Journals of Gerontology: MEDICAL SCIENCES
Cite journal as: J Gerontol A Biol Sci Med Sci. 2014 November;69(11):1375–1388
doi:10.1093/gerona/glu052

Advance Access publication April 16, 2014

Special Issue: Brain Aging

Review

Neuroimaging of Mobility in Aging: A Targeted Review

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Background. The relationship between mobility and cognition in aging is well established, but the relationship between mobility and the structure and function of the aging brain is relatively unknown. This, in part, is attributed to the technological limitations of most neuroimaging procedures, which require the individual to be immobile or in a supine position. Herein, we provide a targeted review of neuroimaging studies of mobility in aging to promote (i) a better understanding of this relationship, (ii) future research in this area, and (iii) development of applications for improving mobility.

Methods. A systematic search of peer-reviewed studies was performed using PubMed. Search terms included (i) aging, older adults, or elderly; (ii) gait, walking, balance, or mobility; and (iii) magnetic resonance imaging, voxel-based morphometry, fluid-attenuated inversion recovery, diffusion tensor imaging, positron emission tomography, functional magnetic resonance imaging, electroencephalography, event-related potential, and functional near-infrared spectroscopy.

Results. Poor mobility outcomes were reliably associated with reduced gray and white matter volume. Fewer studies examined the relationship between changes in task-related brain activation and mobility performance. Extant findings, however, showed that activation patterns in the cerebellum, basal ganglia, parietal and frontal cortices were related to mobility. Increased involvement of the prefrontal cortex was evident in both imagined walking conditions and conditions where the cognitive demands of locomotion were increased.

Conclusions. Cortical control of gait in aging is bilateral, widespread, and dependent on the integrity of both gray and white matter.

Key Words: Cognition—Neuroimaging—Gait—Balance—Brain aging.

Received October 21, 2013; Accepted March 11, 2014

Decision Editor: Stephen Kritchevsky, PhD

MOBILITY impairments and limitations are common among older adults, have detrimental impact on the affected individuals and their families and constitute a major public health challenge to society (1,2). Hence, identifying modifiable risk factors for and mechanisms of mobility impairments and disability in aging is paramount. Converging evidence points to the important role cognitive processes, attention and executive functions in particular, have in explaining variance in mobility performance in healthy, frail and demented older adults (3–5). However, less is known about brain structures and functional regions that are directly involved in mobility performance and decline in the elderly (see Rosso et al. (6) for review). This, in part, is attributed to methodological limitations of most traditional neuroimaging procedures, which require the individual to be in a supine position and immobile during the scanning procedures. Nonetheless, traditional and more recent innovative neuroimaging methods have begun to shed light on brain structures, regions, and functional networks that are involved in mobility. Herein, we provide a targeted review of neuroimaging studies of mobility to provide a better understanding of the relationship between mobility and the structure and function of the aging brain.

Methods

Selection of Studies

PubMed was used to systematically identify studies investigating functional and structural neural correlates of mobility in aging. The search strategy was restricted to original studies published in English up to June 30, 2013. Only studies that examined healthy older adults (60 years of age and older)

were included. Search terms included (i) aging, older adults, or elderly; (ii) gait, walking, balance, or mobility; and (iii) magnetic resonance imaging (MRI), voxel-based morphometry, fluid-attenuated inversion recovery (FLAIR), diffusion tensor imaging, positron emission tomography (PET or FDG-PET), functional MRI (fMRI), electroencephalography, event-related potential, and functional near-infrared spectroscopy (fNIR). The identified studies were screened (N.E. and H.M.B.) for content to assure compliance with the aforementioned inclusion/exclusion criteria. Disease-specific (eg, stroke) studies were included only when a healthy older control group was available. A total of 86 studies were included in the current review.

Findings by Neuroimaging Procedure

Structural MRI Studies

Voxel-based morphometry is a common neuroimaging analysis approach that involves segmenting a structural image of the brain into gray matter (GM), white matter (WM), and cerebrospinal fluid. These segmented images can then be used to perform voxel-based comparisons between groups or correlations with behavioral measures. Another common approach is to compute GM and WM volumes of particular brain structure or structures (eg, prefrontal cortices) and then compare them between groups or correlate them with behavioral measures. Finally, structural images can be used to quantify WM hyperintensities (WMH) and small vessel disease. Several cross-sectional and longitudinal studies of cognitively healthy older adults have linked increased WMH burden with poor gait performance (7–10) and balance (11) (Table 1).

