Imaging on mobility and cognition

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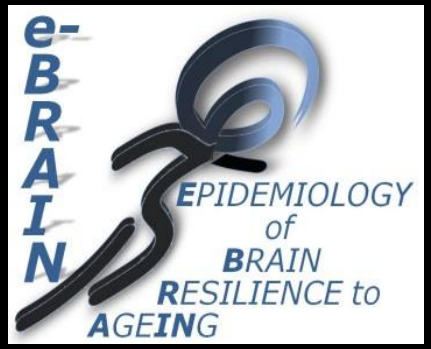
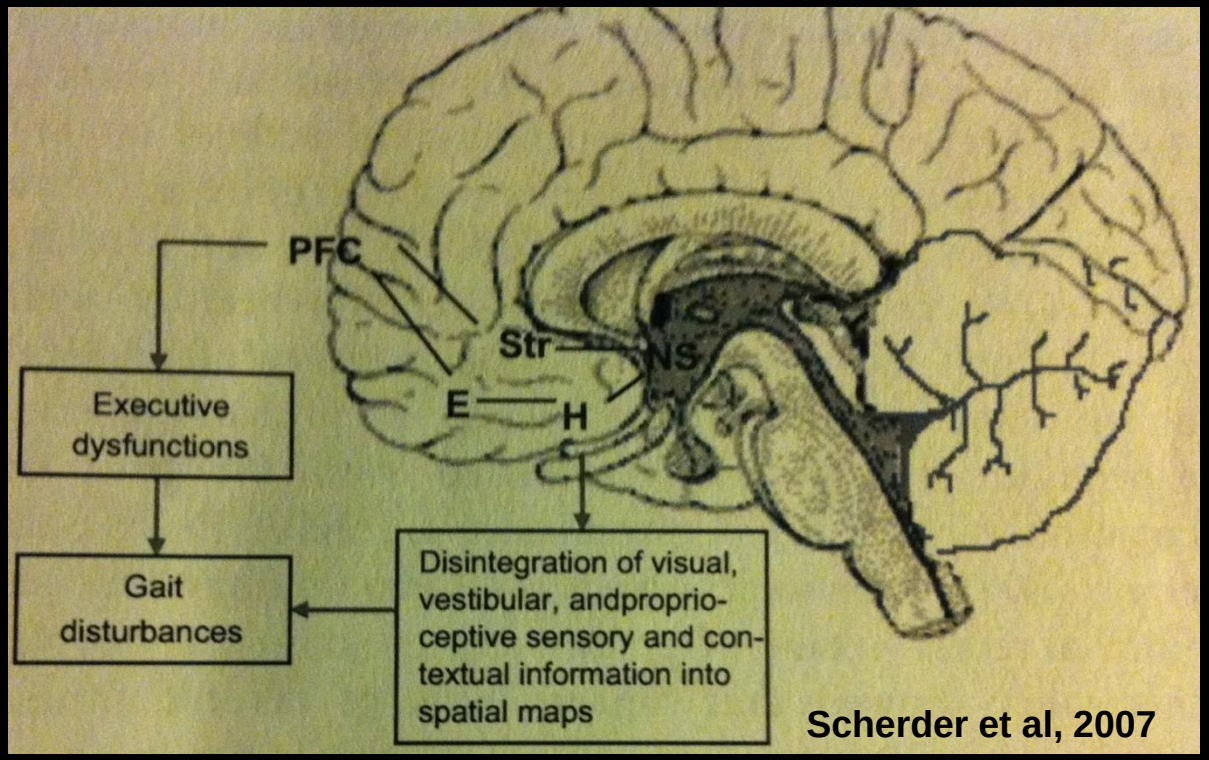


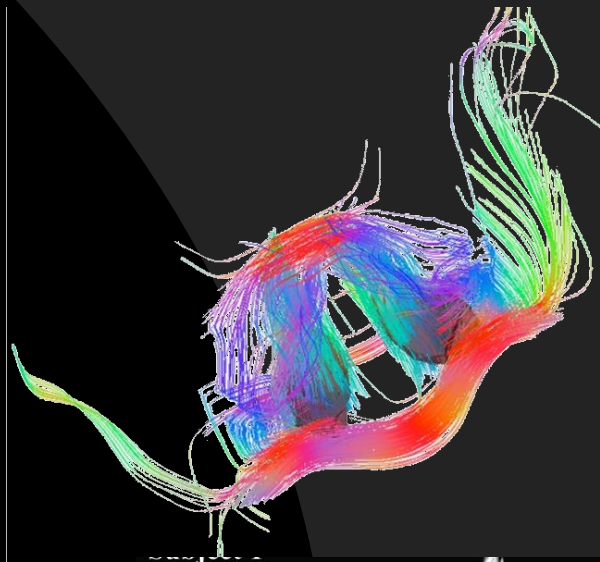


Motor science.
Established in disease models.

OUTLINE

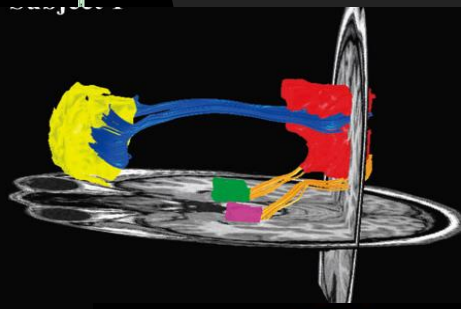
1. Brain structure and gait characteristics
2. Brain activation while dual-tasking on gait
3. Implications for mechanisms:
   - mobility-related networks and ECF-related networks
   - navigation-related networks and memory-related networks

Multimodal neuroimaging



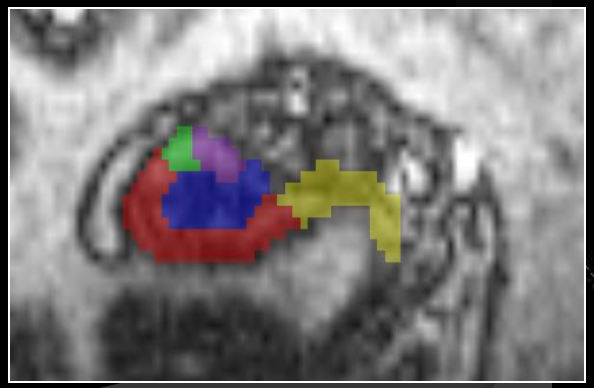
MACRO-structure (volume)

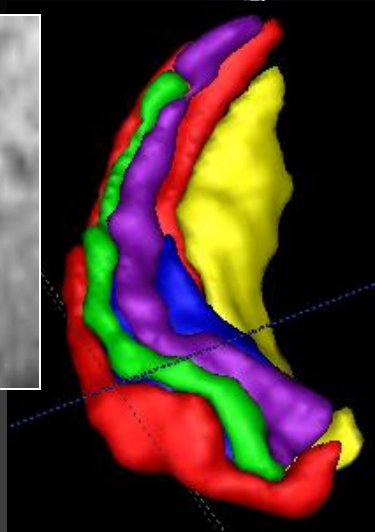
MICRO-structure (MTI, DTI)



