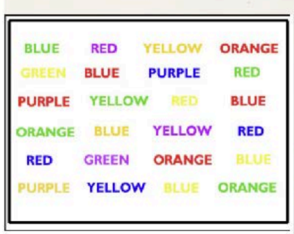
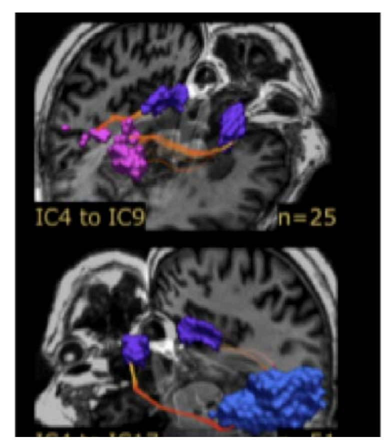
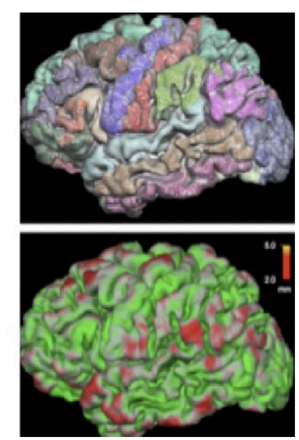
AGING
COGNITION, BRAIN IMAGING
AND
GENETICS



Astri J. Lundervold

BERGEN, 2013/03/01

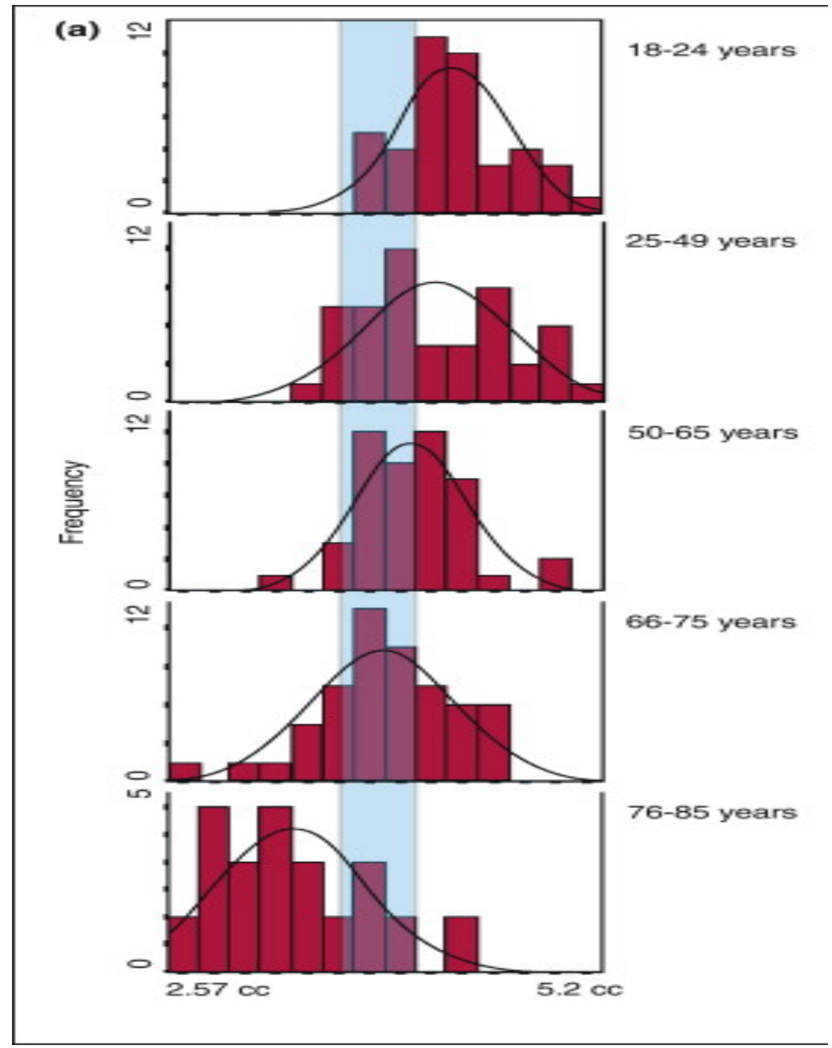




COGNITIVE AGING

GENETIC VARIATION & BRAIN MAINTENECE

Lars Nyberg , Martin Lövdén , Katrine Riklund , Ulman Lindenberger , Lars Bäckman



- Sexual reproduction has the potential to produce tremendous genetic variation in offspring.
- This variation is due to independent assortment and crossing-over during meiosis, and random union of gametes during fertilization.

http://www.ck12.org/book/CK-12-Biology-Concepts/r10/section/2.38/Cell-Biology/

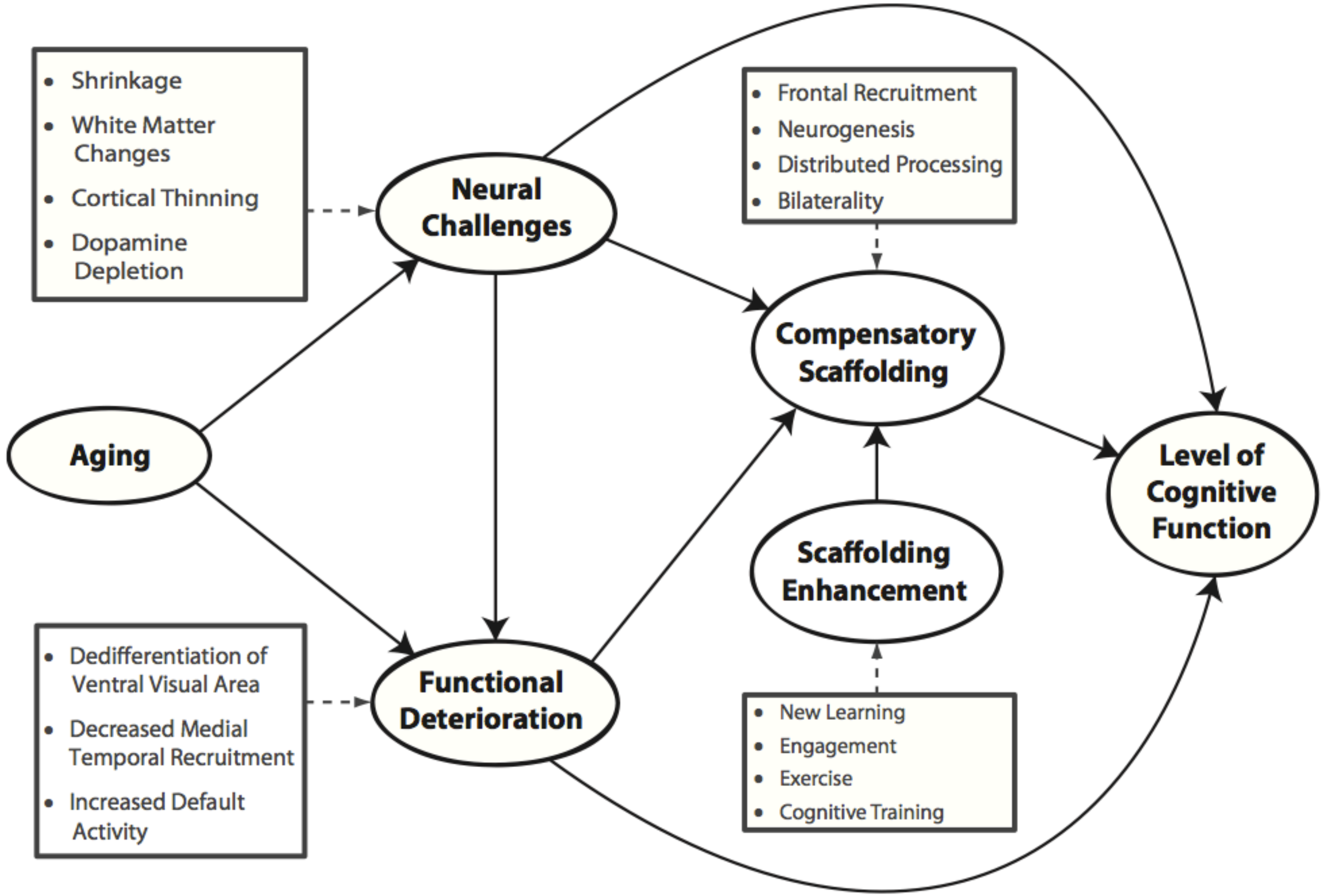


Figure 4

A conceptual model of the scaffolding theory of aging and cognition (STAC).

