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Association between gait variability and brain ventricle attributes: a brain mapping study

Cedric Annweiler [a,b,c,*], Manuel Montero-Odasso [b], Robert Bartha [c], John Drozd [c], Vladimir Hachinski [d], Olivier Beauchet [a]

[a] Department of Neuroscience, Division of Geriatric Medicine, Angers University Hospital, University Memory Clinic of Angers, UPRES EA 4638, University of Angers, UNAM, Angers, France
[b] Department of Medicine, Division of Geriatric Medicine, Parkwood Hospital, St. Joseph's Health Care London, Gait and Brain Lab, Lawson Health Research Institute, University of Western Ontario, London, Ontario, Canada
[c] Center for Functional and Metabolic Mapping, Robarts Research Institute, Department of Medical Biophysics, Schulich School of Medicine and Dentistry, University of Western Ontario, London, Ontario, Canada
[d] Department of Clinical Neurological Sciences, University Hospital, University of Western Ontario, London, Ontario, Canada

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ABSTRACT

Background: It remains unknown which brain regions are involved in the maintenance of gait dynamic stability in older adults, as characterized by a low stride time variability. Expansion of lateral cerebral ventricles is an indirect marker of adjacent brain tissue volume. The purpose of this study was to examine the association between stride time variability and the volume of sub-regions of the lateral cerebral ventricles among older community-dwellers.

Methods: One-hundred-fifteen participants free of hydrocephalus from the GAIT study (mean, 70.4 ± 4.4 years; 43.5% female) were included in this analysis. Stride time variability was measured at self-selected pace with a 10 m electronic portable walkway (GAITRite). Participants were separated into 3 groups based on tertiles of stride time variability (i.e., <2.0%; 2.0–2.8%; >2.8%). Brain ventricle sub-volumes were quantified from three-dimensional T_1-weighted MRI using semi-automated software. Age, gender, Cumulative Illness Rating Scale for Geriatrics, Mini-Mental State Examination, Go-NoGo, brain vascular burden, 4-item Geriatric Depression Scale, psychoactive drugs, vision, proprioception, body mass index, muscular strength and gait velocity were used as covariates.

Results: Participants with the highest (i.e., worst) tertile of stride time variability exhibited larger temporal horns than those with the lowest ($P = 0.030$) and intermediate tertiles ($P = 0.028$). They also had larger middle portions of ventricular bodies than those with the intermediate tertile ($P = 0.018$). Larger temporal horns were associated with increase in stride time variability (adjusted $\beta = 0.86$, $P = 0.005$), specifically with the highest tertile of stride time variability (adjusted OR = 2.45, $P = 0.044$).

Conclusions: Higher stride time variability was associated with larger temporal horns in older community-dwellers. Addressing focal neuronal losses in temporal lobes may represent an important strategy to prevent gait instability.

1. Introduction

Gait instability is a public health concern in older adults because of its high prevalence ranging between 30 and 50%, and its adverse outcomes including falls, hospitalization, loss of independence, institutionalization and death (Alexander, 1996; Montero-Odasso et al., 2005). To delay as long as possible adverse medico-socio-economic consequences, it proves necessary to rapidly develop effective prevention strategies of gait instability, based on a better understanding of its mechanisms. Human walking has long been regarded as a simple motor task due to its predominant automatic component (Alexander, 1996). However, it is now recognized that this view was overly simplistic and that walking in the real world actually requires brain involvement for adopting a motor behavior appropriate to multiple sensory inputs and environmental constraints to avoid stumbles or falls (Beauchet et al., 2008; Mirelman et al., 2012; Montero-Odasso et al., 2012). The most recognized gait parameter to assess gait instability is the stride-to-stride variability of gait cycle duration (i.e., stride time variability, STV) (Beauchet et al., 2008; Hausdorff, 2005; Hausdorff et al., 2001; Mirelman et al., 2012; Montero-Odasso et al.,

* Corresponding author at: Department of Neuroscience, Division of Geriatric Medicine, Angers University Hospital, 49933 Angers Cedex 9, France.
E-mail address: CeAnnweiler@chu-angers.fr (C. Annweiler).

