CHAPTER 1
General introduction
1. GENERAL INTRODUCTION

Natural aging is associated with adverse changes in various structures and functions, such as declines in muscle strength [1,2], sensory acuity [3-6], cognitive abilities [7], nerve conduction velocity [8], and gray and white matter [9-13]. It is therefore not surprising that postural control, in this thesis defined as the control of upright standing, is compromised in old compared with young adults [14-16]. Although the effects of motor and sensory decline on postural control have been studied extensively, age-related changes in neural control of posture are largely unknown. A better understanding of such changes would help in developing new and improving existing exercise- and drug-based balance interventions.

1.1. Cortical involvement in postural control

Although standing is often considered a static postural task, destabilizing gravitational forces caused by minor deviations from the vertical require corrective joint torques to maintain the upright position [17]. Visual, proprioceptive, and vestibular systems provide means to sense the orientation and movement of the body. The muscular system then generates the corrective joint torques to control center of mass movement. The current thesis focusses on the system linking these sensory and motor aspects of postural control; the central nervous system.

The central nervous system can be divided into spinal, subcortical, and cortical structures. Early work on neural control of posture in decerebrated animals suggested that standing relies mainly on spinal reflexes and subcortical centers [18,19]. However, behavioral studies [20] indicated that cortical lesions do affect postural control [20-23] and that expectation and context can influence postural responses after a perturbation [24]. Imaging studies also revealed that several cortical structures are active during actual or imagined standing [25,26]. Moreover, electro-physiological studies reported that cortical activity precedes predictable postural perturbations [27] and that motor cortical excitability increases during the long latency postural response and during unsupported versus supported standing [28]. In summary, there is ample evidence from a variety of experimental approaches that the cerebral cortex plays a role in postural control.

1.2. Age-related changes in postural control: influence of neural circuits unknown

Aging is associated with increases in magnitude and decreases in complexity of center of pressure movements during upright standing [14,29-31]. This deterioration in postural control can already be detected in middle-aged individuals and increases exponentially after age 60 [14]. The age-related differences in postural control are even more pronounced in conditions of high postural challenge [29,32,33] or when a cognitively demanding task is added [34]. Functional significance of these findings is emphasized by the fact that old adults with greater center of pressure
displacement [35,36] or worse dual-task performance [37-40] exhibit a higher incidence of falls.

At least part of the postural control decrements in old adults can be explained by declines in sensory acuity and muscle performance. Age-related deficits in proprioception (joint position and motion sense) [3], vision [4,41], and vestibular function [5,6,42] are associated with worse postural control [43-46]. Furthermore, fallers compared with non-fallers exhibit lower muscle strength and power [47,48]. Especially muscle power seems to be important, as high-velocity muscle power training is more effective than traditional resistance training in improving postural control in old adults [49,50].

In addition to the sensory and muscular systems, age also affects the central nervous system. For example, quality and quantity of cortical grey and white matter significantly declines with age [9-13]. Until now, the majority of studies have used manual tasks to investigate the effect of these structural changes on how the brain operates during motor performance [51-55]. The emerging picture from these studies is that aging causes a reorganization of cortical control of voluntary movement, with an increase in brain activation and decrease in cortical inhibition. As the neural circuits affected by age-related degeneration are also involved in postural control, it is likely that changes in brain activation and inhibition also occur during standing. However, the functional changes in neural control of posture with age and their relation to postural deficits are not yet known.

1.3. Modulating intracortical inhibition to regulate motor cortical excitability

In the human brain, the major inhibitory neurotransmitter is the amino acid gamma-amino-butyric-acid (GABA) [56]. GABAergic intracortical inhibitory neurons constitute 10-25% of all cortical neurons and play an important role in regulating neural activity levels [57]. Intracortical inhibitory neurons are also involved in motor control, indicated by a reduction in intracortical inhibition when voluntarily contracting a muscle [58-61]. This down-modulation of intracortical inhibition most likely reflects a mechanism to selectively increase the excitability of pyramidal neurons projecting to the spinal motor neurons of the contracted muscle [58,62]. Accordingly, intracortical inhibition is also modulated with contraction intensity [59,61], directionality of movement [63], and movement phase [64]. Although intracortical inhibition also decreases during postural contractions in standing [65], and the excitability of the corticospinal pathway increases with postural task difficulty [66-69], the influence of postural task difficulty on cortical measures as intracortical inhibition is still unclear.

1.4. Thesis aim and outline

The aim of this thesis is to determine the age-related changes in neural control of posture, as quantified by measures of motor cortical excitability and brain activation, and how such changes affect body sway during standing. Chapter 2 elaborates on the current knowledge of structur-
al and functional changes with aging in the central nervous system and their relation to motor performance. This chapter also identifies the knowledge gaps of which some will be addressed in the remainder of the thesis. Chapters 3 to 5 describe a series of experiments designed to systematically investigate modulation of motor cortical excitability with postural task difficulty in young and old adults. Motor cortical excitability was quantified by intracortical inhibition and facilitation as assessed in the soleus and tibialis anterior muscles using transcranial magnetic stimulation (TMS). Although TMS has the advantage that measurements can be performed during standing, it is limited to the motor cortex and cannot measure neuronal activation. Therefore, we also conducted a functional magnetic resonance imaging (fMRI) study (chapter 6). For this study, we developed a system to simulate standing in the MRI scanner. The main question that this chapter addresses is whether the decreased ability of old adults to perform a motor-cognitive dual-task is related to the age-related increase in brain activation. Finally, chapter 7 will provide a general discussion of the findings reported in this thesis.

REFERENCES


10. Raz N, Gunning-Dixon F, Head D, Rodrigue KM, Williamson A, Acker JD. Aging, sexual dimorphism, and