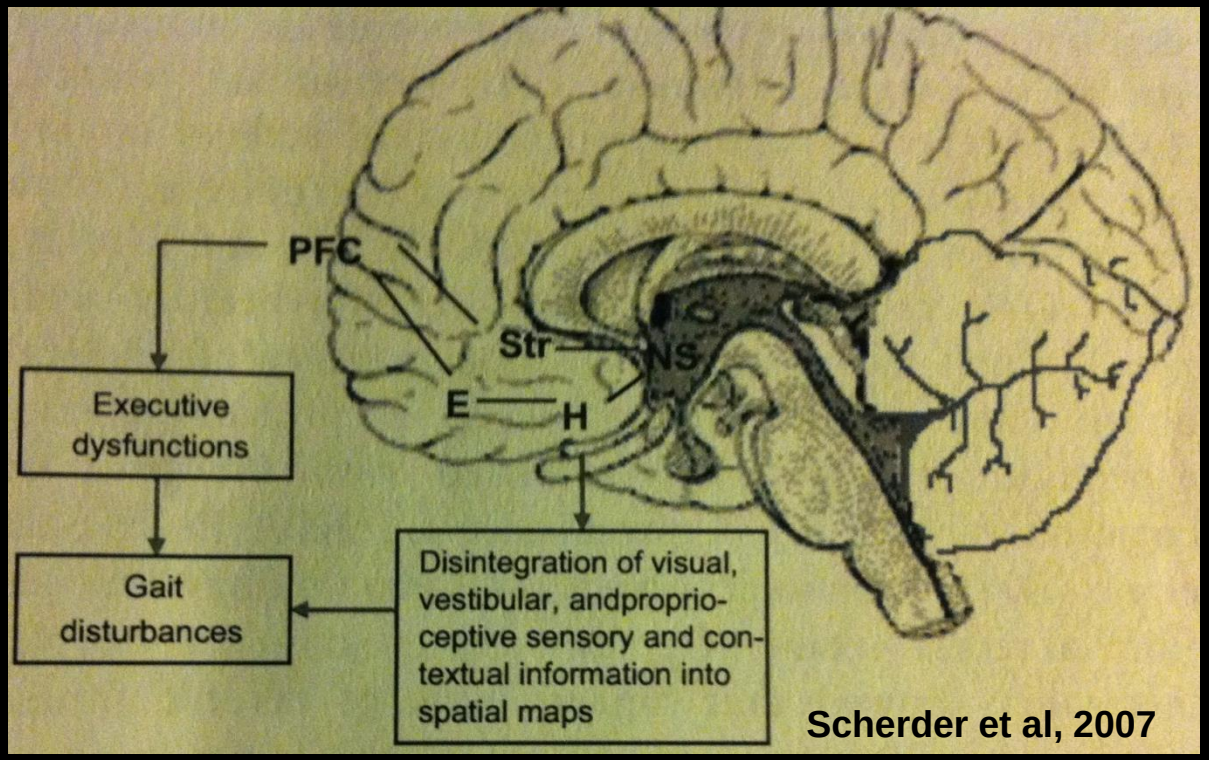
Function
Neuronal activation, resting activity, blood flow
(task-related, resting state arterial spin labeling)

ULTRA-structure
(7 Tesla, 100 micron)





Quantitative, complementary information of network integrity.



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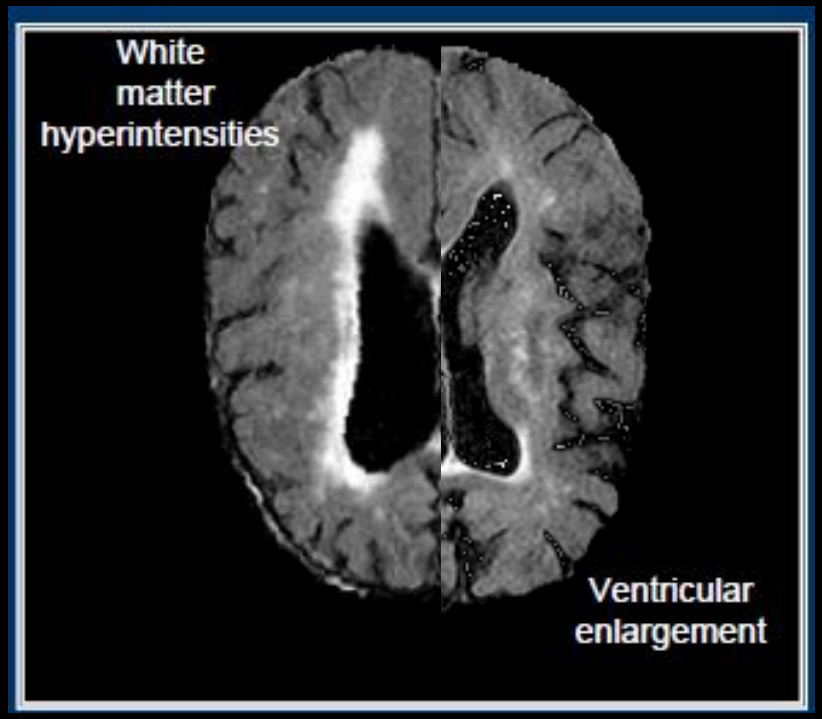
Macro-structure Semiquantitative ratings, total brain



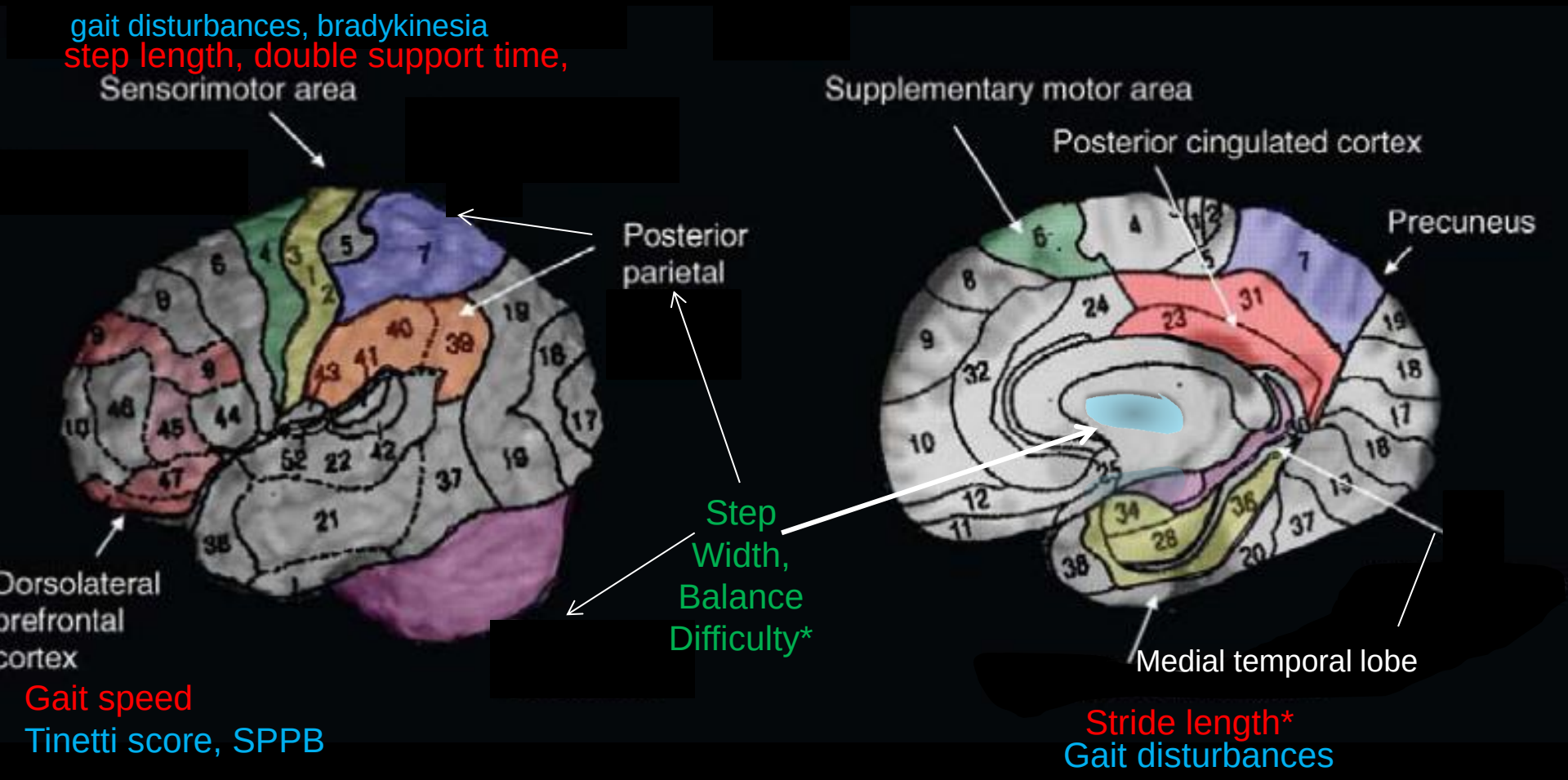
In older adults living in the community, white matter hyperintensities, ventricular enlargement and lacunar infarcts are associated with slower gait,* balance difficulty and with greater risk of developing physical disability, independent of other risk factors

