata AB, Bromma, Sweden) was used to estimate the energy intake from the reported dietary intake. This software is based on the Swedish National Food Administration’s food database. For the analyses, the mean energy intake based on the four days of measurement was calculated per time-point.

**Anthropometry and body composition**

These measurements were taken at the Clinical Research Centre at the University Hospital in Umeå, Sweden. For more information about these measurements, see Papers 1 and 2. Briefly, anthropometric measurements included body height and length, BMI, waist and hip circumference, sagittal abdominal diameter, systolic and diastolic blood pressure and resting heart rate. Body composition was measured using Dual X-ray absorptiometry (DXA) (Lunar Prodigy X-ray Tube Housing Assembly, Brand BX-1 L, Model 8743; GE Medical Systems, Madison, WI; USA). For whole-body measurements, DXA has shown excellent precision (141). From the DXA measurements, we analysed fat mass, lean soft tissue, android and gynoid fat mass.

**Metabolic function**

After an overnight fast, blood samples were drawn to measure lipids (triglycerides, cholesterol, apolipoprotein B and A1), long-term glucose control (Haemoglobin A1c), inflammation (C-reactive protein), hepatic enzymes (alanine aminotransferase (ALT) and aspartate aminotransferase (AST)), fasting glucose and fasting insulin. The hyperinsulinaemic euglycaemic clamp is considered to be the gold standard for measuring peripheral insulin sensitivity. This is, however, a rather time-consuming method, and surrogate indices can, therefore, be used to reduce the burden of the participant and the cost of measurement. We estimated insulin sensitivity according to the Homeostasis Model Assessment for insulin resistance index, calculated as (fasting glucose * fasting insuline)/22.5, which is one of the fasting indices showing the best correlation with clamp studies (142).

**Stress, energy, depression, anxiety and salivary cortisol levels**

Stress was measured with both objective and subjective measurements. Salivary cortisol was collected at 4 time-points (at 07.00 am, 11.00 am, 16.00 pm and
23.00 pm) during one day at the three time-points when collected. Self-reported stress and energy was measured using the stress- and energy scale (143). Depression and anxiety were measured using the Hospital anxiety and Depression Scale (144). A more thorough description of these measurements is given in paper number 1 and 2.

**Cognitive function**
To test cognitive function, a test battery consisting of eight tests was used. We used the Free recall and Word recognition tests to test episodic memory function; the N-back, Flanker and Trail making test to test the executive functions of inhibition, updating and shifting; the Backward digit span to test working memory; and the Similarities task and the Digit symbol task to test processing speed. Figure 6 shows the order of the tests. A thorough description of the included tests is given in paper number 1 and 3.
Figure 6. The cognitive test battery.
**Magnetic Resonance Imaging**

Structural images of the brain were created in order to investigate the hippocampus and the PFC cortical thickness. High-resolution T1 images were created to examine hippocampus volume and PFC grey matter thickness.

To segment the brain, Freesurfer (145) version 6 was used for automatic segmentation of the brain. The volume of the left and right hippocampus (mm$^3$) was based on the subcortical segmentations. These were then added together to calculate the total volume of the hippocampus. PFC thickness (mm) was based on the cortical segmentations. Different regions-of-interest of the PFC were calculated as the mean values of the bilateral superior and middle frontal gyri (dIPFC); bilateral opercular, orbital and triangular gyri (vIPFC); and the bilateral anterior and middle-anterior cingulate gyri and sulci (ACC). The left and right PFC cortical thickness were then averaged.

**Interviews**

By using a convenience sampling at 13 months, 20 of the participants from the intervention group participated in an interview, held with the aim of investigating their experiences of taking part of the study and barriers and facilitators to using the treadmill workstations. A modified Grounded Theory approach (146) was used for the analyses of the interview data. The interviews were based on a semi-structured interview guide and were conducted by two researchers and/or two physiotherapy students, where one or two of the researchers or students participated in each interview. After the interviews had been held, they were transcribed word by word for later coding.

Using constant comparison, the emerging codes were merged into subcategories and categories, and a core category was created, showing the connection between the different categories. The emerging codes, subcategories and categories were constantly compared to the underlying data, making sure that the results were grounded in the data. Data was triangulated between four researchers who had all participated in the coding process.

**Statistical analyses**

In Papers 2 and 3, linear mixed models were used for the statistical analyses. In Paper 2, analyses of three-way interactions between group (intervention/control), time-point (baseline, 2-, 6-, 10-, and 13 months) and day of week (weekday/weekend) were carried out on the activity measurements for total time awake. Furthermore, in Paper 2, data was analysed for work time and non-work time, energy intake and body measurements investigating two-way
interactions between group and time-point. In Paper 3, two-way interactions between group and time-point was used to investigate effects of the intervention on cognitive function, grey matter volume and thickness, and BDNF levels. All mixed models in Papers 2 and 3 further included sex (man or woman) as fixed effect, subject as random intercept, and age at baseline as a covariate. Intracranial volume was also included as a covariate in the models for hippocampal volume and PFC thickness in Paper 3.

In Paper 3, a mediation analysis was also performed to compare changes from baseline and 13 months in LPA, hippocampus volume and BDNF levels. Further in Paper 3, Orthogonal Partial Least Squares (OPLS) was used to investigate multivariable correlations of the baseline data in an exploratory manner, with percentage of time spent sitting as the response.
Results

The findings from each of the measurements in the study is presented in detail in each individual article. A summary of the results is given here.

