Neurokognitivt åldrande

”Normalt åldrande”
och/eller
åldrande med sjukdom eller ?

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UNIVERSITY OF GOTHENBURG

Varför intresse sig för åldrande och äldre?

- Demografiska förändringar – vi lever allt längre - åldrande befolkningar världen över
- Åldrandet – en alltmer betydande del av livet
- Vi kan förbättra villkoren för att åldras med samhällsförändringar, prevention, behandling, vård och omsorgsinsatser
- **Kognitiv funktion och hälsa under allt större hot med stigande ålder**

ADA-GERO

Vad behöver du som psykolog veta om hur kognition påverkas under åldrandet?

- Teoretiskt perspektiv
  - ✓ Hur ser påverkan ut?
  - ✓ Hur mycket påverkan?
  - ✓ Påverkas alla?
  - ✓ Vad är normalt?
  - ✓ Vilka är orsakerna?

- Kliniskt perspektiv
  - ✓ Hur kan vi skilja mellan normal och patologisk påverkan?
  - ✓ Hur ser påverkan ut vid olika sjukdomar?
  - ✓ Hur kan vi behandla – påverka och/eller återställa funktion?

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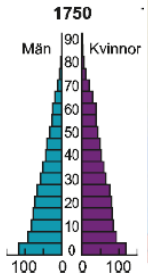
Varför intresse sig för åldrande och äldre?

Demografiska förändringar – vi lever allt längre - åldrande befolkningar världen över

Medellivslängd – ett historiskt perspektiv

- 18 – 29 Neandertal människa
- 22 Mesolitiska perioden, 8000-6000 fKr
- 30 Grekland 400 fKr
- 30 Rom, 600 fKr
- 31 England, 800 e Kr
- 35 England, 1250
- 35 Sverige, 1750
- 40 England, 1850
- 55 Sverige, 1900



Department of Economic and Social Affairs
Population Division

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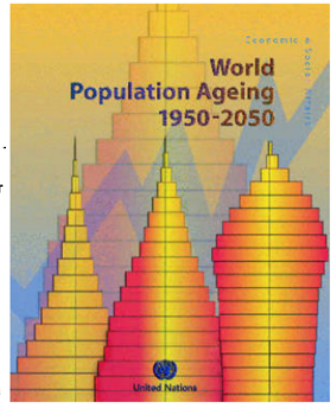
World Population Ageing: 1950-2050



This report was prepared by the Population Division as a contribution to the 2002 World Assembly on Ageing and its follow-up. The report provides a description of global trends in population ageing and includes a series of indicators of the ageing process by development regions, major areas, regions and countries. The report shows that:

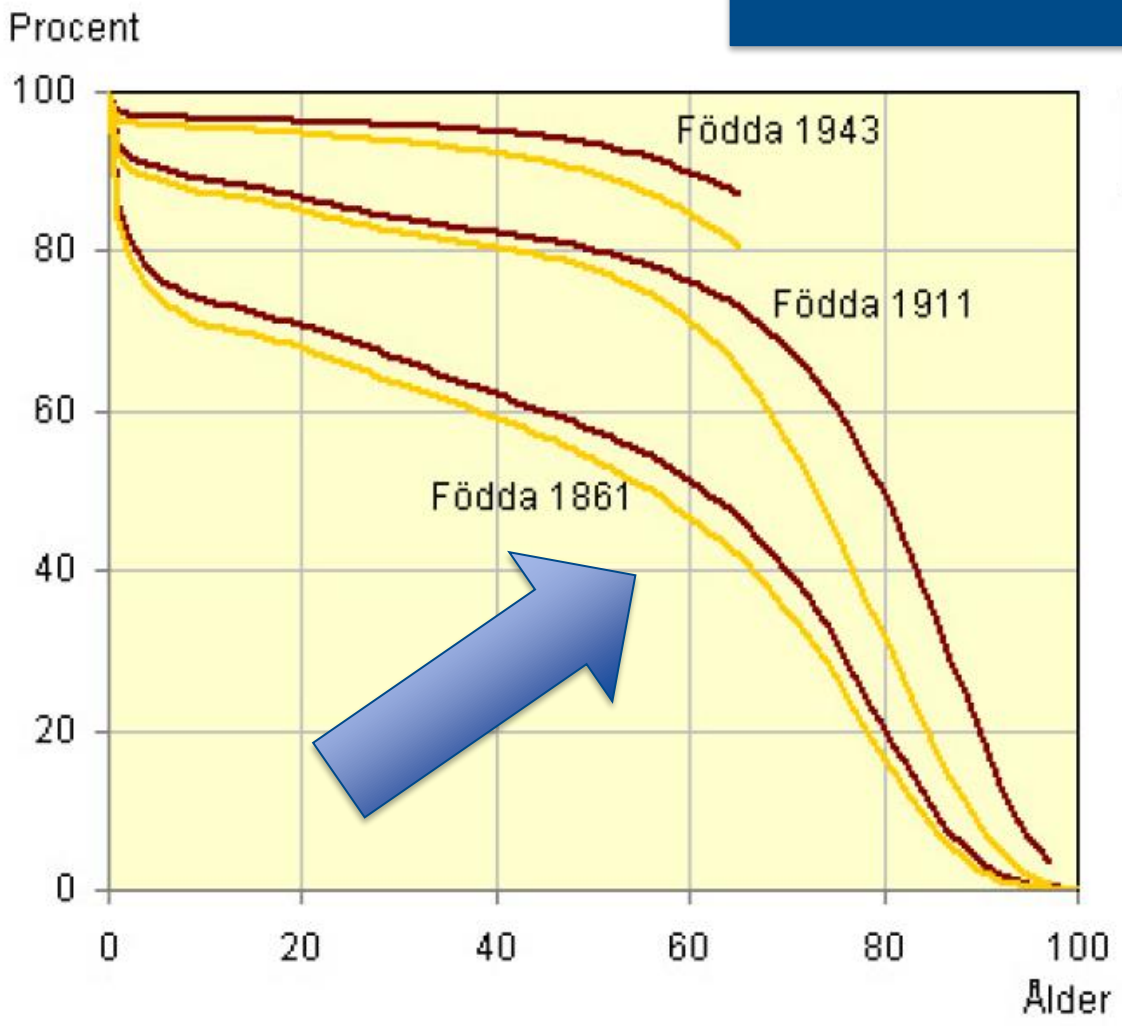
- Population ageing is unprecedented, without parallel in human history—and the twenty-first century will witness even more rapid ageing than did the century just past.
- Population ageing is pervasive, a global phenomenon affecting every man, woman and child—but countries are at very different stages of the process, and the pace of change differs greatly. Countries that started the process later will have less time to adjust.
- Population ageing is enduring: we will not return to the young populations that our ancestors knew.
- Population ageing has profound implications for many facets of human life.

ADA-GERO

Rektangularisering av överlevnadskurvan

Antal kvarlevande av 100 födda

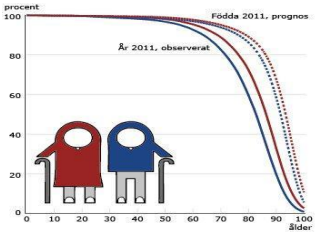
Efter kön och födelseår



Källa: SCB

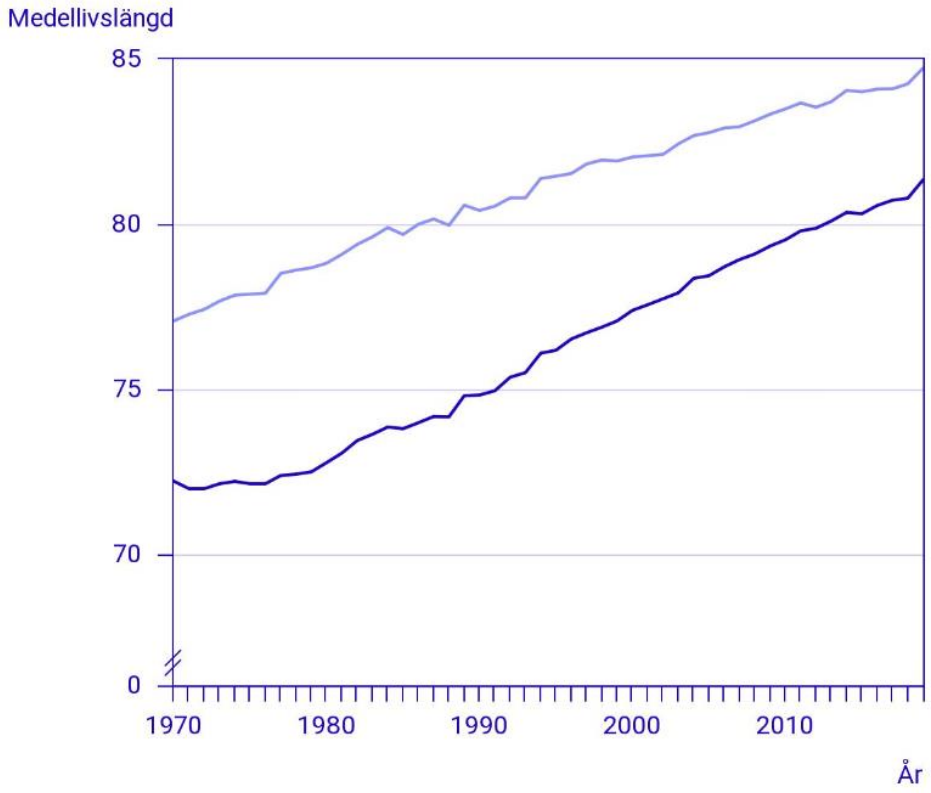
*Hälften av de flickor som föddes 2011 beräknas uppnå **93** års ålder.*

*För pojkarna beräknas hälften leva vid **91 år**.*



Medellivslängd i Sverige

Medellivslängd från födseln per år från 1970



Diagramförklaring

— Män

— Kvinnor

Medellivslängd kvinnor	Medellivslängd män
2019	2019
84,7	81,3
år	år

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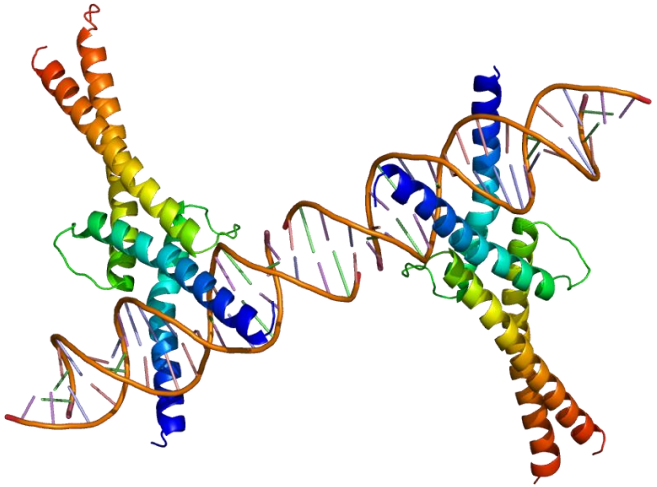
Genetic influence on human lifespan and longevity

Approximately 20–30% is accounted for by genetics



Hjelmborg, Iachine, Skytthe et.al, Hum Genet *(2006)*

Aging
”what is it all about”?

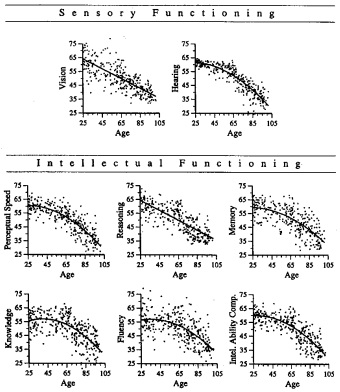
Change past maturity

- **due to inner biological influences/factors**
- occuring in all individuals with increasing chronological age
- occuring/accumulating over an extended time period
- irreversible
- **environmentally modifiable** in terms
  - of rate and magnitude of change

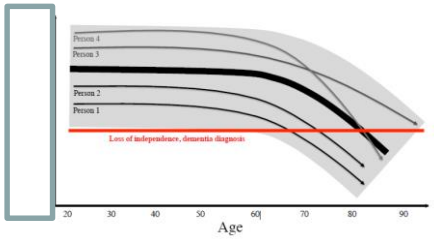
- … affecting overall functioning and survival

Age Differences or Change

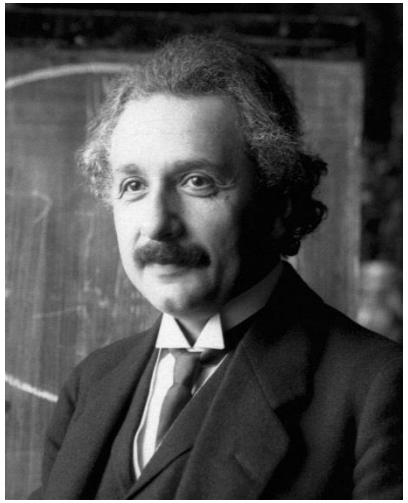
- Inter-individual differences
  - Cross-sectional design
    - *age differences*

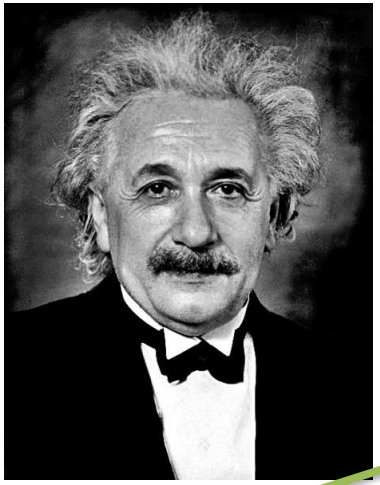


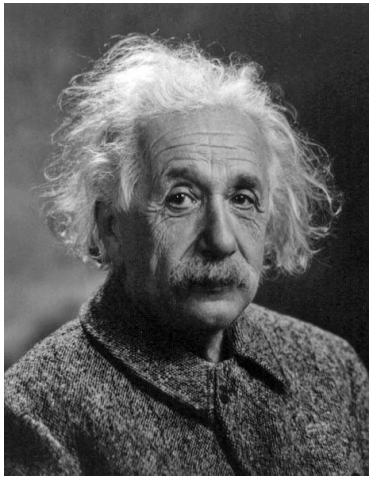
- Intra-individual change
  - Longitudinal design
    - *age related changes*



Intellectual growth should commence at birth and cease only at death







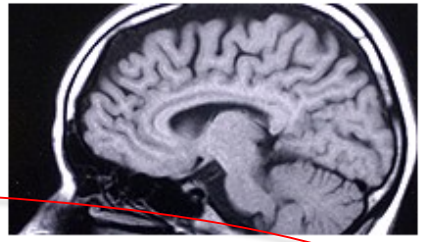
Albert Einstein
1879-1955

VETENSKAP

Vid 45 års ålder börjar förfallet

Publicerat: fredag 06 januari kl 20:43 , Nyheter P4 Kalmar | Dela

Redan vid 45 års ålder börjar den kognitiva förmågan försämras, visar fransk och brittisk forskning.



