Plasticity and Brain Aging

U13 Bench-to-Bedside Conference
"Sensory Impairment and Cognitive Decline"

Caterina Rosano,MD, MPH
Professor of Epidemiology
Graduate School of Public Health
University of Pittsburgh,
Pittsburgh PA, 15261

DISCLOSURE

- Current funding:

1 R01 AG029232-01;

1R01AG037451-01A1;

RO1DK089028;

3P30AG024827-13S1

P30AG024827

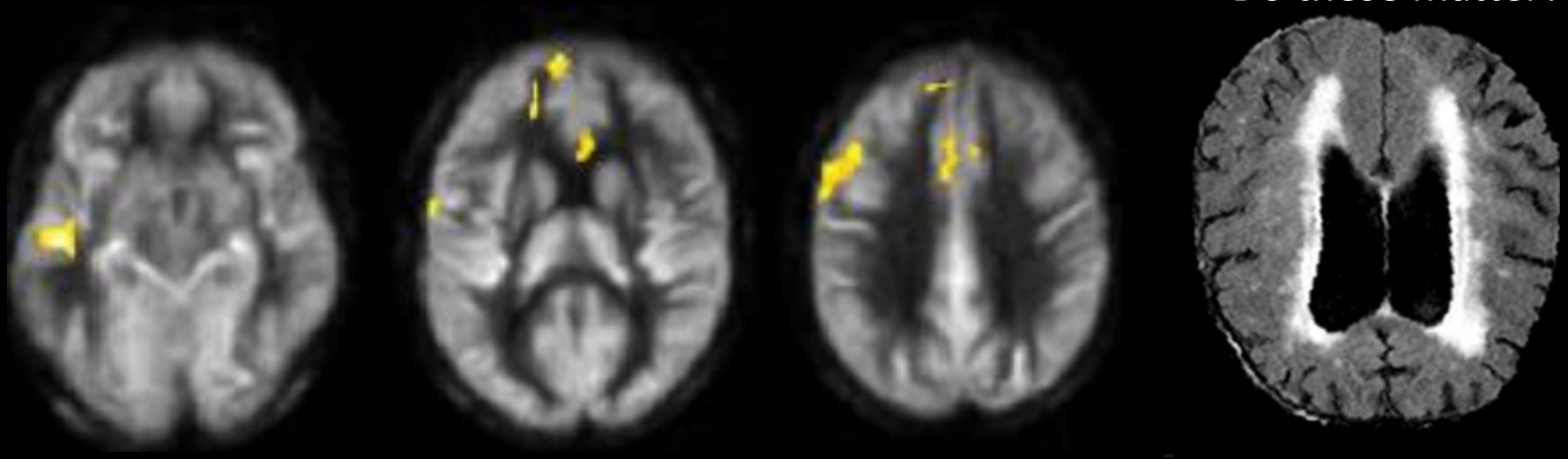
- Other financial relationships: none
- Conflicts of interest: none

Cerebral Cortex February 2015;25:396–405
doi:10.1093/cercor/bht234
Advance Access publication August 28, 2013

Neural Mechanisms of Brain Plasticity with Complex Cognitive Training in Healthy Seniors

Sandra B. Chapman[1], Sina Aslan[2], Jeffrey S. Spence[1], John J. Hart Jr[1], Elizabeth K. Bartz[1], Nyaz Didehbani[1], Molly W. Keebler[1], Claire M. Gardner[1], Jeremy F. Strain[1], Laura F. DeFina[3] and Hanzhang Lu[4]

Do these matter?



GAPS of studies on brain plasticity and aging:

--Limited information on underlying age-related CNS changes

--Healthy and high functioning young old

REVISITED FOCUS : **age-related CNS changes**

- can drive functional decline either directly or by weakening the potential for plasticity.

Next slides: examples of age-related CNS characteristics that have recently emerged with advanced neuroimaging technologies.

Focus: structure of gray and white matter and vessels.