Demographic data

Table 4 shows the demographic data at baseline. The mean age of the participants was 51.3 years, and the mean BMI was 29.1 kg/m². The waist circumference for women was 94 cm and for men 101.5 cm, which is greater than the upper limit associated with increased metabolic risks for women, but slightly less for the men (88 cm and 102 cm recommended levels, respectively) (147). The majority of the waking and working hours at baseline were spent sitting (556 and 263 minutes, respectively), and they spent about one hour of walking during work hours at baseline.
Table 4. Demographic data of all participants included (n=80) at baseline.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean (SD)</td>
<td>51.3 (±6.8)</td>
</tr>
<tr>
<td>Women/men, n (%)</td>
<td>44/36 (55/45)</td>
</tr>
<tr>
<td>Marital status, n (%)</td>
<td></td>
</tr>
<tr>
<td>Married/living together</td>
<td>72 (90)</td>
</tr>
<tr>
<td>Living alone/divorced</td>
<td>7 (8.75)</td>
</tr>
<tr>
<td>Missing</td>
<td>1 (1.25)</td>
</tr>
<tr>
<td>Education, n (%)</td>
<td></td>
</tr>
<tr>
<td>Compulsory</td>
<td>2 (2.5)</td>
</tr>
<tr>
<td>Upper secondary</td>
<td>30 (37.5)</td>
</tr>
<tr>
<td>University</td>
<td>36 (45)</td>
</tr>
<tr>
<td>Other tertiary</td>
<td>11 (13.8)</td>
</tr>
<tr>
<td>Missing</td>
<td>1 (1.3)</td>
</tr>
<tr>
<td>Weight (kg), mean (SD)</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>81.7 (±10.4)</td>
</tr>
<tr>
<td>Men</td>
<td>93.6 (±13.1)</td>
</tr>
<tr>
<td>BMI (kg/m²), mean (SD)</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>29.0 (±3.3)</td>
</tr>
<tr>
<td>Men</td>
<td>29.3 (±3.1)</td>
</tr>
<tr>
<td>Waist circumference (cm), mean (SD)</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>94.0 (±8.7)</td>
</tr>
<tr>
<td>Men</td>
<td>101.5 (±7.9)</td>
</tr>
<tr>
<td>Percent fat mass, mean (SD)</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>44.6 (±4.8)</td>
</tr>
<tr>
<td>Men</td>
<td>31.2 (±5.5)</td>
</tr>
<tr>
<td>Time spent sitting (min), mean (SD)a</td>
<td></td>
</tr>
<tr>
<td>Total time awake</td>
<td>556 (±133)</td>
</tr>
<tr>
<td>Working hours</td>
<td>263 (±103)</td>
</tr>
<tr>
<td>Time spent standing (min), mean (SD)a</td>
<td></td>
</tr>
<tr>
<td>Total time awake</td>
<td>314 (±125)</td>
</tr>
<tr>
<td>Working hours</td>
<td>217 (±104)</td>
</tr>
<tr>
<td>Time spent walking (min), mean (SD)a</td>
<td></td>
</tr>
<tr>
<td>Total time awake</td>
<td>107 (±41)</td>
</tr>
<tr>
<td>Working hours</td>
<td>52 (±25)</td>
</tr>
<tr>
<td>Daily number of steps, mean (SD)a</td>
<td></td>
</tr>
<tr>
<td>Total time awake</td>
<td>9,001 (±3,808)</td>
</tr>
<tr>
<td>Working hours</td>
<td>4,587 (±2,313)</td>
</tr>
</tbody>
</table>

aThe daily sitting, standing, and walking time and number of steps is presented for weekdays and weekends combined for total time awake, and for working hours during weekdays.
Paper 2

Physical activity and sedentary behaviour measurements

Walking time and number of steps
The intervention group increased their daily walking time and their number of steps during total time awake on weekdays at all follow-ups, while the control group remained at the same level throughout the study. The observed changes for walking time and number of steps were mainly due to changes within the intervention group during working hours (Figure 7). The differences were greatest initially during the study but were still significant at 13 months. No differences were observed between or within the groups at weekends or during non-working hours on weekdays.

Figure 7. Walking time (a) and number of steps (b) during working hours. Estimated means (SE). ***p<0.001 difference between groups.

Standing and sitting time
No major changes were observed for daily standing time during total time awake on weekdays or weekends. Further, no major effects were observed on time spent standing during working hours (Figure 8a) or non-working hours on weekdays for either of the groups. Compared to baseline, the intervention group reduced their daily sitting time at all follow-ups but the 13-month follow-up during total time awake on weekdays. The control group remained at the same level throughout the study. The same pattern was observed during working hours (Figure 8b).
Figure 8. Standing time (a) and sitting time (b) during working hours. Estimated means (SE). *p<0.05 difference between groups.

No major effects were observed for sitting time at weekends. The intervention group reduced their time spent sitting during non-working hours on weekdays at all follow-ups, and the control group at all follow-ups except at 13 months (Figure 9).

Figure 9. Sitting time during non-working hours. Estimated means (SE).

Sedentary patterns
The intervention group took fewer short breaks (<3 minutes long), and slightly more long breaks (>20 minutes long) during their total time awake on weekdays, while no differences were observed within the control group. The same pattern was observed during working hours (Figure 10). No major effects were observed at weekends or during non-working hours on weekdays.
Light- and moderate-to-vigorous physical activity
The intervention group increased their LPA levels at 2 months on weekdays, but then went back to baseline levels again (Figure 11a). No differences were observed within the control group. At weekends, the intervention group reduced their LPA at 13 months while the control group increased their LPA compared to baseline, leading to a difference of 44 minutes per day between the groups at this time point (Figure 11b).

Figure 10. Number of short (a) and long breaks (b) during working hours. Estimated means (SE). *p<0.05 difference between groups.

Figure 11. Daily light-intensity physical activity during total time awake on weekdays (a) and weekends (b). Estimated means (SE). **p<0.01 difference between groups.

Compared to baseline, the intervention group reduced their MVPA at all follow-ups and the control group reduced their MVPA at 13 months during total time awake on weekdays (Figure 12a) and at weekends (Figure 12b). No differences were observed between the groups at any time point.
Energy intake
The intervention group reduced their daily energy intake at all follow-ups compared to baseline, but there was no difference between the groups at any time point.

Body measurements and metabolic function
No major effects or between-group differences were observed regarding anthropometric measurements, body composition or metabolic function.

Stress, energy, depression, anxiety and salivary cortisol
No major effects or between-group differences were observed regarding subjective stress and energy levels, depression and anxiety scores, or salivary cortisol measurements.

Paper 3
Cognitive functions and structural brain imaging
No effects of the intervention were observed for cognitive functions, hippocampal volume or PFC cortical thickness, except for dIPFC thickness which slightly decreased within the intervention group from baseline to the 13-month follow-up. Both groups improved their performance in the domains of executive function and processing speed, and thus also in the composite cognitive score measurement, compared to baseline.

We did not observe any effects on BDNF levels in any of the groups during the study. The mediation analyses revealed that, within the intervention group, changes in LPA between baseline and 13 months had a positive direct effect on hippocampal volume change between baseline and 13 months, but this was not mediated by changes in BDNF levels between baseline and 13 months, as there

Figure 12. Daily moderate-to-vigorous physical activity during total time awake on weekdays (a) and at weekends (b). Estimated means (SE).
was no indirect mediating effect. No relationship, neither direct nor indirect, between change in LPA, BDNF and hippocampus volume was observed in the control group.

**Exploratory analysis of baseline data**

The main finding from the OPLS analyses was that, among participants older than 51 years, a higher percentage sitting time was associated with a smaller hippocampal volume (Figure 13).

**Figure 13.** Variables contributing significantly to the orthogonal partial least squares models with percent sitting time as the response variable for the group (a) aged ≤ 51 years and (b) aged > 51 years. Stalpes with positive values indicate a positive association and staples with negative values indicate a negative association with percent sitting time. DXA = dual X-ray absorptiometry. ACC = anterior cingulate cortex. vIPFC = ventrolateral prefrontal cortex. LPA = light-intensity physical activity. ALT = alanine aminotransferase.