Förmågan att lösa matematiska problem minskar

Läs studien i British Medical Journal

Genom att studera drygt 2 000 kvinnor och 5 000 män under en tioårsperiod kunde forskarna se att flera funktioner, som slutledningsförmåga, börjar försämras redan i 45-årsåldern.

Deltagarna har exempelvis fått testa förmågan att resonera och dra slutsatser från matematiska och språkliga problem, att komma ihåg saker och skriva ner så många djur som möjligt på en minut.

Omdiskuterad fråga

Frågan om när människors förmåga att dra slutsatser och komma ihåg saker börjar gå ner har varit omdebatterad.

Tidigare har mindre undersökningar visat att människors kapacitet börjar gå ner först vid 60-årsåldern. Men den nya undersökningen gjord av forskare i Frankrike och Storbritannien visar alltså tydliga nedgångar redan från 45-årsåldern och som sedan förstärkts upp till 70-årsåldern.

Förmågan att resonera och dra slutsatser minskade på tio år med drygt tre procent för män som från början var mellan 45 och 49 år och med knappt tio procent för män som från början var mellan 65 och 70.

Snabbare bland välutbildade

För kvinnor var resultatet detsamma förutom i den äldre gruppen där försämringen var mindre, drygt sju procent.

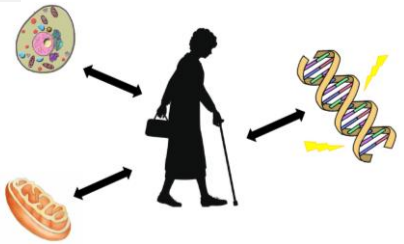
De som deltagit i undersökningen är anställda vid regeringskansliet i London. Det är alltså ovanligt många välutbildade i gruppen och möjligen kan det betyda att nedgången i hjärnans förmåga skulle kunna gå snabbare bland folk i allmänhet, enligt forskarna.

BMJ 2011

Ett livslångt utvecklings- och åldrandeperspektiv

Biologisk ålder

Våra cellers, organ och organsystems funktion i förhållande till återstående livslängd – överlevnadsförmåga

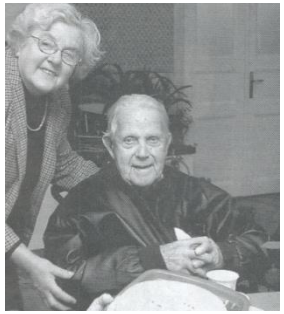


Vad klarar den "åldrande hjärnan"?

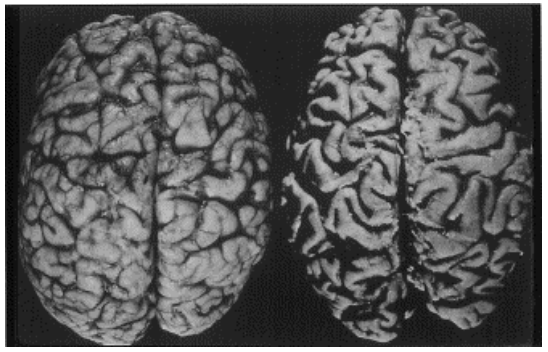
122

119

115



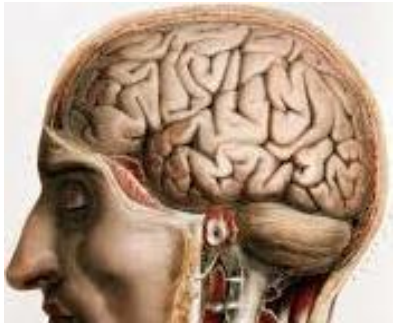
102



Ett livslångt utvecklings- och åldrandeperspektiv

Psykologisk ålder

Vår förmåga att anpassa oss och hantera inre och yttre förändringar i en komplex verklighet



Psykologiskt åldrande

Biologiskt åldrande

Tid

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Ett livslångt utvecklings- och åldrandeperspektiv

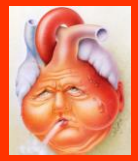
Social ålder

Vår roll och funktion i samhället, egen och andras värdering och bedömning

Psykologiskt åldrande

Socialt åldrande

Biologiskt åldrande



Tid

Ageism - Ålderism

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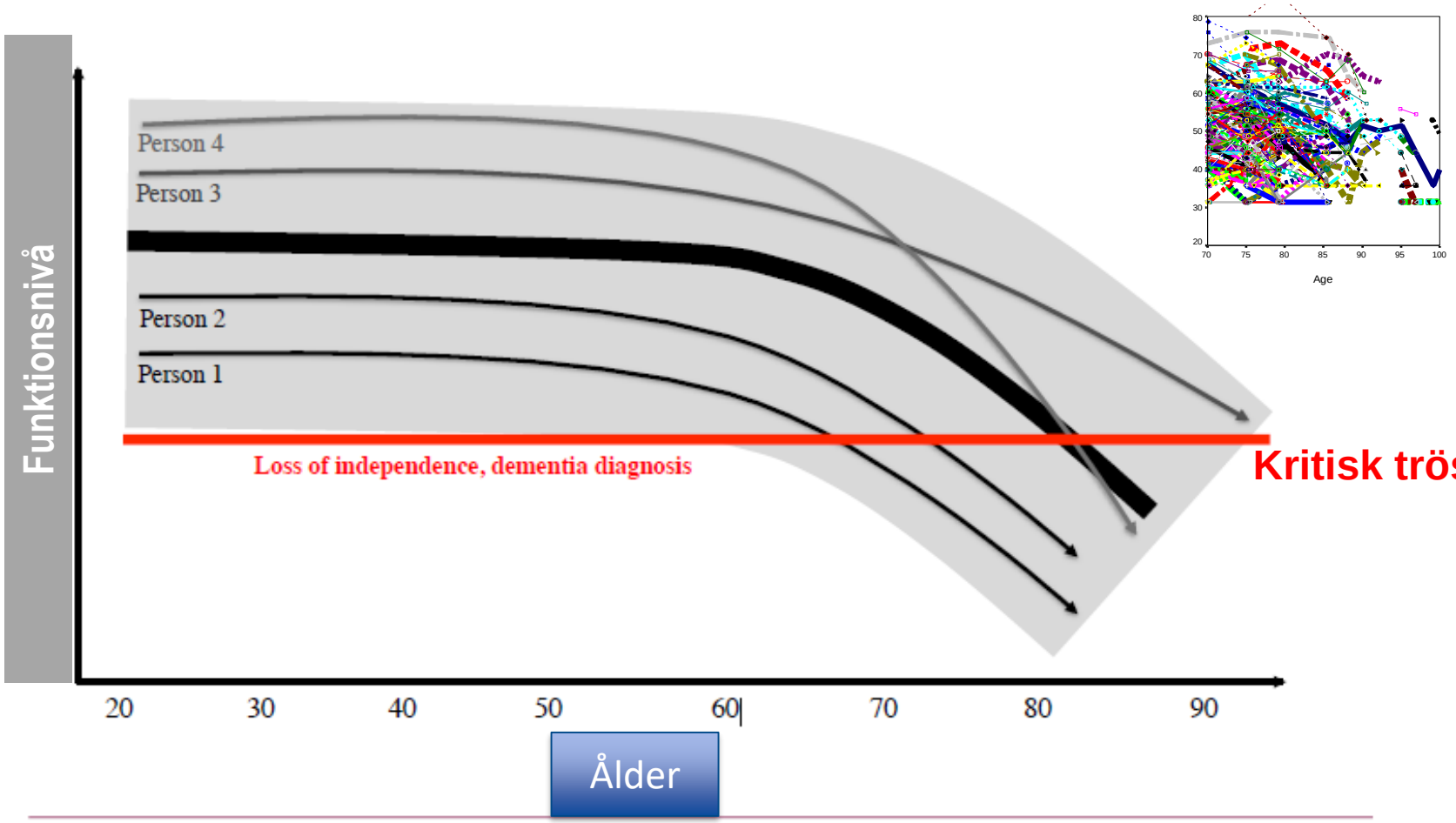
Vi ”åldras” olika



Kritisk tröskel

Informed by e.g., SLS; e.g., Schaie, 1996, *American Psychologist*; Betula longitudinal study; e.g., Rönnlund et al., 2005, *Psychology and Aging*; de Frias, Lövdén, Lindenberger, & Nilsson, 2007, *Intelligence*

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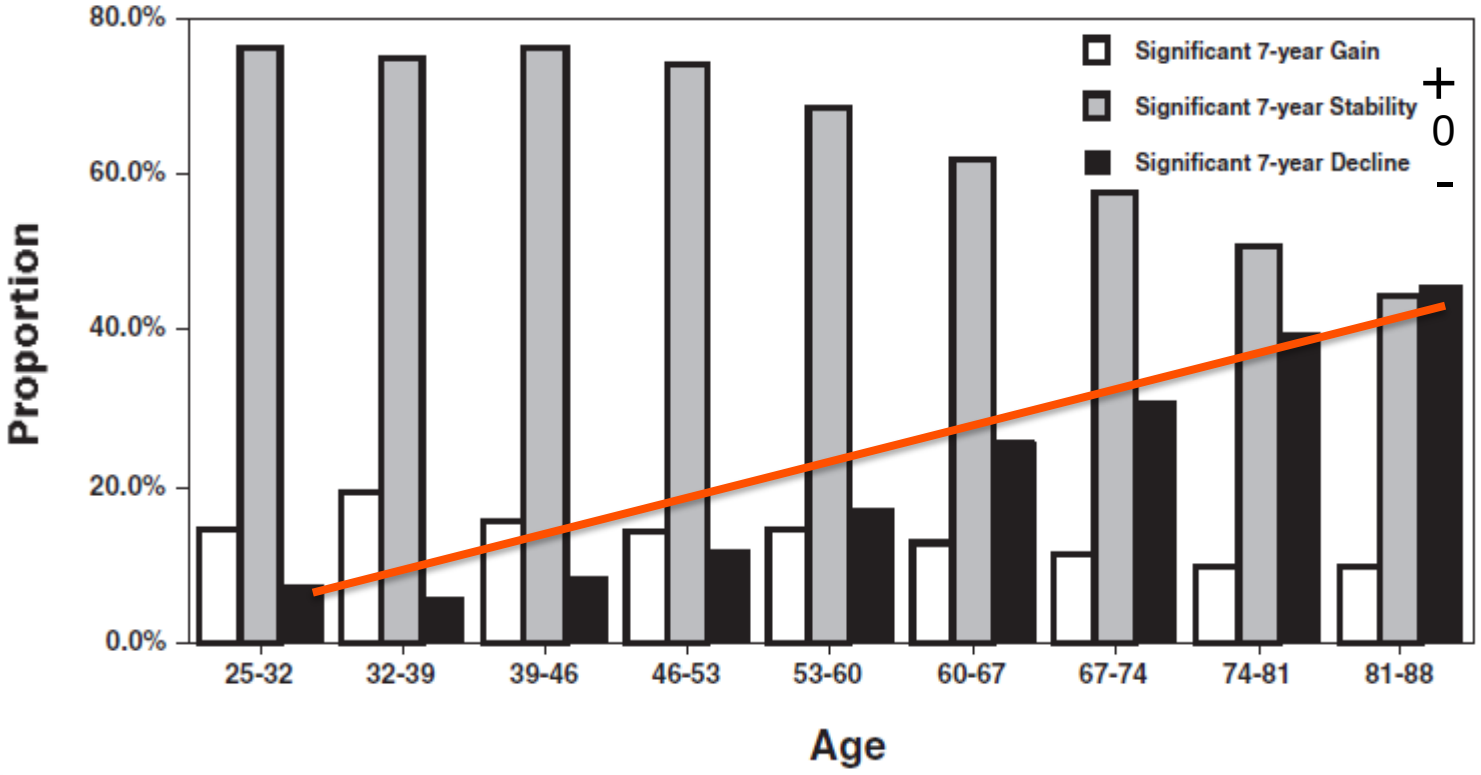
Stabil eller förändrad kognition i olika åldrar



Proportions of study participants showing significant gain, loss or stability over 7 years

明星大学心理学年報 2010, No.28, 021－035

講演録

Adult Cognitive Development from a Lifespan Developmental Perspective[1]

K. Warner Schaie *Department of Psychiatry and Behavioral Sciences, University of Washington*

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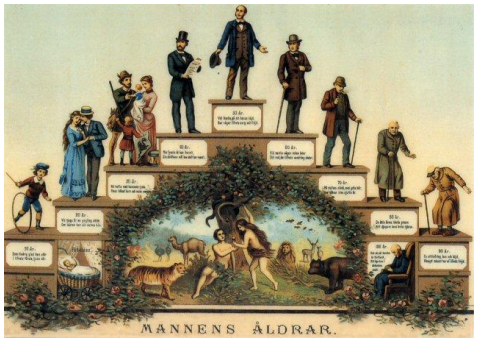
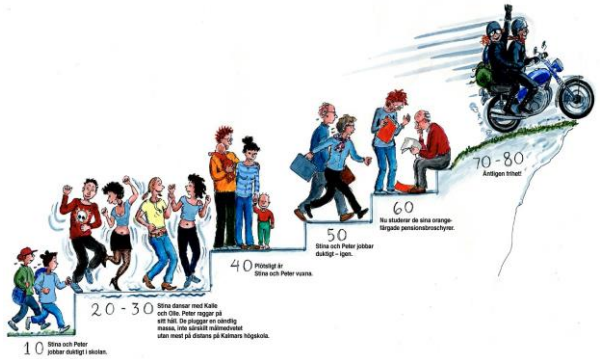
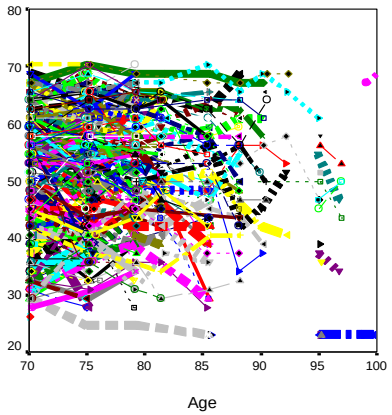
”The Goal”
An Accurate Portrayl of Differential Aging





No single trajectory



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Kaskadmodellen (J. Birren)

Med stigande ålder blir kronologisk ålder en allt sämre prediktor för kognitiv hälsa

Primärt / ”Normalt” åldrande

Sekundärt åldrande

sjukdomsrelaterat

Tertiärt åldrande -

terminal nedgång

Psykisk snabbhet
Episodiskt minne
Exekutiv förmåga/ multi-tasking, logisk - spatial förmåga, verbal fluency

Kristalliserade/erfarenhets-baserade förmågor; språk - semantiskt minne

Global kognitiv nedgång =
alla domäner är påverkas

MMSE / MMT

Världens mest använda screening test för kognitiv svikt på äldre dar

Mini Mental Test/MMT

(Efter Folstein MF et al. J Psychiatr Res 1975;12:189–198)

Testning skall ske utan tidspress eller distraherande moment och med värnande om patientens självkänsla. Vid nedsatt allmäntillstånd, sänkt vakenhetsgrad, grav hörselnedsättning, språksvårigheter eller andra faktorer som kan ge orättvisande resultat bör testningen uppskjutas eller ifrågasättas. Testresultatet ger en objektiv värdering av patientens kognitiva funktioner och kan ge vägledning vid utredning av demens eller demensliknande tillstånd. Vid screeningundersökningar har man använt gränsvärden runt 24 poäng för identifiering av kognitiva störningar. Man har ofta god hjälp av upprepad testning för att följa ett förlopp. Observera att demenssjukdom kan föreligga trots gott resultat vid MMT och att avsevärt poängavdrag vid MMT kan avspegla en depression eller konfusion med reversibel kognitiv svikt. CSK -98.