Example 1: dormant neurogenesis

a) Ultra-high field imaging: in vivo "dissection" of hippocampal formation into its subregions.
---Dentate gyrus: neuroregenerative potential.
----Cornu ammonis: Vulnerable to ischemia, stress; atrophy predates cognitive impairment.
- Rodent/ non human primates

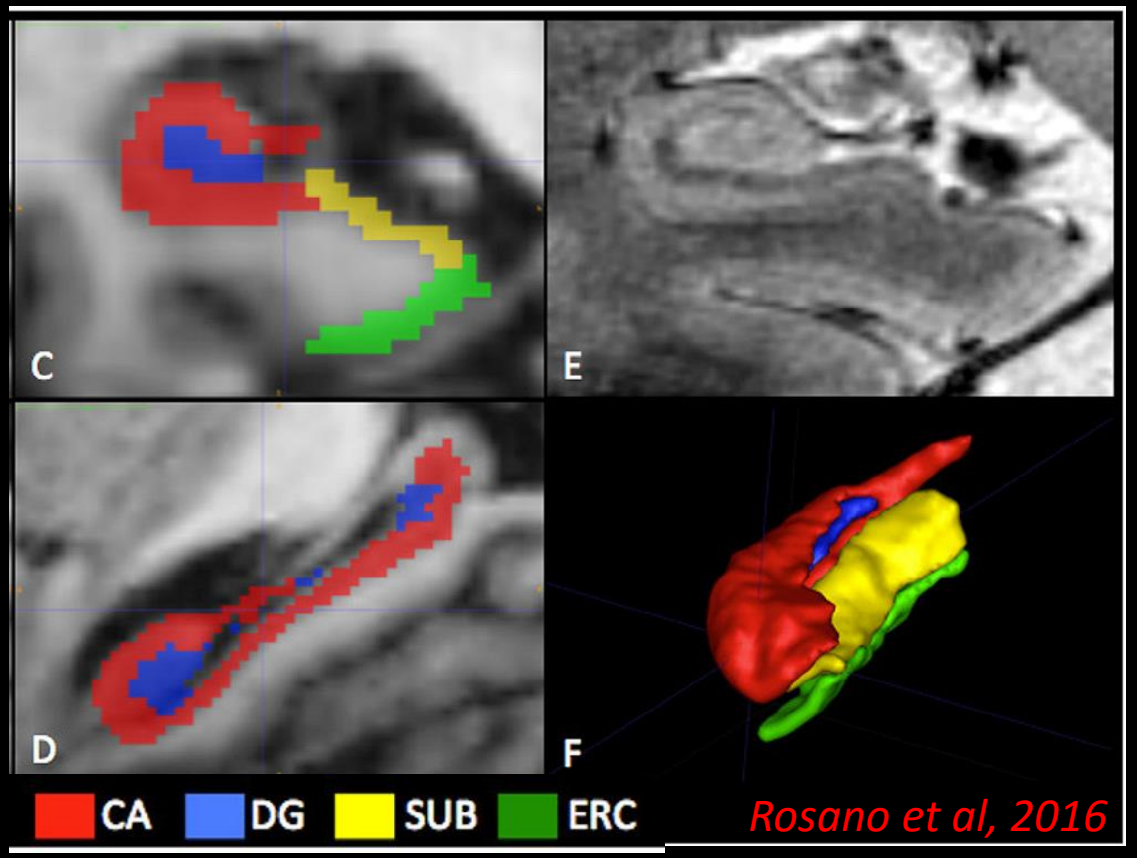
b) Experimental/proof of concept studies : PA, transcranial MRI-guided focused ultrasound.

RESEARCH OPPORTUNITIES:
- Underlying mechanisms (new neurons , viable, richer dendritic arborizations, more blood)

Adult hippocampal neurogenesis and cognitive flexibility — linking memory and mood

NATURE REVIEWS | NEUROSCIENCE

Christoph Anacker[1] and René Hen[1–]