**Paper 4**

**Interview data**

The analyses of the interview data identified a core category called “the Capacity to Benefit”. This represents the knowledge among and the ability of all participants to reach a better health by increasing physical activity at work. The categories that emerged from the data were presented as “ideal types” (148), that should not be interpreted as individual subjects, but rather as representing
abstract conceptualizations of the participants attitudes, ideas and experiences, identified during the coding processes. The ideal types are labelled the Convinced, the Competitive, the Responsible and the Vacillating. These ideal types should not be considered as static, since the participants can move in between these ideal types during different phases of their life, depending on e.g. internal or external factors. Different strategies are being used by these different ideal types to reach the goal, mainly due to different motivational status.

The Convinced knows what is right and live accordingly. They have a high motivational level, with no difficulties in detecting facilitators. They rarely see any barriers – if they do, they can easily find strategies to overcome them.

The Competitive is inspired and motivated by challenges and by competition – as long as they are better than anyone else, their goal is reached.

The Responsible is very concerned about doing the right thing. Their motivational level is based on their belief that if they have made a promise, they must try to keep it.

The Vacillating has a more struggling path to get to the target, always fighting to keep up the motivational level. They try to do their best, but constantly struggles with the barriers experienced on the way.

Internal and external factors are constantly affecting the participants in different ways. Different ideal types have different abilities to see facilitators and barriers. Where some ideal types can more easily disregard and remove barriers, others tend to “get stuck” on them. The design of the treadmill, being clumsy with a cheap design affected some of the participants, whereas others did not mind the design. Further, factors in the workplace, such as the type of work task and the type of office, also affected the use, where many stated that having an individual office is preferable in order not to disturb the co-workers or others. The attitudes of managers and co-workers also affected the participants. Again, different ideal types respond in different ways to these environmental cues.
Discussion

We found it possible to increase daily physical activity in office environments by installing treadmill workstations. A reduced amount of MVPA, mainly at weekends, was, however, observed within the groups, which could imply negative compensatory effects of the intervention. However, a decreased sitting time during non-working hours was also observed. No effects were observed on body measurements, metabolic functions, stress, energy, depression or anxiety, or on cognitive functions and brain volumes. Interestingly, a cross-sectional negative association between sedentary time and hippocampal volume was observed in our exploratory analyses, however only in participants older than 51 years. Based on what the participants said during interviews, four different ideal types emerged from the data. These included the Convinced, the Competitor, the Responsible and the Vacillating. All the participants had the capacity to reach the goal of benefitting from the treadmill intervention, although different ideal types tend to use different strategies to reach this goal, primarily based on their motivational level. Moreover, physical and social factors in the environment also influenced the ideal types differentially regarding the use of the treadmill workstations.

The study population

Umeå is a university city and thus has relatively well-educated inhabitants. The city has many large sport centres, and a culture of being physically active, including a city planning that promotes active commuting to work. Our study participants had a high level of MVPA at baseline of between 50 and 70 minutes per day. This level of MVPA is similar to that observed in a Swedish population-based study on people aged 50 to 64 years, in which 49 minutes per day was spent in MVPA (149). In addition, the mean total standing time at baseline in our study was more than five hours per day, which is rather a lot compared to studies performed in other countries (150) but also in other parts of Sweden (151). One of the most important determinants for physical activity is education, where a higher amount of physical activity is observed among people with higher socioeconomic status (152). Our population consisted of healthy overweight or obese, non-smoking, middle-aged adults, of whom many had a university degree or other tertiary educational level qualification; it was thus a socioeconomically advantaged group. Performing this study on another study population, including for example subjects with metabolic diseases, or in a city with other sociodemographic conditions would likely have given different effects on, for example, metabolic function. Those who chose to participate in this study are thus already at the start a selective group of people who, due to the rather demanding nature of our study with several time-consuming measurements, most likely had
some sort of interest in health questions. Our study population might therefore not be representative of the general population in Sweden, resulting in differences in, for example, MVPA-levels between our study participants and previous population-based studies, in which around 30 minutes of daily MVPA was observed (153, 154). However, one important aspect to take into consideration is that previous studies, showing a lower amount of MVPA, used uniaxial data from the vertical axis from the Actigraph (153, 154), and the data from these studies might thus not be fully comparable to ours and others using VM data, which tends to give a higher amount of MVPA compared to uniaxial accelerometer data (155).

Fitness and/or MVPA levels may moderate the deleterious effects of sitting. Ekelund et al. showed in their meta-analyses of self-reported data that those who spend more than 60 minutes per week in MVPA do not have any increased risks of all-cause, cardiovascular or cancer mortality with a large amount of sitting, as is observed among those who do not have that large amount of MVPA (58, 59). Furthermore, a large amount of LPA might be especially important for women with low MVPA levels (156). McCarthy et al. showed that cardiorespiratory fitness modified the effects of the regular activity breaks on postprandial glucose levels, where those with higher fitness had less effect of regularly breaking up sitting. They thus reason that breaking up sitting might be most important for people with lower fitness levels (157). Similar results were observed in the study by Ekblom-Bak et al., using an isotemporal substitution model, showing that individuals with lower fitness levels had greater effects on measurements on insulin resistance by replacing sedentary time with LPA compared to those with greater fitness levels. The same was observed for individuals with higher compared to lower fasting glucose levels (149). Other studies show that low cardiorespiratory fitness, large amounts of sedentary time, and low amounts of physical activity (of light, moderate and/or vigorous intensity level) is independently associated with the metabolic syndrome and T2D (158, 159). The associations between these different factors thus need to be further investigated.

We did not measure physical fitness in our study and it is not clear how pronounced the health risks related to a large amount of sitting at baseline were in our group of participants.

Even in this relatively homogenous group of people, we could observe four different ideal types, and different factors affecting their motivation to use the treadmill. This implies that an intervention like this could be even more difficult to implement in the “real world”, outside of a research project, which might be directed towards a more heterogenous sample than in our study. Our participants were recruited from 13 different companies (17 offices). All of these workplaces had some sort of structured health-promoting programme for their employees,
and studies investigating effects in other countries or in other workplaces in Sweden might therefore have another “starting point”.

Physical activity has been shown to be one important factor distinguishing between healthy and unhealthy overweight and obese individuals, where those who are healthy tend to have larger amounts of physical activity than those who are unhealthy (113). For meeting the recommended levels of MVPA, in combination with an active everyday life, approximately 7,000–8,000 steps per day is needed, with more steps per day giving greater health effects (54). In our study, our participants took about 9,000 steps at baseline, which increased to about 10,500 steps per day in the intervention group at 13 months. They thus had a high level of physical activity already to start with. The increase in daily steps could possibly induce other health effects than seen on, for example, our anthropometric or metabolic measurements, i.e. other factors of health that we may not be aware of and have not measured in this study.

Earlier interventions to increase physical activity in offices

Our study is to our knowledge the first randomized study in this field and forms a good platform for further studies in this research area. Earlier interventions on treadmill workstations with various study designs have had various results. The few long-term studies that exist have shown positive results on various body measurements and metabolic parameters, but no clear pattern has been observed, in line with our results.