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2012). STV is a particularly fine marker of fall risk (Beauchet et al., 2008; Hausdorff, 2005; Hausdorff et al., 2001; Mirelman et al., 2012; Montero-Odasso et al., 2012), and represents a window into brain function and higher-level gait control (Beauchet et al., 2008; Mirelman et al., 2012; Montero-Odasso et al., 2012). Importantly, while the propulsion component of gait — traditionally explored with gait velocity or step length — has been linked to the trophism and integrity of sensorimotor networks (i.e., basal ganglia, motor cortex and white matter in the corticospinal tract) (Annweiler and Montero-Odasso, 2012; Rosano et al., 2008), the maintenance of a regular walking pattern is a more complex motor task that may involve different brain regions such as the prefrontal lobes (Beauchet et al., 2012), temporal lobes (Lafleur et al., 2002), precentral gyrus (Gottlieb, 2007) and parietal lobes (Graziano et al., 2002).

Brain atrophy has been described while aging in parallel to increase in STV (Annweiler and Montero-Odasso, 2012), leading to the assumption that loss of neurons in these different brain regions may explain loss of gait dynamic stability in older adults (Annweiler et al., 2012a). A simple, automatic and reproducible way to explore brain volume reduction is to measure the adjacent sub-volumes of lateral cerebral ventricles for differential changes (Annweiler et al., 2012b; Chance et al., 2003). Indeed, cerebrospinal fluid is under pressure and any parenchymal loss results in passive ventricle expansion (Bradley and Orrison, 2000). Modern software can segment ventricles in sub-volumes providing insight into the volume of adjacent brain structures. For instance, atrophy of the temporal lobes leads to ventricle temporal horn enlargement; expansion of the anterior part of the ventricular bodies reflects prefrontal lobe shrinkage; expansion of the middle part of the ventricular bodies illustrates atrophy of the posterior portion of frontal lobes including the precentral gyrus; and expansion of the posterior part of the ventricular bodies gives insight into parietal lobe atrophy (Annweiler et al., 2012b; Chance et al., 2003).

We hypothesized that, among older adults, focal atrophy of the frontal lobes and/or the temporal lobes and/or the parietal lobes, as illustrated by the multi-point expansion of the lateral cerebral ventricles, may be responsible for an increase in STV. The purpose of this study was to examine the associations between STV and the different sub-volumes of the lateral cerebral ventricles among older community-dwellers.

2. Material and methods

2.1. Participants

We studied 154 community-dwellers followed in Angers University Memory Clinic, France, from November 2009 to July 2011 and recruited into the 'Gait and Alzheimer Interactions Tracking' (GAIT) study. The GAIT study is an observational cross-sectional study designed to examine gait in older community-dwellers reporting subjective memory complaint. Sampling and data collection procedures have been described elsewhere in detail (Annweiler et al., 2012c). In summary, subjective memory complaint was documented using the Subjective Memory Complaints Questionnaire (Vannier-Nitenberg et al., 2013), and the main exclusion criteria were age <60 years, Mini-Mental State Examination (MMSE) score <10 (Folstein et al., 1975), inability to walk independently, history of stroke, history of any acute medical illness within the past 3 months, current delirium, severe depression, and inability to understand or answer the study questionnaires. For the current analysis, participants were excluded when a hydrocephalus was diagnosed based on the neurological evaluation (triad of obvious gait disturbances, cognitive dysfunction, and urinary incontinence), or for MMSE < 24 in order to examine the relationships between gait and brain ventricles only in people without advanced cognitive decline. Studied participants received a medical examination, consisting of structured questionnaires, standardized clinical and neurocognitive examination, gait and balance assessments and MRI of the brain.