Denise C. Park and Patricia Reuter-Lorenz, 2009

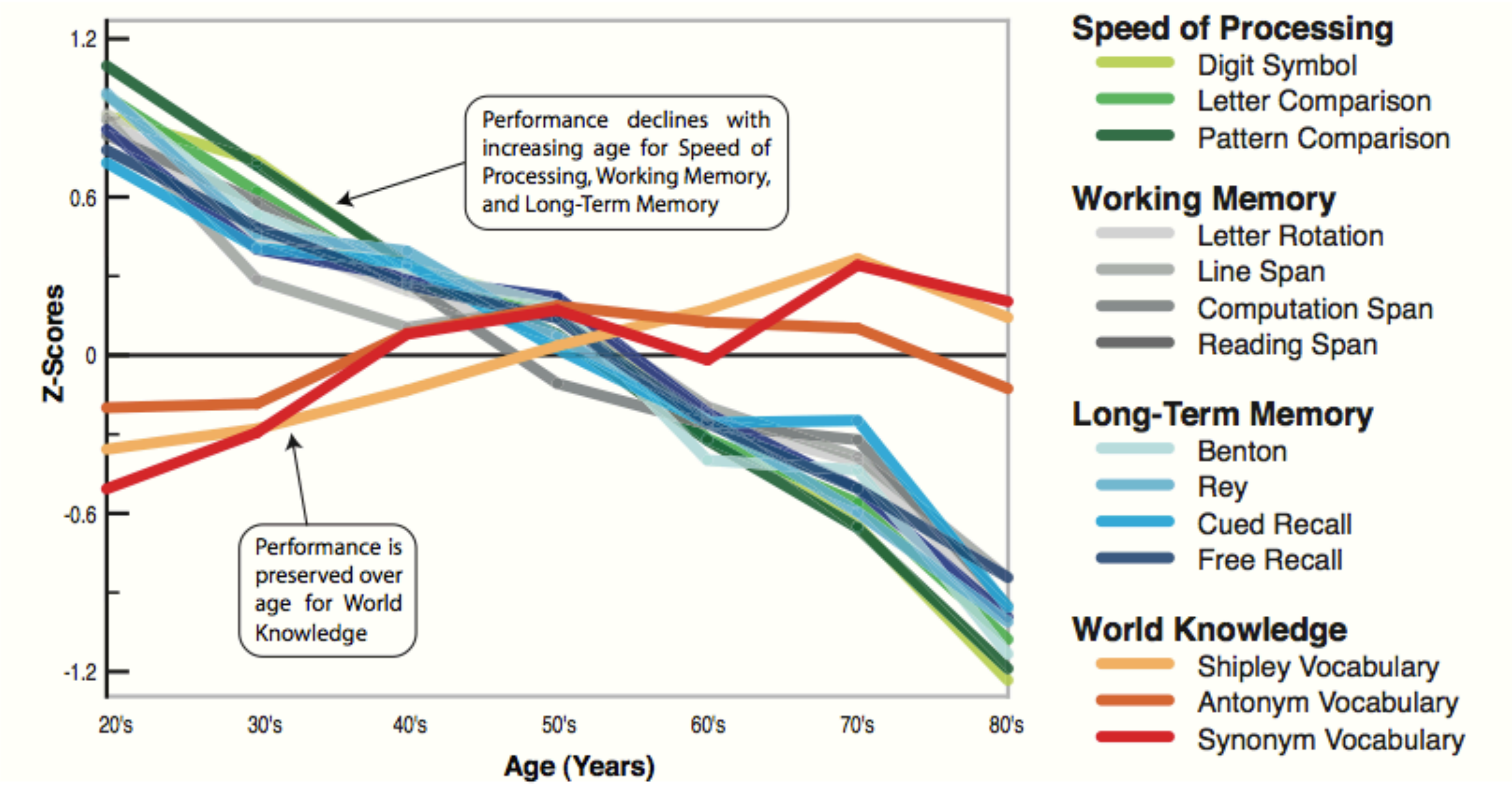


Figure 1

Cross-sectional aging data adapted from Park et al. (2002) showing behavioral performance on measures of speed of processing, working memory, long-term memory, and world knowledge. Almost all measures of cognitive function show decline with age, except world knowledge, which may even show some improvement.

Denise C. Park and Patricia Reuter-Lorenz, 2009

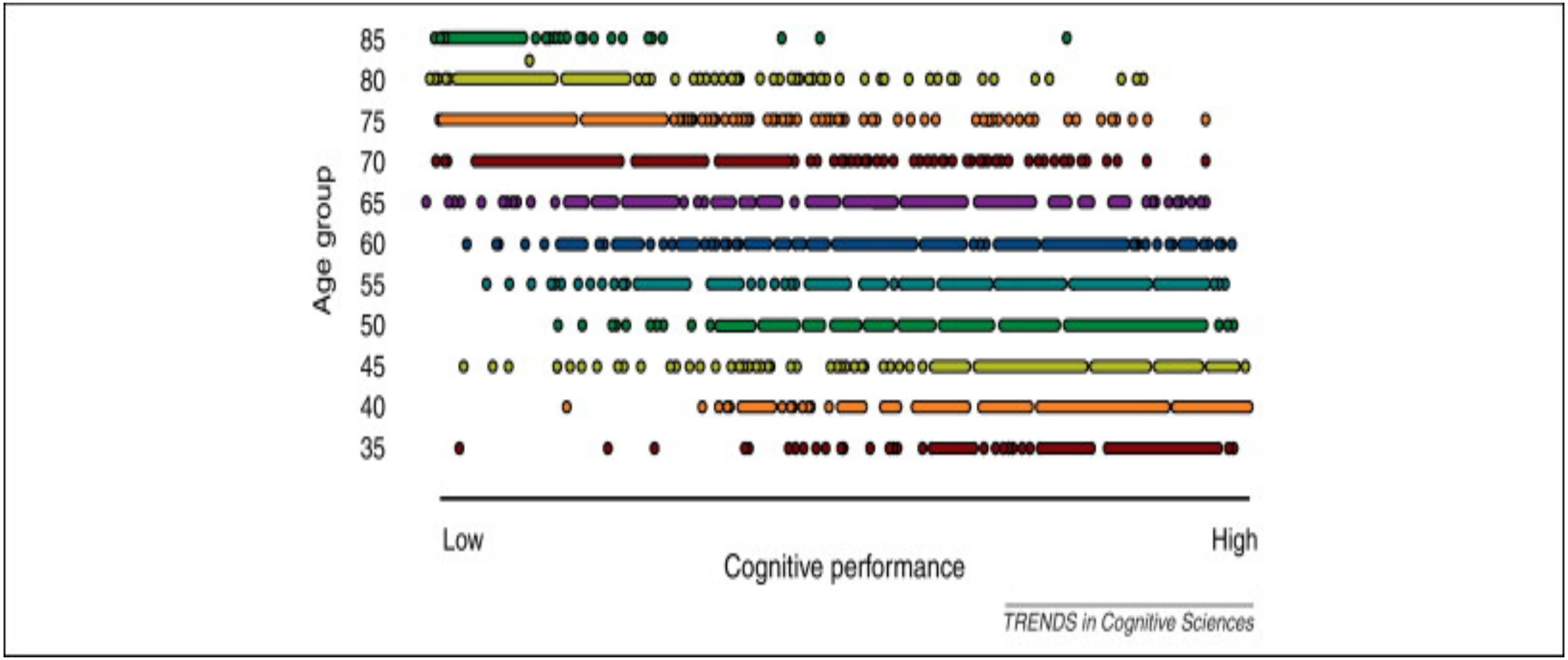


Figure 2 Illustration of variability in memory aging. The graph shows the results of a Q-mode factor analysis that sorted individuals into high versus low cognitive performers (each circle denotes the average score of an individual). Although a n...