Trends over time in long-term interventions

A tendency for larger increases in time spent walking in the beginning of the study, as in our study, has also been observed in previous treadmill workstation studies (121, 122), bike desk studies (128) and in different multicomponent interventions including sit-stand table installations (160, 161). Ben-Ner et al. observed an increased work performance over time, with an initial decline followed by an increased performance compared to baseline (123). Changes in cardiometabolic risk factors have been reported in the later phase of the intervention, but not in the early phases (162, 163). If the adherence to the intervention is maintained over time, some improvements can thus be observed in the long term that were not observed at the short-term follow-up (123, 162), implying that some physiological and/or cognitive effects could require some time before they can be observed. This emphasizes the importance of long-term follow-up in these types of interventions, as short-term studies may not give results that can be extrapolated to long-term effects. Hence, even longer-term follow-ups than in our study may be required to see any effects.
**Compensatory effects**

There may be several reasons for our lack of results on other than the activity measurements. Firstly, our participants were healthy to start with, and they were already relatively active already at baseline. This can have made it difficult for us to induce effects on body functions and structures. It may also be that the intensity of the treadmill walking was too low to actually influence these or other parameters. Due to the low intensity of the intervention, even longer follow-up times can be required to improve, for example, body or cognitive measurements. The decrease that we observed regarding MVPA, although not significant between the groups, may however be a key factor regarding the lack of effects on body and brain measurements. The reduction of leisure-time MVPA can thus have prevented potential effects from the increase in daily walking time during working hours, since it is the total amount of physical activity that is of importance.

Other studies have also observed compensatory effects on physical activity at leisure-time after installing sit-stand tables in offices (164, 165). Interestingly, Nooijen et al. observed, based on self-reported population-based cohort data from Stockholm, that those who changed from sedentary to physically active occupations reduced their leisure-time exercise levels, while those who changed from physically active to sedentary occupations increased their leisure-time exercise levels (166), implying a compensatory effect of occupational-based physical activity. However, other studies have not observed any compensatory effects on sedentary behaviour and/or physical activity during non-working hours or at weekends when installing treadmill workstations in offices in the USA (123), or when installing sit-stand tables with or without a multicomponent intervention (160, 161, 167-170). The reported differences between studies are difficult to explain. It might be due to the fact that the studies have been performed in different countries, with different norms or built environments, where different possibilities for e.g. active commuting to work might exist. It could also be due to socioeconomic and cultural differences between corporates with different levels of systematic health-promoting work in the workplaces. Furthermore, differences in study population phenotypes, such as age and BMI status, or differences in study protocols and instructions to the participants may exist.

Another plausible compensatory effect that might occur from increasing physical activity at work is changes in energy intake. We observed a decrease in energy intake within the intervention group at all follow-ups compared to baseline. This can suggest a reduced energy intake due to lowered appetite levels as a compensatory response. More likely, however, this is due to the reporting of energy intake being very time-consuming and demanding for the participants, as was often mentioned during the interviews. All the measurements performed
during the study were rather time-consuming, and the food registration was something that many of the interviewed participants felt was the most tiresome. This could lead to a larger underestimation of the energy intake, due to the participants not reporting everything that they ate, or to a larger adaption of the eating habits during the days of registration in the later phases of the study, when the participants might be more tired of these measurements.

Compensatory responses that might be a barrier to weight loss in response to exercise interventions could be of behavioural or metabolic nature, and both volitional and automatic compensatory responses have been identified. For example, a reduced RMR after an exercise-induced weight-loss is an automatic metabolic response (171). This is assumed to be a defensive mechanism where the body strives to prevent a negative energy balance and thus reduces RMR to save energy (87). Choosing to eat a bag of crisps after an exercise session is a volitional choice, whereas other behavioural responses are more difficult to classify as automatic or volitional, such as slightly increasing the portion-size or reducing the NEPA levels after beginning to exercise (171). Whether the compensatory responses on physical activity observed in our study were of volitional and/or automatic nature is difficult to assess. The participants might have had a smaller perceived need for MVPA due to the increase of walking time at work, or it could have been a physiological response aiming to restore energy levels. Our interview data did not however support a behavioural volitional response among our participants, since very few participants mentioned during the interviews that the treadmill walking had affected their physical activity outside of work. There might also have been some sort of biological processes behind this, but there can only be speculations regarding that. Only one minor adverse event was reported, so injuries connected to the treadmill walking were most likely not causing the decrease.

Future larger studies need to investigate whether these compensatory effects of increasing physical activity in, for example, the occupational domain leads to a decrease in physical activity in other domains, determining the extent of, the reasons for, and the best strategies to handle these putative effects. It would be of importance to investigate whether the compensatory effects are greater when increasing physical activity in the occupational domain compared to when increasing physical activity in other domains, to better know when and how to target this compensation.

**Breaking up sitting**

Another potential explanation for the lack of effects on body and brain measurements is the reduction in the number of breaks that we observed within the intervention group. This decline in the number of breaks was observed in the
accelerometer data and implied in the interview data, where some participants indicated during the interviews that, once they had begun to use the treadmill, they might as well use it for the desired hour in one stretch and then not use it more that day. Previous research has indicated that it is not only the total amount of sitting that is important for metabolic functions, but perhaps more important is the way that the sitting time is accumulated. Acute experimental studies show that by breaking up sitting time every 20–30 minutes performing some sort of physical activity of either light or moderate intensity or of light resistance characteristics, positive effects are observed regarding postprandial glucose and/or insulin levels (172-174), mean nocturnal or 24 hour glucose levels (103, 175), systolic (176, 177) and diastolic blood pressure (176, 177), improved lipidomic profile (178) and reduced fatigue levels (108). Notably, by pooling data from three studies on acute effects of interrupting prolonged sitting in overweight or obese people, Dempsey et al. concluded that the effects on postprandial glucose or insulin levels from regularly breaking up sitting were higher the more insulin resistant the individual was (179).

Mechanisms behind the effects of reducing and regularly breaking up sitting are just starting to be investigated. Some researchers have proposed inactivation of lipoprotein lipase, negatively affecting e.g. triglyceride uptake and HDL cholesterol production, to be one important physiological reason for the harmful effects of sedentariness, which could be distinctly separated from the physiological benefits of exercising (180). This, however, needs to be further studied in humans (97). One more commonly mentioned and studied explanation of the positive effects observed by breaking up sitting on, for example, glucose and insulin is that the spreading out of activity throughout the day when regularly taking breaks from sitting stimulates the muscle contraction uptake of glucose (181).

Based on previous studies, it is thus possible that the reduction in number of short breaks and the small increase of longer breaks that we observed prevented positive effects that could potentially have been observed from increasing walking time. More information to the participants before the study about the health effects of regularly breaking up sitting might have prevented this behaviour. However, since the planning and the start of the study, much more research has become available regarding the benefits of regularly breaking up sitting, as opposed to only reducing the total amount of sitting, and this was therefore not as well-known during the planning of the study. Future studies need to take this into consideration. It might also be that another option than the treadmill desk might be more feasible if the aim is to increase the number of breaks and change the sedentary patterns. Simpler advice, such as using a printer further away from the office, taking the stairs, or walking over to the workmate instead of sending them an e-mail, might work just as well in that purpose, but these strategies need
to be further investigated with the “right” instructions for the aim of increasing number of breaks.