GAIT SPEED : lacunar infarcts in frontal lobe (De Laat, *Stroke*. 2010)
BRADIKINESIA: lacunar infarcts in the frontal lobe (De Laat, 2012)

* longer DST, longer stride length

See “Understanding Gait in Aging: Finding the way forward” - Camicioli and Rosano, 2012 for references

Macro-structure VOLUMETRIC METHODS: GM regions



*pallidum

See “Understanding Gait in Aging: Finding the way forward” - Camicioli and Rosano, 2012 for references

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Gait Measures Indicate Underlying Focal Gray Matter Atrophy in the Brain of Older Adults

Caterina Rosano[1], Howard Aizenstein[2], Jennifer Brach[3], Allison Longenberger[1], Stephanie Studenski[4], and Anne B. Newman[1]

Step Width

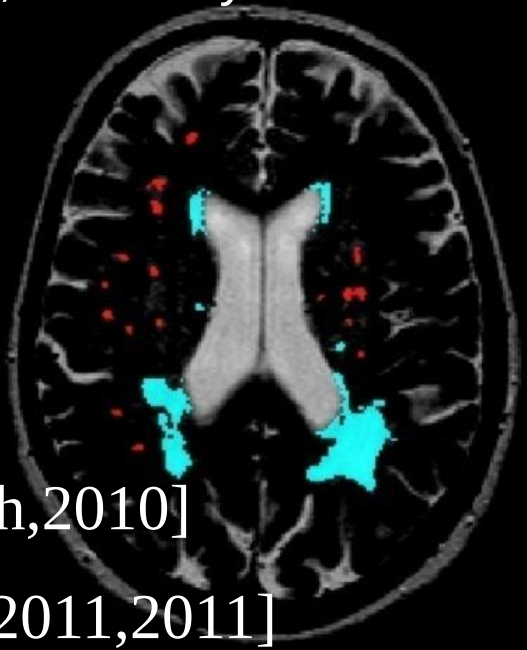
Regions of Interest	Standardized β (p Value)
Pallidum, right	-.13 (.04)
Inferior parietal lobule, right	-.17 (.03)
Adjusted model, r^2	0.14

Associations remained similar when all the covariates entered the model forced in blocks.

for step width (adjusted r^2 from models: 0.18)

Characteristics	Study Populatio 220)
Demographics	
Age, mean (*SD*)	78.0 (3.9)
Education, y, mean (*SD*)	14.0 (2.5)
Race, *n* (%) white	171 (77.7)
Gender, *n* (%) male	81 (36.8)
Gait characteristics	
Gait speed, mean (*SD*) m/s	1.05 (0.22)
Step length, mean (*SD*), m	0.58 (.10)
Step width, mean (*SD*), m	0.21 (0.04)
Stance time, mean (*SD*), s	0.73 (.10)
Step time, mean (*SD*), s	0.56 (0.06)
Double support time, mean (*SD*), s	0.16 (0.04)
Peripheral risk factors of gait abnormalities	
Body mass index, kg/m^2, mean (*SD*)	26.1 (3.9)
Hip/knee arthritis, *n* (%)	74 (33.6)
Impaired vibration sensitivity*, *n* (%)	111 (50.5)
Hypertension, *n* (%)	71 (32.3)
Ankle arm ratio ≥0.9, *N* (%)	183 (85.1)
Prevalence of stroke, *N* (%)	8 (3.6)
Central risk factors of gait abnormalities	
Brain structure measures (global markers)	
Brain infarcts ≥1, *N* (%)	61 (27.7)
White matter hyperintensities ≥3, *N* (%)	70 (32)
Total brain volume, cm^3, mean (*SD*)	1335.3 (131.2)
Brain function measures	
Modified Mini-Mental State Examination, mean (*SD*)	93.7 (5.3)
Digit Symbol Substitution Test, mean (*SD*)	47 (12.3)
CES-D score, mean (*SD*)	5.2 (4.3)
Dementia, *n* (%)	11 (5)

Macro-structure: VOLUMETRIC METHODS, WMH by Tract



Frontal
- SPPB [Benson,2002]
- Sway [Novak 2009]
- GAITRite composite [Srikanth,2010]
- Speed /stride length [DeLaat, 2011,2011]
- UPDRS [DeLaat,2012]

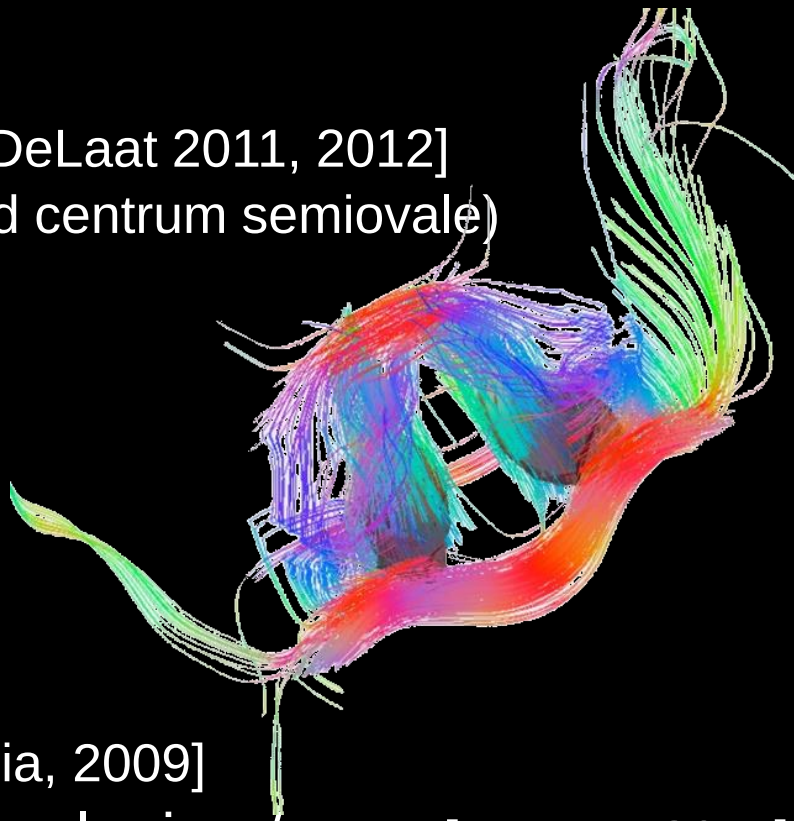
Corpus callosum
- Speed/SPPB [total*- Ryberg, 2007]
- Gait disorders [genu*-Moretti, 2005]
- Speed [splenium - Moscufo,2011]