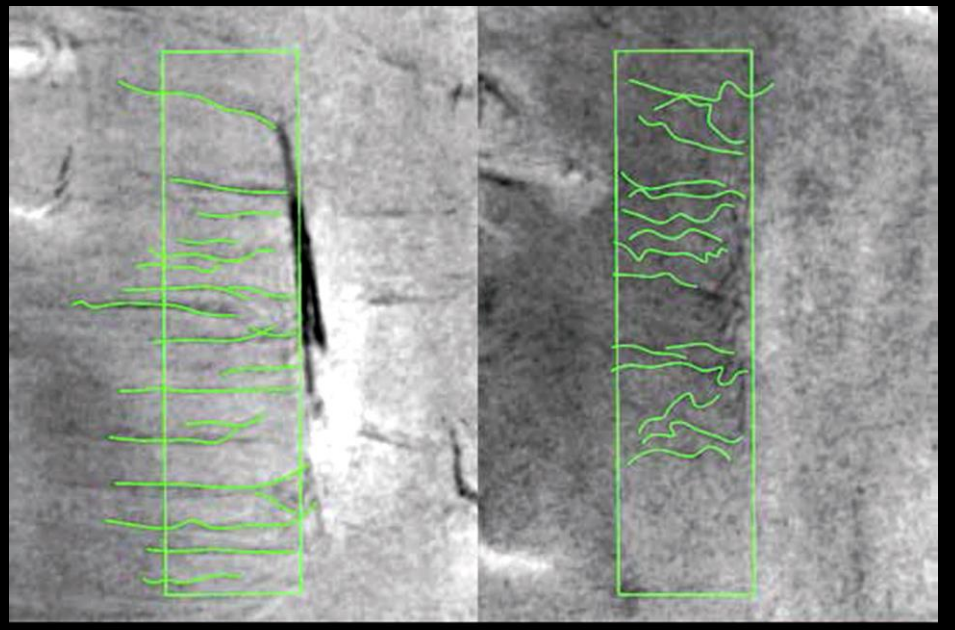


Rosano et al, 2016

Example 2: small arteries and veins

a) Time of flight, ultra-high field susceptibility weighted images: direct visualization of small arteries and veins w/out contrast. # and tortuosity.

b) Small veins' tortuosity/lower arterial density: AD, APOe4, Physical activity

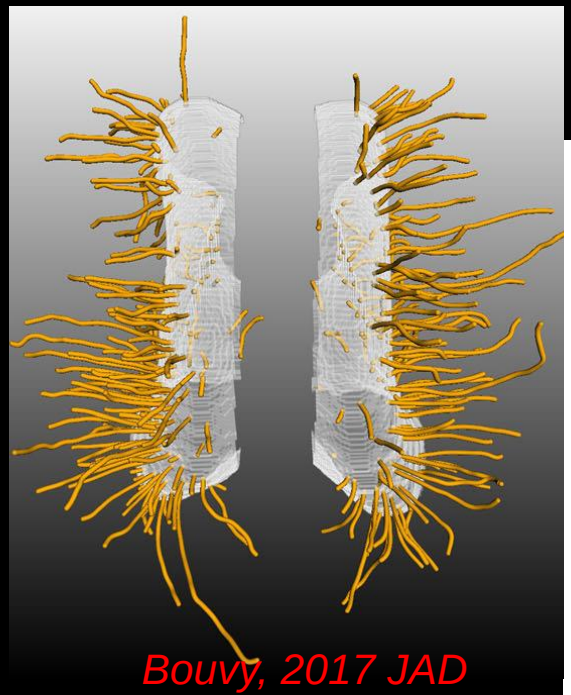


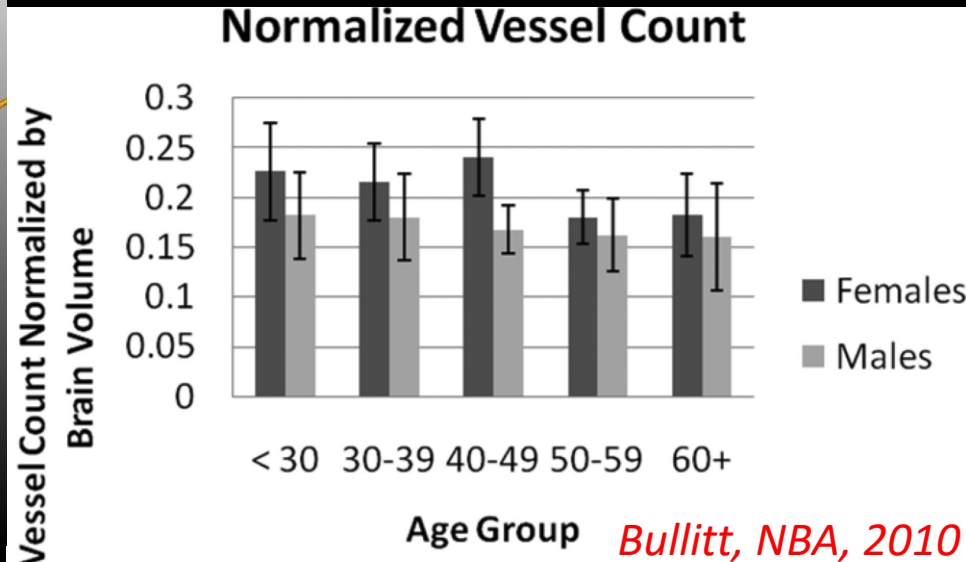
Shabaan, AJNR 2017

RESEARCH OPPORTUNITIES

-- mechanisms (inefficient angiogenesis?)