Uppgifterna i denna MMT-version är huvudsakligen formulerade enligt Svensk Förening för Kognitiva Sjukdomar (SFK). Stockholm feb 2000.

Patientbricka Datum /

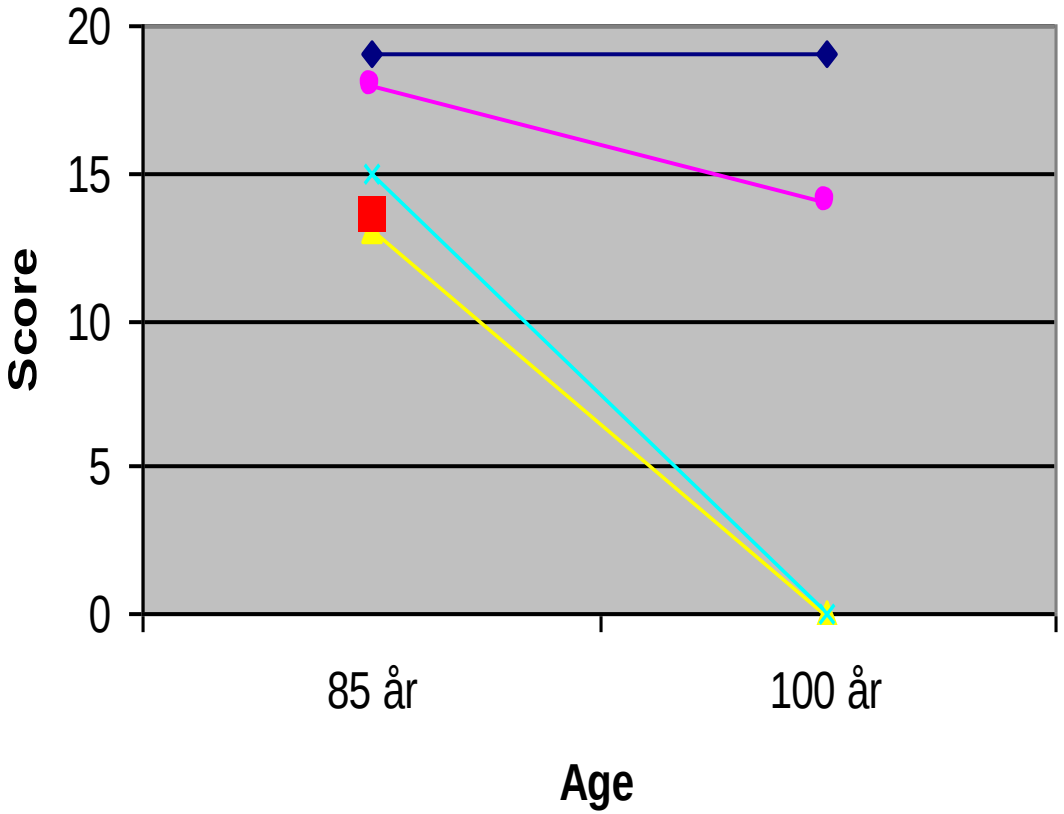
Patient: .....

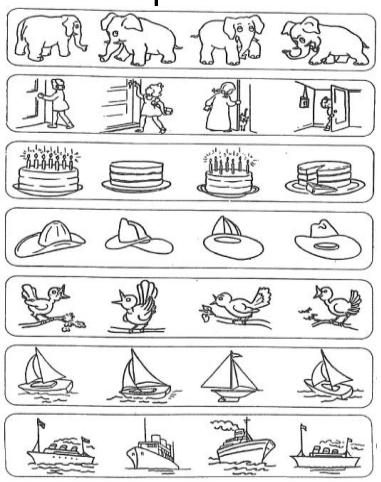
Datum: ..... Testansvarig: .....

Pat poäng	max poäng	
.....	(5)	**ORIENTERING** Fråga patienten vad det är för: År. Årstid. Datum. Veckodag. Månad.
.....	(5)	Fråga patienten var han/hon är ... Land. Län. Kommun (Stad). Sjukhus (Vårdcentral/Bostadsområde). Våningsplan.
.....	(3)	**REGISTRERING** Nämn tre föremål (ex nyckel, tandborste, lampa). Be patienten repetera dem. Den första repetitionen avgör antalet poäng, men fortsätt repetera orden till patienten lärt sig dem (upp till 6 ggr). Antal försök som krävdes för inlärning: .....
.....	(5)	**UPPMÄRKSAMHET OCH BERÄKNING** Be patienten börja vid 100 och dra ifrån 7, och sedan fortsätta dra ifrån 7 tills Du säger stopp (93-86-79-72-65). *Ett poäng för varje rätt svar.* Om patienten inte kan eller inte vill medverka ges 0 poäng. Be patienten bokstavera ordet "konst" baklänges. Om patienten gör fel men sedan fortsätter rätt, räkna antalet rätt (ex tsnok 5p, tsonk 3p). OBS! Vid förnyad testning av samma patient ska det alternativ som användes första gången användas.
.....	(3)	**MINNE** Be patienten återge de tre ord du tidigare bad honom/henne lägga på minnet.
.....	(2)	**SPRÅK** Pröva benämningsförmågan genom att peka på en klocka och fråga patienten vad det är. Gör samma sak med en penna.
.....	(1)	Be patienten repetera: "INGA OM, MEN ELLER VARFÖR". Instruera/tala tydligt! Tillåt bara ett försök.
.....	(3)	Utför 3-stegsuppmaning: Ge patienten ett blankt papper och säg tydligt: "Tag det här papperet i höger hand, vik det på mitten och lägg det i knät!" Ge ett poäng för varje riktigt utförd uppgift.
.....	(1)	Visa patienten texten "BLUNDA" (se baksidan). Be patienten läsa texten och göra som det står. Ge bara poäng om patienten verkligen blundar.
.....	(1)	Be patienten skriva en mening (längst ned på blankettens baksida). Diktera inte. Meningen måste innehålla subjekt och predikat och vara förståelig.
.....	(1)	**SPATIAL FÖRMÅGA/KOPIERING** Be patienten rita av figuren på blankettens baksida. Alla 10 vinklarna skall finnas och överlappningen skall forma en fyrhörning. Tremor och rotation ignoreras.
.....	(30)	**TOTAL POÄNGSUMMA**

Folstein et al. *Mini-Mental State: a practical method for grading the cognitive state of patients for the clinician.* J Psychiat Res 1975;12:189-198

Thurstone memory test





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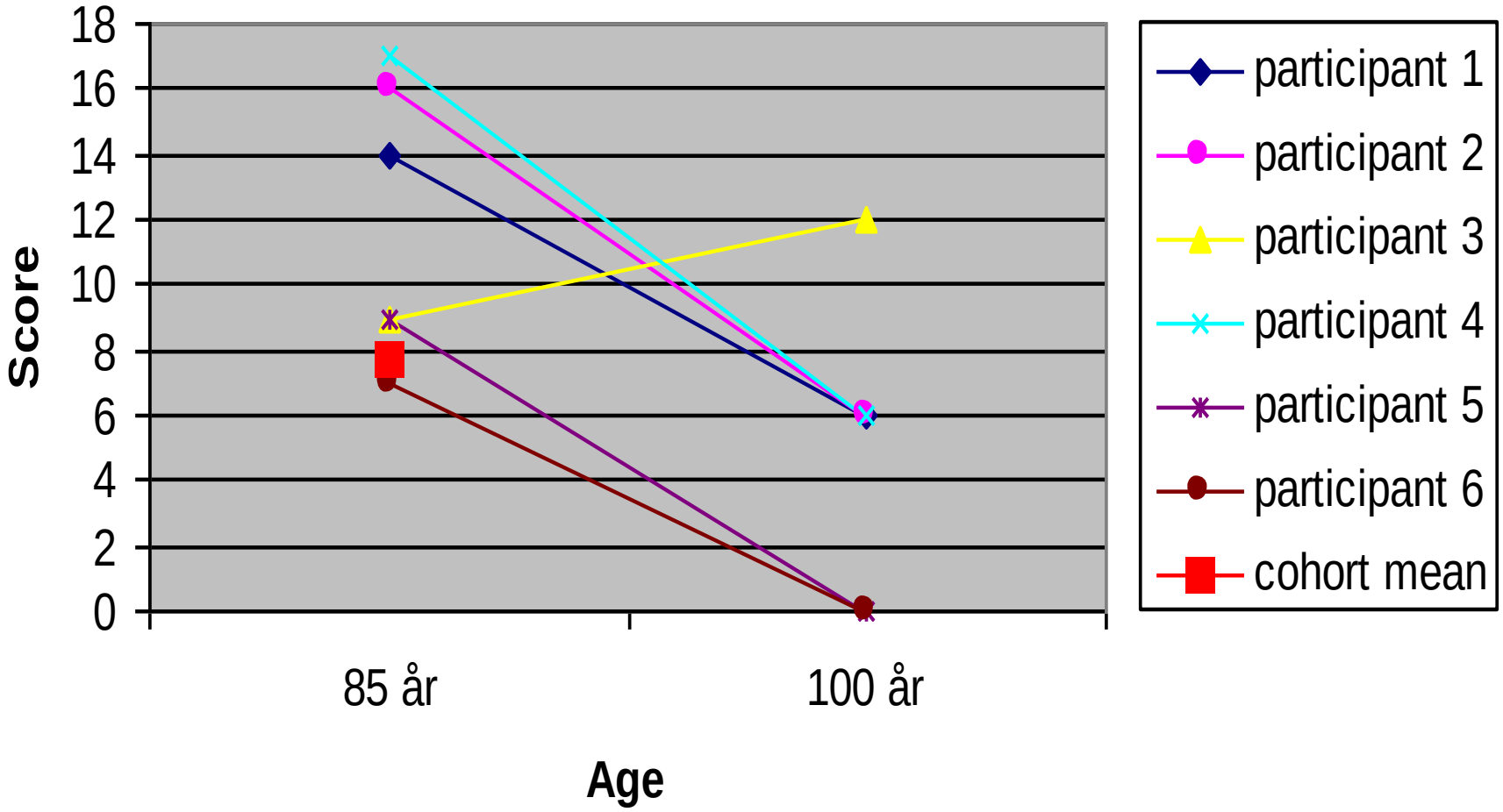
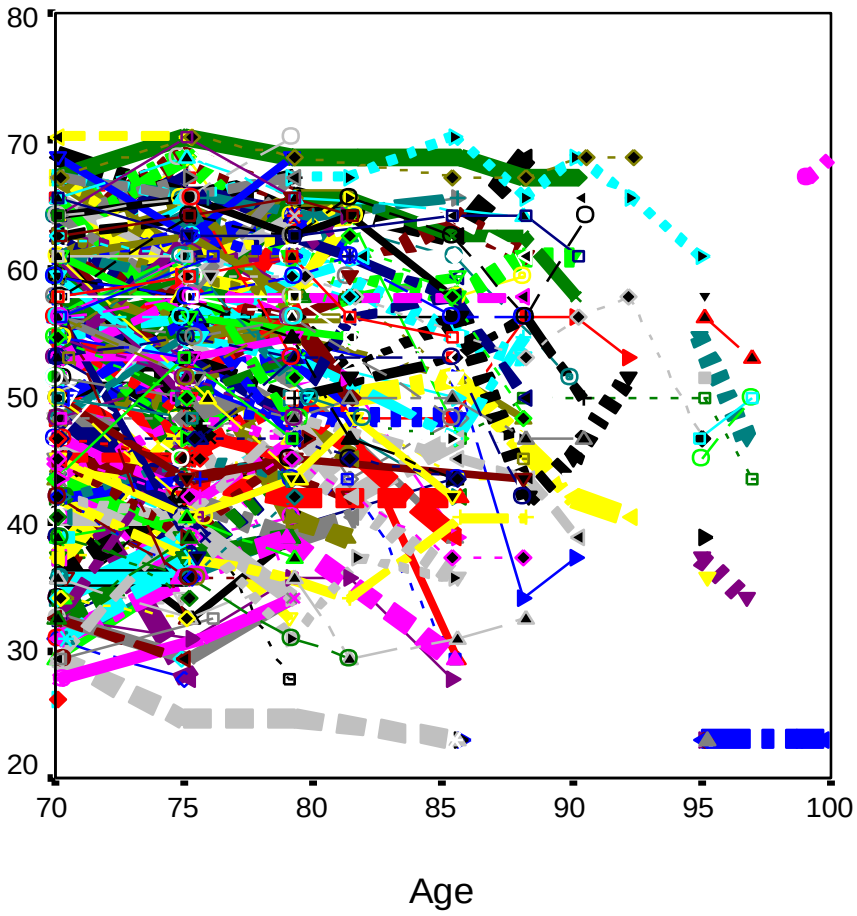
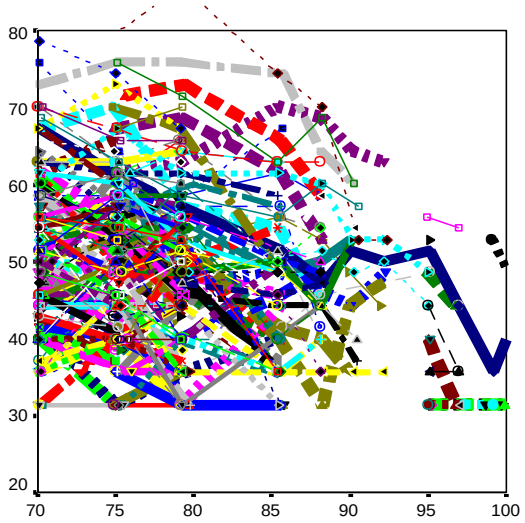
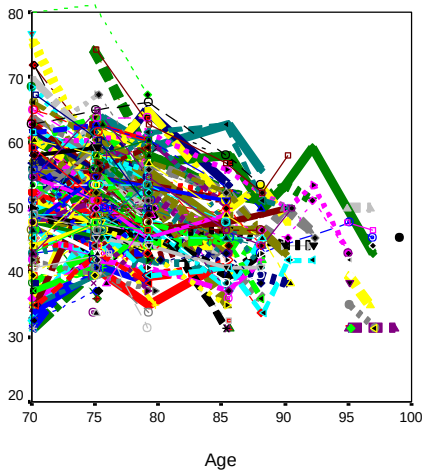
Spatial ability



How to make sense of observed intra-individual trajectories?