Specifically, WM disease, small vessel disease, and subclinical stroke have been associated with poor quantitative gait markers, mobility decline, and increased risk for physical disability (16,17,23). Relationships between GM volume and mobility have also been identified using voxel-based morphometry procedures. Brain atrophy was associated with decreased trunk stability during walking while talking (26), while GM volume of the primary sensorimotor and medial temporal areas was associated with bradykinesia and gait disturbance (19,29). GM volume in the left cerebellum, basal ganglia, and left prefrontal regions was strongly associated with mobility (18,27,28). Furthermore, subcortical hyperintensities were linked to slower gait velocity in Alzheimer's disease patients and healthy controls (21). Reciprocally, physical activity has also been shown to predict greater volumes of frontal, occipital, entorhinal, and hippocampal regions (22). In summary, substantial research demonstrates that both WMH burden and cortical volume are related to mobility outcomes in aging.

Fluid Attenuated Inversion Recovery

FLAIR is a structural MRI sequence that is particularly suitable for detecting WMH because it masks the cerebrospinal fluid that cloud other structural MRI sequences (eg, T2-weighted images) (30). Several studies that have used a FLAIR sequence in cognitively healthy older adults implicated increased WMH burden in poor gait performance (31–35) and increased risk for falls (36,37) (Table 2).

WMH in prefrontal regions (32,46) and the splenium (and other corpus callosum regions) (41,47–49) appear to be specifically detrimental to gait performance. This is presumably because these regions coordinate the processing of visuospatial information during walking (44,48,49) and play an essential role in executive functions (37,44). In fact, executive functions have been shown to be more affected by WMH than memory or language functions (44). Several reliable and valid manual, semi- and fully automated methods for quantifying WMH in FLAIR sequences exist (51–54). The Age-Related White Matter Changes (ARWMC) (51) scale, a manual ratings scale, is comparable to semiautomated methods for detecting associations between WMH and gait (39) and simpler scales (see Fazekas (53)) may be sufficient for clinical settings (38).

Diffusion Tensor Imaging

Diffusion tensor imaging is a reliable method for evaluation of WM integrity (WMI) that is capable of detecting abnormalities in the WM that appear normal on conventional MRI (55,56). To date, only a small number of studies have thoroughly investigated the relationship of WMI and mobility outcomes in aging (Table 3).

Specifically, findings reveal that WMI is associated with gait disturbances (46,59,61) and that WMI in the corpus callosum is a critical marker of gait impairments in aging (58). In studies examining relationships between gait, balance, and postural stability, evidence for greater age-related microstructural deterioration was reported in frontal brain regions (32,57,62). Studies examining the function of the pedunculopontine nucleus in healthy and impaired older adults have revealed the importance of intact connectivity from pedunculopontine nucleus to locomotion centers, including cerebellum, for independent walking (60,63,65). Thus, there is evidence to support the notion that specific patterns of WM abnormalities in aging are related to various mobility outcomes including gait, balance, and fall risk.

Positron Emission Tomography

PET is an invasive neuroimaging technique that can be used to track glucose utilization after injection of a radioactive tracer such as fludeoxyglucose-18 (FDG). PET studies have shown that in healthy older adults gait, balance, and sensory integration are related to striatal pathways of the dopaminergic system of the basal ganglia (66–69) (Table 4).

These pathways, which tend to denervate in normal aging, are also implicated in the executive control of gait