Lars Nyberg , Martin Lövdén , Katrine Riklund , Ulman Lindenberger , Lars Bäckman

Memory aging and brain maintenance

Trends in Cognitive Sciences Volume 16, Issue 5 2012 292 - 305

http://dx.doi.org/10.1016/j.tics.2012.04.005

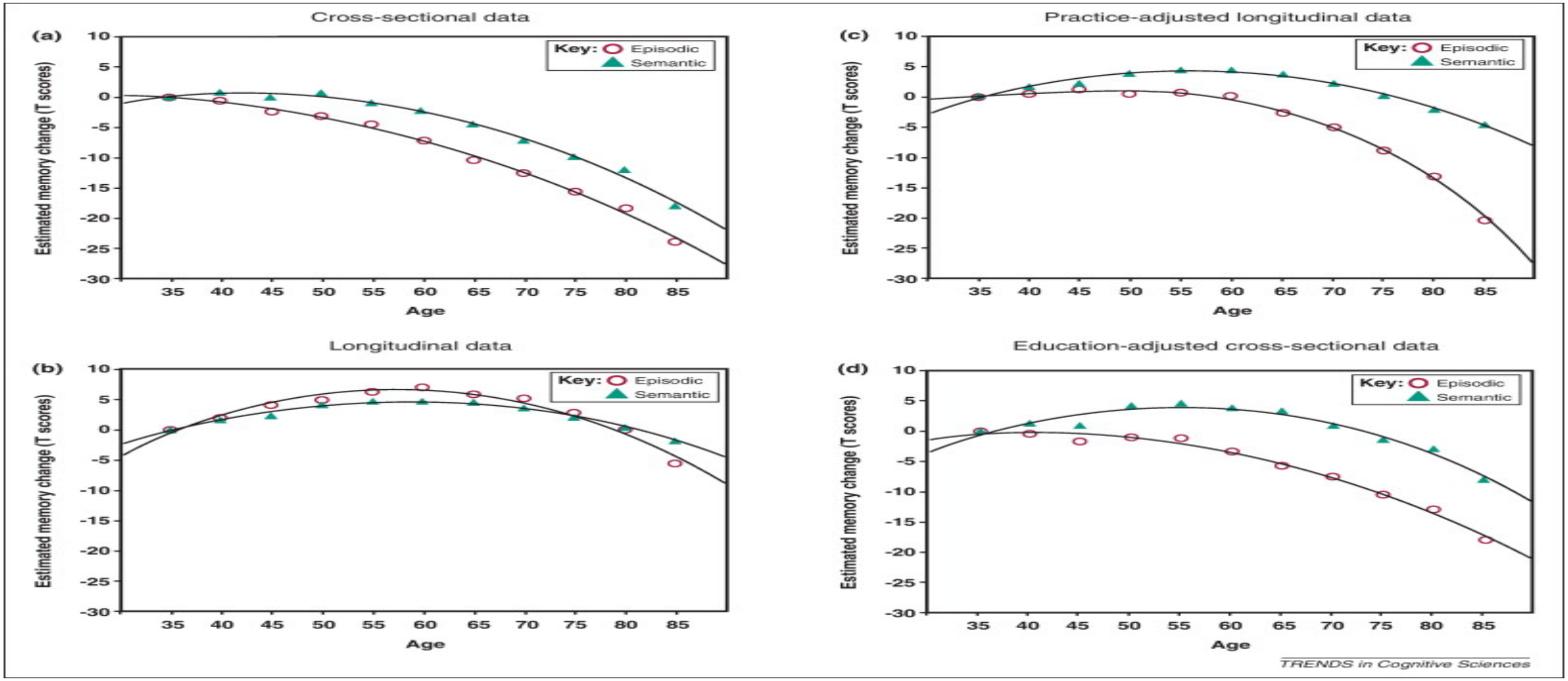
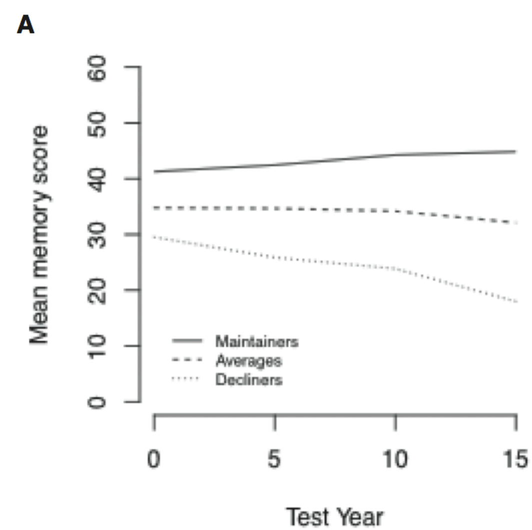


Figure 1 Illustration of assessment of age-related episodic-memory change with cross-sectional a
Cross-sectional data reveal early onset of decline. (b) Longitudinal data indicate a positive gradie



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http://dx.doi.org/10.1016/j.tics.2012.04.005

Aging – cognition, imaging and genetics

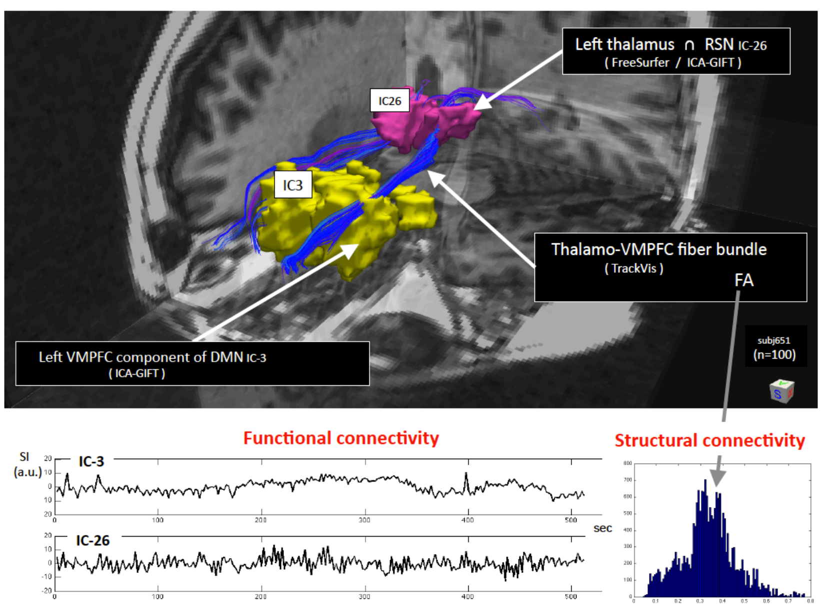
OSLO and BERGEN

Sensory and motor function
Attention/executive function
Memory function
Language function
Visual Cognition
Self-reports of cognitive problems; depression and sleep

Astri J. Lundervold

Genotyping: Stephanie LeHellard, Thomas Espeset et al.

Structural and functional connections using series 2, 3, 4 & 5



Genome wide scans (using Illumina 610 quad CHIP) for 600k SNPs.
Used in international collaborations.