**Light-intensity physical activity and cognitive function**

We could not observe any effects of our intervention on cognitive functions, hippocampus volume or cortical thickness. A suggested mediator of improved brain plasticity following exercise is BDNF (94). However, we could not observe any effects on BDNF in our study, which may have limited the possibilities for the intervention to produce plastic effects on brain and to improve cognitive function. Either the effect of treadmill walking is too small to produce any effects on cognitive function, brain structure or BDNF, or the total volume of treadmill walking was too small, i.e. one might need to walk much more in order to gain any effects due to the lower intensity of the physical activity. It is also possible that the decrease in MVPA and in number of breaks observed among our participants (see paper 2) might have hindered potential benefits from increasing walking time. Further, when it comes to BDNF, the question is also what we can say regarding the effects on the central nervous system, based on a peripheral measurement of BDNF. Based on the positive effects of MVPA on the brain (94, 95), interventions like ours might need to focus not only on increasing LPA levels, but to also keep the levels of MVPA remained, in order to gain putative effects on the brain. However, the relationship with BDNF and LPA, sedentary behaviour and breaks from sitting needs to be further investigated.

Kennedy et al. (182) discuss potential physiological mechanisms interplaying between exercise and cognitive function. Improvement of parameters such as reduced central arterial stiffness, which reduces the risk of small cerebral vessel damages, reduced endothelial dysfunction, which affects the autoregulation of the cerebral perfusion rate and the distribution of the cerebrovascular blood flow to active parts of the brain (functional hyperaemia), reduced stress and anxiety levels, improved levels of chronic inflammation and an improved insulin sensitivity are all observed after exercise interventions (182). We could not observe any differences in any of these proposed mechanisms that we measured in our study, and nor did our participants lose any weight, which previously has been related to improved hippocampus structure and function (33, 34). These factors may contribute to the lack of effects on the brain measurements. However, our study participants were, except from overweight and obesity, healthy already at baseline, and the total dose of walking might thus need to be higher in order to gain effects due to the low intensity. Once again, studies investigating acute effects can be of guidance in which mechanisms that underlies putative positive effects of breaking up and/or reducing the total amount of sitting, but the results and mechanisms need to be further established in larger prospective studies.
Other types of office interventions

Research on bike workstations
Other types of active workstations in offices can include bike or pedalling workstations used at a regular office desk. There are only a few studies available investigating the effects of this type of intervention with follow-ups after 4 and 5 months (127, 183). These show a positive effect on physical activity when installing bikes or pedalling workstations in offices (127, 183) with up to 50 minutes per day (183). No effects have been observed on cardiometabolic, productivity, musculoskeletal or cognitive outcomes (127, 183), apart from a reduction in fat percentage after using the bike workstation (127). These results indicate that bike or pedalling workstations could be a feasible option as well to increase physical activity in offices.

Research on sit-stand tables
All participants in our study had access to sit-stand tables already at study start, which is a common thing in workplaces in Sweden where about 68 % of office workers who spend more than 25 % of the worktime in the office have access to sit-stand tables (184). However, just because you have a sit-stand table does not mean that you actually use the function of raising it to work in a standing position. Another question regarding sit-stand tables is, therefore, how much they are actually being used during a normal working week, i.e. the habitual use. Mazzotta et al. observed a mean change in table position of 1.7 times per day in a group of employees most of whom had been using the sit-stand table for less than a year. Also, they spent about 60 % of the time at the workstation standing (185). Carr et al. observed that those employees who have had access to a sit-stand table for more than 6 months sat about 66 minutes less, stood about 60 minutes more and had less sit-stand transitions compared to employees at the same company who did not have had access to a sit-stand desk (150). As previously mentioned, our participants seemed to use the sit-stand function a great deal, with over five hours of standing time per day. If this is the “true” habitual pattern of usage can be difficult to capture with regards to the Hawthorne effect, where those who are being measured change their movement pattern during the time of measuring.

The effects of standing is, however, not clear from an energy balance perspective. A recent meta-analysis concluded that energy expenditure is increased by 0.15 kcal/minute during standing compared to sitting. A replacement of 6 hours per day from sitting to standing would then lead to an additional 54 kcal expenditure per day in a person of 65 kilograms, and a loss of 2.5 kilogram body fat per year (186). This increase in energy expenditure is relatively small and assumes that no compensatory effects, like increased energy intake or decreased BMR, is happening simultaneously. It thus needs to be further explored in prospective studies what effects can be observed from standing alone, and also what effect
MVPA has in moderating the associations between sitting and/or standing behaviours with health-related outcomes (187).

In an experimental study, breaking up sitting time with LPA breaks has been shown to improve insulin sensitivity, whereas breaking up sitting with standing breaks did not (188). Comparing effects of uninterrupted sitting to different types of activity breaks, consisting of standing, light-intensity walking or cycling, in individuals either with prehypertension or impaired glucose tolerance, it was observed that the mean 24-hour glucose concentration was lower in all conditions compared to sitting. Of all active break conditions, standing breaks produced the least reduction in glucose concentrations (175). This might imply that standing breaks alone are not enough to improve metabolic function, and that a greater energy expenditure is needed for improvement.

Short- to medium-term studies investigating the effects of installing a sit-stand table in offices, with or without counselling, has observed decreased sitting and/or increased daily time spent standing at work ranging between 65 and 150 minutes per day (165, 167, 168, 189-191). While Alkhajah et al. observed an increase in HDL-cholesterol, no effect was observed on other metabolic markers (165), similar to the results of MacEwen et al. (168). The methodological quality of these studies varied, and a recent Cochrane review summarizes that sit-stand workstations can be effective in reducing sitting time at work at short- and medium-term follow-up, but that the evidence is of low quality (129). As discussed in Shrestha et al., the increase in standing time is on average 89 minutes per day and probably leads to negligible effects on energy expenditure compared to sitting, based on the minor increases in energy expenditure during standing compared to sitting (129). However, having the possibility to vary the body position while working can have other positive effects than only on energy expenditure, such as reductions in low back discomfort, especially when the employees have the possibility to decide for themselves when to sit and when to stand during the day (192). The effects on work productivity also needs to be further explored (129).