Table 1. Voxel-Based Morphometry Studies of Mobility

Studies	*N*	Mean Age Years (±*SD*)	% Female	Mobility Outcome	Conclusion
Gass et al. (12)	37 subcortical vascular encephalopathy; 11 controls	70 (55–82); 68 (63–71)	54; 36	Composite gait abnormality (dynography)	No overall correlation of total lesion area with neuropsychological score or gait abnormality
Kwa et al. (13)	17 isolated PHL; 17 controls	66 (47–80); 65 (47–77)	NS; NS	Quantitative and clinical gait	PHLs may be a cause of disequilibrium in patients with atherosclerosis
Whitman et al. (10)	70 healthy	79 (4)	NS	Tinetti scale	Some older people develop gait and balance dysfunction that is associated with gradual onset of cerebral WM disease
Starr et al. (11)	97 healthy	79 (1)	40	Gait speed, Tinetti scale	WML, periventricular, and brain stem lesions were associated with impaired balance
Lee et al. (14)	21 NPH; 20 controls	71 (6); 74 (5)	43; 45	Clinical balance	Midbrain atrophy is significantly associated with gait disturbance in NPH
Moretti et al. (15)	30 gait disturbance with LA; 8 controls	73 (6); 61 (9)	30; 50	Clinical gait	CC atrophy associated with gait impairment independently of LA and other brain abnormalities
Rosano et al. (16)	2,450 healthy	74 (5)	57	Quantitative gait, timed chair rise	Subclinical structural brain abnormalities can increase risk of disability and decline in mobility
Rosano et al. (17)	321 healthy	78 (NS)	60	Quantitative gait	Quantitative gait performance is associated with high WM disease and subclinical strokes
Rosano et al. (18)	327 healthy	78 (4)	57	Gait speed, tandem stance	Smaller GM volumes in regions crucial for mobility control are associated with worse gait and balance, independent of other diffuse brain abnormalities such as WMH
Rosano et al. (9)	331 healthy	78 (4)	NS	Quantitative gait	Step length variability associated with subclinical vascular abnormality burden
Rosano et al. (19)	220 healthy	78 (NS)	63	Quantitative gait	Spatial and temporal characteristics of gait are associated with distinct brain networks
Rosano et al. (20)	3,156 healthy	74 (5)	57	Gait speed	Lower DSST score and slower gait speed may indicate early structural and functional brain changes that are treatable
Franch et al. (8)	30 gait disorders of unknown cause; 30 controls	80 (6); 77 (4)	50; 50	Tinetti scale, TUG	Gait disorders of unknown cause associated with WML and hypertension
Nadkarni et al. (21)	42 mild AD; 33 controls	74 (8); 73 (8)	60; 47	Quantitative gait	Subcortical hyperintensities burden may have relatively stronger association with slower gait velocity in controls than in patients with mild AD
Dumurgier et al. (7)	3,604 healthy	73 (5)	62	Quantitative gait	Persistent hypertension associated with slower gait in the elderly may be partly explained by WMH and support vascular risk factors in mobility dysfunction
Erickson et al. (22)	299 healthy	78 (4)	61	Number of blocks walked over 1 wk	Increased walking associated with greater GM volume
de Laat et al. (23)	485 SVD	65 (13)	49	Quantitative gait, Tinetti scale, TUG	MB may be associated with gait disturbances independently of other coexisting markers of SVD
Kim et al. (24)	1,744 healthy	78 (4)	60	Quantitative gait	Retinal microvascular signs associated with slow gait and poor EF
Rosano et al. (25)	643 healthy	74 (NS)	57	Gait speed	Older adults with uncontrolled hypertension had slower gait decline and faster WMH progression than those with controlled hypertension
Doi et al. (26)	110 healthy	75 (7)	50	Quantitative gait, trunk movements	Decreased trunk stability during dual-task walking is associated with brain atrophy
Dumurgier et al. (27)	1,623 healthy	73 (4)	61	Quantitative gait	GM subcortical structures associated with age-related decline of mobility performances
Manor et al. (28)	29 DPN; 68 DM; 89 controls	67 (8); 68 (8); 65 (8)	48; 46; 52	Quantitative gait	Strong relationships between brain volumes and walking outcomes in DPN and to lesser extent DM but not controls
Rosano et al. (29)	307 healthy	83 (±3)	55	UPDRS	Primary sensorimotor and medial temporal atrophy may relate to development of bradykinesia and gait disturbances

Notes: 26 studies reviewed. AD = Alzheimer's disease; CC = corpus callosum; DM = diabetes mellitus; DPN = diabetic peripheral neuropathy; DSST = Digit Symbol Substitution test; EF = executive functions; GM = gray matter; LA = leukoaraiosis; MB = microbleeds; MCI = mild cognitive impairment; NPH = normal pressure hydrocephalus; NS = not specified; PHL = pontine hyperintense lesions; SH = subcortical hyperintensities; SVD = small vessel disease; TUG = Timed "Up-and-Go" test; UPDRS = Unified Parkinson's Disease Rating scale; WMH = white matter hyperintensities; WML = white matter lesions; WWT = walking while talking.

