Neurobiology of Aging 50 (2017) 47–59

Contents lists available at ScienceDirect

Neurobiology of Aging

journal homepage: www.elsevier.com/locate/neuaging

Individual differences in brainstem and basal ganglia structure predict postural control and balance loss in young and older adults

Matthieu P. Boisgontier [a,*], Boris Cheval [b], Sima Chalavi [a], Peter van Ruitenbeek [a,c], Inge Leunissen [a], Oron Levin [a], Alice Nieuwboer [d], Stephan P. Swinnen [a,e]

[a] Movement Control & Neuroplasticity Research Group, Department of Kinesiology, KU Leuven, Leuven, Belgium
[b] Methodology and Data Analysis Research Group, Faculty of Psychology and Educational Sciences (FAPSE), Geneva University, Geneva, Switzerland
[c] Department of Clinical Psychological Science, Faculty of Psychology and Neuroscience, Maastricht University, Maastricht, the Netherlands
[d] Research Group for Neuromotor Rehabilitation, Department of Rehabilitation Sciences, KU Leuven, Leuven, Belgium
[e] Leuven Research Institute for Neuroscience & Disease (LIND), KU Leuven, Leuven, Belgium

ARTICLE INFO

Article history:
Received 15 July 2016
Received in revised form 14 October 2016
Accepted 25 October 2016
Available online 1 November 2016

Keywords:
Aging
Basal ganglia
Brainstem
Falls
Pedunculopontine nucleus
Posture

ABSTRACT

It remains unclear which specific brain regions are the most critical for human postural control and balance, and whether they mediate the effect of age. Here, associations between postural performance and corticosubcortical brain regions were examined in young and older adults using multiple structural imaging and linear mixed models. Results showed that of the regions involved in posture, the brainstem was the strongest predictor of postural control and balance: lower brainstem volume predicted larger center of pressure deviation and higher odds of balance loss. Analyses of white and gray matter in the brainstem showed that the pedunculopontine nucleus area appeared to be critical for postural control in both young and older adults. In addition, the brainstem mediated the effect of age on postural control, underscoring the brainstem's fundamental role in aging. Conversely, lower basal ganglia volume predicted better postural performance, suggesting an association between greater neural resources in the basal ganglia and greater movement vigor, resulting in exaggerated postural adjustments. Finally, results showed that practice, shorter height and heavier weight (i.e., higher body mass index), higher total physical activity, and larger ankle active (but not passive) range of motion were predictive of more stable posture, irrespective of age.

1. Introduction

Falls are a leading cause of injury, affecting all age groups. In 2000, the total cost of fall injuries in the United States was estimated at $81 billion (Corso et al., 2015). Compared to younger adults, older adults have higher mortality and hospitalization rates (Kennedy et al., 2001). By 2030, 1 in 5 Americans will be 65 years and older (Colby and Ortman, 2015). Older adults are also becoming healthier and more active, which puts them at risk for similar injuries to those sustained by their younger counterparts, such as non–ground-level falls, associated with a higher burden of injury and mortality (Gelbard et al., 2014). In 2000, the incidence of fatal and nonfatal fall injuries in adults aged over 65 years was estimated at 10,300 and 2.6 million, respectively, for a total cost exceeding $19 billion (Stevens et al., 2006). Traumatic brain and lower extremity injuries were the most frequent injuries, accounting for 78% of fatalities. The most frequent nonfatal injuries were fractures of the lower and upper extremities (Stevens et al., 2006). In adults aged 65–74 years, the fatal fall injury rate was 17%, with higher rate for males than females, and the nonfatal fall injury rate was 31%, with higher rate for females than males (Stevens et al., 2006). Accordingly, a better understanding is needed of the neurobiological factors that underlie poor postural control that may result in falls.

Postural control is fundamental for preventing falls, for both young and older adults (Boisgontier et al., 2016a; Heijnen and Rietdyk, 2016). This becomes increasingly critical with aging, especially for prolonging functional independence and preventing the kinds of falls that cause catastrophic injuries (Corso et al., 2015; Gelbard et al., 2014; Kennedy et al., 2001; Stevens et al., 2006; Tinetti and Williams, 1997). Postural control involves a set of mechanisms (e.g., sensory integration, motor command generation, and muscle contraction) that stabilize the center of the total body mass relative to the support base (Shumway-Cook and Woollacott, 2007). Balance is the state of equilibrium resulting from the ability of the postural control system to keep the vertical projection of the

---

* Corresponding author at: Movement Control & Neuroplasticity Research Group, Department of Kinesiology, KU Leuven, Tervuursevest 101, 3000 Leuven, Belgium. Tel.: +32 16376471; fax: +32 16329197.
E-mail address: Matthieu.Boisgontier@kuleuven.be (M.P. Boisgontier).

0197-4580/$ – see front matter © 2016 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.neurobiolaging.2016.10.024

center of mass within the support base. The better controlled the posture, the less likely that balance will be lost. Recently, whole-brain gray matter structure has been shown to predict both postural control and the odds of balance loss (Boisgontier et al., 2016a). These findings at the whole-brain level concur with evidence that shows or suggests associations between postural performance and many brain regions, encompassing almost the entire brain, including the cerebral cortex (Burciu et al., 2013; Mihara et al., 2008; Slobounov et al., 2005, 2006; Taubert et al., 2016), cerebellum (Drijkoningen et al., 2015; Horak and Diener, 1994; Morton and Bastian, 2004; Ouchi et al., 1999), basal ganglia (Visser and Bloem, 2005), and brainstem (Drijkoningen et al., 2015; Honeycutt et al., 2009; Karachi et al., 2010). However, the relative predictive power of these structures remains unclear. Given the technical difficulty of accurately testing deep brain functional activity in a standing balance task, and given the correlation between brain volume and brain activity (Qing and Gong, 2016), structure-based predictions are needed to improve the understanding of the underlying neural mechanisms of postural control and falls.