2.2. Gait assessment

STV (i.e., coefficient of variation of stride time = [mean / standard deviation] × 100) was measured at self-selected usual pace using a computerized walkway with embedded pressure sensors (GAITRite® Gold walkway, 972 cm long, active electronic surface area 792 × 610 cm, total 29,952 pressure sensors, scanning frequency 60 Hz, CIR System, Havertown, PA) (Beauchet et al., 2011). As participants walked along the mat, imbedded sensors were activated by the pressure of their feet and deactivated when the pressure was released. A trained evaluator gave standardized verbal instructions to the participants. Participants walked in a quiet, well-lit room wearing their own footwear according to European guidelines for spatio-temporal gait analysis in older adults (Kressig and Beauchet, 2006). To avoid acceleration and deceleration effects, participants started walking 1 m before reaching the electronic walkway and completed their walk 1 m beyond it. For this analysis, participants were separated into 3 groups based on the tertilization of STV: lowest tertile (i.e., 0.71–1.99%; n = 38), intermediate tertile (i.e., 2.00–2.80%; n = 39) and highest tertile (i.e., 2.81–22.37%; n = 38).

2.3. Lateral cerebral ventricle volume

Imaging of the brain was performed with a 1.5-Tesla MRI scanner (Magnetom Avanto, Siemens Medical Solutions, Erlangen, Germany) using a standard MRI protocol (Dubois et al., 2009) including 3D T_1-weighted magnetization prepared rapid acquisition gradient echo (MP-RAGE) axial images (acquisition matrix = 256 × 256 × 144, FOV = 240 mm × 240 mm × 187 mm, TE/TR/TI = 4.07 ms/2170 ms/1100 ms), and fluid-attenuated inversion recovery (FLAIR) axial images (acquisition matrix = 256 × 192, FOV = 240 mm × 180 mm, slice thickness = 5 mm, slice gap = 0.5 mm, 30 slices, TE/TR/TI = 122 ms/9000 ms/2500 ms). Measurements of ventricle volume were made from the 3D T1-weighted MP-RAGE images, while white matter hyperintensities (WMH) were rated using the FLAIR images.

All volumetric analyses were performed on a PC workstation running Windows XP 64-bit operating system, using Brain Ventricle Quantification Suite (BVQ; Merge Healthcare, Mississauga, ON), a semi-automated analysis package designed to segment and quantify lateral ventricular volume and sub-volumes using T_1-weighted MRI images (Accomazzi et al.). A single researcher (CA), who was blinded to age, gender and all clinical information, performed all volumetric analyses. The measurement of whole ventricle volume is highly reproducible with intra- and inter-operator correlation coefficients greater than 0.98 (Nestor et al., 2008). Normalization of volumes to other brain structures was not performed as it has previously been demonstrated that this normalization does not significantly affect results (Carmichael et al., 2007). Operator-selected seed points were placed in each lateral ventricle and a region-growing algorithm automatically expanded the seed points within the 3D space of the image to the margin of the periventricular tissue. The region-growing procedure combines image intensity and shape analysis (using morphological operators) and was specifically optimized for the segmentation of the lateral ventricles (Accomazzi et al.). The lateral ventricles were then automatically rendered in three dimensions and in the coronal, sagittal and axial planes for inspection (Fig. 1). In certain cases extraneous anatomical volumes (usually third and fourth ventricular volumes) were removed by identifying the tissue connecting the ventricle proper and the extraneous volumes. BVQ then automatically removed the extraneous tissue to the border of the lateral ventricles. This type of minimal manual interaction was required in approximately one-third of all participants (Nestor et al., 2008). Finally, BVQ identified the anterior and posterior commissures and used these two anatomical landmarks to define the position of two coronal planes. The intersection of these planes with the 3D rendering of the main ventricle bodies was used to define the three sub-volumes: the anterior portion of the ventricular bodies (anterior to the