Table 2. Fluid Attenuated Inversion Recovery Studies of Mobility

Studies	*N*	Mean Age Years (±*SD*)	% Female	Mobility Outcome	Conclusion
Gouw et al. (38)	79	74 (5)	55	SPPB	Simple visual rating scales of WMH may be sufficient for detecting disturbances in gait and balance in clinical settings
van Straaten et al. (39)	639	74 (5)	53	Gait disturbance	The sensitivity for detecting gait disturbance associations differs between WMH measures
Acharya et al. (40)	79	PD: 67 (7); Control: 70 (6)	47	Quantitative gait	Age, not WMH, is associated with worse gait in PD and controls
Ryberg et al. (41)	569	74 (5)	55	Gait difficulty, falls, SPPB, and gait speed	Atrophy of CC is an important predictor of mobility disability in older adults with WMH
Sparto et al. (42)	8	Range (75–83)	50	Step initiation	Central processing time during voluntary step initiation is affected by WMH
Novak et al. (43)	76	65 (7)	53	Gait speed and postural control	Focal and periventricular WMH contributes to mobility decline among the elderly by altering a feedback mechanism needed for long-term postural control
Srikanth et al. (36)	294	72 (7)	45	Falls and quantitative gait	WMH are strong predictors of falls in the elderly
Murray et al. (44)	148	79* (range 73–91)	56	UPDRS and quantitative gait	WMH in the parietal lobe contribute to balance and posture by altering integration of visuospatial information
Rosano et al. (31)	795	76 (6)	59	Gait speed	Magnetic transfer ratio can be used as an additional biomarker for mobility decline in the elderly, particularly elderly women
Srikanth et al. (32)	385	72 (7)	44	Quantitative gait	Frontal and periventricular WMH reflecting major anterior fibers and association fibers correlate with gait
Wakefield et al. (45)	99	82 (4)	60	SPPB, Tinetti scale, gait velocity, walk down stairs	Total WMH was associated with all mobility measures, but walk down stairs. Total WMH predict mobility as well as regional measures of WMH
de Laat et al. (46)	429	65 (9)	45	Quantitative gait	WMH in interconnecting and prefrontal regions are associated with reduced gait in SVD
Griebe et al. (47)	34	69 (7)	68	Gait velocity, single-leg stance and SPPB	WM reductions of the CC can be detected early in healthy older adults
Moscufo et al. (48)	99	83 (4)	58	SPPB, gait speed, strength, and balance	The association between WMH and gait differs across gait measures. Strength is associated with WMH in the splenium, but balance does not correlate with any WMH measures
Choi et al. (35)	395	72 (7)	44	Quantitative gait and falls risk	Total burden of cerebrovascular disease is important for identifying individuals risk of gait decline and falls
de Laat et al. (33)	415	65 (9)	46	Quantitative gait	The association between WMH and gait and differ across quantitative gait measures
Moscufo et al. (49)	77	Baseline: 82 (4); follow-up: 84 (4)	46	Standing balance, chair rise, gait speed, and Tinetti scale	WMH in the splenium restricts interhemispheric integration of visuospatial information and contributes to age-related mobility decline
Zheng et al. (37)	287	78 (5)	54	Falls	Techniques to reduce the development and progression of WMH are key to preventing falls in the elderly
Nadkarni et al. (50)	GOI:21; TOI: 23	GOI:78 (5); TOI: 76 (6)	GOI: 55; TOI: 82	Gait speed pre- and postintervention	A task-oriented intervention that focuses on timing and co-ordination can benefit older adults with WMH in tracts associated with gait and cognition
Willey et al. (34)	701	80 (6)	67	Gait speed at baseline and follow-up (4.7 y later)	Reducing WMH is important for the prevention of gait decline

Notes: 20 studies reviewed. CC = CC = corpus callosum; GOI = gait intervention; PD = Parkinson's diesease; SPPB = short physical performance battery; SVD = small vessel disease; TOI = task-oriented intervention; UPDRS = Unified Parkinson's Disease Rating scale; WMH = white matter hyperintensities.

*Median.

Table 3. Diffusion Tensor Imaging Studies of Mobility

Studies	*N*	Mean Age Years (±*SD*)	% Female	Mobility Outcome	Conclusion
Sullivan et al. (57)	49 participants	44 (16)	37	Fregly–Graybiel ataxia battery	Age-related microstructural deterioration of regional WM related to gait and balance performance
Bhadelia et al. (58)	173 elders	73 (8)	75	Tinetti scale	WM integrity in CC is an important marker of gait in aging
Srikanth et al. (32)	385 elders	72 (7)	44	Quantitative gait	Worse gait was associated with bilateral frontal and periventricular WM lesions
de Laat et al. (59)	484 elders with cerebral SVD	66 (9)	43	Quantitative gait	Integrity of normal and abnormal WM is associated with gait disturbances
de Laat et al. (46)	429 elders with cerebral SVD	65 (9)	45	Quantitative gait	Elders with SVD displayed widespread disruption of WM integrity
Yeo et al. (60)	55 stroke patients; 22 age-matched controls	55 (range 34–73); 52 (range 33–73)	29; 50	Functional Ambulation Category (FAC) scale	Increased neuronal activity of the PPN in patients who were able to walk independently
Koo et al. (61)	125 elderly participants; (78 without fall risk and 47 with fall risk)	72 (8); 71 (7); 73 (9)	73; 76; 68	Tinetti scale	Participants with fall risk evidenced clusters of abnormal WM in multiple brain regions
Van Impe et al. (62)	31 young adults; 36 elders	25 (range 20–34); 69 (range 62–81)	55; 50	Balance	WM integrity of frontal and fronto-occipital tracts were predictive of balance older adults
Yeo et al. (63)	43 stroke patients; 20 age-matched controls	54 (range 34–74); 50 (range 30–72)	30; 55	FAC scale	Connectivity between the PPN, ipsilesional cerebellum, and contralesional pontine locomotor center appears to be related to walking ability
Kafri et al. (64)	13 elders with high-level gait disorders (HLGD), 9 elderly; 13 middle-aged controls	77 (4); 75 (5); 47 (9)	62; 66; 69	Clinical gait	HLGD patients had lower fractional anisotropy and higher displacement values in multiple brain regions
Youn et al. (65)	40 participants; (14 FOG) and 26 controls	81 (6); 79 (5)	43; 42	FOG questionnaire	Bilateral PPN, superior premotor cortex, right orbitofrontal area, and left supplementary motor area were related to FOG