- Few studies
- small N


Bouvy, 2017 JAD



Bullitt, NBA, 2010

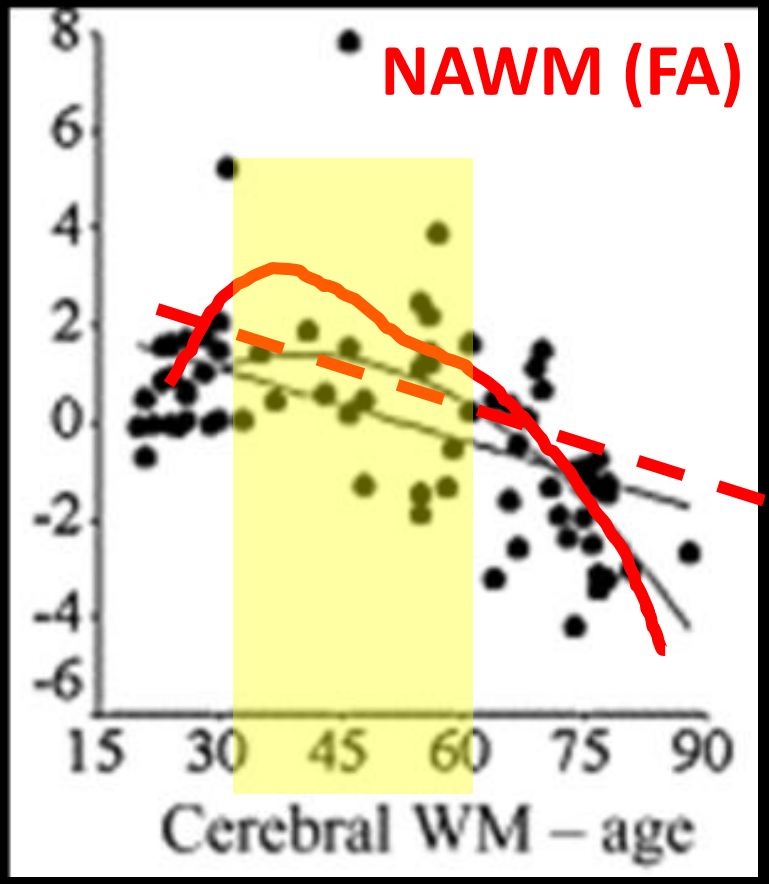
Example 3: microstructure of normal appearing parenchyma

a) Multi directional diffusion tensor imaging: characterization of fibers' properties.

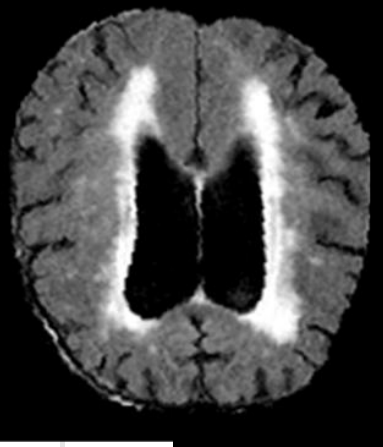
b) Emerging as a "resilience factor" in stroke and older age.

RESEARCH OPPORTUNITIES:

- Spatio-temporal patterns of change indicate window of opportunity in early/late middle age.
- Influence of risk factors
- Interactions w/ demographics, multi-morbidities



Example 4: WMH.