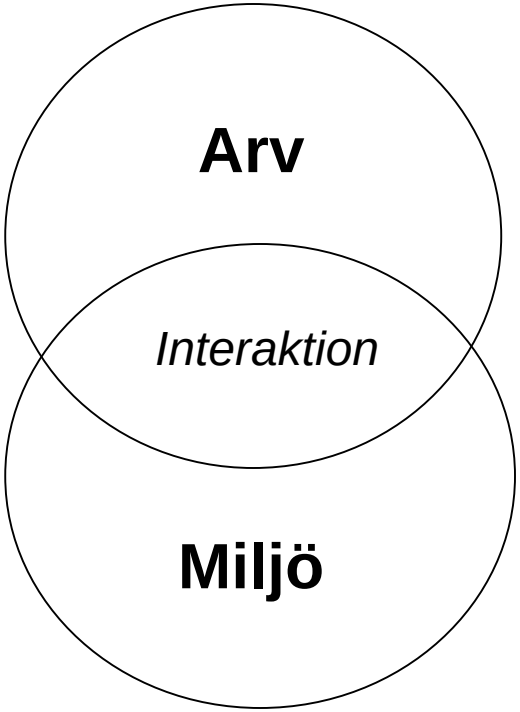




Interagerande system och livslång utveckling
Life-Span Development

Förutsättningar

Typ av påverkan



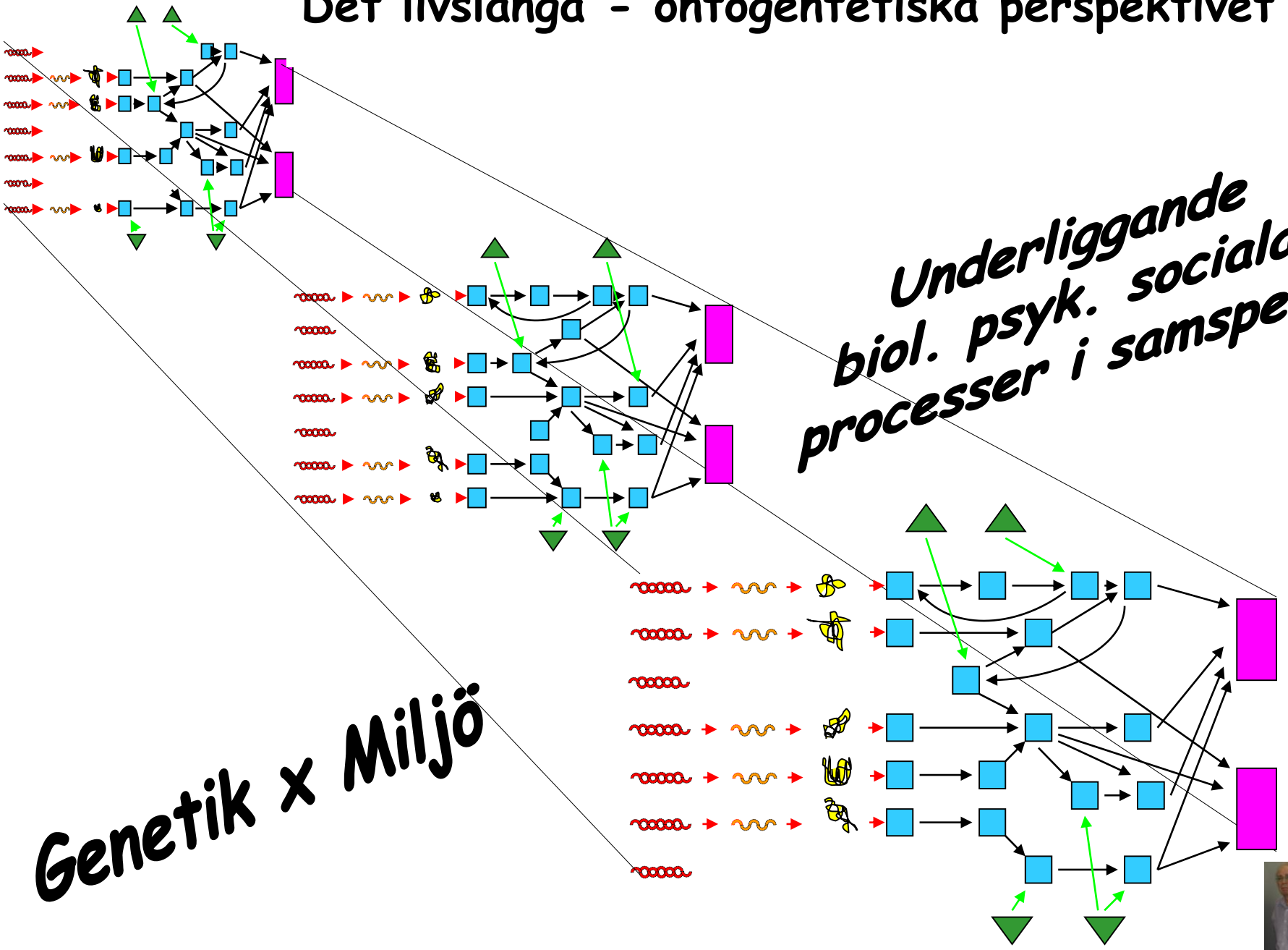
Normativ ålders-relaterad påverkan

Normativ historie-relaterad påverkan

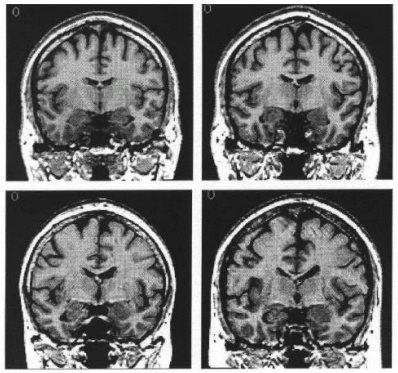
Icke-normativ påverkan

Tid

Det livslånga - ontogentetiska perspektivet



Brain structure is heritable



Estimated proportion of genetic variance (heritability) was:

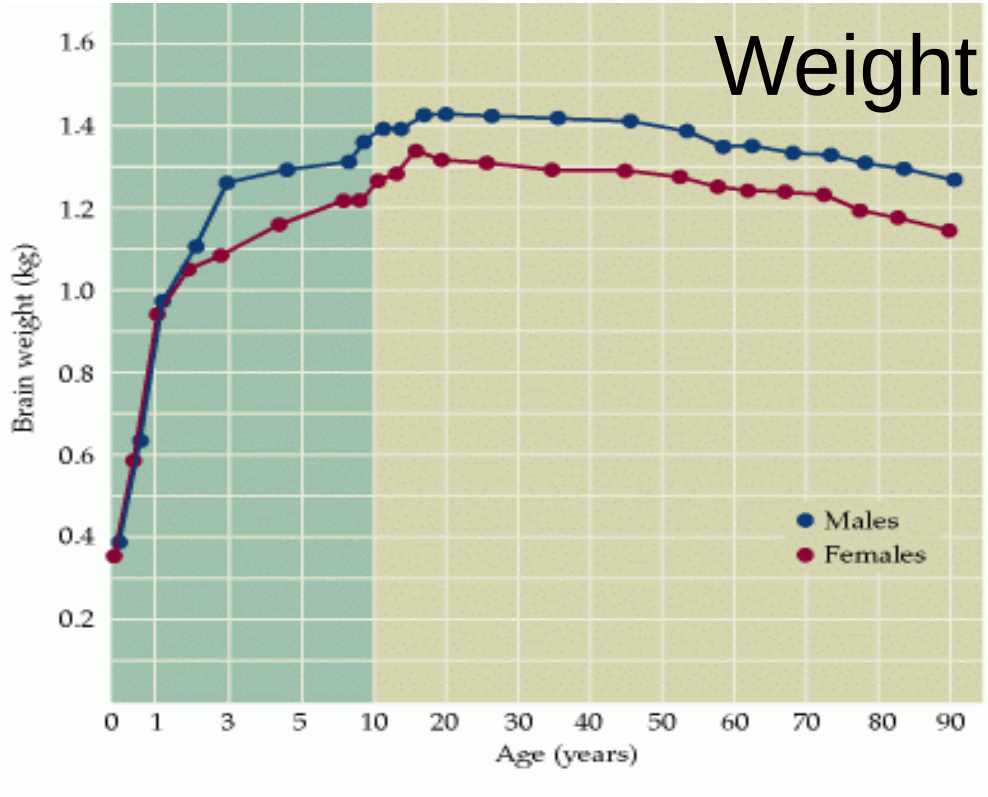
81% for midline cross-sectional area of corpus callosum

79% for lateral ventricle size

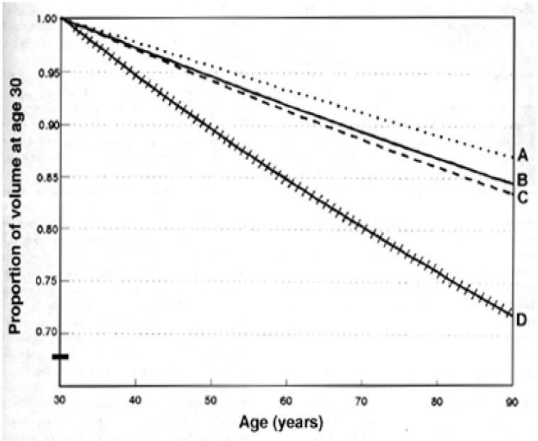
45 MZ and 40 DZ male twin pairs aged 68-78

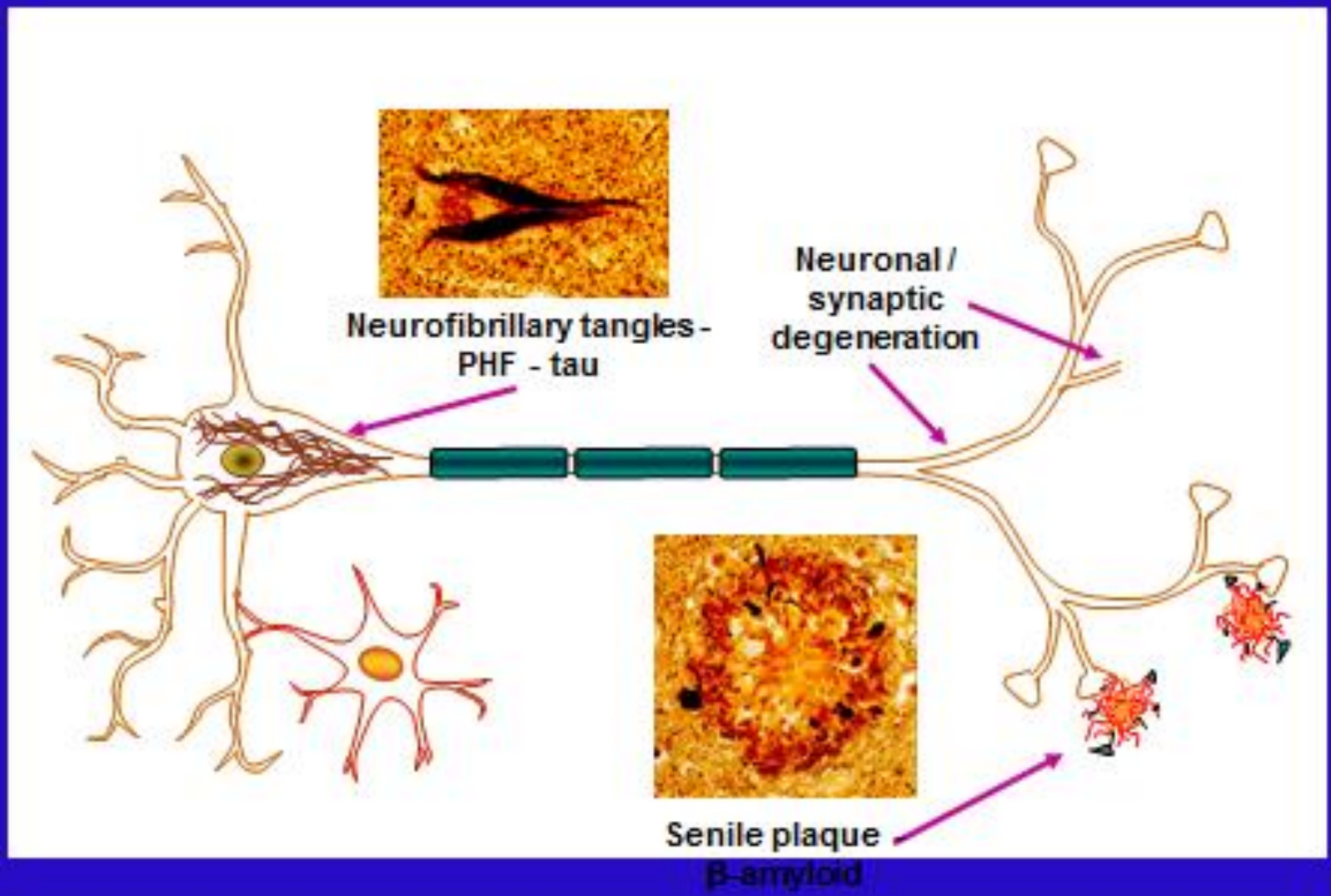
Pefferbaum, Sullivan & Caremlli (2000): Brain structure in men remains highly heriable in the seventh and eight decades of life. Neurobiol. Aging 21(1):63-74.