Other workplace modifications than only the office desk may be needed to reduce sitting time at offices. Mazzotta et al. investigated habitual use of a sit-stand table and observed that participants in their pilot study spent almost as much time sitting in other places in the workplace as they did at their office desk (185). This implies that the whole office design is important, and that focus also needs to be on other environments in the office such as stairs, meeting or lunch rooms. Walking meetings is, for example, something that could be implemented at low cost without the demand of large resources and seems feasible among office workers (193). The feasibility and acceptance of such interventions however needs to be examined in larger long-term trials.
Research on multi-component interventions

Our interview data confirm that individuals are affected by multiple factors at multiple levels, as stated in the ecological model of health behaviour (75). In the interviews, participants commonly reported that they were affected by, for example, the physical environment, with some participants stating that those in individual offices had a better possibility to use the treadmill, not disturbing the co-workers as much as if working in an office landscape without the possibility of closing the door. Co-workers and managers also affected the usage, although in different ways for different ideal types. Some participants reported that they did not want to disturb their co-workers, and some reported not using the treadmill when co-workers were nearby due to the feeling of disturbing them, even though some of them had never really asked their co-workers whether the noise actually was disturbing. They also reported being affected by comments from their co-workers in both positive and negative ways. Furthermore, work tasks affected some of the individuals who reported that they could only use the treadmill while working on some of their work tasks. Others reported that they could use the treadmill regardless of the work task at hand. Motivational levels among the participants affected their usage of the treadmill, and their tendency to see facilitators and barriers in their surroundings. According to the transtheoretical model, a person who is about to or is currently making a change of behaviour goes through six different stages along the way: precontemplation, contemplation, preparation, action, maintenance and termination. At the beginning of the process, during the precontemplation phase, the disadvantages of changing are often greater than the advantages. For a person to move through the different phases, the advantages of changing must increase, becoming greater than the disadvantages (194). This is represented by the ideal types presented, where different ideal types perhaps tend to see barriers more easily than others and respond accordingly. However, the ideal types are not a static behaviour – rather, individuals can move between these ideal types. This makes it more difficult to succeed in interventions like these, since individuals respond differently between each other and also have different individual patterns of response depending on their current life situation and context. Adding an even more personalized component to the interventions, including even more individual consultations with weekly follow-ups, might be useful (195). This was asked for by many participants in our interview data, who reported that the health consultation that they received at the beginning of the study should have included more individual feedback.

Working with factors on many levels makes it more difficult to discern which factors had major effects, and which ones that had a smaller effect, or how the combination of the different factors worked. In complex interventions, multiple factors influence the outcome. The Inphact treadmill study can be classified as a complex intervention, since it has worked with factors on different levels of
influence. The most obvious factor that we worked with was on the environmental level, installing the treadmills. We also worked to some extent with information and guidance of the company managers/leaders, and additionally, all interested employees at the companies were invited to the information meeting at the beginning of the recruitment period, at which they were given information about the field of research. This might have affected the other employees and leaders of the companies, potentially creating more awareness about the health-risks of prolonged sitting within the organizations, possibly affecting the norms at the company. Participants in the intervention group also received boosting e-mails at four occasions, aiming to inspire them to use the treadmills. The interview conducted at the end of the study shed some light on the adherence to the intervention and how it was received among the participants. A process evaluation was not performed in our study, which could have clarified the influence of the different factors on these different levels.

Most studies that have worked with multicomponent interventions have investigated the effects of installing sit-stand tables on the environmental level, in combination with targeting other levels of influence. In a short-term follow-up study of three months, Neuhaus et al. were able to show that installing sit-stand desks in combination with organizational support and individual coaching and support gave better results on workplace sitting compared to installing sit-stand desk alone (196). Results from the Take a Stand-trial in Denmark indicated that the multicomponent intervention was effective in reducing sitting time, replacing it with standing time, both at one- and three-months follow-up. Moreover, an increase in fat free body mass was observed (161). Also, less expensive methods than sit-stand tables, such as the relocation of bins and printers, have been shown to be able to improve the sedentary patterns in offices, for example, reducing the prolonged sitting (197).

Longer-term interventions have also shown to be effective when including multi-component strategies. In Stand Up Victoria, a cluster-randomized controlled trial in a governmental organization in Australia, different strategies were implemented with organizational, environmental and individual strategies aimed to reduce sitting time at work, a reduction in sitting time, an increase in standing time and a decreased prolonged sitting and usual sitting bout duration was observed after both 3 and 12 months compared to controls (160). Furthermore, an improvement in cardiometabolic risk score and fasting glucose was found at 12 months, although this was due to a long-term worsening in the control group, with no changes observed within the intervention group (163). The intervention was also reported to be acceptable among the study participants (198). Even though both environmental and educational strategies did result in reduced sitting among white-collar workers, the meta-analysis by Chu et al. supports the
use of multi-component interventions, as these interventions seem to give the most pronounced effects in reducing sitting time in offices (199).

Factors influencing sedentary behaviour

Different reasons exist for why people in general and office workers in particular spend so much time sitting. To be able to better develop and implement intervention strategies to reduce sitting in different domains, it is of importance to better understand these different factors that work at different levels within each domain, based on the ecological model of sedentary behaviour (75). In a systematic review investigating correlates of sedentary behaviour in adults, Prince et al. concluded that intrapersonal correlates, such as higher educational level, higher occupational class and higher income, were associated with higher occupational sedentary behaviour. Also, they concluded that active workstations, such as sit-stand desks or standing prompting software, were associated with less occupational sedentary behaviour in the occupational domain (200). This was also observed in our study, implying the importance of environmental attributes in improving physical activity and reduce sedentary behaviour in the occupational domain. However, mainly cross-sectional studies have been performed investigating these correlates, and there is a need for longitudinal, well-designed studies to further investigate these factors. Most of the studies included in the review by Prince et al were performed in the USA, United Kingdom, Canada or Australia (200). In Swedish middle-aged adults, being male and having a high educational level has also been associated with more time spent sedentary (153). More studies from other countries, with different cultures, norms and built environments, would also be of interest, since these factors might affect sedentary behaviour in different ways (75).

Nooijen et al. reported that the most common reason for sitting among Swedish office workers in their study was that it is a habit. Other important barriers to reducing sedentary time at work were that standing is tiresome and uncomfortable, and that the respondents lacked the motivation to stand and work, although these factors seemed to differ between different age groups and/or between genders (151). The same study also reported that employees with a higher educational level and who were younger were more prone to the idea of changing the environment in the office to improve standing time, and they thus suggested that some level of individualization of the interventions should be done to get the best effects (151). This was also concluded by McGuckin et al., as one intervention might not suit all individuals in a company (201). That the individual has a motivation for change and the ultimate responsibility is also emphasized as an important factor, alongside the importance of having support from the managers at the company (198, 202, 203). These observations are in line with our interview data, where the motivational levels among the participants seemed to
have affected treadmill workstation usage, indicating that interventions need to include an individualized aspect as well.