Basal ganglia/ Limbic system : gait speed [DeLaat, 2011];

Micro-structure: DIFFUSION TENSOR– normal appearing White M.

Frontal:

-Parkinsonian signs- [DeLaat 2011, 2012]
(n.s. in posterior horns and centrum semiovale)

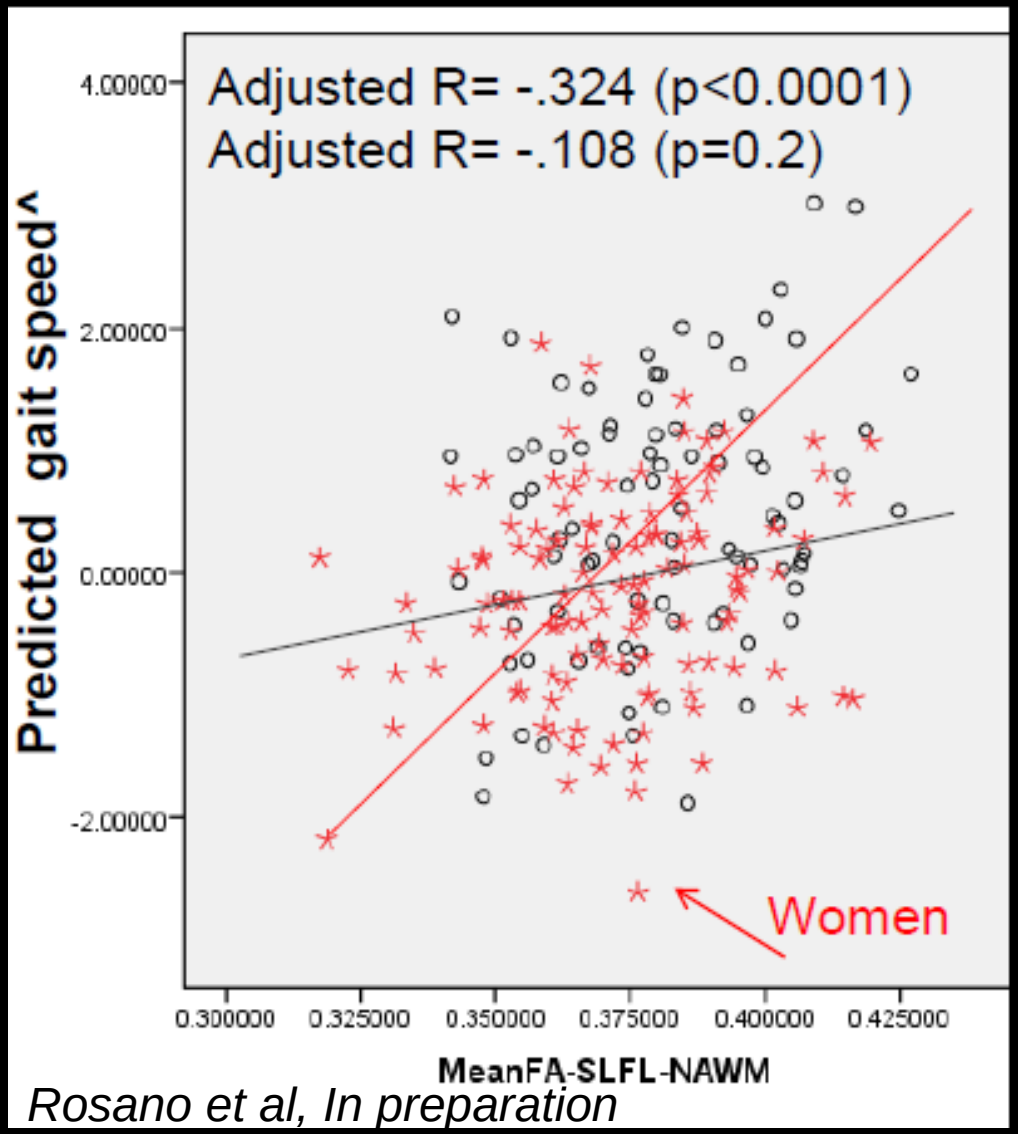


Corpus Callosum :

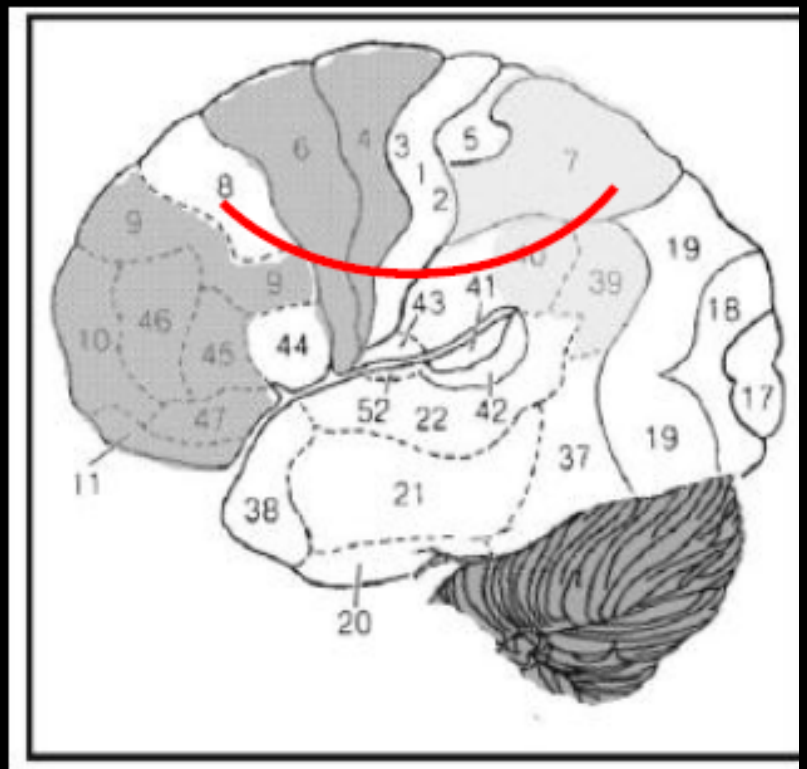
Tinetti - genu* [Bhadelia, 2009]

Gaitmat measures -- splenium/genu [DeLaat, 2011]