a) Volumetric, semi-automated methods

b) Many risk factors well known, in large, longitudinal studies

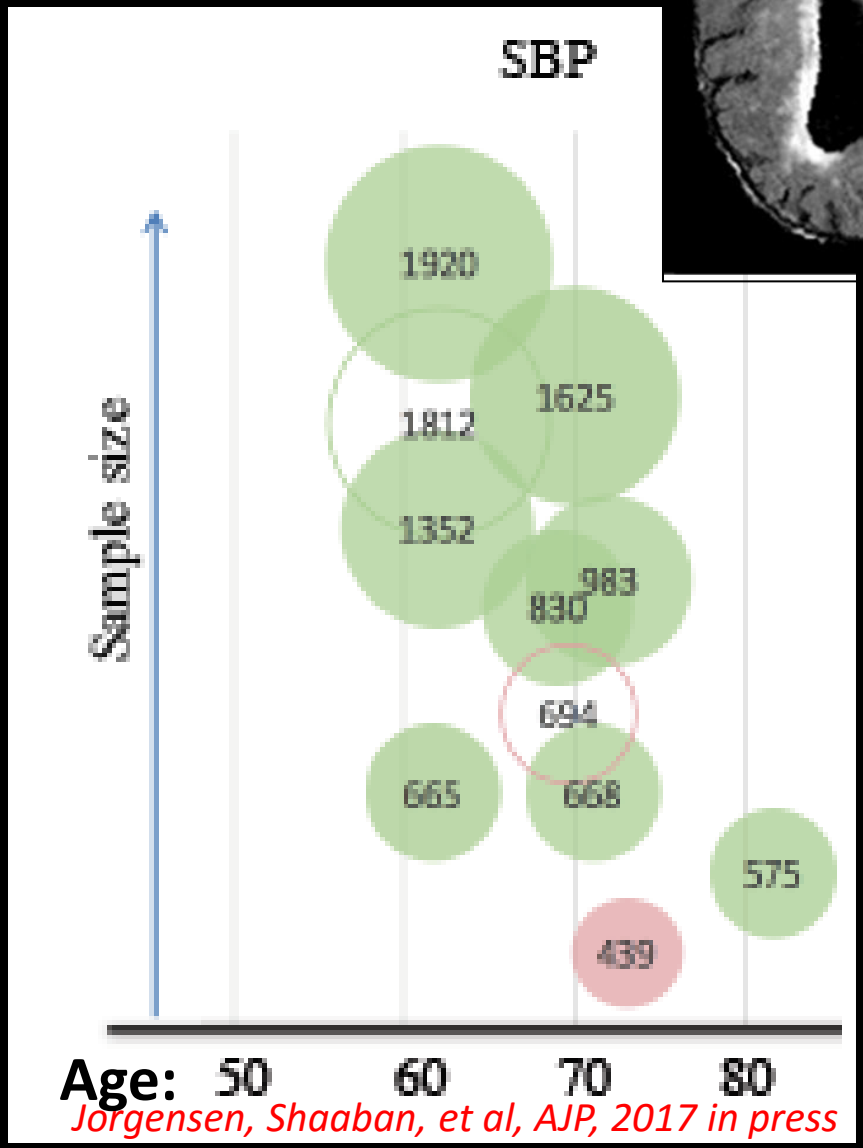
c) As early as middle-age.

d) Complex interactions w/ age, race, sex, APOe4

e) RCT targeting RF for WMH : modest/no results

RESEARCH OPPORTUNITIES :

- interactions w/ demographics, length of exposure, other morbidities.



Jorgensen, Shaaban, et al, AJP, 2017 in press

Knowledge gaps to understand plasticity

- Better understand age-related CNS characteristics and underlying mechanisms.

- Moderating effects of these CNS changes on plasticity: threshold effects?

- Moderating effects of demographics, length of exposure to risk factors, multi-morbidities.

Research Opportunities.

- Multi-modal and repeated CNS assessments in vivo w/ ex-vivo validations.

- Careful sample selection to leverage the heterogeneity of aging processes to explain inter-subject variability:

  -wide range of age (e.g. prior to middle- age) and of health-related factors;

  - information on time of exposure to risk factors;

http://www.humanconnectomeproject.org/
https://abcdstudy.org/

Conclusions:

- Age-related CNS change can drive functional decline either directly or by weakening the potential for plasticity.
- Whether intervening on age-related CNS change can also promote plasticity needs to be studied.
- Studies should integrate cutting edge CNS assessments w/ traditional methods, both in vivo and ex-vivo, and maintain a focus on state of the art study designs and careful population selection.

THANK YOU

Claude Pepper-Pittsburgh

1 P30 AG024827 Geriatric Medicine

PI: Greenspan/Newman

Geriatric Psychiatry Neuroimaging

H.J. Aizenstein

Magnetic Resonance Center

H. Hetherington

T. Ibrahim

Center for Aging and Population Health

Department of Epidemiology

Graduate School of Public Health

University of Pittsburgh

Director: A. B. Newman , MD, MPH

Collaborators

S. Stephanie, NIA,
Boudreau, Pitt
Lopez, Neurology
Guralnik, Maryland;

car2350@pitt.edu