De Cocker et al. summarized from focus group interviews with questions regarding sitting time among Flemish office workers, that the most acceptable strategies to reduce occupational sitting reported by the participants were on the social, organizational and environmental level, and strategies on the individual level came last. Strategies that they reported would be acceptable to reduce occupational sitting included the introduction of standing meetings or the instalment of standing desks for the individual workers (204). It may be that working with factors on levels other than the individual level is more easily acceptable among office workers, but as individual strategies may be of major importance for success in implementing a change of sedentary behaviour, this needs to be further explored. Further, Brakenridge et al. reported on the experiences of employees participating in an intervention, designed to be driven from within the organization, with the aim of reducing sitting. One important finding was that the acceptability of the different parts of the intervention, such as standing or walking meetings, was highly influenced by the norm of the company, and that this norm changed as the intervention was implemented (202). Working with the social norm in the company to encourage the employees to take regular breaks from sitting is thus another factor that is important when aiming to reduce sedentary behaviour. If the office workers perceive that others may think that they are not doing their job as well when walking on a treadmill or taking short breaks from sitting, they may not be as prone to actually do this (201). Hadgraft et al. reported from their qualitative study that the possibility of actually reducing and breaking up sitting also largely depends on the office furniture, where the absence of a sit-stand table makes it more difficult to change the behaviour. Furthermore, if more people in the company are using a sit-stand desk when working, the social norm of the company probably shifts to making it acceptable to not sit while working (203). This was further stated by participants who had participated in a longitudinal multicomponent study (198). No one in our interviews mentioned the norms of the company as an issue, but, since all of our participants had sit-stand tables at the beginning of the study, it may be that the social norms of our companies were already different to begin with than those in other studies. Also, the companies all accepted that the employees would participate in our study and perform all the measurements during work hours, so perhaps the norms in our companies had already shifted to making activity at work more acceptable.

Additionally, involving the organization in the study implementation process, by having a person from within the organization involved throughout the whole process, was one very important strategy for raising the awareness about health risks of sitting and in affecting the cultural norms, and in implementing the
intervention according to what suited the organization in question the best (202). Even though the upper administration at the company is supportive, there may still be difficulties in recruiting participants if the day-to-day supervisors are not involved. Furthermore, the participants own perceptions of a lowered productivity when using treadmill desks could be a factor that needs to be handled (126). For better adherence to interventions, it is thus important to include all levels of the organization.

A limited knowledge of the health risks on e.g. cardiometabolic factors of prolonged sitting, has been mentioned as a barrier to reducing sitting among different groups of people (203-205). Interventions aiming to reduce sitting among office workers could perhaps thus be more effective by increasing the awareness of how sedentary and physically inactive the participants actually are, increasing the general knowledge of the health risks of prolonged sitting and providing information on how the reduction of sitting can actually be achieved. Although the general knowledge of the health risks of sitting might have increased since the studies by de Cocker and Martinez-Ramos were performed (204, 205) and results from qualitative studies may not be generalizable in the same way as quantitative data, this might imply the importance to continue to work with the general knowledge of this behaviour, thereby providing a knowledge base to the individuals that can make it easier for them to apply strategies to change their behaviour. Interventions at workplaces are thus important to increase the awareness of sedentary behaviour patterns and health in general among the employees (198). This is also discussed in the study by McGuckin et al., where some of the participants interviewed indicated that education about the health risks of sitting should be given (201). However, if companies are to work harder at reducing sedentary time among their employees, the evidence needs to be strengthened and dose-response relationships are needed, as highlighted by some of the interviewed managers in the study by Hadgraft et al. (203). Further investigating the dose-response relationship between sitting and negative health effects, elucidating the relationship between sedentary behaviour and MVPA, is thus one of the factors that are of major importance. The results from the qualitative studies are intriguing and, although many factors mentioned might be culturally bound, they imply the importance of working with factors on multiple levels to reach a behaviour change.

Methodological discussions

Our study is, to the best of our knowledge, the first long-term study of treadmill workstations, and also the first outside the USA in this research area. The environments, corporate cultures and norms might thus not be the same in our study compared to the previous studies. We included participants from 13 companies (from 17 different offices) in the City of Umeå, which increases the
generalizability to companies residing in Sweden or countries with similar working contexts.

Our study participants all had sedentary jobs, meaning that, according to their self-report at screening, they spent most of the day sitting. When measuring them during baseline we observed, however, that they spent a lot of time standing as well, and that they also spent a lot of time in MVPA each day. This illustrates the problems with self-reporting of physical activity. One major strength in our study was thus the use of two accelerometers during the study period, with measurements performed for 7 – 14 days at several time-points during the study. By using both the thigh-worn activPAL and the waist-born Actigraph, we were able to capture the two different aspects of sedentary behaviour and physical activity in different intensity levels.

However, regarding accelerometer measurements many issues remain so as to standardize the measurements to make them more comparable between studies. Differences between devices regarding wear time protocol is one issue where some devices, such as the activPAL is commonly worn for 24 hours, while others, such as the Actigraph, are commonly worn during waking hours only. This can affect the adherence rate to the monitors in different ways. Another important question is how missing data and non-wear time, including sleep time, should be captured and handled. This needs to be easy for both study participants and researchers, without losing quality of the data. With activPAL, it is most common to use self-reported non-wear times captured using log books. This method is rather time-consuming, and, if participants forget to report that they did not wear a device at a certain time-point, that period will be included as sitting or standing time. A few studies have tested an automatic algorithm to find non-wear time data, showing promising results (206, 207). One common method to define non-wear periods with the Actigraph is to use different automatic algorithms. By automatically classifying non-wear time as any period of 20 minutes or longer with zero counts produces the lowest misclassification error, i.e. non-wear time being classified as sedentary behaviour. However, since this algorithm results in a greater loss of data, the use of a 60 minute time-period with zero counts has been recommended, as this had similar accuracy as when using a 20-minute time-period but with lower loss of data (137). It needs to be further examined which “cut-off” for non-wear time that is most valid to use. Another thing to consider when interpreting data from these devices is the possibility that the cut-points used in Actigraph to define MVPA might be too low, and that some of the activity classified as MVPA in our study might actually be LPA.

To capture food intake in individuals, prospective methods, i.e. a food diary, or retrospective methods, i.e. a 24-hour recall or a food frequency questionnaire, can be used. No gold standard method to capture the actual food intake exists today,
and the methods used have different limitations and benefits. We used a food diary during four consecutive days. Food diaries have the possibility of providing a good picture of the typical food patterns, and does not rely on the subject's memory, if filled in immediately at the time of eating. However, using a prospective method might affect the person and alter their eating behaviour, such as the selection and amount of food, thus not capturing the true, habitual intake. It is also a quite demanding method for the subjects. Furthermore, underreporting the food intake is also more common among people with obesity, among women and elderly people, and those with a lower socioeconomic class (208), which needs to be considered when interpreting the results. The database used for the analysis of the food registrations could also be one source of error, since the products that the participants ate might have different energy and nutrient composition than what is available in the database. Additionally, if any of the reported food products did not exist in the database, a similar product had to be chosen in the database, causing a source of error.

Since the study was not planned to control for the potential effects of season, an uneven number of participants were measured each season and this could thus not be controlled for in the analyses. Previous research has observed various results on the effects of season on physical activity. Koepp et al. did not observe any group by time pattern regarding seasonal differences (121), in line with the results of Hagströmer et al. on a Swedish population (209). However, a study from the United Kingdom indicated that season might have an effect on physical activity, with more LPA during summer and spring, and more sedentary behaviour during winter (210). The effects of season thus needs to be further investigated.