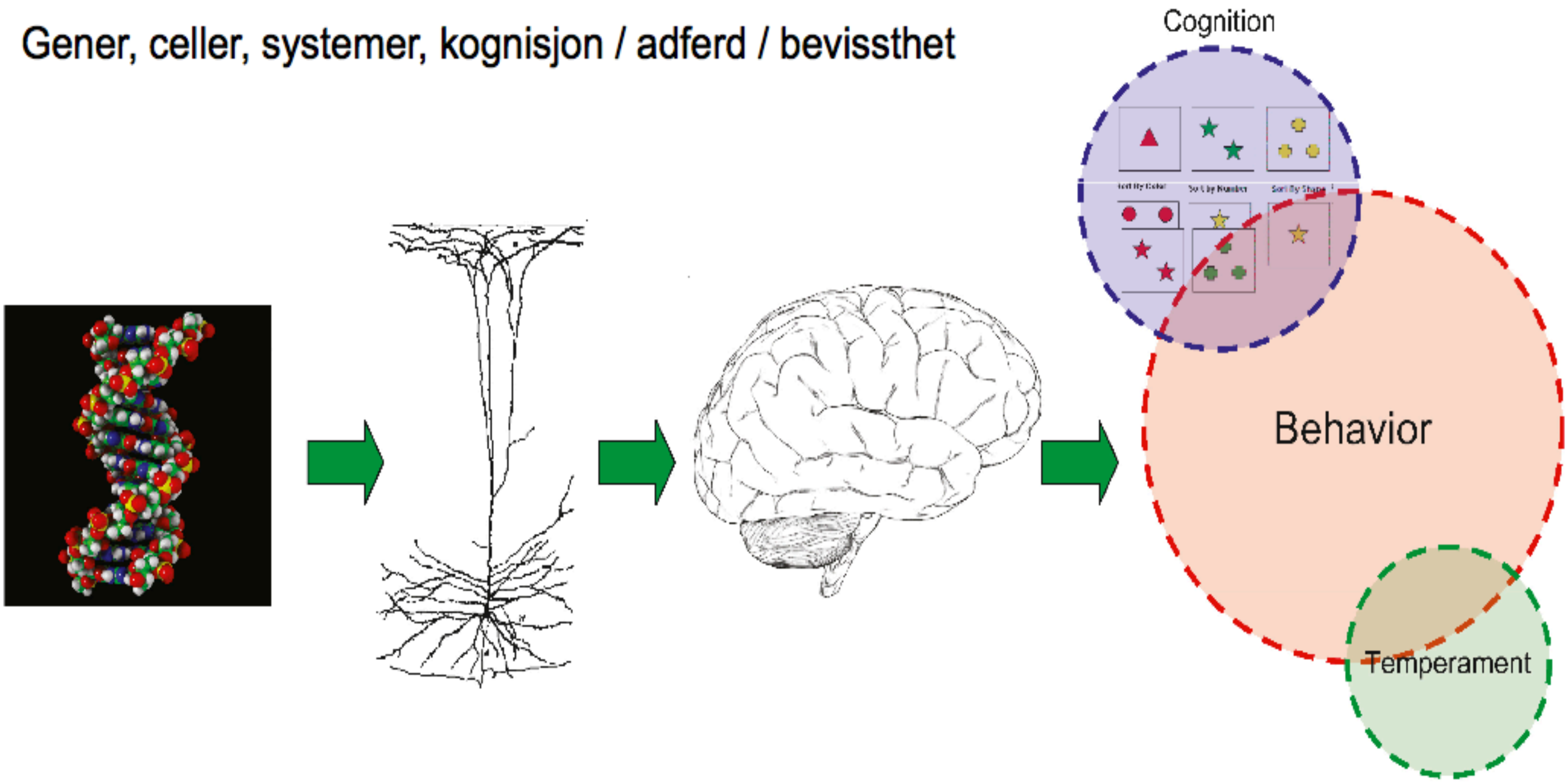
Participants

- WAVE-1 (2004/2005)
  - Neuropsychological test results n = 165
  - MRI n = 120
  - Blood samples

- WAVE-2 (2008/2009)
  - Neuropsychological test results n = 134
  - MRI n = 118

- WAVE-3 (2011/2012)
  - Neuropsychological test results n n=109
  - MRI n = 94

Gener, celler, systemer, kognisjon / adferd / bevissthet



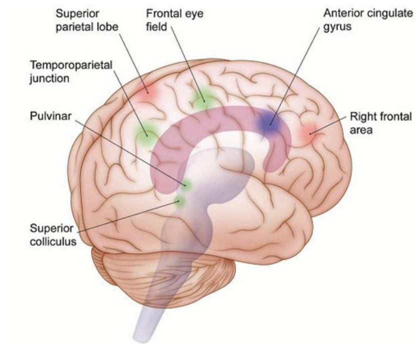
Genes:
Multiple alleles of small effect

Cells:
Subtle molecular bottlenecks

Systems:
Variable development/information processing

Behavior:
Complex functional interactions and emergent phenomena

Fra Baars & Gage: *Cognition, Brain, and Consciousness* (2010) p.587

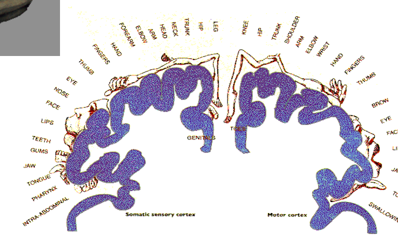


Clinical Neuropsychology

* To understand the relation between behavior and the underlying neural systems.
* Even simple cognitive tasks are dependent on a neural network involving different brain areas.
* Each network represents a specific subfunction

Posner, M. (1988). Structures and function of selective attention. I T. Boll & B.K. Bryant (red) Clinical neuropsychology and brain functions. Washington DC, APA, s. 173-202).

Neuropsychological function



Sensori-motor function

Perception, tempo, coordination

Cognitive function

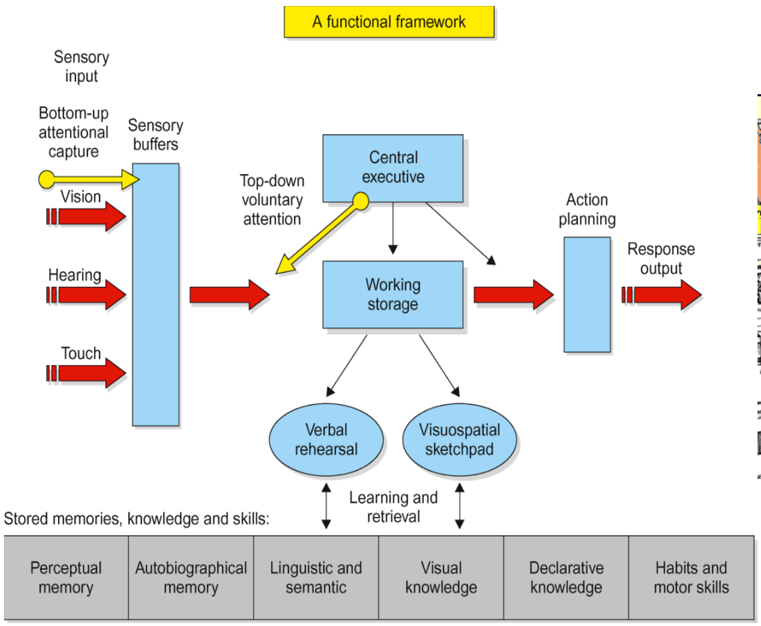
Attention, psychomotor tempo, memory function, language, visual cognition, executive function