Age & Brain



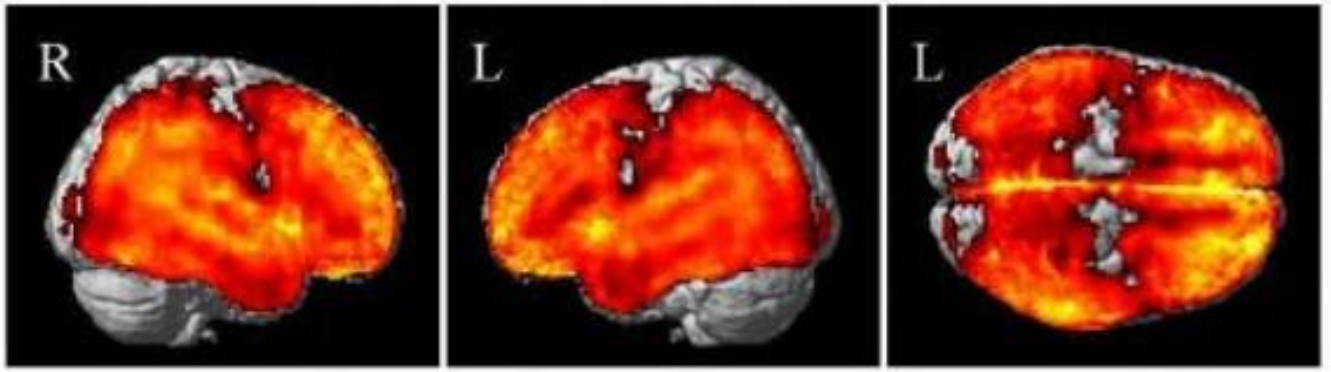
Volume




Neurofibrillary tangles -
PHF - tau
Neuronal /
synaptic
degeneration
Senile plaque
β-amyloid

Impact of diagnosis and APOE ε4 genotype status on cerebral amyloid deposition

Main Effect of *APOE* (ε4+ > ε4-)



Voxel-wise analysis of PET scans showed a main effect of APOE ε4 carrier status such that **APOE ε4+ participants had greater amyloid deposition than APOE ε4- participants in nearly the entire cortex.**

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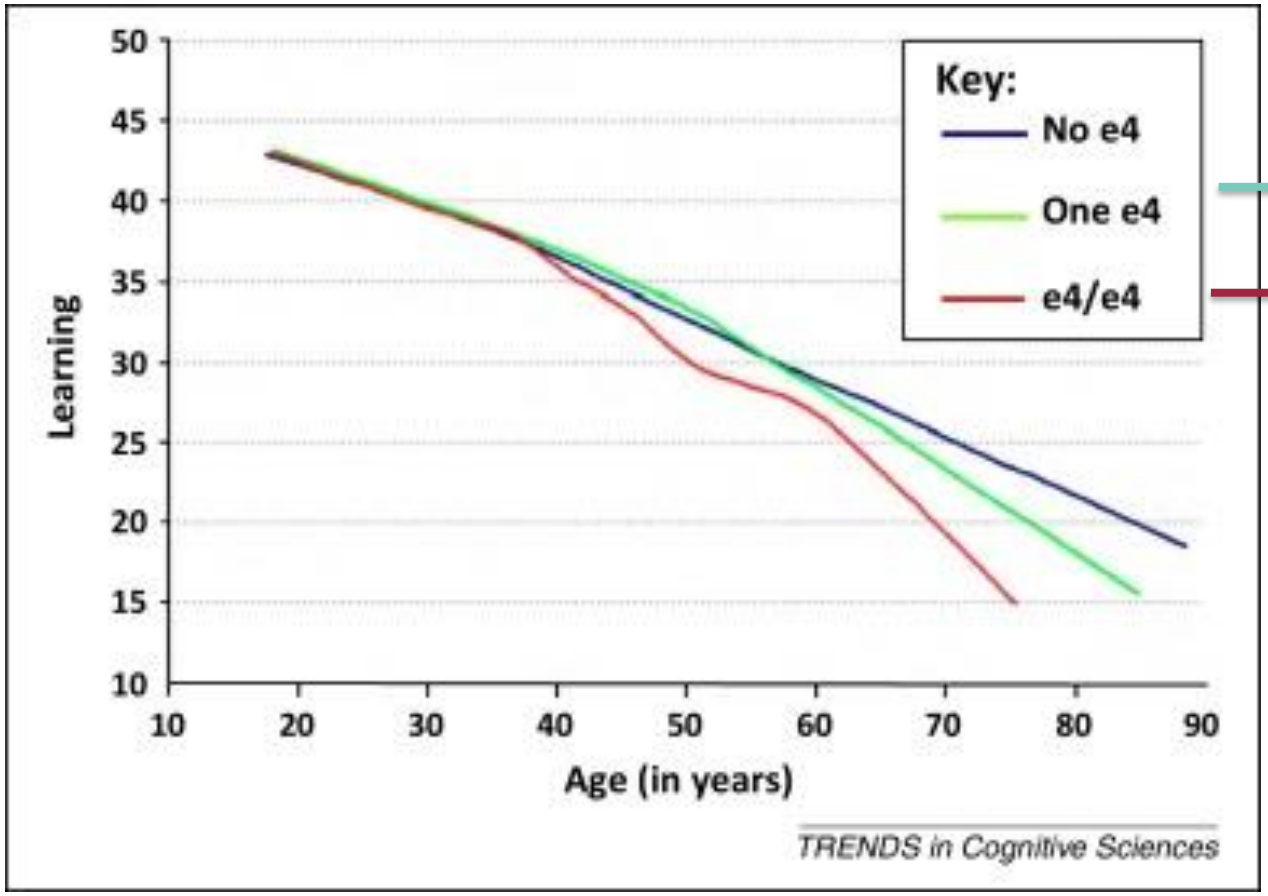
APOE och kognition



Heterozygote
a carrier of two different alleles at a specific genetic locus.
Homozygote
a carrier of two identical alleles at a specific genetic locus.

Effects of the apolipoprotein E (APOE) polymorphism on learning, with increased negative dose–response effects of the e4 allele across adult age. Learning reflects the number of correctly recalled words in the Rey Auditory Verbal Learning Test. Adapt...

ADA-GERO

Nervcellsförlust och åldrande

Innan seniet förloras främst nervceller i cortex

Under seniet förloras även nervceller i vitsubstans (myeliniserade celler), främst i corpus callosum (hjärnbalken)

Generellt drabbar nervcellsförluster i mindre utsträckning de utvecklingsmässigt äldre delarna av hjärnan.

Development and aging of cortical thickness correspond to genetic organization patterns

Anders M. Fjell[a,b,1], Håkon Grydeland[a], Stine K. Krogsrud[a], Inge Amlien[a], Darius A. Rohani[a], Lia Ferschmann[a], Andreas B. Storsve[a], Christian K. Tamnes[a], Roser Sala-Llonch[a], Paulina Due-Tønnessen[a,c], Atle Bjørnerud[a,d], Anne Elisabeth Sølsnes[e], Asta K. Håberg[f,g], Jon Skranes[e], Hauke Bartsch[h], Chi-Hua Chen[h], Wesley K. Thompson[i], Matthew S. Panizzon[j], William S. Kremen[j,k], Anders M. Dale[i,l], and Kristine B. Walhovd[a,b]

[a]Research Group for Lifespan Changes in Brain and Cognition, Department of Psychology, University of Oslo, 0373 Oslo, Norway; [b]Department of Physical Medicine and Rehabilitation, Unit of Neuropsychology, Oslo University Hospital, 0424 Oslo, Norway; [c]Department of Radiology, Rikshospitalet, Oslo University Hospital, 0424 Oslo, Norway; [d]The Interventional Centre, Rikshospitalet, Oslo University Hospital, 0424 Oslo, Norway; [e]Department of Laboratory Medicine, Children's and Women's Health, Norwegian University of Science and Technology, 7491 Trondheim, Norway; [f]Department of Medical Imaging, St. Olav's Hospital, N-7006 Trondheim, Norway; [g]Department of Neuroscience, Norwegian University of Science and Technology, 7491 Trondheim, Norway; [h]Department of Radiology, University of California at San Diego, La Jolla, CA 92093; [i]Department of Psychiatry, U… San Diego, La Jolla, CA 92093; [j]Center of Excellence for Stress and Mental Health, VA San Diego Healthcare System, La Joll… Behavioral Genomics Twin Research Laboratory, University of California at San Diego, La Jolla, CA 92093; and [l]Department … of California at San Diego, La Jolla, CA 92093

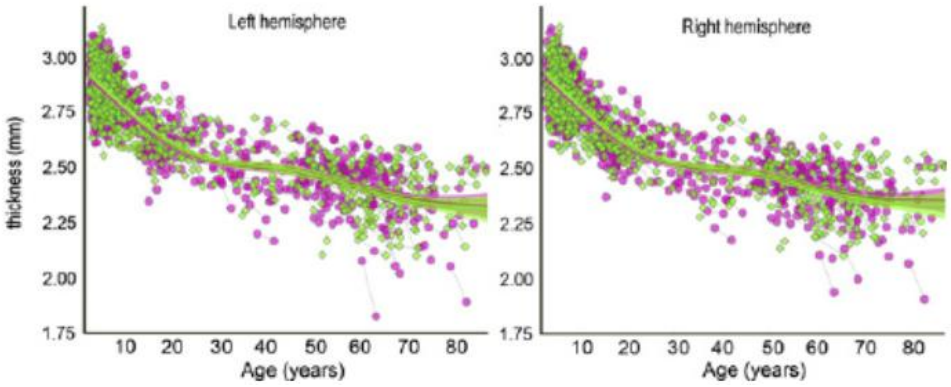


Fig. 1. Global change in cortical thickness. GAMM was used to estimate the lifespan trajectory of cortical thickness separately for each hemisphere, based on both the cross-sectional and the longitudinal information in the 1,633 observations in the total sample. The shaded area around the fit line represents the 95% CI. Green signifies female and pink signifies male.

0 COMMENTS

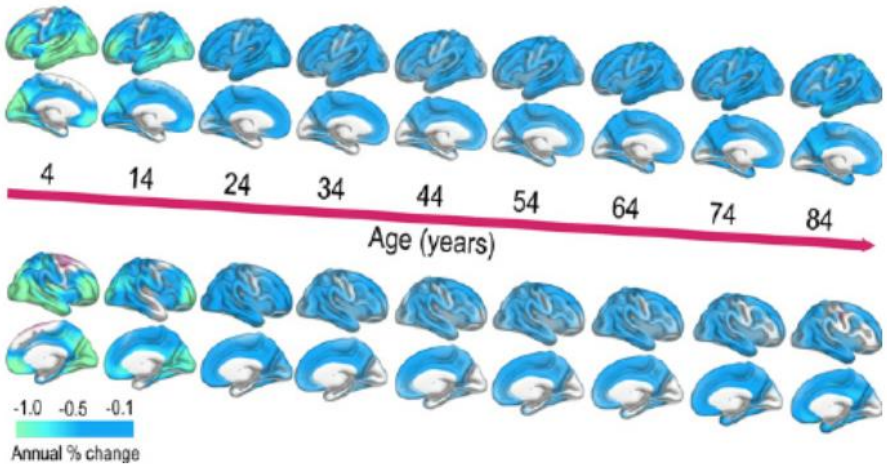
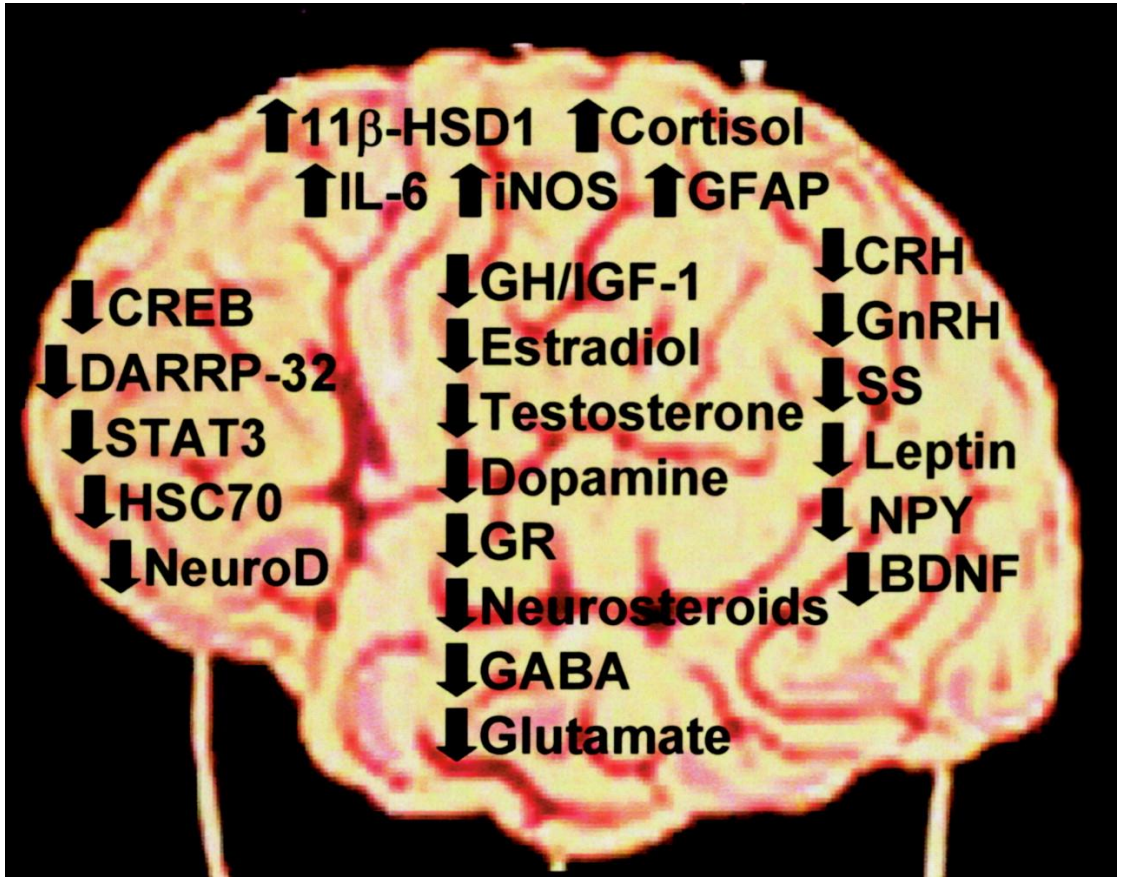


Fig. 3. Annual percent thickness decrease across the lifespan. APC in cortical thickness was estimated from a surface-based smoothing spline function, yielding APC estimates at each decade from 4 y. (Upper) Left hemisphere. (Lower) Right hemisphere. Blue–cyan colors indicate thinning.