We used individual randomization to the different groups instead of cluster randomization. This most likely increased the contamination risk between participants in the different groups working in the same company, but instead reduced the risk that other factors on the different corporates would influence the results.

We used mixed models for our statistical analyses in papers two and three. It can be questioned whether the traditional statistical models, such as linear regression, are the best way to account for the different contributions of physical activity and sedentary behaviour, since linear models do not take the co-dependency between the variables into account. A better approach might be to use a statistical model that accounts for the fact that the day has a total fixed limit of 24 hours and that when relocating time to one behaviour (e.g. LPA), time must be taken from another behaviour (e.g. sedentary behaviour); thus, the behaviours affect one another. A few studies have used such a compositional data analysis method, in which this co-dependency between variables and fixed time-limit of a
day are accounted for. Most of these studies have been of cross-sectional design (211, 212), but one study by Winkler et al. (162) used the compositional data analysis method on longitudinal data from the Stand Up Victoria study. By using this model, they observed a significant association between reductions in sitting and improvements in, for example, triglycerides, total/HDL cholesterol ratio, weight, body fat, insulin and waist circumference. Overall improvement in cardiometabolic risk score was observed by replacing sitting with either standing or stepping, whereas some of the metabolic variables, such as fasting insulin and insulin sensitivity, were improved more when sitting was replaced with walking compared to standing (162). Further development of these models can shed more light on how we should distribute our 24 hours a day between these different behaviours to gain optimal effects on health.

The participants in the intervention group received boosting e-mails on four occasions during the study. It is difficult to disentangle the effects of these e-mails compared to the effects of the treadmill itself. During the interviews, many participants stated that they did not remember receiving any e-mails, and that they probably just “got lost” among all the other e-mails that they receive during a week. Others instead felt that they were positive and facilitated the use of the treadmill. Similar findings were reported by Brakenridge et al., where some of the participants suggested weekly meetings or regular presentations including the time for discussion as one alternative (202). Other ways of reaching out to the participants, such as phone calls, would perhaps have had a greater effect in our study. These findings, in combination with other studies, further indicate the need to individualize the intervention, in combination with factors in the environment, to better reach the needs of the different participants.

**Ethical aspects**

This study was conducted in accordance with the Declaration of Helsinki. Ethical approval was granted by the Regional Ethical Review Board, Umeå, Sweden. All participants gave oral and written informed consent before inclusion.

Participating in studies where the management of the company have encouraged their employees to participate might induce some ethical considerations. How easy is it for the individual to say no to participation if they somehow feel that the manager thinks that they should participate? Moreover, how easy is it to drop out of the study if that is the case? The individuals might experience some social pressure from both managers and co-workers regarding the adherence to the use of the treadmill, especially if the norm in that the workplace is to be physically active. If the participants feel that it is not working for them with the treadmill or with other parts of the study, it might be an additional stress if they feel that they should still use the treadmill since the managers or other people in their
surrounding think that they should. Feelings of disappointing the researchers if choosing to drop out of the study before it has been completed is also always possible in studies like ours.

We wanted to investigate the effects of increasing physical activity among overweight and obese individuals at different workplaces, since evidence when we planned the study indicated that these groups of individuals might have the worst health risks of a large amount of sitting. Weight issues might, however, be a sensitive thing to discuss, and people participating in this study might have felt that they were “alleged” to be less healthy than the co-workers of normal weight, possibly causing feelings of shame or discomfort.

Any possible medical disorders found during the examinations were taken care of by referring them to the proper instance in the hospital or elsewhere. The participants received feedback after the study had ended on many of the measurements taken during the study, such as the activity measurements, which was one way to give something back to the participants. However, wearing the two accelerometers for 7–14 days and reporting all the food intake for four days might have made the participants feel supervised, and might have caused feelings of inconvenience.

**Implications for public health**

The use of treadmill workstations is one method to use in order to improve physical activity in a normally sedentary environment. However, different organizations need to analyse and develop interventions appropriate for their context. Our description of the ideal types, that emerged from our interview data, might provide guidance for companies in the process of implementing interventions aiming to increase physical activity in office environments. By further working with both environmental as well as individual factors, it may be possible to influence sedentary behaviour and health in a more extensive manner. Individualizing the interventions in combination with the work at other levels of impact, for example, the physical and social environment and the organizational level, might thus be the best way to proceed.
Conclusions

We show that, by introducing treadmill workstations at offices, it is possible to increase the daily physical activity level with regards to walking and number of steps in healthy overweight and obese office workers. This did not, however, induce any effects on different body and cognitive measurements. Interestingly, our exploratory analyses revealed a negative relationship between sitting time and hippocampal volume among participants older than 51 years of age. When performing interventions like this, it is important not only to focus on the occupational domain, but to further consider the activity patterns of the whole day and the whole week, with a particular focus on potential compensatory effects that might occur in the long-term. It is also important to work with a multifactorial approach, introducing strategies and actions on different levels of impact. Physical environmental factors, such as treadmill workstations, are important in order to make it possible for office workers to increase their physical activity. Individual factors, such as motivational level, social environmental factors, such as norms at the company, and organizational factors, working with including the managers and adapting the intervention to the workplace in question, are also important. Within our selected group of participants, who most likely had a good level of knowledge about the positive health effects of physical activity, we could still observe different motivational levels, with different strategies and paths being used to reach the capability of benefiting from the intervention with treadmill workstations. This implies that it is necessary to meet the individual at their motivational level if interventions like this are to succeed even better in the long term.
Future research needs

- There is a need to study how multifactorial interventions should be implemented to give the most beneficial effects in the long-term on increasing NEPA in office environments. Our study gives some guidance, and the interview data creates hypotheses that can be tested in future research.
- The general health effects of increasing LPA need to be investigated. This should be explored using objective measurements.
- Of particular interest and importance for a working population is to further explore what effect an increased LPA and a decreased sitting time may have on cognitive function, related to hippocampal volume, based on our exploratory findings.
- The dose-response relationship between sitting and health effects needs to be further established, including objective measurements of this relationship.
- The relationship between MVPA and sedentary behaviour on different aspects of health needs to be established.
- Future interventions could be even longer than our intervention. It may be that, due to the low intensity of the intervention, more pronounced effects can be found over a longer time period.
- How interventions like this affect the productivity of the participants needs to be further explored.
- Effects on fatigue levels and musculoskeletal health from these interventions are also of interest.
- Health economic evaluations of reducing sitting should be made – if reduced sitting can be shown to be economically beneficial for companies or the society in whole, it may have a major impact on the development of office environments.
- Our population was not as inactive as we might have thought they would be. If this intervention were implemented in an even more inactive population, a more distinct impact could possibly be seen on public health with larger effects on metabolic or other body functions. Future multicomponent interventions could target subjects with more metabolic disturbances.
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