Lifespan Changes in Brain and Cognition:

Neurodevelopmental Origins and Plasticity

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Magnetic Resonance Imaging in lifespan studies

Nyberg et al., 2012, Trends Cogn Sci
Fjell et al., 2014 Cerebral cortex.
Ex: What is next?

The timing of influences

• When does aging begin?

• Quest to find age-specific, age-exclusive and distinct pathological mechanisms of change
The lifespan approach

• understand mechanisms at work early in life

• identify what and how residual variance may be affected by late-life factors

• neurodevelopmental origins
Rationale for a lifespan approach

• 2010 NIH ‘State of the Science’ report: insufficient evidence to support the use of pharmaceutical agents, dietary supplements or other means for the prevention of cognitive decline or Alzheimer’s

• Roberts & Petersen (Brain, 2014): “studies that have investigated modifiable lifestyle risk factors for MCI or dementia have typically assessed risk factors in midlife at best, or more often than not, in late life.”
The lifespan approach

• A number of risk factors for poor cognitive function and decline in aging are likely similar to those for aberrant development

• In some respects, aging starts in the womb

Time machine, anyone?
Early factors

Brain development - of early priority in life!

- CNS fundamentals form early in gestation
- Multiple neurodevelopmental processes exclusively prenatal
• Cerebral and cognitive differences in children exposed to opioids and other substances in utero Walhovd et al. 2007; 2010; 2012; Nygaard et al., 2016

• No such differences found in children born to mothers detoxified in a hospital setting Walhovd et al. 2015

• and no differences in birth weight
Long-term influence of normal variation in neonatal characteristics on human brain development


Fig. 1. Relationships of birth weight and cortical surface area, controlling for age, sex, GA,F, household income, and scanner, thresholded for multiple comparison corrections (FDR = 5%). (A) Lateral left hemisphere. (B) Lateral right hemisphere. (C) Medial left hemisphere. (D) Medial right hemisphere.
Early genetic influences on later cortical change

Genetic topography of brain morphology

- The adult cortex can be divided into regions of maximal shared genetic influence
- Hypothesis: Genetically programmed neurodevelopmental events cause a lasting impact on the organization of the cortex – observable decades later
Early genetic influences on later cortical change

Does cortical change (thickness) in development and aging follow the same genetic divisions?

- Changes in cortical thickness in development AND aging followed closely the genetic organization of the cortex

*Fjell et al., PNAS, 2015 Dec 15;112(50):15462-7.*
Early life factors and cognition in late adulthood

• late preterm birth – risk for neurocognitive impairment in late adulthood (Heinonen et al 2015)

• cardiovascular fitness and cognitive performance in early adulthood - risk of early-onset dementia and mild cognitive impairment (MCI) > 40 yrs later (Nyberg et al., 2014)
Early life factors and cognition in late adulthood

- The Lothian birth cohort: general cognitive ability scores from age 11 to old age (Deary et al.)

Neurodevelopmental origins of lifespan changes in brain and cognition

- n = 973, 4-88 yrs, total of 1633 scans
- Half recruited though the Norwegian Mother-Child Cohort study (MoBa)
- M= 2.3 yrs (0.2-6.6 yrs) follow-up
- Cortical area and general cognitive ability (GCA)
Neurodevelopmental origins of lifespan changes

Relationship of cortical area and general cognitive ability (GCA) in child sample (MoBa, 4-12 yrs)

$r = .28$ (ctrl sex, age and site)

Walhovd et al., PNAS, 2014

Neurodevelopmental origins of lifespan changes

- Full sample split based on GCA

- Area from identified GCA region extracted for each participant, fitted to age

- Effect of age ($p < .0001$), and of GCA group ($p < .0001$)

- No interaction with age ($p = .83$)

Walhovd et al., PNAS, 2014
Beginning to target prenatal origins of lifespan changes

• Select potentially important variables from the MoBa database collected at pre- and neonatal stages

• Investigate relationship to GCA and cortical area of GCA region

• Gestational Age
• Birth weight
• Apgar score
• Parental education
• Parental income
• Single parenthood

Beginning to target prenatal origins of lifespan changes

• BW related to cortical area of GCA region, $r = .16$
• Ctrl for parental height, $r = .15$
• Excl LBW ($< 2500g, n = 11$), $r = .21 / .20$

• Parental education related to GCA, $r = .18$

• Parental income: no relationships, vs recent American study (Noble et al., 2015)
Are the effects genetically mediated?