Notes: 11 studies reviewed. CC = corpus callosum; FOG = freezing of gait; PPN = pedunculopontine nucleus; SVD = small vessel disease; WM = white matter.

Table 4. Positron Emission Tomography Studies of Mobility

Studies	*N*	Mean Age Years (±*SD*)	% Female	Mobility Outcome	Conclusion
Cham et al. (66)	35 healthy	65 (13)	49	Dynamic posturography testing	Ability to inhibit balance destabilizing vision-related postural control processes depends at least partially on striatal dopaminergic pathways
Ouchi et al. (70)	8 iNPH; 8 controls	72 (4); 67 (5)	38; 25	Clinical gait	Postsynaptic D2 receptor hypoactivity in dorsal putamen may predict severity of gait impairment in iNPH
Cham et al. (67)	40 healthy	61 (17)	55	Quantitative gait	Quantitative gait markers were significantly lower than age-based predictions in adults with lower striatal dopamine transporter activity
Bohnen et al. (68)	77 healthy	61 (16)	56	Prospective falls	AASDD may contribute to recurrent falls
Ouchi et al. (69)	7 PD; 6 healthy	66 (7); 65 (6)	16; 29	Quantitative gait	Dopaminergic activity in the putamen plays an important role in the execution of gait
Bohnen et al. (71)	44 PD; 15 controls	69 (10); 64 (10)	23; 53	History of falls	Cholinergic hypofunction is associated with fall status in PD
Park et al. (72)	11 PAGF; 14 PSP; 13 PD; 11 controls	74 (6); 69 (6); 65 (7); 72 (6)	45; 21; 39; 45	Clinical gait	PAGF and PSP may represent variable entities along a disease continuum encompassing both conditions
Gilman et al. (73)	12 PD; 13 MSA-P; 4 PSP; 22 controls	67 (11); 63 (8); 68 (7); 58 (10)	50; 38; 75; 68	Clinical balance and gait	Substantial decreases in subcortical cholinergic activity may account for greater gait disturbances in early stages of MSA-P and PSP compared with PD
la Fougère et al. (74)	16 healthy	61 (8)	44	Imagined walking and actual walking	Basic activation and deactivation patterns of actual locomotion correspond to that of imagined locomotion
Nath et al. (75)	50 healthy	65 (15)	NS	Peak slip velocity	AASDD may impact the ability to recover from large perturbations during walking in fast walkers
Shimada et al. (76)	24 healthy	78 (2)	100	Quantitative gait	Primary sensorimotor, prefrontal, and temporal activation (especially hippocampus) associated with gait adaptability during unaccustomed walking
Zwergal et al. (77)	12 PSP; 12 controls	68 (7); 68 (8)	33; 33	Quantitative gait	During walking, prefrontal, subthalamic, pedunculopontine/cuneiform nucleus, and thalamic functional activation reduced in patients with PSP
(78)*	20	65–85	NS	Quantitative gait	Abnormalities in basal ganglia-thalamo cortical loops contribute to gait disturbance in elderly with ARWMC

Notes: 12 studies reviewed. AASDD = age-associated striatal dopaminergic denervation; ARWMC = Age-Related White Matter Changes scale; iNPH = idiopathic normal pressure hydrocephalus; MSA-P = multiple system atrophy, Parkinsonian type; NS = not specified; PAGF = pure akinesia with gait freezing; PD = Parkinson's disease; PSP = progressive supranuclear palsy.