Översikt av åldersrelaterade neuorkemiska förändringar i CNS

Smith, R. G. et al. Endocr Rev 2005;26:203-250



11{beta}-HSD1, BDNF, CREB, CRH, dopamine and DARPP-32, GABA, glial fibrillary acidic protein (GFAP), GH/IGF-I, GnRH, GR, HSC70, IL-6, iNOS, NPY, somatostatin (SS), och signal transducer and activator of transcription 3 (STAT3)

Main causes of age-related cognitive decline

– *”the wear and tear” hypothesis -*

- **Long-lived post-mitotic cells, such as neurons**, retinal pigment epithelium, cardiac myocytes, and skeletal muscle fibers **show more prounanced age-related changes**. These cells are all highly vulnerable to aging due to their intensive oxygen metabolism and a consequent extensive ROS (reactive oxygen species)
- **Neurons** - richness of interconnections **atrophy with age**

–include **cortical as well as sub-cortical neuclei** related to sensation, motor control, memory-cognition, and affect

- **Metabolic decline**

–and down-regulation of neuronal populations **preceede cell death**

- **Physical/chemical deterioation**

–and emergent neuropathology are **correlated with specific behavioral losses**

– **changes are universal** but **substantial variability**

in time of onset, course and magnitude of functional impairment

Heritability

Substantial Genetic Influence on Cognitive Abilities in Twins 80 or More Years Old

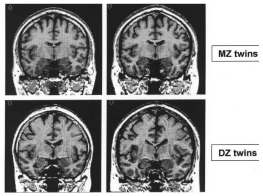
Gerald E. McClearn, Boo Johansson, Stig Berg, Nancy L. Pedersen, Frank Ahern, Stephen A. Petrill, Robert Plomin*

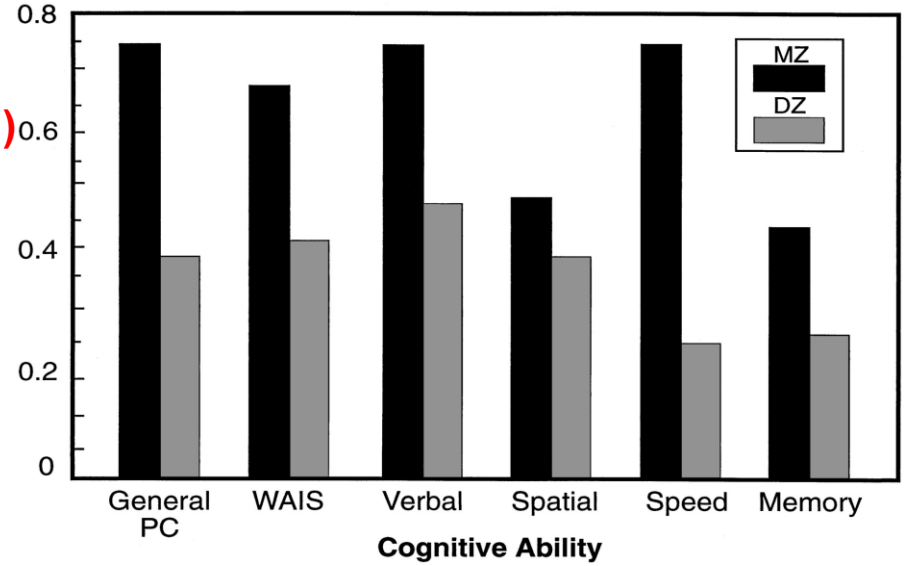
General and specific cognitive abilities were studied in intact Swedish same-sex twin pairs 80 or more years old for whom neither twin had major cognitive, sensory, or motor impairment. Resemblance for 110 identical twin pairs significantly exceeded resemblance for 130 fraternal same-sex twin pairs for all abilities. Maximum-likelihood model-fitting estimates of heritability were 62 percent for general cognitive ability, 55 percent for verbal ability, 32 percent for spatial ability, 62 percent for speed of processing, and 52 percent for memory. There was also evidence for the significant influence of idiosyncratic experience as the environmental component that most determines individual differences in cognitive abilities late in life

SCIENCE • VOL. 276 • 6 JUNE 1997 • www.sciencemag.org

62% för general cognitive ability (”g”)

55% för verbal förmåga
32% för spatial förmåga
62% för perceptuell snabbhet





Posthuma et.al Genetic correlations between brain volumes and the WAIS-III dimensions of verbal comprehension, working memory, perceptual organization, and processing speed

Heritability differs at various levels of cognitive performance

Low cognitive functioning in nondemented 80+-year-old twins is not heritable

Stephen A. Petrill[a,*], Boo Johansson[b], Nancy L. Pedersen[c], Stig Berg[b], Robert Plomin[d], Frank Ahern[e], Gerald E. McClearn[e]

[a]*Department of Psychology, Wesleyan University, 207 High Street, Middletown, CT 06459-0408, USA*
[b]*Institute of Gerontology, Jönköping, Sweden*
[c]*The Karolinska Institute, Stockholm, Sweden*
[d]*Social, Genetic, and Developmental Psychiatry Research Centre Institute of Psychiatry, London, UK*
[e]*Center for Developmental and Health Genetics, The Pennsylvania State University, Pennsylvania, USA*

Received 2 March 1999; received in revised form 31 January 2000; accepted 29 March 2000

Abstract

Late-onset dementia is moderately heritable, but little is otherwise known about the origins of low cognitive functioning very late in life. We investigated genetic influence of low cognitive functioning in 200 pairs of 80+-year-old twins identified as nondemented. Twin analyses of groups selected below the 40th percentile of cognitive functioning showed no genetic influence, suggesting that low cognitive functioning is due to nongenetic factors. Although the entire range of cognitive functioning shows moderate genetic influence, this masks very high heritability for the high end of the distribution and very low heritability at the low end. Preclinical dementia and/or terminal decline may account for nonsignificant heritability at the low end of ability. These results have implications for molecular genetic attempts to identify genes associated with late-onset dementia. The results should also stimulate the search for nongenetic factors responsible for low cognitive functioning in late life, a critical aspect for quality of life.

Keywords: Late-onset dementia; Cognitive functioning; Heritability

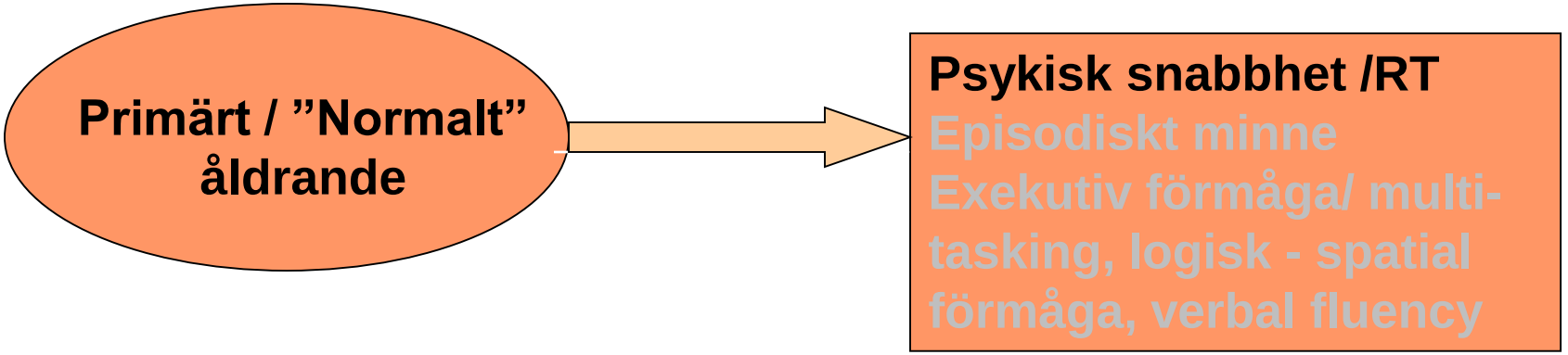
Identical (MZ) and fraternal (DZ) familiality estimates, group heritability (h_g^2), standard errors (S.E.), and significance levels for nondemented extremes in cognitive functioning

	Familiality estimates				
Cutoff (%)	MZ (*n*)	DZ (*n*)	h_g^2	S.E.	P<.05
≥90	0.75 (24)	0.25 (17)	0.75	0.27	*
≥80	0.79 (46)	0.23 (39)	0.79	0.26	*
≥70	0.80 (63)	0.35 (60)	0.80	0.27	*
≥60	0.79 (79)	0.41 (85)	0.75	0.29	*
≤40	0.66 (64)	0.37 (88)	0.59	0.35	NS
≤30	0.56 (47)	0.45 (64)	0.21	0.34	NS
≤20	0.40 (31)	0.53 (40)	0.00	0.32	NS
≤10	0.42 (10)	0.61 (25)	0.00	0.46	NS

n refers to number of probands.

2001

Kaskadmodellen (J. Birren)



Korrelation / flerval RT x ålder = -.52

1,5 ms ökning av flervals RT per år

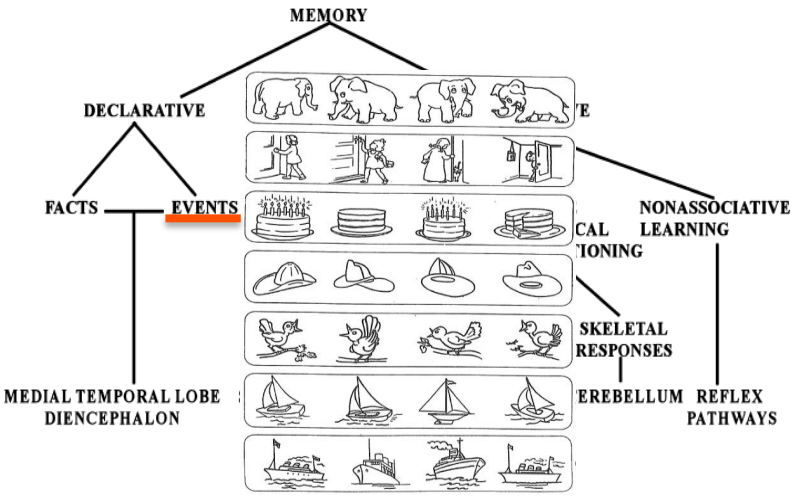
Ung. samma snabbhet för 8 och 70-åring

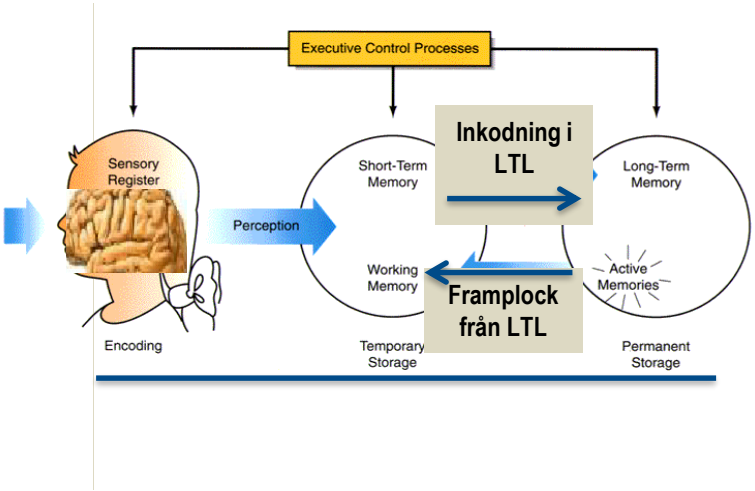
- Liten effekt - lexikala uppgifter
- Moderat effekt - enklare beslutsfattande
- Störst effekt - spatiala uppgifter

Kaskadmodellen (J. Birren)

Primärt / ”Normalt” åldrande

Psykisk snabbhet /RT
Episodiskt minne
Exekutiv förmåga/ multi-tasking, logisk - spatial förmåga, verbal fluency





Kaskadmodellen (J. Birren)

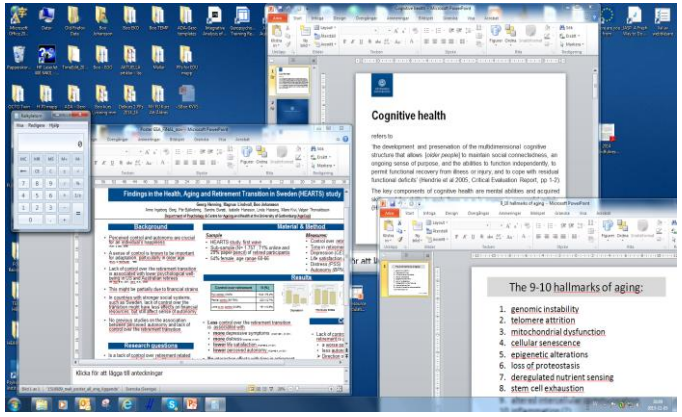
Primärt / ”Normalt” åldrande

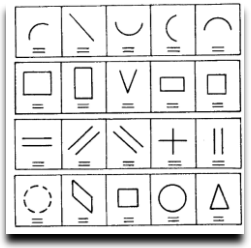
Psykisk snabbhet /RT
Episodiskt minne
Exekutiv förmåga/ multi-tasking, logisk - spatial förmåga, verbal fluency

Exekutiv förmåga/ multi-tasking, logisk - spatial förmåga, verbal fluency

Exekutiv förmåga – 3 komponenter:

- Uppdatering (uppmärksamhet/relatera nytt till tidigare förvärvat) ex n-back
- Byte av fokus och strategier (ex TMT)
- Inhibition (ex Stroop)





S-A test

Kaskadmodellen (J. Birren)

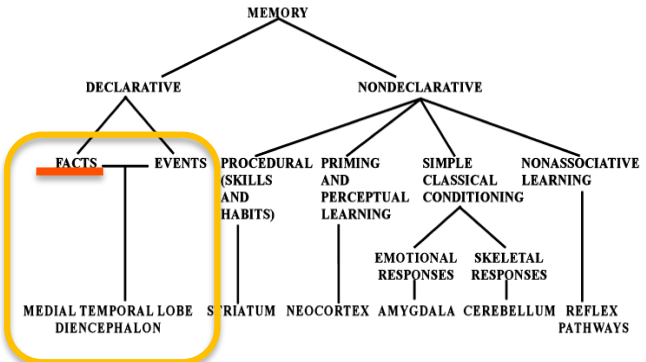
Primärt / ”Normalt” åldrande

Sekundärt åldrande

sjukdomsrelaterat

Psykisk snabbhet
Episodiskt minne
Exekutiv förmåga/ multi-tasking, logisk - spatial förmåga, verbal fluency

Kristalliserade/erfarenhets-baserade förmågor; språk - semantiskt minne



Kunskapsminne - facts
Ordförråd - aktivt / passivt ordförråd
Ordförståelse / Synonymtest

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Ohälsa - sjukdomar med kognitiva effekter: ökad förekomst med stigande ålder

- Förhöjt blodtryck
- Stroke / Hjärt-kärl sjukdom/
- Bristtillstånd
- Depression
- Diabetes
- Övervikt/fetma - BMI
- Demenssjukdom
    - *Comorbiditet / läkemedelsbiverkan*

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Samband mellan BMI i medel-åldern och kognition i hög ålder hos icke-demenssjuka

Dementia and Geriatric Cognitive Disorders

Dement Geriatr Cogn Disord 2010;29:543–552
DOI: 10.1159/000314874

Accepted: May 7, 2010
Published online: July 3, 2010

Overweight in Midlife Is Related to Lower Cognitive Function 30 Years Later: A Prospective Study with Longitudinal Assessments

Linda B. Hassing[a] Anna K. Dahl[b] Nancy L. Pedersen[c, d] Boo Johansson[a]