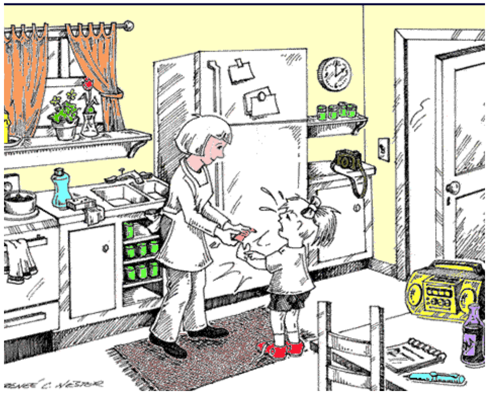
Emotional function

Behavior, self-perception, regulation, emotions

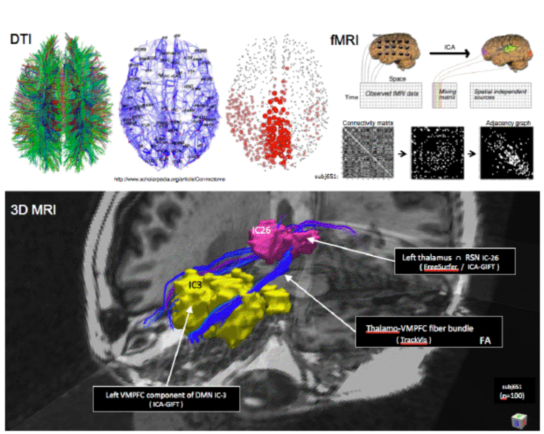
Clinical Neuropsychology

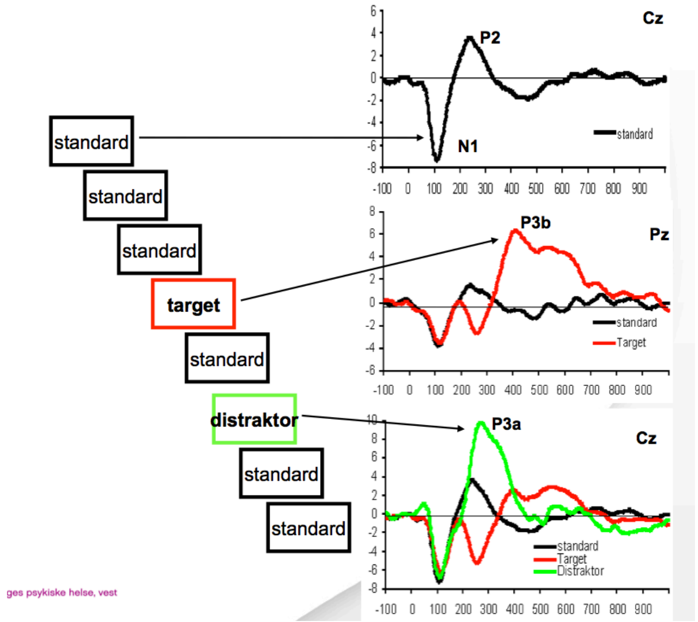
Baars & Gage, 2010

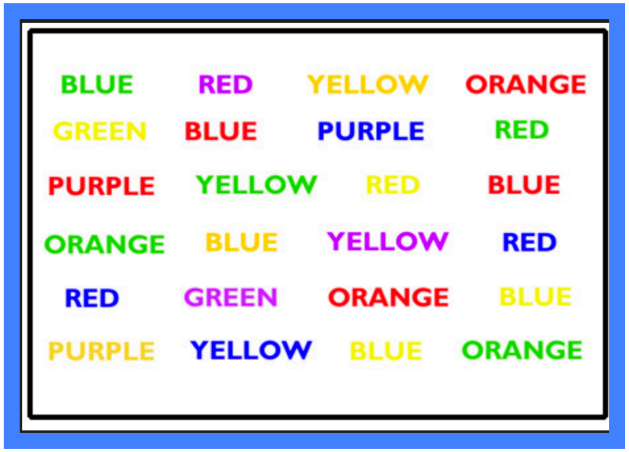




'Graphing' the functional resting state network in subj651

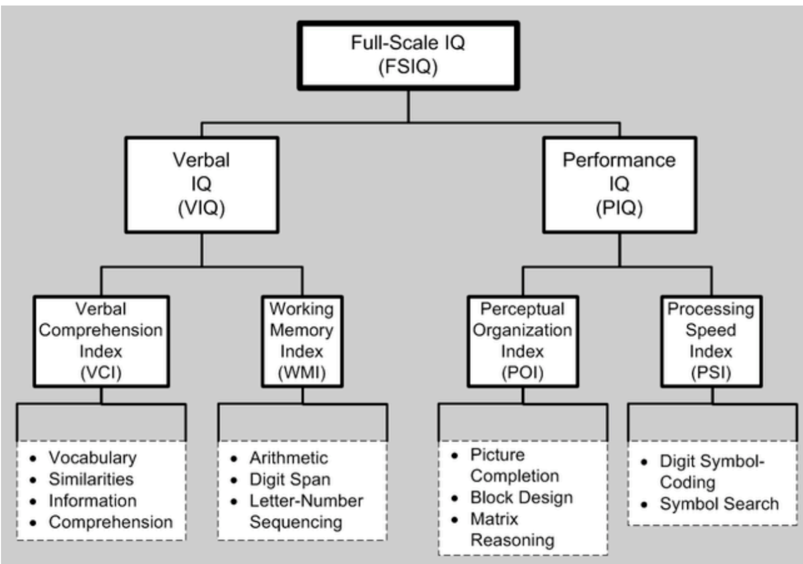




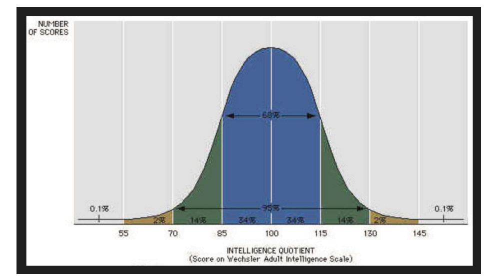

BLUE RED YELLOW ORANGE
GREEN BLUE PURPLE RED
PURPLE YELLOW RED BLUE
ORANGE BLUE YELLOW RED
RED GREEN ORANGE BLUE
PURPLE YELLOW BLUE ORANGE

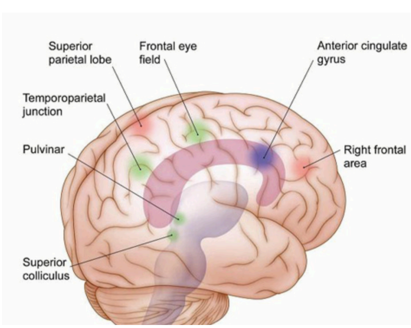

STIMULUS BOOKLET
MANUAL

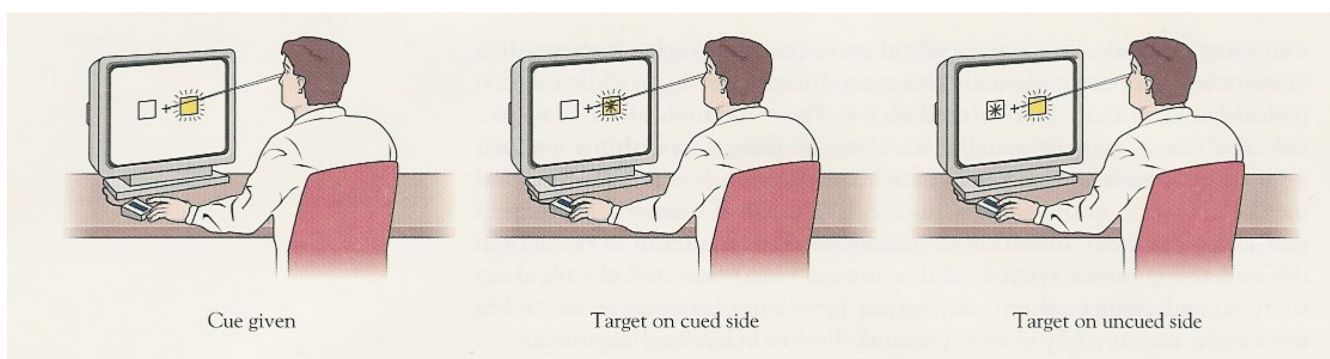

CVLT-II


Full-Scale IQ
(FSIQ)
Verbal
IQ
(VIQ)
Performance
IQ
(PIQ)
Verbal
Comprehension
Index
(VCI)
Working
Memory
Index
(WMI)
Perceptual
Organization
Index
(POI)
Processing
Speed
Index
(PSI)
• Vocabulary
• Similarities
• Information
• Comprehension
• Arithmetic
• Digit Span
• Letter-Number
Sequencing
• Picture
Completion
• Block Design
• Matrix
Reasoning
• Digit Symbol-
Coding
• Symbol Search