*SPECT study.

Table 5. Functional Magnetic Resonance Imaging Studies of Mobility

Studies	*N*	Mean Age Years (±*SD*)	% Female	Mobility Outcome	Key Contrast	BA/Brain Region	Conclusion
Godde and Voelcker-Rehage (82)	51	69 (3)	75	Imagined walk backward and forward	Backward > forward	6, 7, 10, 13, 22 24, caudate, thalamus, claustrum, putamen	Brain regions associated with EF were engaged to a greater extent during imagined walk backward than forward
la Fougère et al. (74)	16	61 (8)	44	FDG-PET, walk and rest fMRI: imagined walk and rest	Walk > rest; imagined walk > imagined rest	Walk > rest: 3, 4, 13, 18, 19, 31, 36, 37, 47, cerebellum, and tegmentum; imagined walk > imagined rest: 6, 7, 9, 10, 13, 18, 19, 22, 24, 31, 32, 36, 40, caudate, putamen, cerebellum, and tegmentum	Actual walk and imagined walk engaged motor, SMA, multisensory, parahippocampal and cerebellar regions
Rosano et al. (83)	30	Successful aging (SA): 81 (3); physical activity (PA): 81 (4)	73	DSST and self-reported physical activity	PA > SA	BA 9	PA group was more active, performed better on the DSST and used the DLPFC more than the SA group
Snijders et al. (84)	45	PD with freezing of gait (PD-FOG): 59 (9); PD without FOG: 63 (7); controls: 57(9)	40	Motor imagery (MI) and visual imagery (VI)	MI > VI (PD > controls); MI > VI (PD-FOG > PD without FOG)	MI >VI (PD > controls): 5, 24; MI > VI (PD-FOG > PD without FOG): 5, 6, and mesencephalon	PD group showed less activation in superior parietal and anterior cingulate regions during MI. PD patients with FOG showed less activation in mesencephalon during MI
Wai et al. (81)	40	PD: 64 (13); old: 65 (6) young: 22 (2)	53	Imagined gait initiation (iGI), stepping over obstacle (iSO), and gait termination (iGT)	PD > old (iGI); old > young (iGI); PD > old (iSO); old > young (iSO); PD > old (iGT); old > young (iGT)	PD > old (iGI): no significant clusters; old > young (iGI): 7, 18, 37; PD > old (iSO): 4, 6, 7, 17, 18, 19, 31, 37, 40 44, 45, 46; old > young (iSO): 5, 6, 7, 19, 37, 40; PD > old (iGT): 7, 19; old > young (iGT): 6, 7, 8, 19, 32, 37, 39, 40, and thalamus	Imagined gait engaged SMA, pre-SMA, dorsal premotor, visual, and posterior parietal regions. Activation in these regions were affected by PD and by healthy aging
Zwergal et al. (80)	60	50 (24)	50	Imagined walk, run, stance, and lying	Walk > lying	6, 7, 31, caudate, thalamus, and cerebellum	The basic locomotor and posture network is preserved in aging

Notes: Six studies reviewed. BA = Brodmann area; DLPFC = dorsolateral prefrontal cortex; DSST = Digit Symbol Substitution test; EF = executive function; FDG-PET, fludeoxyglucose-18-positron emission tomography; fMRI = functional magnetic resonance imaging; PD = Parkinson's disease; SMA = supplementary motor area.

when balance is challenged (68,75). Thus, dopaminergic physiology may relate to certain aspects of gait, independent of age-related changes, and may partially explain recurrent falls in older adults (71). "In-vivo" locomotion studies, where patients are injected with FDG, walk on a treadmill, and then undergo a static PET scan, reveal that "real" locomotion uses a direct pathway via the primary motor cortex. Conversely, imagined locomotion (as measured via fMRI) uses an indirect pathway via the supplementary motor cortex and basal ganglia loop implicating the primary sensorimotor area, prefrontal area, and temporal lobe in more cognitively demanding gait protocols (74,76).

Functional Magnetic Resonance Imaging

fMRI is a noninvasive but stationary neuroimaging technique that provides a blood-oxygen-level-dependent signal of neural activity (79). Actual gait cannot be studied with fMRI, but imagined gait studies provide a window into the functional correlates of actual gait in the elderly (74,80–82) (Table 5).