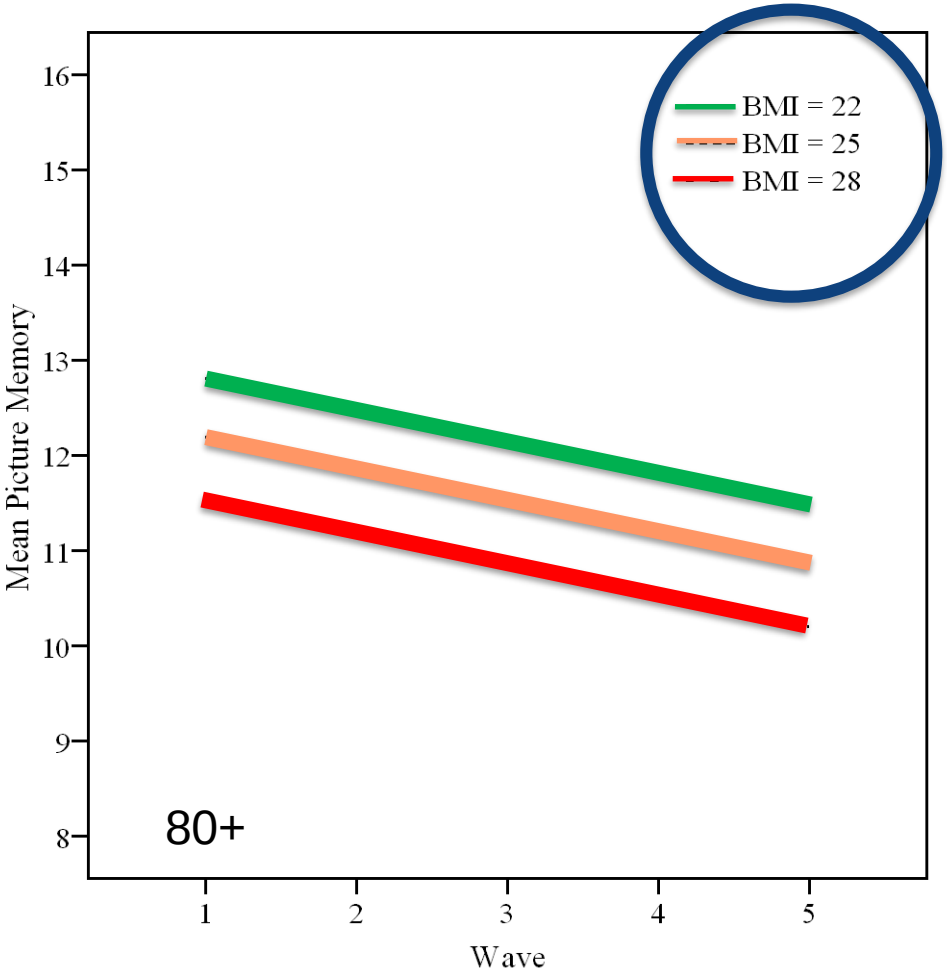
[a]Department of Psychology, University of Gothenburg, Gothenburg, [b]Institute of Gerontology, School of Health Sciences, Jönköping University, Jönköping, and [c]Department of Medical Epidemiology, The Karolinska Institute, Stockholm, Sweden; [d]Department of Psychology, University of Southern California, Los Angeles, Calif., USA

Key Words
Adiposity · Obesity · Cognition · Mental ability

Abstract
Aim: To examine if the body mass index (BMI) in midlife is related to cognitive function 30 years later in a dementia-free sample. ***Methods:*** BMI was reported in 1963 at age 50–60 years, and cognitive abilities were examined 30 years later in a longitudinal design with 5 measurement occasions at 2-year intervals (n = 417). The cognitive abilities examined included tests of long-term memory, short-term memory, speed, verbal and spatial ability. ***Results:*** Multilevel modeling adjusting for demographic and lifestyle factors, and relevant diseases showed that a higher BMI in midlife predicted lower test performance 30 years later. Significant associations between BMI and level of performance were found in all cognitive abilities; however, a higher midlife BMI was not associated with steeper cognitive decline. ***Conclusion:*** Our results indicate that midlife overweight is related to lower overall cognitive function in old age. The fact that BMI-related effects were noted in mean-level cognitive performance, whereas only one ability showed differences in slopes, suggests that the negative effect of overweight has an onset before the entry into very old age.

The evidence that overweight in middle age is related to increased dementia risk in old age is growing [1–4]. However, few studies have addressed the question if overweight affects cognitive abilities among those who do not develop dementia. Our hypothesis is that overweight is likely to assert a negative effect on cognition even in individuals who remain nondemented.

Cross-sectional studies on the association between body mass index (BMI) and cognitive function in midlife have produced mixed and nonconclusive findings. Significant associations between high BMI and low cognitive test performance have been reported in two studies using samples covering the whole adult age span [5, 6]. However, in the study by Dore et al. [6], the association between BMI and cognition was to a large extent attenuated by adjusting for physical activity. In another study, a significant association between BMI and cognition was found only in executive function [7]. In one further study, based on an older sample (54–81 years), significant associations were found in only 3 out of 11 cognitive tests [8]. Cross-sectional studies on older age cohorts show even more contradictory results, where some indicate that higher BMI is associated with better cognitive function [9–11], whereas others have found that higher BMI is associated with lower cognitive function [12, 13]. Taken together, findings based on cross-sectional studies do not



Hassing, L. B., Dahl, A., Pedersen, N. L. & Johansson, B. (2010) *Overweight in midlife is related to lower cognitive function 30 Years Later: A prospective study with longitudinal assessments.* Dementia and Geriatric Cognitive Disorders.

ADA-GERO

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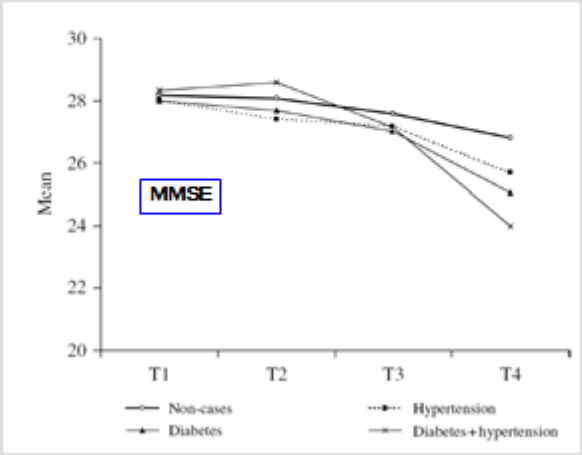
Diabetes och hypertension

- Ingen negativ effekt av högt blodtryck
- Negativ effekt av diabetes
- Individer med diabetes och högt blodtryck utgör en högriskgrupp för kognitiv svikt och demens



Age and Ageing 2004; **33:** 355–361
DOI: 10.1093/ageing/afh100

Published electronically 10 May 2004

Comorbid type 2 diabetes mellitus and hypertension exacerbates cognitive decline: evidence from a longitudinal study

LINDA B. HASSING[1], SCOTT M. HOFER[2], SVEN E. NILSSON[4], STIG BERG[4], NANCY L. PEDERSEN[5,6], GERALD MCCLEARN[3], BOO JOHANSSON[1]

[1]Department of Psychology, Göteborg University, Göteborg, Sweden
[2]Department of Human Development and Family Studies and [3]Center for Developmental and Health Genetics, Pennsylvania State University, University Park, PA, USA
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[5]Department of Medical Epidemiology and Biostatistics, Karolinska Institute, Stockholm, Sweden
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Abstract

Background: diabetes and hypertension are two highly prevalent diseases in the old population. They are highly related such that comorbidity is common.
Objectives: to examine (i) the independent impact of the respective diseases on cognitive decline in very old age and (ii) the interactive impact of the two diseases on cognitive decline.
Subjects: 258 individuals (mean age = 83 years), all non-demented at baseline. Of these, 128 individuals (non-cases) were free from diabetes and hypertension, 92 individuals had a diagnosis of hypertension, 16 had a type 2 diabetes mellitus diagnosis without hypertension, and 22 had comorbid diabetes and hypertension.
Method: a population-based longitudinal study of ageing (The OCTO-Twin Study), including four measurement occasions 2 years apart. The Mini-Mental State Examination was used to measure general cognitive function. Data were analysed using SAS Proc Mixed multilevel modelling.
Results: longitudinal trajectories indicated a steeper decline in cognitive function related to diabetes but not related to hypertension. However, the results indicated greatest cognitive decline among persons with comorbid diabetes and hypertension.
Conclusions: it is concluded that comorbidity of diabetes and hypertension produce a pronounced cognitive decline. This finding emphasises the importance of prevention and treatment of those highly prevalent diseases in the old population.

Keywords: *hypertension, type 2 diabetes mellitus, cognitive decline, older age, longitudinal study, vascular disease*

ADA-GERO

Published in final edited form as:
Psychol Aging. 2009 June ; 24(2): 373–384. doi:10.1037/a0015713.

Depression as a Risk Factor or Prodomal Feature for Dementia? Findings in a Population-Based Sample of Swedish Twins

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University of Southern California

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Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Sweden, and Department of Psychology, University of Southern California

Boo Johansson,
Göteborg University, Sweden

John J. McArdle,
University of Southern California

Laura Fratiglioni, and
Aging Research Center, Karolinska Institutet, Sweden

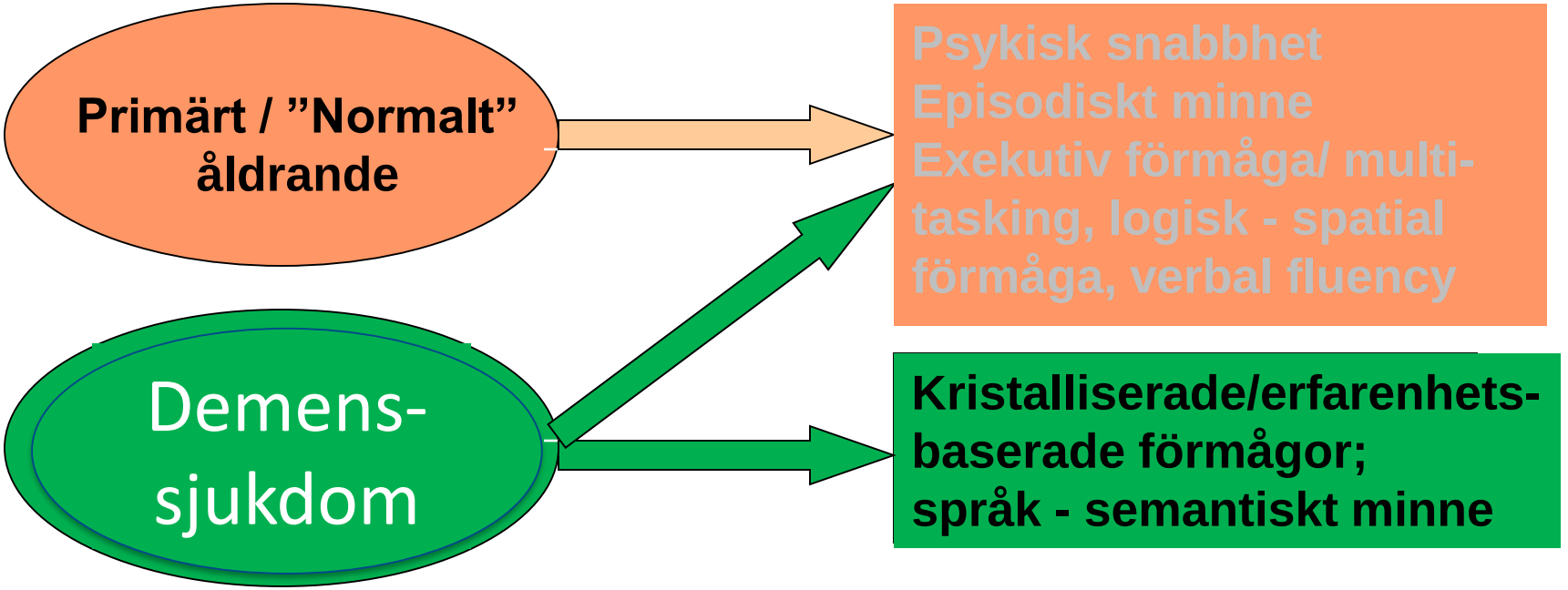
Nancy L. Pedersen
Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Sweden, and Department of Psychology, University of Southern California

Abstract

This study tested whether history of depression is associated with an increased likelihood of having dementia, and to verify whether a first depressive episode earlier in life is associated with an increased likelihood of dementia, or whether only depressive episodes occurring close in time to dementia diagnosis are related to dementia. Depression information was collected from national hospital discharge registries, medical history, and medical records. Dementia was clinically diagnosed using DSM-IV criteria. Case-control results showed that individuals with recent registry-identified depression were 3.9 times more likely than those with no registry-identified depression history to have dementia, while registry-identified depression earlier in life was not associated with an increased dementia risk. Each 1-year increase in the difference between depression onset and dementia onset or censored age decreased the likelihood of dementia by 8.4%. Co-twin control analyses found that individuals with prior depression were 3.0 times more likely to have dementia than their non-depressed twin partner, with a similar gradient of age of depression onset. Taken together, these findings suggest that after partially controlling for genetic influences, late-life depression for many individuals may be a prodrome rather than a risk factor for dementia.

Taken together, these findings suggest that after partially controlling for genetic influences, **late-life depression for many individuals may be a prodrome rather than a risk factor for dementia.**

Kaskadmodellen (J. Birren)



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FACT FILE

World Health Organization

10 FACTS ON DEMENTIA

Next

1 2 3 4 5 6 7 8 9 10

Cathy Greenblat

Dementia is not a normal part of ageing

Although dementia mainly affects older people, it is not a normal part of ageing. Dementia is a syndrome, usually of a chronic or progressive nature, caused by a variety of brain illnesses that affect memory, thinking, behaviour and ability to perform everyday activities.