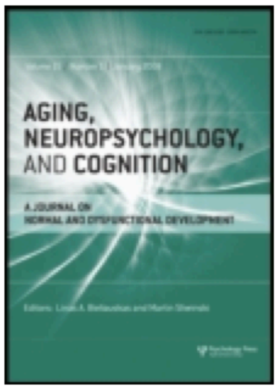

WISC-IV
Manual
WISC-IV
Stimulus Book
WISC-IV
Manual


NUMBER
OF SCORES
68%
95%
0.1%
0.1%
55
70
85
100
115
130
145
INTELLIGENCE QUOTIENT
(Score on Wechsler Adult Intelligence Scale)


Superior
parietal lobe
Frontal eye
field
Anterior cingulate
gyrus
Temporoparietal
junction
Pulvinar
Right frontal
area
Superior
colliculus


Cue given
Target on cued side
Target on uncued side

Eike Wehling



Aging, Neuropsychology, and Cognition

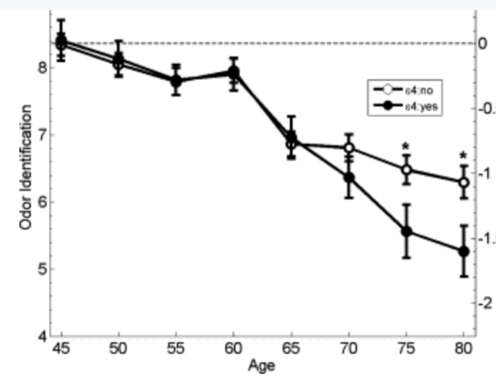
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/nanc20

Familiarity, Cued and Free Odor Identification and Their Association with Cognitive Functioning in Middle Aged and Older Adults

Eike Ines Wehling [a] , Steven Nordin [b] , Thomas Espeseth [c] , Ivar Reinvang [c] & Astri J. Lundervold [a]

Neurobiology of Aging

Volume 31, Issue 4, April 2010, Pages 567–577



Odor identification impairment in carriers of ApoE-ε4 is independent of clinical dementia

Jonas K. Olofsson[a, b, c], Steven Nordin[a, d], Stefan Wiens[b, c], Margareta Hedner[b, c], Lars-Göran Nilsson[b, c], Maria Larsson[b, c]

Full Text (HTML)

Unawareness of Olfactory Dysfunction and its Association with Cognitive Functioning in Middle Aged and Old Adults

Arch Clin Neuropsychol (2011) 26(3): 260-269 first published online April 6, 2011

Cognitive tests/questionnaires

Test	Wave 1	Wave 2	Wave 3
WASI (2 subtests, IQ est.)	X	X	X
Odour identification (SOIT)	X	X	X
Trail Making Test	X	X	X
Coding	X	X	X
Stroop (D-KEFS)	X	X	X
FAS (D-KEFS)	X	X	X
CVLT-II	X	X	X
Rey Complex Figure		X	X
Letter-number		X	X
PASAT	X	-	X
CDP and memory (exp.)	X	X	
Grooved Pegboard		X	X
Benton/Dichotic listening	X	-	-
Self-reports (depression, memory, sleep)	X	X	X

	Name	Type	Width	Decimals	Label	Values	Missing	Columns	Align	Measure	Role
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3	cvlt_tri_1_s	Numeric	8	2	CVLT-II - Immediate Recall - Trial 1 - Number Correct - standard score	None	None	8	Right	Scale	Input
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10	cvlt_tri_5_r	Numeric	8	2	CVLT-II - Immediate Recall - Trial 5 - Number Correct - raw score	None	None	8	Right	Scale	Input
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13	cvlt_tri_tot_t	Numeric	8	2	CVLT-II - Immediate Recall - Trial 1-5 Total - Number Correct - t-score	None	None	8	Right	Scale	Input
14	cvlt_tri_b_r	Numeric	8	2	CVLT-II - Immediate Recall - Trial B - Number Correct - raw score	None	None	8	Right	Scale	Input
15	cvlt_tri_b_s	Numeric	8	2	CVLT-II - Immediate Recall - Trial B - Number Correct - standard score	None	None	8	Right	Scale	Input
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17	cvlt_sd_fr_s	Numeric	8	2	CVLT-II - Delayed Recall - Short Delay Free Recall - Number Correct - standard score	None	None	8	Right	Scale	Input
18	cvlt_sd_cr_r	Numeric	8	2	CVLT-II - Delayed Recall - Short Delay Cued Recall - Number Correct - raw score	None	None	8	Right	Scale	Input
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33	cvlt_mid_s	Numeric	8	2	CVLT-II - Learning Characteristics, Trials 1-5 Total - % Recall from Middle - scaled score	None	None	8	Right	Scale	Input
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39	cvlt_consis_s	Numeric	8	2	CVLT-II - Learning Characteristics, Trials 1-5 Total - Across-Trial Recall Consistency - scaled score	None	None	8	Right	Scale	Input
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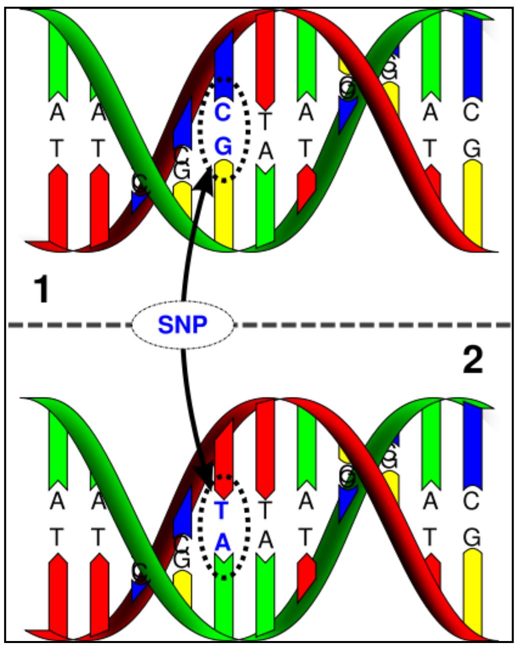
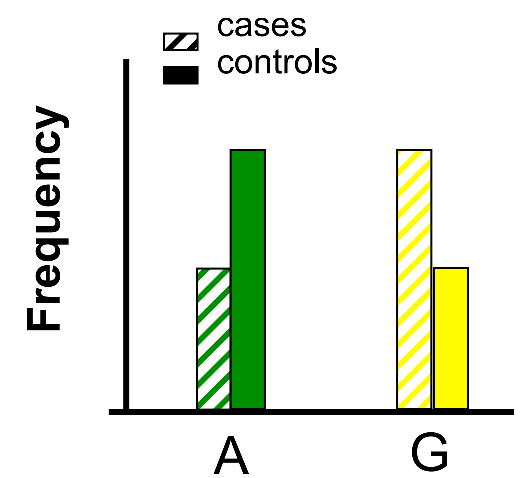
43	cvlt_sd_ret_s	Numeric	8	2	CVLT-II - Recall Contrast Measures - Short-Delay Retention/Retroactive Interference - Short Delay Free Recall vs. Trial 5 - scale...	None	None	8	Right	Scale	Input
44	cvlt_ld_ret_...	Numeric	8	2	CVLT-II - Recall Contrast Measures - Long-Delay Retention - Long Delay Free Recall vs. Short Delay Free Recall - %	None	None	8	Right	Scale	Input

Association study

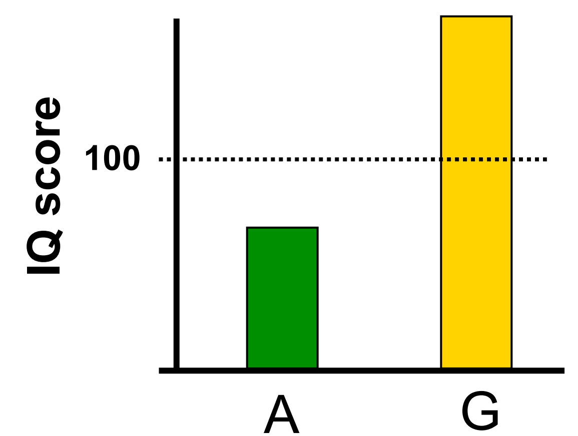
Tests whether the presence of a specific genetic variant (e.g. SNP allele) is correlated to a particular disease status or trait value.