Micro-structure: DIFFUSION TENSOR– normal appearing White M

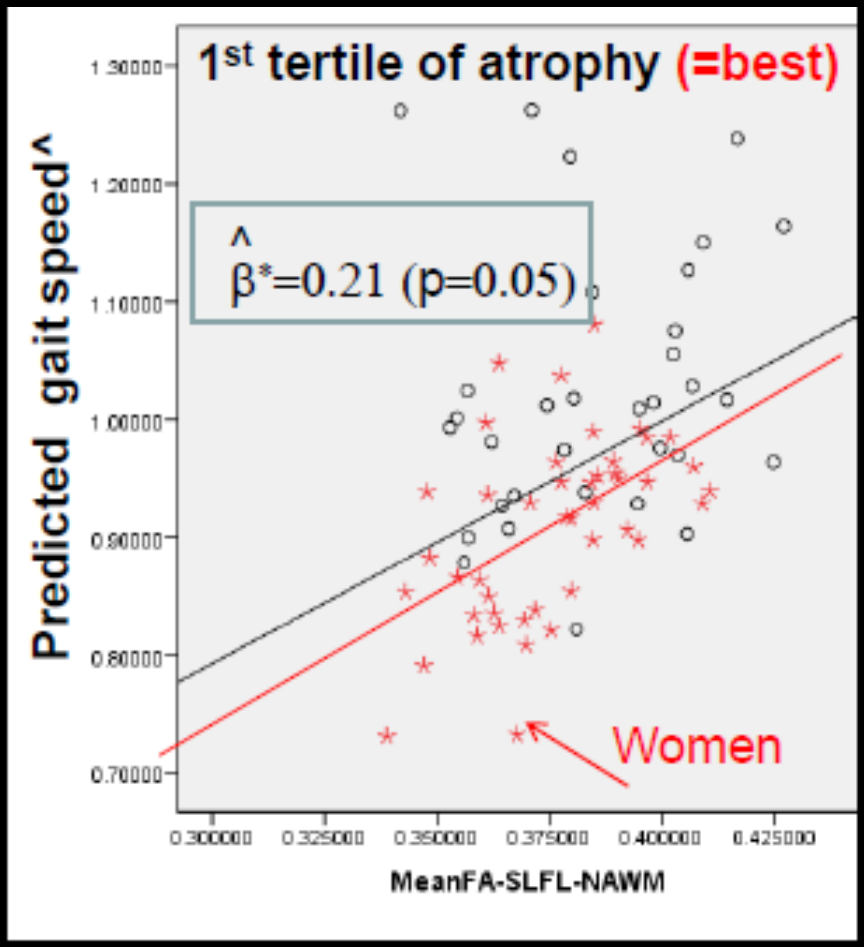


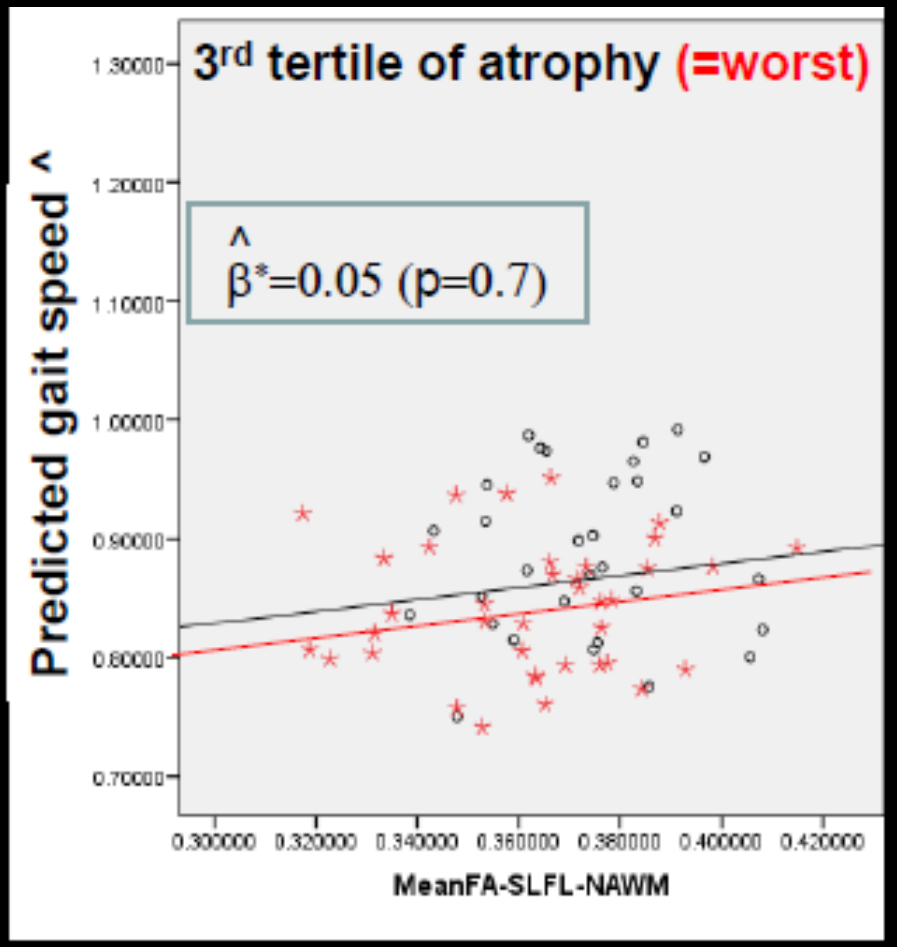
Rosano et al, In preparation



^ Gait speed values adjusted for: age, BMI, quadriceps strength, painknee/OA, in past 12 mo physical activity, gender specific Gray matter atrophy

Micro-structure: DIFFUSION TENSOR– normal appearing White M.