Older adults activate supplementary motor areas (SMA), caudate, visual, and cerebellar regions to the same extent as younger adults during imagined walk relative to imagined stance (80). Older adults also activate primary motor, SMA, parietal, thalamic, and caudate regions during imagined walk backward to a greater extent than imagined walk forward (82). Moreover, highly fit individuals activate primary motor cortices to a greater extent during imagined walk backward than forward while less fit individuals activate prefrontal regions a greater extent during imagined walk backward than forward (82). SMA are also activated to a greater extent in older than younger adults during imagined stepping over obstacle and terminating gait (81). Finally, SMA and other prefrontal regions are activated to a greater extent during imagined walking-while-talking relative to imagined walking or talking alone (85). Taken together, imagined gait fMRI studies suggest that gait engages SMA, pre-SMA, posterior parietal and cerebellar regions, and that older adults (particularly less fit older adults) engage SMA and other prefrontal regions during gait—presumably because locomotion necessitates executive functions. The results of these fMRI studies are comparable to FDG-PET studies of actual gait (74).

Electroencephalography

Electroencephalography is a noninvasive method of measuring complex neural activity where brain responses to specific events are recorded. This electrical activity consists of positive (P) and negative (N) components or voltage deflections that occur at specific latencies. To date, there is a paucity of studies investigating the relationship of neural activation and mobility outcomes in aging; nevertheless, significant age-related differences in amplitude and latency have been reported (Table 6).

Table 6. Electroencephalography Studies of Mobility

Studies	*N*	Mean Age Years (±*SD*)	% Female	Mobility Outcome	Conclusion
Shibata et al. (86)	7 female	69 (4)	100	Treadmill walking	Walking at low to moderate intensities provides neural relaxation for elderly women
Duckrow et al. (87)	8 young; 13 old mobile; 20 old frail	30 (5); 80 (5); 83 (4)	63; 39; 60	Balance	Delays in sensory conduction play a subsequent role in maladaptive motor responses
Vogt et al. (88)	18	Females: 62(6); males: 64 (5)	45	Self-paced walking	Significant increase in theta and alpha band activity was associated with walking and exercise
Shoushtarian et al. (89)	20 PD patients; 12 young adults; 8 elders	66 (7); 26 (7); 62 (9)	33; NS; NS	GI/stride length	Compared with young, healthy old adults demonstrate diminished central activity during GI

Notes: Four studies reviewed. GI = gait initiation; NS = not specified; PD = Parkinson's disease.

Table 7. Functional Near-Infrared Spectroscopy Studies of Mobility

Studies	*N*	Mean Age Years (±*SD*)	fNIR System*	Mobility Outcome	Conclusion
Miyai et al. (108)	8	35 (8); 4 males, 4 females	a	Treadmill walking	Medial portion of the primary sensorimotor regions and SMA were bilaterally activated during treadmill walking
Suzuki et al. (109)	9	28 (7); 7 males, 2 females	b	Treadmill walking/running	PFC, PMC, and medial SMC were activated at the acceleration phases of walking and running and may be involved in the adaptation to increased speed during locomotion
Mihara et al. (110)	23	12 stroke patients, 53(17); 11 healthy subjects, 43 (12)	c	Treadmill walking	Cortical activation was observed in PFC, SMA, and SMC regions in both controls and stroke patients during acceleration but persisted in the patient group throughout the gait protocol
Suzuki et al. (111)	7	31 (5); 4 males, 3 females	b	Simple (SW) and prepared walking (PW) on treadmill	Activations in the PFC, SMA, PMC, medial SMC before walking and during the acceleration phase of walking were increased in PW as compared with SW
Harada et al. (112)	15 (divided into low [$n = 8$] and high [$n = 7$] gait capacity groups)	63 (4); 2 males, 13 females	b	Treadmill walking at predefined speeds	Increases in walking intensity enhanced cortical activations in the left PFC and SMA. Greater increase was observed in low vs. high gait capacity group
Holtzer et al. (113)	22	Young adults (range 19–29); elders (range 69–88)	d	Normal walking (NW), walking while talking (WWT)	Increased bilateral activation in the PFC was observed in WWT as compared with NW
Huppert et al. (114)	10	Young adults (range 21–47), 5 males, 5 females	e	Choice-step reaction time task with congruent and incongruent directional cues	Task-related activation was increased in incongruent compared with congruent choice stepping condition in the inferior frontal gyrus
Kurz et al. (115)	13	Young adults, 24 (1)	f	Forward (FW) and backward walking (BW) on a treadmill	BW elicited greater activation within medial SMC than FW. Activations in the precentral gyrus and SMA were correlated with stride-time during FW
Koenraadt et al. (116)	11	Young adults 23 (4); 3 males, 8 females	g	NW and precision stepping (PS) on a treadmill	SMA was activated prior to the start of NW and PS. More PFC activation was observed during the first half of the PS as compared with NW

Notes: Nine studies reviewed. m-SMC = medial-supplementary motor cortex; PFC = prefrontal cortex; PMC = premotor cortex; SMA = supplementary motor area; SMC = sensorimotor cortex.
*See Supplementary Appendix 1.