Case-control phenotype



Quantitative/continuous trait



Andrea Christoforou

Critical advances

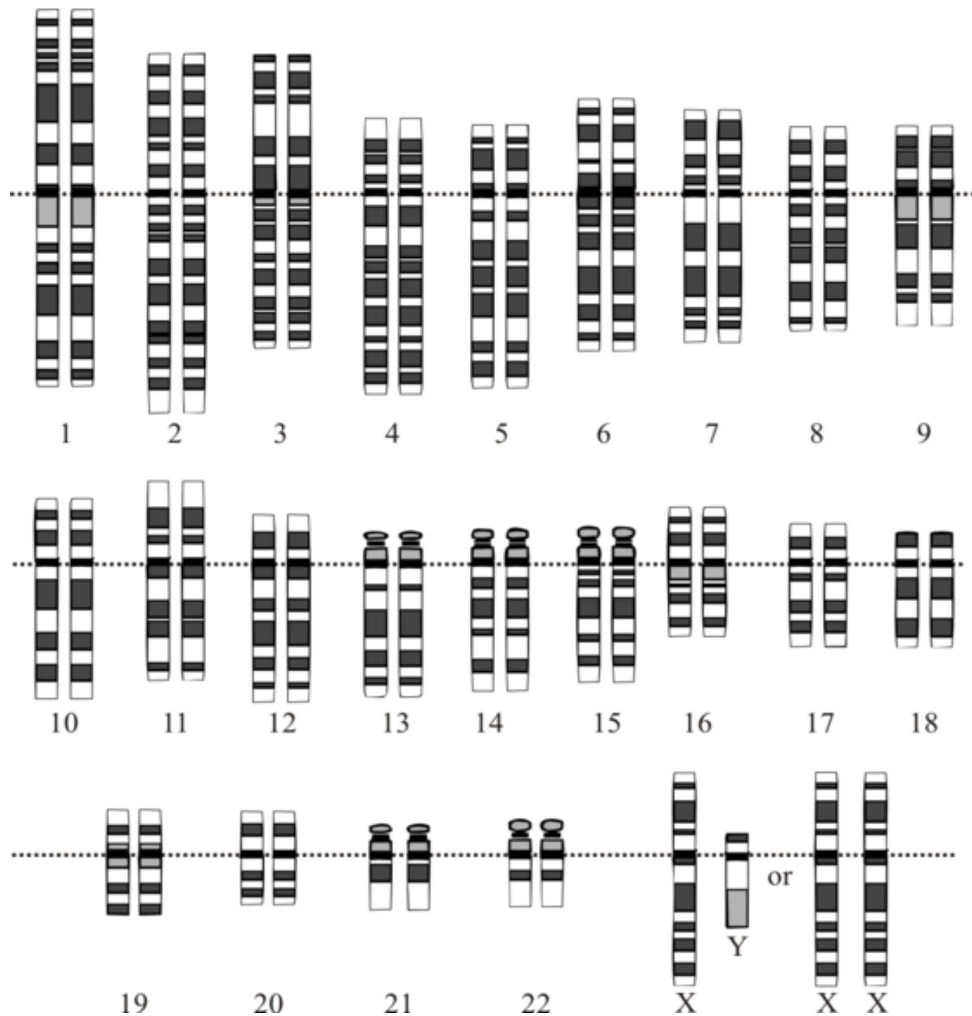
GWAS: hypothesis-free genomewide approach

Completion of the Human Genome Sequence

Mutation screening; SNP identification and cataloging

Realization of the International HapMap Project

Advances in Genotyping technologies



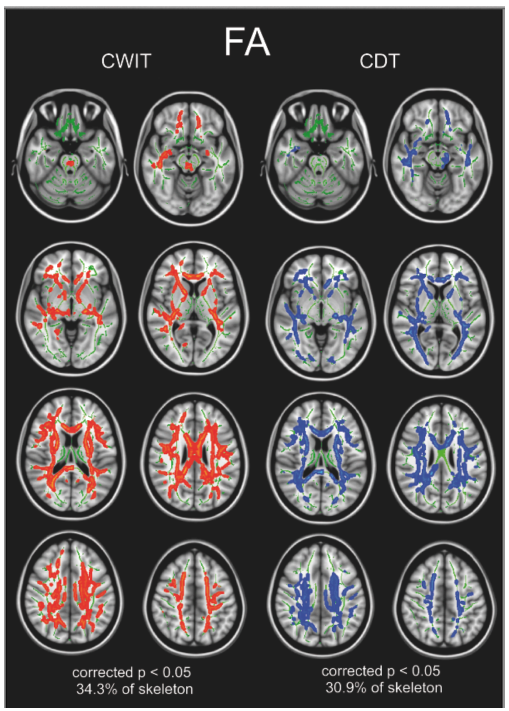
"GWAS is the study of genetic variation across the entire genome that is designed to associate genetic variations (SNPs) with traits or with the presence or absence of disease or condition."

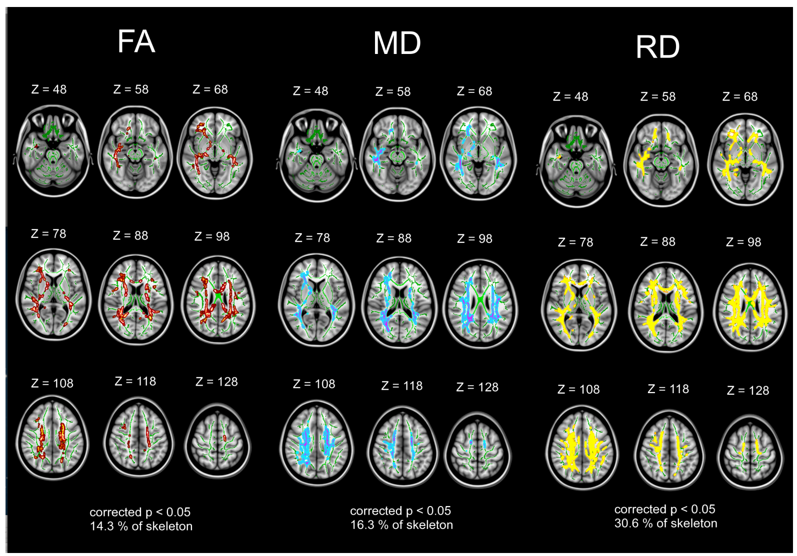
Andrea Christoforou

General fluid-type intelligence is related to indices of white matter integrity in middle-aged and old adults

White matter structure of general fluid-type intelligence

Judit Haász*[1, 2, 3], Erling T. Westlye*[2], Thomas Espeseth[1, 4, 5], Arvid Lundervold[2, 6], Astri J. Lundervold[1, 7]