Posturography has been widely used to investigate the mechanisms involved in postural control (e.g., Boisgontier et al., 2013). This technique involves measuring the movement of the center of pressure (CoP), which has shown to predict falls in older adults (Pajala et al., 2008). However, it remains unclear whether CoP displacements mediate the effect of age on balance loss events (Boisgontier et al., 2016a). The relative effect of the different brain structures on postural control with aging is also debatable. At the brain level, the impact of aging on synaptic modeling (Bloss et al., 2011) and neuron density (Andersen et al., 2003) varies across brain regions (Boisgontier, 2015), which could explain the varying impact of aging on brain structures (Walhovd et al., 2011; Ziegler et al., 2012). Hence, certain brain structures, such as the brainstem, may account for the relationship between aging and posture better than other regions do.

The objective of this study was to determine which brain regions generally predict human postural control and balance during upright standing, irrespective of static versus dynamic postural conditions, task difficulty, practice, visual condition, joint mobility, physical activity, and age. In sum, we investigated which brain regions are fundamental for postural control and balance. In addition, to determine the extent to which these structures mediate the effect of age on postural control, we examined 10 cortical and subcortical regions of interest (ROIs) that have been associated with posture. We hypothesized that (1) the brainstem is the most critical brain region for postural control and for balance loss prevention and that (2) the brainstem accounts for the age-related decline in postural control. Indeed, the brainstem is essential for posture (Drijkoningen et al., 2015; Honeycutt et al., 2009), owing to its involvement in fast postural responses (Jacobs and Horak, 2007) and startle reflexes (Brown et al., 1991; Nonnekes et al., 2015), which are critical for preventing balance loss. Furthermore, a specific brainstem substructure, the pedunculopontine nucleus, has gained recent attention as a strong predictor of postural stability (Fling et al., 2013; Karachi et al., 2010; Lau et al., 2015; Welter et al., 2015).

2. Methods

2.1. Participants

Thirty young (age, 22 ± 3 years; height, 175 ± 9 cm; weight, 69 ± 12 kg; 16 males, 14 females) and 28 older (70 ± 5 years; 169 ± 8 cm; 77 ± 13 kg; 15 males, 13 females) healthy volunteers participated in this study. All participants had normal or corrected-to-normal vision, and none reported a history of neurologic, psychiatric, cardiovascular, or neuromuscular disorders. In addition, a certified physical therapist with extensive experience in neurorehabilitation (MPB) attended all testing sessions and observed no symptoms or indicators suggesting neural disorders. Older participants were screened for cognitive impairment with the Montreal Cognitive Assessment test using the standard cut-off score of 26. The total score on the International Physical Activity Questionnaire (Craig et al., 2003) was used to determine total physical activity. All participants gave their written informed consent, and procedures were performed according to the guidelines of the ethics committee for biomedical research at KU Leuven, Belgium and in accordance with the World Medical Association International Code of Medical Ethics.

2.2. Postural task

Standing balance was tested on an Equitest balance platform (Neurocom International, Inc, Clackamas, OR, USA). This dynamic postural system consists of a force platform (46 × 46 cm) that moves around a mediolateral axis and is equipped with force transducers to measure X, Y, and Z forces (Fx, Fy, and Fz) and X, Y, and Z moments (Mx, My, and Mz). Participants stood barefoot, with the medial malleoli of the ankles vertically aligned with the platform's axis of rotation. A safety harness was worn to prevent falls due to loss of balance (hereinafter, balance loss). To fully assess balance performance, 7 balance disturbance conditions with different platform frequencies and mean amplitudes were tested in eyes open and eyes closed conditions (Fig. 1). The 0.0 Hz–0.0° couple (static) was the least challenging condition. The 0.1 Hz–5.0° couple (very slow movement) was the most challenging condition in terms of movement perception. The 0.1 + 1.5 + 6.0 Hz–5.0° couple was the most challenging condition in terms of triggering rapid corrective responses. The 4 remaining couples (0.1 Hz–0.7°, 1.5 Hz–0.7°, 1.5 Hz–1.3°, and 1.5 Hz–2.7°) were used to link the previously mentioned extreme couples: the challenge increased progressively with increasing amplitude and frequency. Each trial lasted 1 minute and was repeated twice, for a total of 28 randomized trials per participant (7 patterns × 2 visual conditions × 2 trials). Participants were invited to rest for 10 minutes after the 14th trial. When participants asked for a break at any other time during the test session, they were allowed to rest and they got back onto the platform as soon as they had recovered. Participants were instructed to minimize body sway. When a participant fell (held by the safety harness) or took a step to regain balance, the trial was recorded as a balance loss event and was removed from the CoP analysis. These events were counted and used as an indicator of balance. Participants were given another opportunity to complete the failed trials after performing all 28 trials.

2.3. Analysis of postural sway

The amount of CoP movement along the anteroposterior axis was computed using the root mean square deviation of the time series, and was used as an indicator of postural control (CoP root mean square deviation [RMSD]). The CoP coordinates along the anteroposterior axis (CoPy) of the platform surface were computed in mm as follows:

$$\mathrm{CoPy} = \frac{(\mathrm{CoPz})(\mathrm{Fy}) - \mathrm{Mx}}{\mathrm{Fz}}$$

where CoPz is the distance from the transducers to the platform surface, Fy is the anteroposterior force, Mx is the moment about the mediolateral axis, and Fz is the vertical force.