- VETSA, n = 515
- High heritability within GCA region (A = .94)

An apparent paradox

Brain structure is
- under genetic control

and

- can be influenced by environment and experience
• so is there any residual variance to be explained by stuff happening later in life?
How age affects cognition

Age explains 41% (p < .001) of the variance in memory at baseline:
Memory = 24.44 - 0.19 x age

How age affects cognition ...or not

... after 10 weeks of memory strategy training for the older, age is no longer a significant predictor, explaining < 3%.
Memory = 25.06 - 0.06 x age
Can you change your brain by thinking?

- By mental exercise?
- Even in older age?

Changes with cognitive training

(Engvig et al., 2010, 2011, 2012, 2014)
Results from ERC project

Neurocognitive plasticity
–partly preliminary!

Indebted to the great work of PhD students
Ann-Marie Glasø de Lange & Anne Cecilie Sjølie Bråthen
+ many superb coworkers

Improvement specific to memory intervention

De Lange et al., Neurobiol Aging, 2016
Microstructural changes with training

Older adults

De Lange et al., Human Brain Mapping, in press
What determines the variability of plasticity?

- Baseline brain characteristics moderately predict memory gains

- HC volume (Engvig et al., 2012)

- White matter MD (de Lange et al., 2016)

Slides with preliminary data on plasticity in relation to APOE allelic variation and the temporal dynamics of plasticity removed for publicly available slides at this time
Walhovd et al., Neurobiology of Aging, 2014
The way ahead

• Can we replace age in the equation to explain differences in brain and cognitive function across the lifespan?

  Detailed mapping of numerous factors, and hence large samples of individuals through the lifespan and health span, taking on a dimensional and multifactoral lifespan view of aging.

• Need to study influences in both an experimental and an observational setting to reconcile findings on neurodevelopmental origins and continuous plasticity through life.

• Develop paradigms, apps and experimental designs to better measure different stages and aspects of episodic memory.
Working together: Lifebrain

- Funded by Horizon 2020 SC1-PM-04-2016; Aims to establish a solid foundation of knowledge for understanding how brain, cognitive and mental health can be optimized through the lifespan.

- 14 partners, 8 European nations (Denmark, Germany, Netherlands, Norway, Spain, Sweden, Switzerland, UK)

- Integration, harmonisation and enrichment of 11 major neuroimaging studies of age differences and changes → unique database of fine-grained brain, cognitive and mental health measures, n > 6,000

- Longitudinal brain imaging + genetic and health data available for a major part, + cognitive/mental health measures for extensively broader cohorts, > 40,000 examinations.

- Wish to investigate across European and US cohorts

- www.lifebrain.uio.no

Set to change: new project starting 2018

- Aim: to identify how early life environmental and genetic factors restrict and promote neurocognitive plasticity through life.

- Investigation of plastic brain changes with memory training in VR. Testing differences in neurocognitive plasticity in younger and older adult mono-(MZ) and dizygotic (DZ) twins (n = 400), with varying prenatal environmental differences, as indexed by extent of discordance in birth weight (BW)
Conclusions

• Brain and cognition change at all times
• Similarity of patterns in development and aging
• Neural substrate for relative stability of cognitive functioning level across life?
• Early life factors may significantly impact brain and cognition for the entire life course
• Aspects of brain and cognition can be influenced at all times in life
• How do early and later life factors interact to produce the continuum of brain and cognitive function?

Thank you!