2 scores measuring general cognition

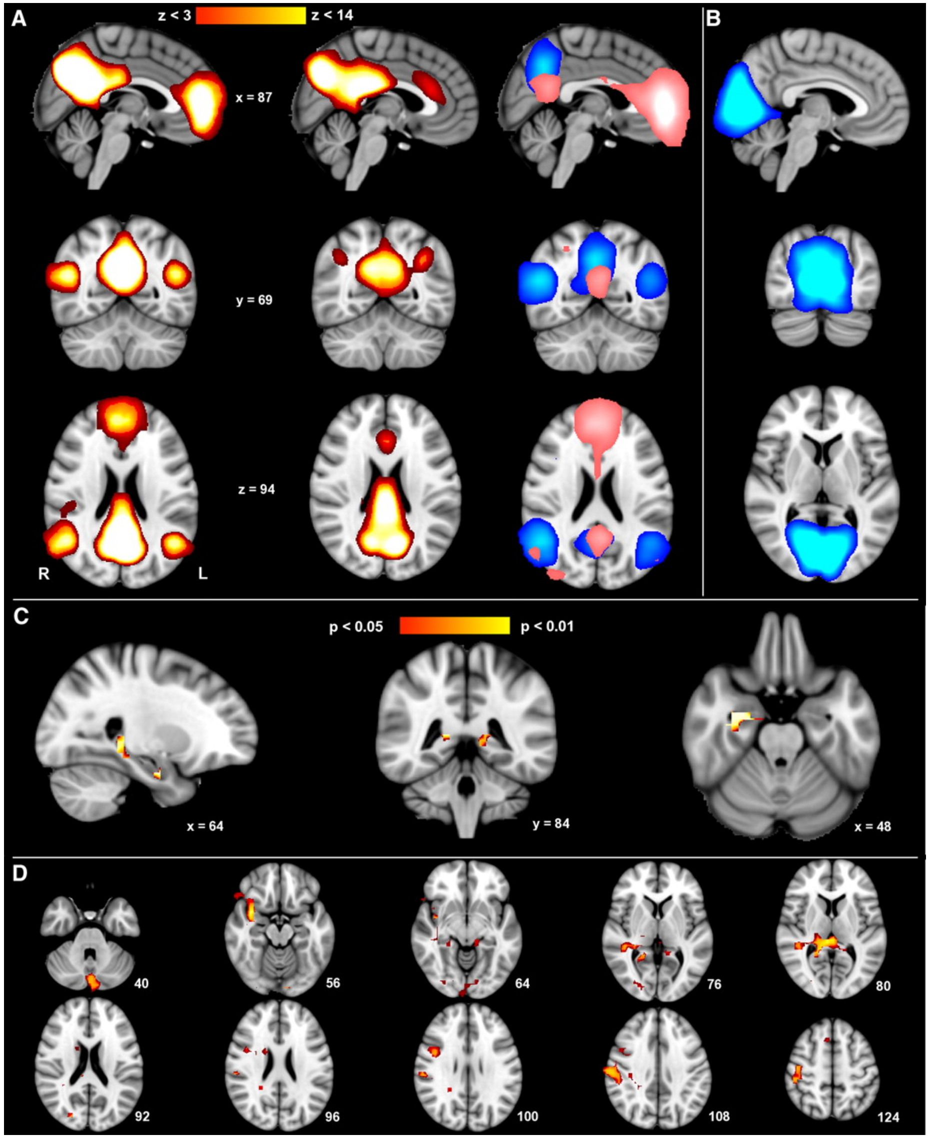
(1) G PCA = G fluid

"*Fluid* intelligence or *fluid reasoning* is the capacity to think logically and solve problems in novel situations, independent of acquired knowledge." (Wikipedia)

(2) WASI V = G crystalized

"*Crystallized* intelligence is the ability to use skills, knowledge, and experience. It should not be equated with memory or knowledge, but it does rely on accessing information from long-term memory." (Wikipedia)

A, In red-yellow to the left is the DMN comprising three components from the gICA.



Westlye E T et al. J. Neurosci. 2011;31:7775-7783

Neurobiology of Disease

Increased Hippocampal Default Mode Synchronization during Rest in Middle-Aged and Elderly APOE ε4 Carriers: Relationships with Memory Performance

Erling T. Westlye[1], Arvid Lundervold[1,2], Helge Rootwelt[3], Astri J. Lundervold[4,5], and Lars T. Westlye[6]

ELSEVIER
NeuroImage
Volume 63, Issue 1, 15 October 2012, Pages 507–516

Episodic memory of APOE ε4 carriers is correlated with fractional anisotropy, but not cortical thickness, in the medial temporal lobe ☆

Erling Tjelta Westlye[a], Erlend Hodneland[a, b], Judit Haász[a], Thomas Espeseth[c, d, e], Arvid Lundervold[a, f], Astri J. Lundervold[d, g]

Age-related disconnection of resting state networks in individuals at genetic risk for Alzheimer's disease

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A LOT OF DATA

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Hypothesis Generation through Interactive Visual Analysis of Heterogeneous Medical Data

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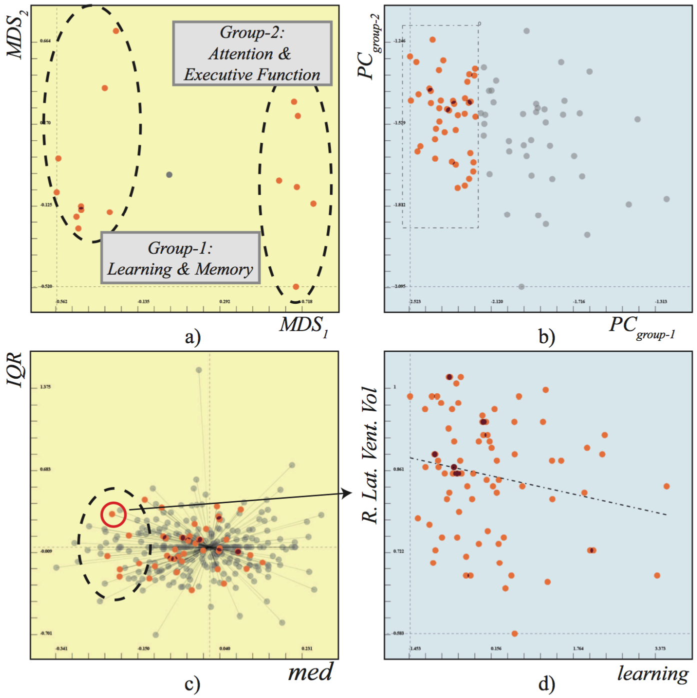

Fig. 2. a) MDS is applied on the *test score* dimensions, where related dimensions are placed closer. Two groups for the test scores show up in the results. b) Each group is represented through an application of PCA and first components for each of the groups are the axes for the scatterplot. A group of participants, who are better in learning and attentive functions is selected c) Some brain regions are smaller for this subgroup, i.e., have smaller *median* value. d) When one of these dimensions is observed closely, we saw that there is really a negative correlation with one of the test scores from the first group (*learning*).

Interactive Visual Analysis of Heterogeneous Cohort Study Data

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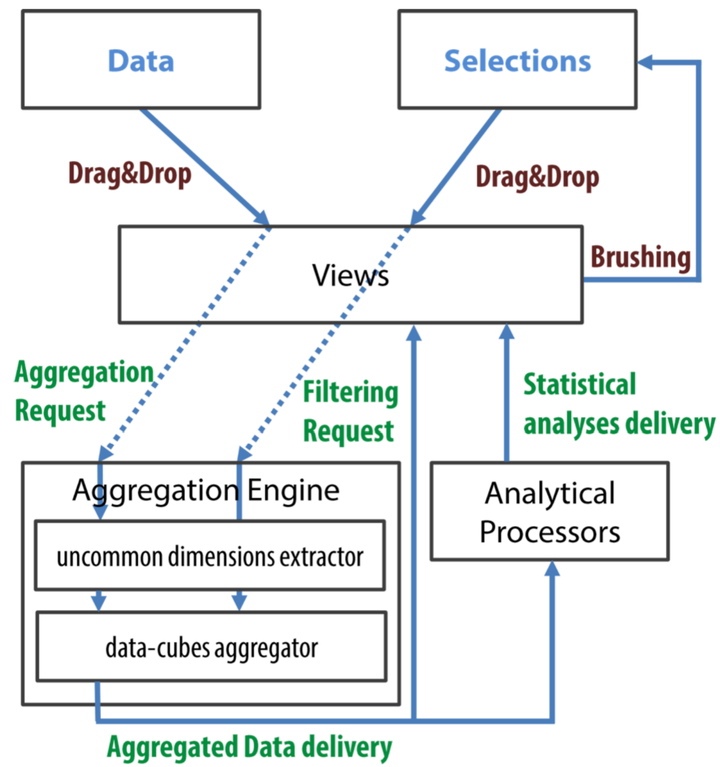

Fig. 2. Simplified illustration of the proposed model. User interactions are colored in red, automatic transparent operations are green, information sources are blue, and in black the components necessary to implement the model.