One study examined whether age-related changes in WM function were associated with mobility impairments using stance perturbation evoked potentials and found delayed onset of the first P component (P1) for older adults, as well as smaller and later activation of the first negative component (N1) for frail elders (87). In other aging studies examining neural oscillations, increased asymmetrical alpha- and theta-band activity were reported, with significant associations between frontocortical right activation and perceived level of physical health/fitness (88) and central activation with neural relaxation (86). Lastly, one study reported significantly greater amplitude of initial componentry at Cz for healthy youngs compared with healthy older adults during a gait initiation task (89). Electroencephalography can be used to identify neural mechanisms of specific mobility outcomes but at present these data are very limited.

Functional Near-Infrared Spectroscopy

fNIR is a relatively new noninvasive neuroimaging technique that provides information about changes in cortical brain oxygenation levels using the light–tissue interaction properties of light within the near infrared range (90–97). fNIR has been validated against traditional neuroimaging methods and is less prone to movement artifacts (98–107). A limited number of recent studies began to utilize fNIR to assess cortical control of mobility in real, as opposed to imagined conditions (Table 7).

In those studies the number of participants was small and the populations under investigation limited to young and older adult samples (108,109,111–116), though stroke patients were also assessed (110). While the mobility tasks and fNIR devices varied across studies (see Supplementary Appendix 1), consistent increases in task-related oxygenation levels in prefrontal cortex, premotor cortex, and SMA were observed. The involvement of these brain regions was increased in response to anticipation of and acceleration during tasks (109–112) and when locomotion became more cognitively demanding (113–116). Furthermore, cortical responses to task demands were moderated by disease status (110), age (113), and walking capacity (112). fNIR can augment traditional neuroimaging methods by establishing associations between brain activation and mobility performance when assessed simultaneously in real time.

Discussion

Although the neuroimaging literature of mobility in aging has been relatively scarce, consistent and complementary findings across different imaging modalities were observed. Structural MRI was most commonly used followed by FLAIR and diffusion tensor imaging. Fewer studies utilized methods that examined the relationship between changes in task-related brain activation and mobility performance. Especially noted is the paucity of studies that aim to determine task-related changes in brain activation during actual mobility.

Models of cortical and brainstem control of gait and posture have been previously described (117), implicating the basal ganglia (118), cerebellum (119), frontal and parietal cortices (120), in the planning and execution of purposeful locomotion. The neuroimaging studies reviewed reveal consistencies with these aforementioned models and provide important insights into the neural substrates of mobility in aging. Cortical control of locomotion is widespread in aging. Damage and reduced volume in multiple regions of GM and WM and worse functional integrity of the latter were related to poor mobility outcomes as evidenced by different neuroimaging methods. These findings support the notion of age-related increases in the size and number of brain regions and networks that are correlated with motor and cognitive functions (121). Widespread involvement of WM in mobility further suggests that among older adults locomotion is dependent on the integrity and communication of multiple tracks across both hemispheres. However, the degree of damage and method used to assess WMI, as well as the type of mobility outcome determine the extent of their relationship (122).

Consistent with existing models of locomotion, the neuroimaging findings revealed that the cerebellum, basal ganglia, parietal and frontal cortices were related to mobility outcomes. Moreover, increased involvement of frontal cortical regions was evident in imagined walking conditions and when cognitive demands of locomotion increased. The involvement of frontal and prefrontal circuits in cognitively demanding locomotion tasks affirms robust behavioral literature that implicates cognitive processes, notably the executive functions, in mobility (3,5,123,124). Building on existing theories of cognitive and brain reserve (125), future research should aim to determine the functional relevance of specific brain regions and networks that might represent compensation, inefficiency, or di-differentiation (cf, Holtzer et al. (126) for further details regarding these models) vis-à-vis purposeful locomotion in aging.

While beyond the scope of this article determining shared and distinct brain regions and functional networks of mobility in normal and pathological aging is of interest (for instance, see two recent reviews on the neural substrates of gait in Parkinson's disease, refs (127,128)). Future studies should also focus on integrating different neuroimaging methods to determine how brain structures, WM, functional networks, and biochemical pathways jointly subserve mobility outcomes in healthy and pathological aging.

Supplementary Material

Supplementary material can be found at: http://biomedgerontology.oxfordjournals.org/

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