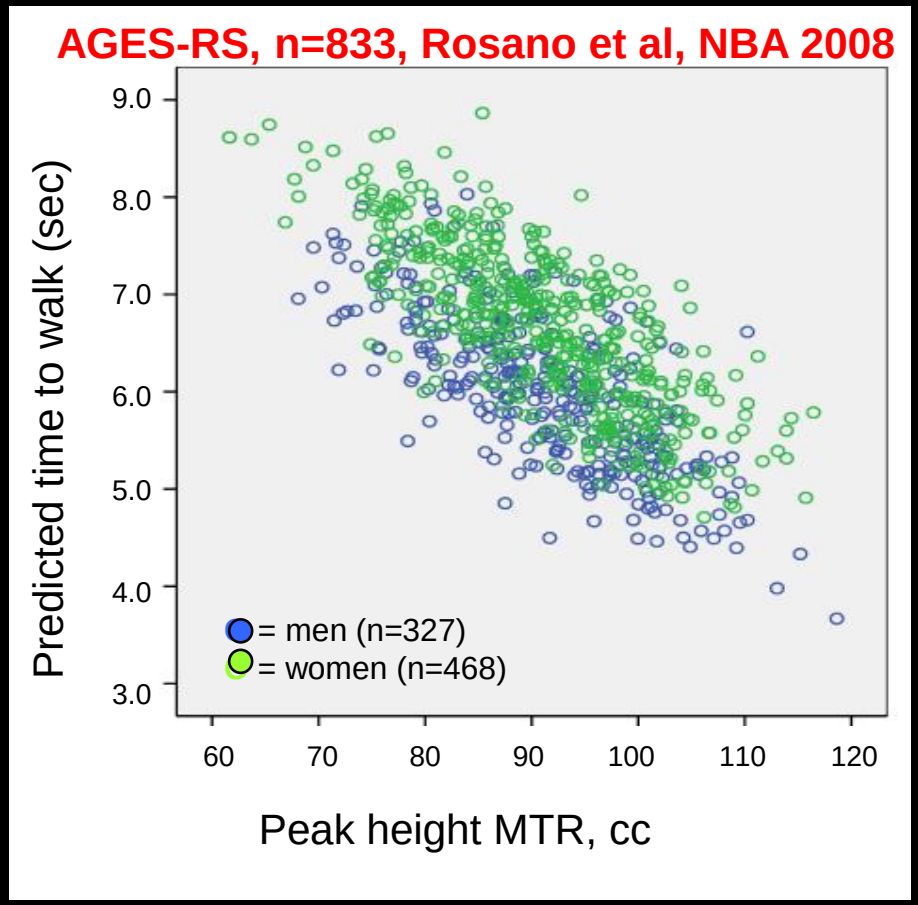


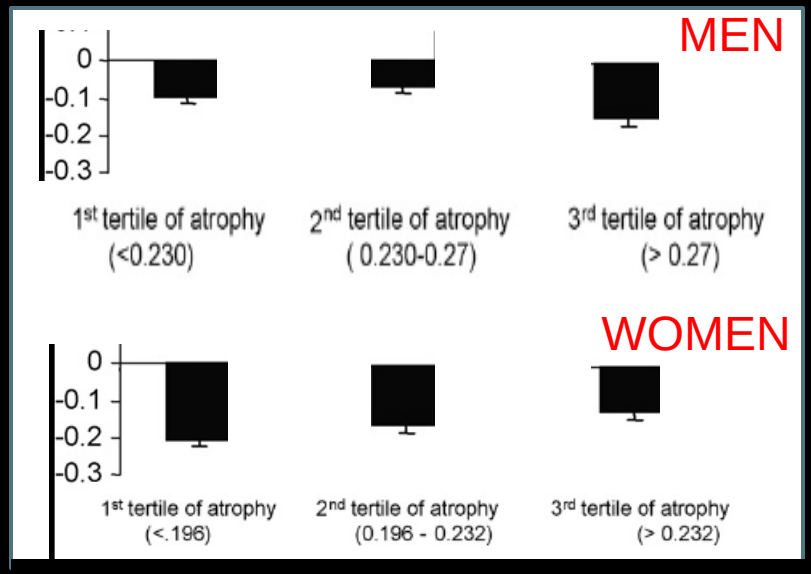


Eliminated in those in the 3rd tertile of atrophy

^ Gait speed values adjusted for: age, BMI, quadriceps strength, painknee/OA, in past 12 mo physical activity, gender specific Gray matter atrophy

Micro-structure: Magnetization transfer– normal appearing White M



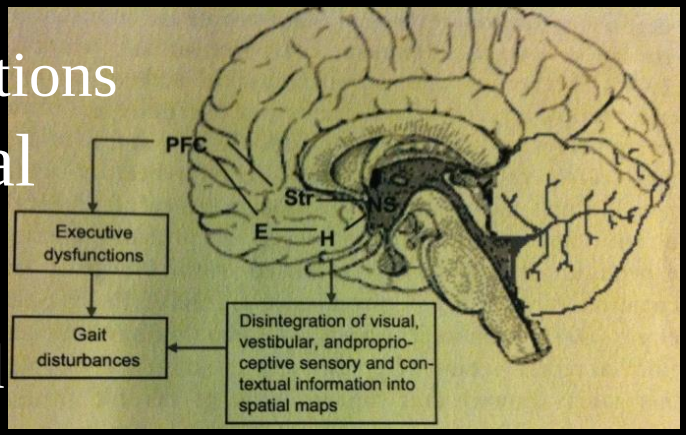


Age head size, BMI, coronary artery calcium, physical activity, hip/knee, OA

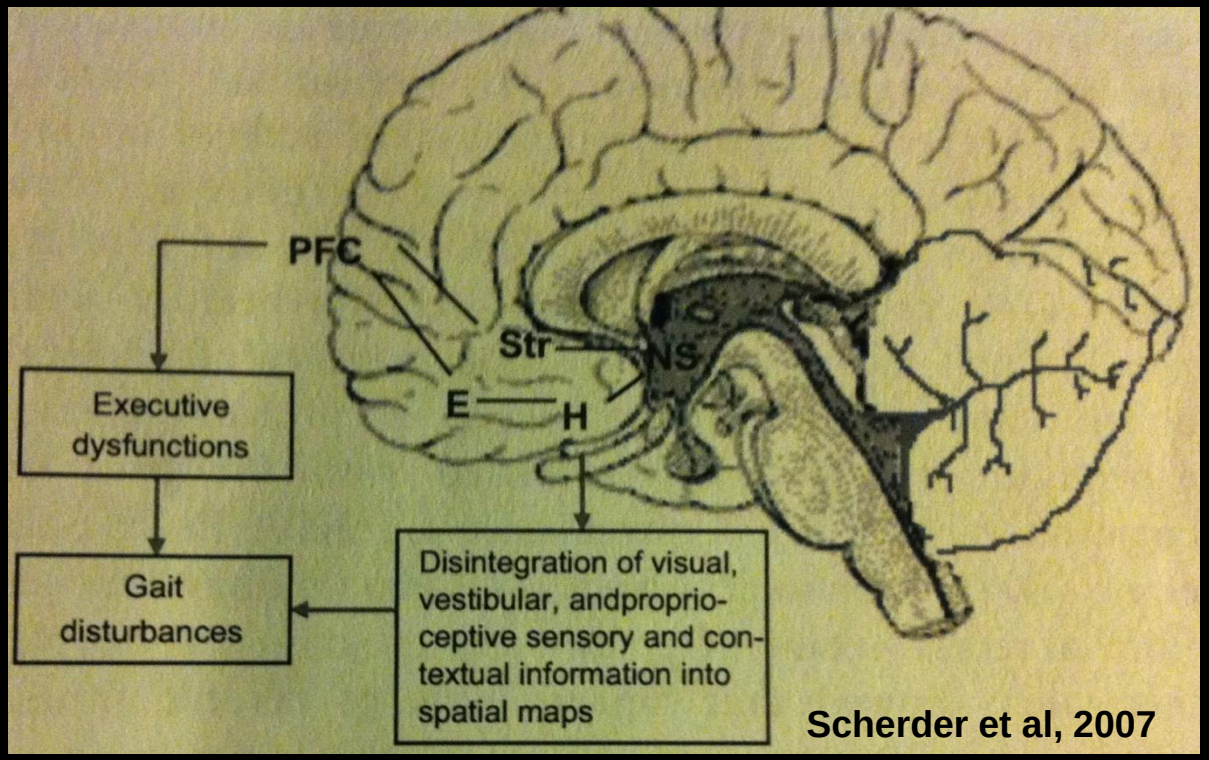
Eliminated in men after adjustment for brain infarcts and WMH.

1. EVIDENCE FOR THE ASSOCIATION BETWEEN BRAIN AND MOBILITY IN OLDER ADULTS: SUMMARY

Findings somewhat consistent with the traditional model of mobility control



- WMH- Frontal, interhemispheric connections
- Lacunar infarcts in fronto-subcortical
- GM atrophy:
  - Dorsolateral prefrontal: gait speed
  - Basal ganglia (-)
  - Sensorimotor: bradykinesia/slowing
  - Medial temporal: gait disturbances
- Micro-structure: *(in those with lower atrophy)*
  - Fronto-parietal , interhemispheric connections



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FUNCTIONAL MRI

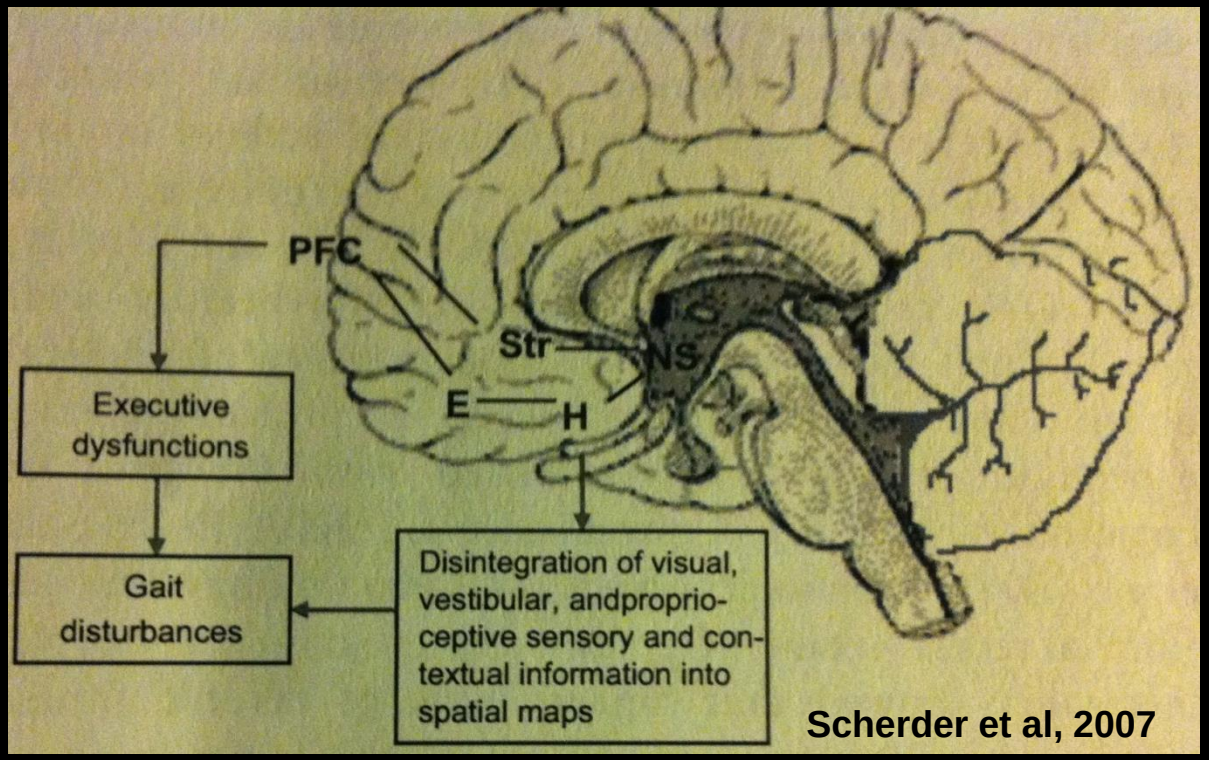
Cross-sectional

Functional neuroimaging studies indicate a role of basal ganglia and prefrontal motor regions in relationship with gait

[Ben-Salem, 2008; Iseki, 2010; la Fougere, 2010, …..]

Need to do.

find papers examining
areas activated while dual-tasking on gait



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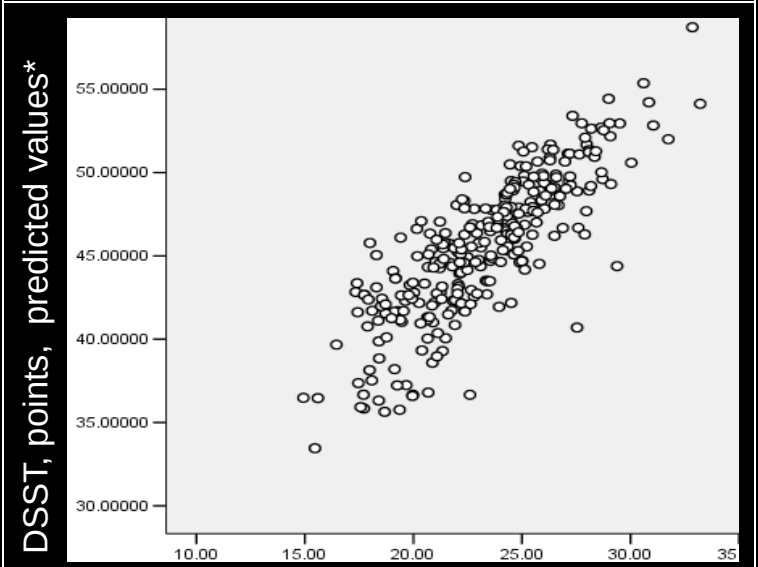
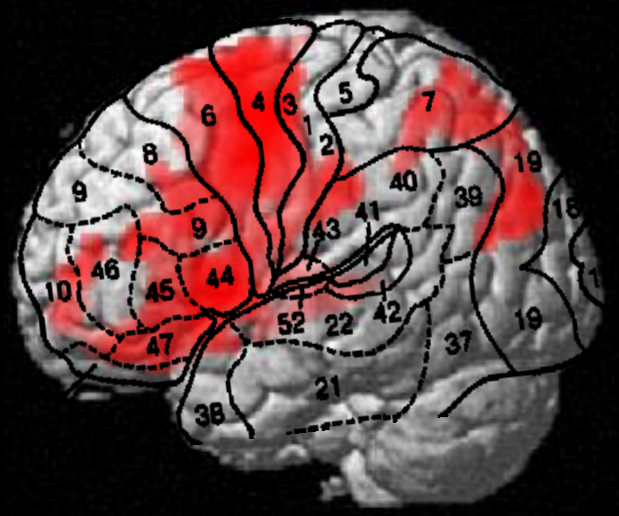
Implications: Insights into mechanisms

The PFC areas associated with gait speed partially overlap with the areas related to information processing speed in aging.

dLPFC atrophy and lower DSST score: volumetric study



dLPFC activation and DSST



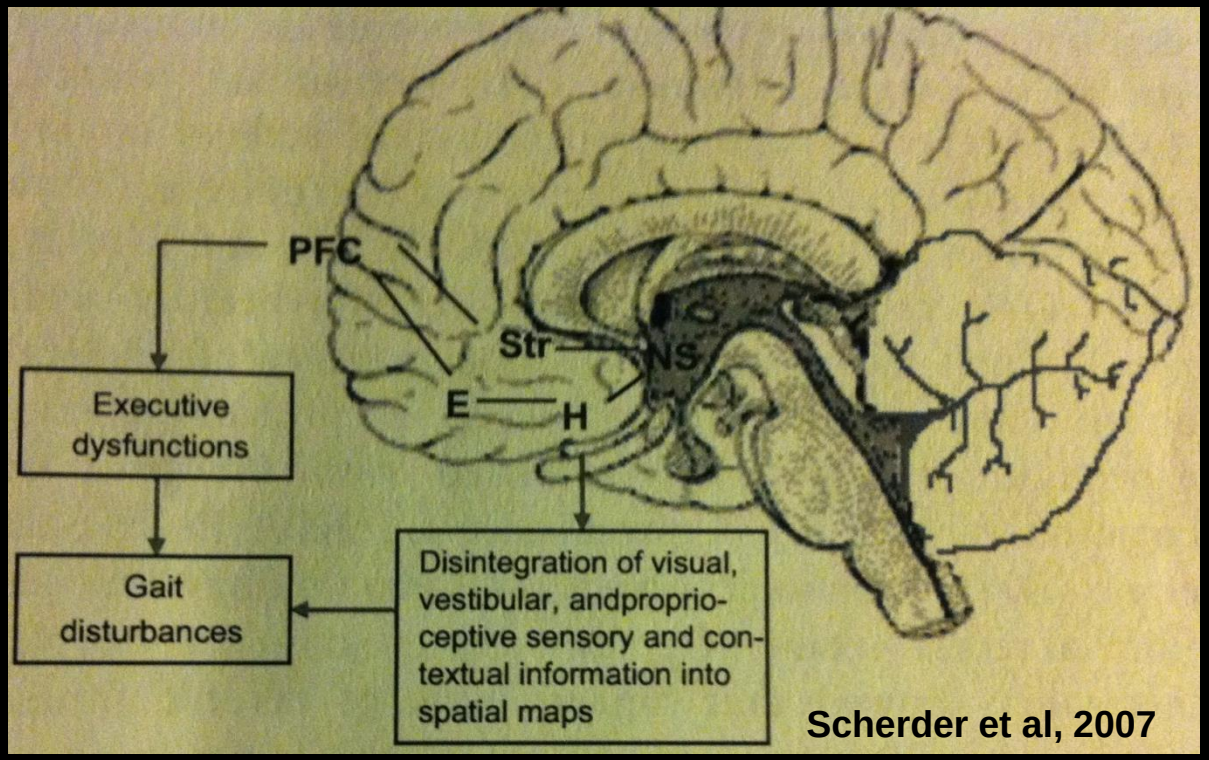
Venkatraman Rosano, Neuroimaging 2010

GMV: β*=0.14; p=0.00002

Adjustment for tests of information processing speed partially explains the associations between dLPFC volume and gait

(Zheng, 2012; Carmelli, 2000; Rosano, 2008; Rosano, 2010)—cross-sectional

Need to do



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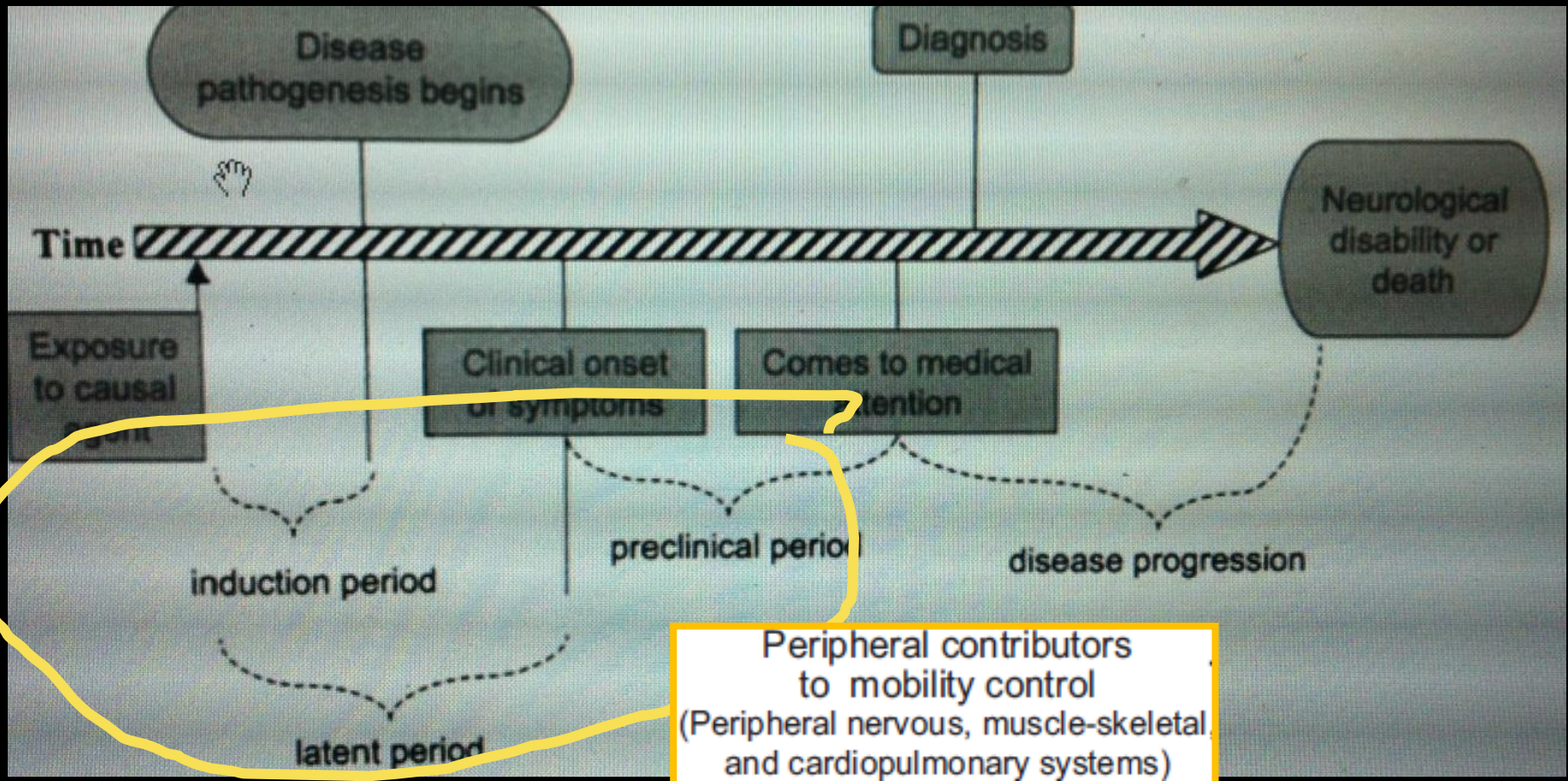
Need to do

Challenges and opportunities

- The manifestations of CNS abnormalities as gait/mobility problems will depend on a number of other conditions that exists outside the CNS.



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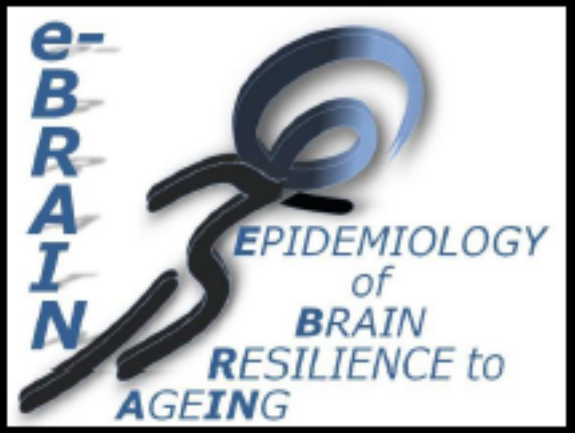

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