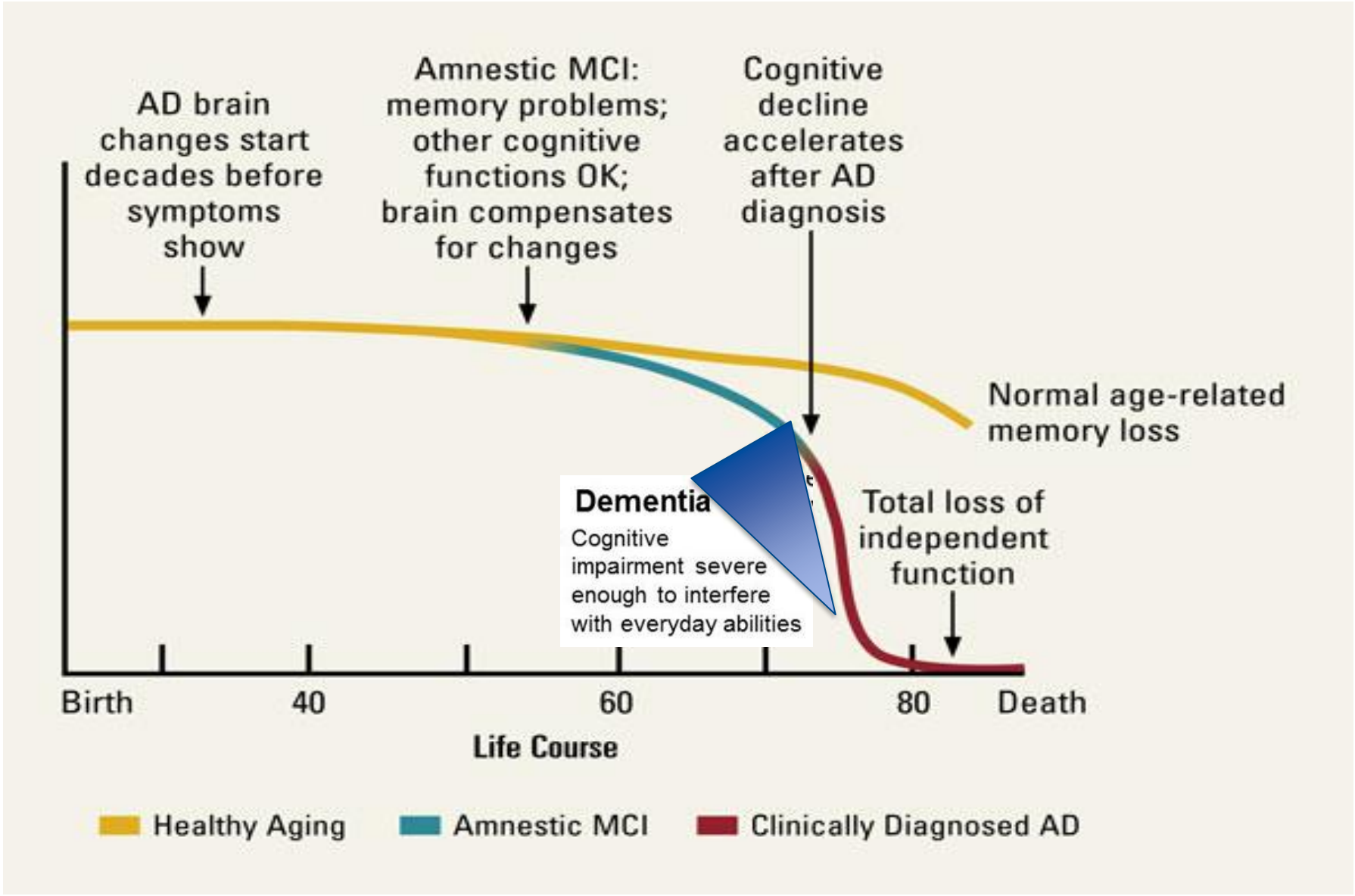
Olika typer av demens

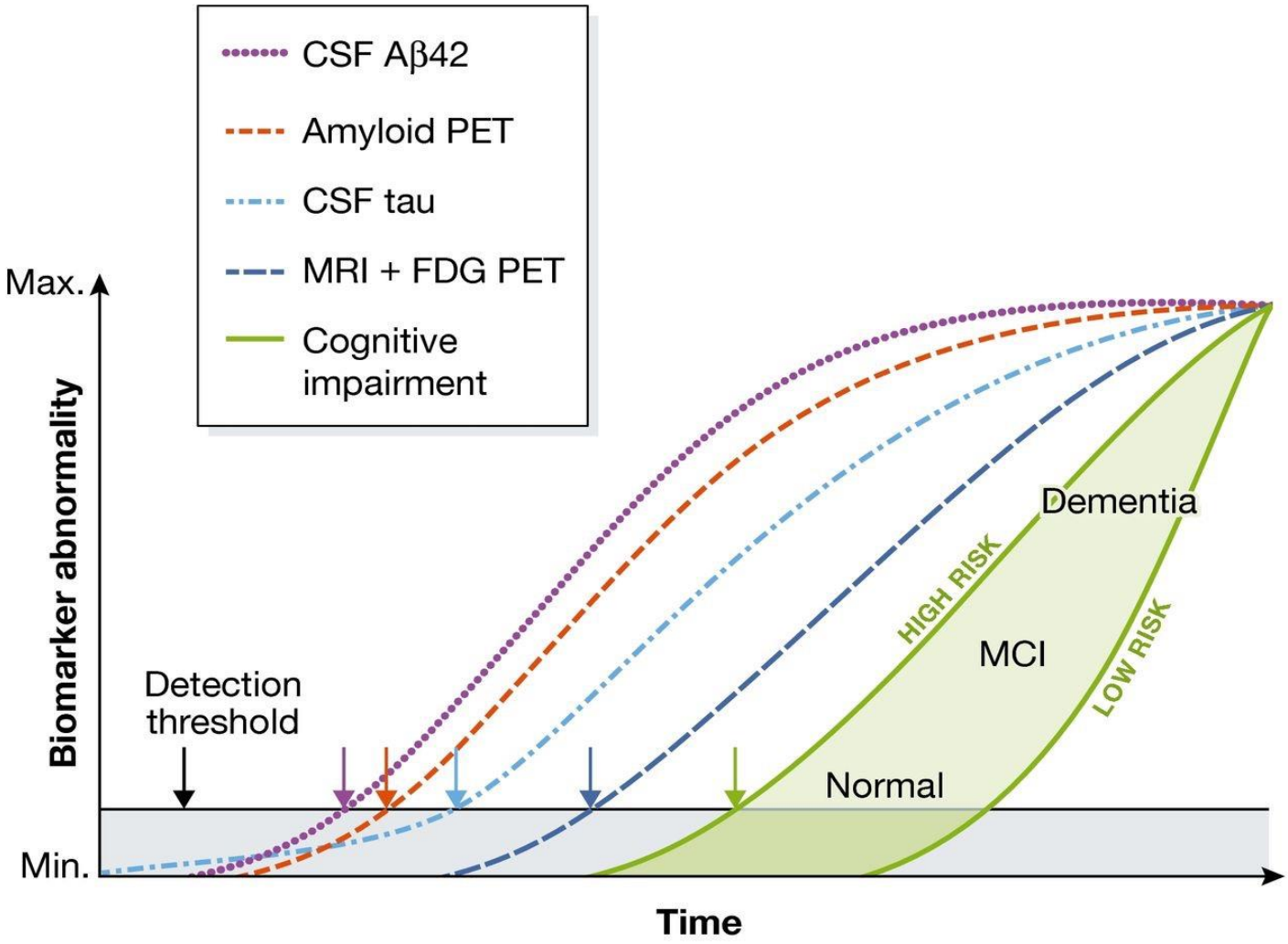
UNIVERSITY OF GOTHENBURG

The clinical challenge in neuropsychology of aging:
? intact or degree of compromised cognition ?

ADA-GERO

Cognitive decline in relation to dementia





Jack, C. R., Jr., Knopman, D. S., Jagust, W. J., Shaw, L. M., Aisen, P. S., Weiner, M. W., Petersen, R. C., & Trojanowski, J. Q. (2010). Hypothetical model of dynamic biomarkers of the Alzheimer's pathological cascade. *Lancet Neurol*, *9*(1), 119-128. https://doi.org/10.1016/S1474-4422(09)70299-6

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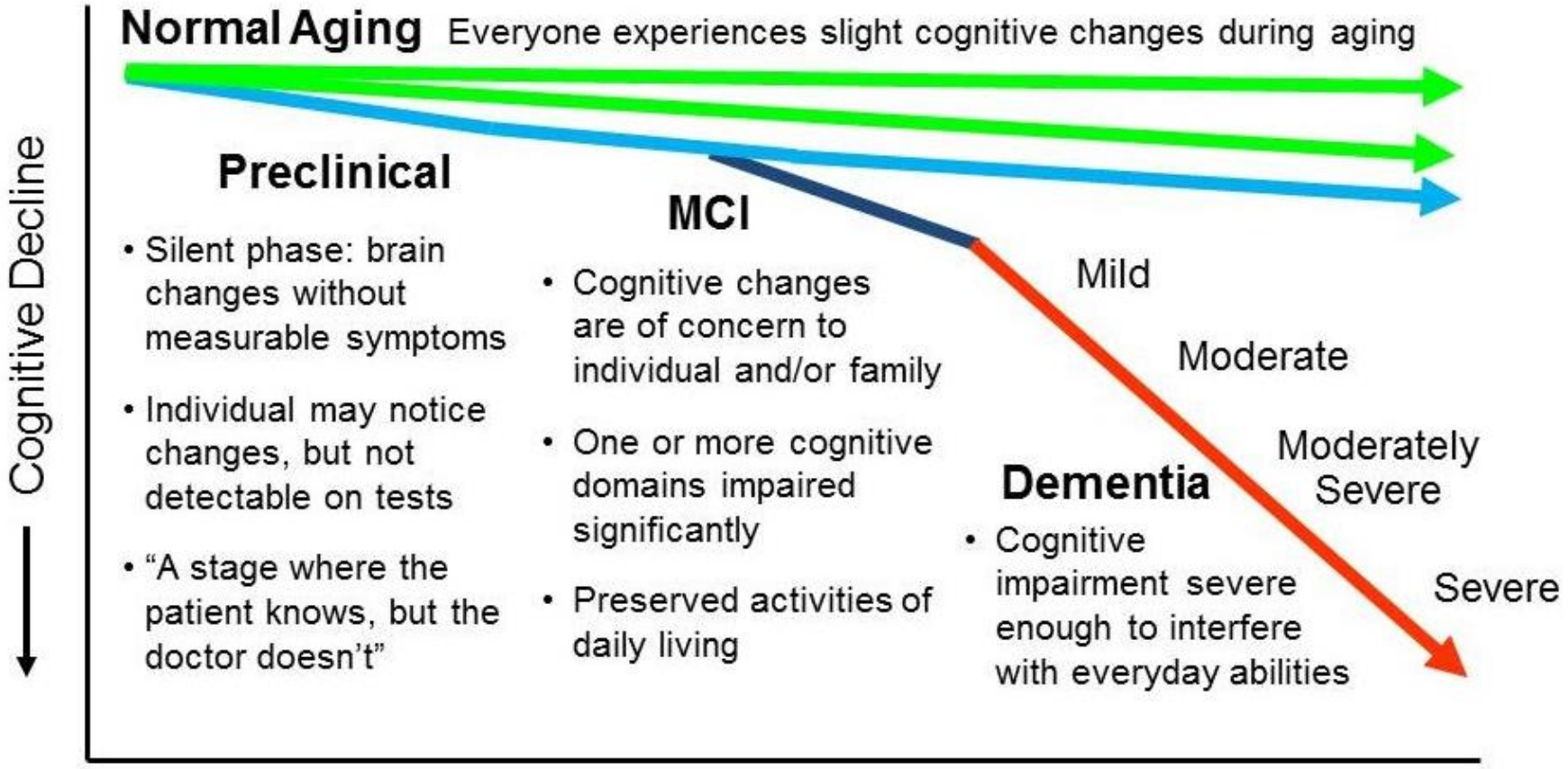


ADA-GERO

Demens • enl. DSM-IV-kriterierna

En nedsättning av flera kognitiva funktioner. Nedsättningen visar sig genom:

1. nedsatt minnesfunktion (bristande förmåga att lära in något nytt och att minnas vad som tidigare lärts in)

2. minst en typ av följande störningar:
   - afasi (språkstörning)
   - apraxi (oförmåga att utföra ändamålsenliga rörelser trots intakta motoriska funktioner)
   - agnosi (bristande förmåga att känna igen eller identifiera föremål trots intakt sensorisk funktion)
   - störning av exekutiva funktioner (d v s planera, organisera, rangordna, tänka abstrakt)

Den kognitiva funktionsnedsättningen förorsakar en betydande försämring av sociala eller yrkesmässiga funktioner och representerar en betydande sänkning från en tidigare funktionsnivå.
Den kognitiva funktionsnedsättningen förekommer inte enbart i samband med konfusionstillstånd

DSM-V

Demens ersätts med begreppet neurokognitiv störning

WHO

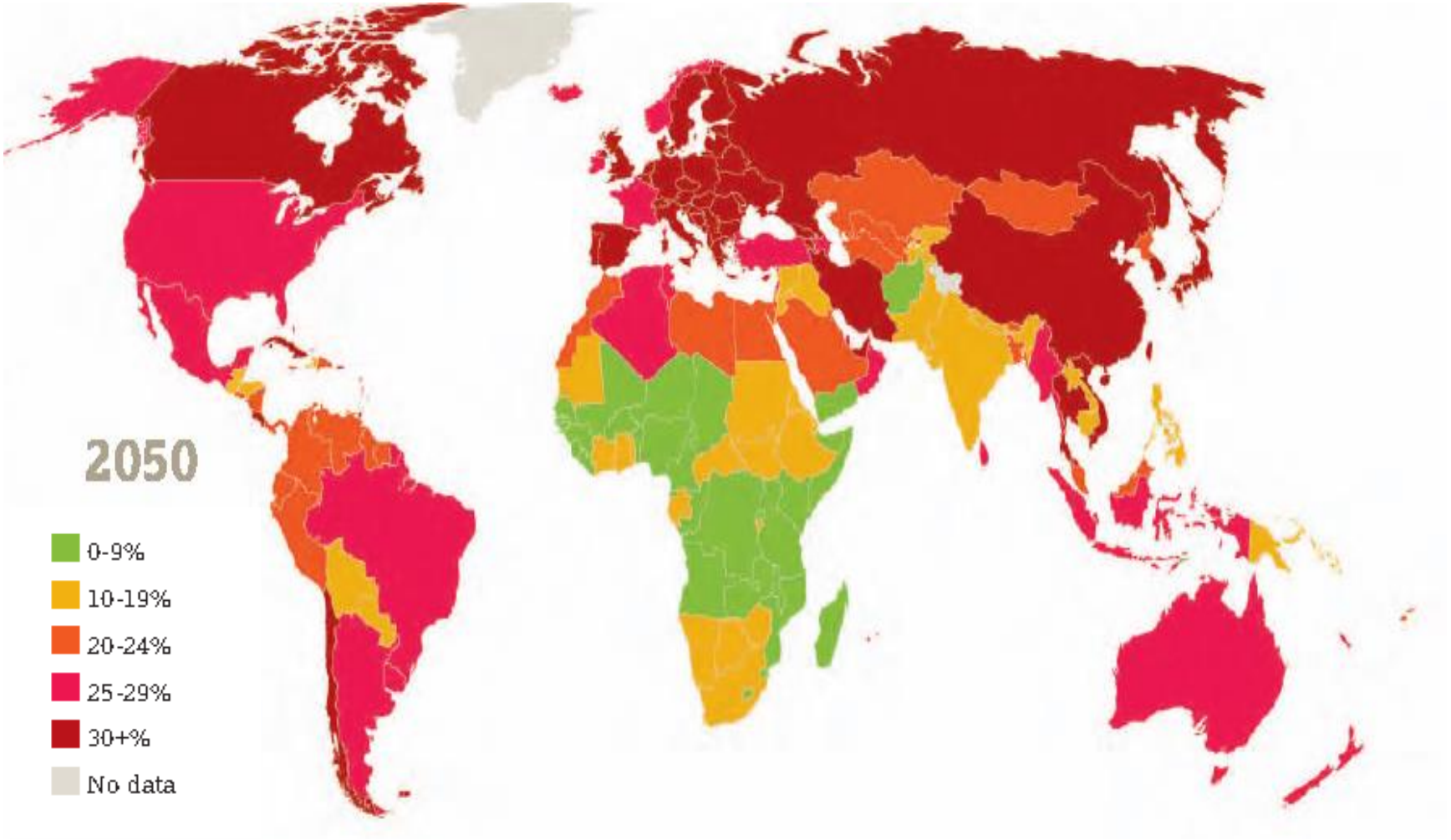
Dementia is a syndrome – usually of a chronic or progressive nature – in which there is deterioration in cognitive function (i.e. the ability to process thought)

beyond what might be expected from normal ageing.

Typ av “ demenssjukdomar “

- Alzheimers sjukdom 55 - 75 %
- Vaskulär demens 20 - 30 %
- Mixed (Alzheimer/vaskulär demens)
- Frontallobsdemens
- Sekundära demenssjukdomar
  - -Bristsjukdomar
  - -Infektioner
  - -Hjärntumörer
  - -Skalltrauma

The prevalence of dementia



Source: UNDESA Population Division, Population Ageing and Development 2012, Wall Chart, 2012

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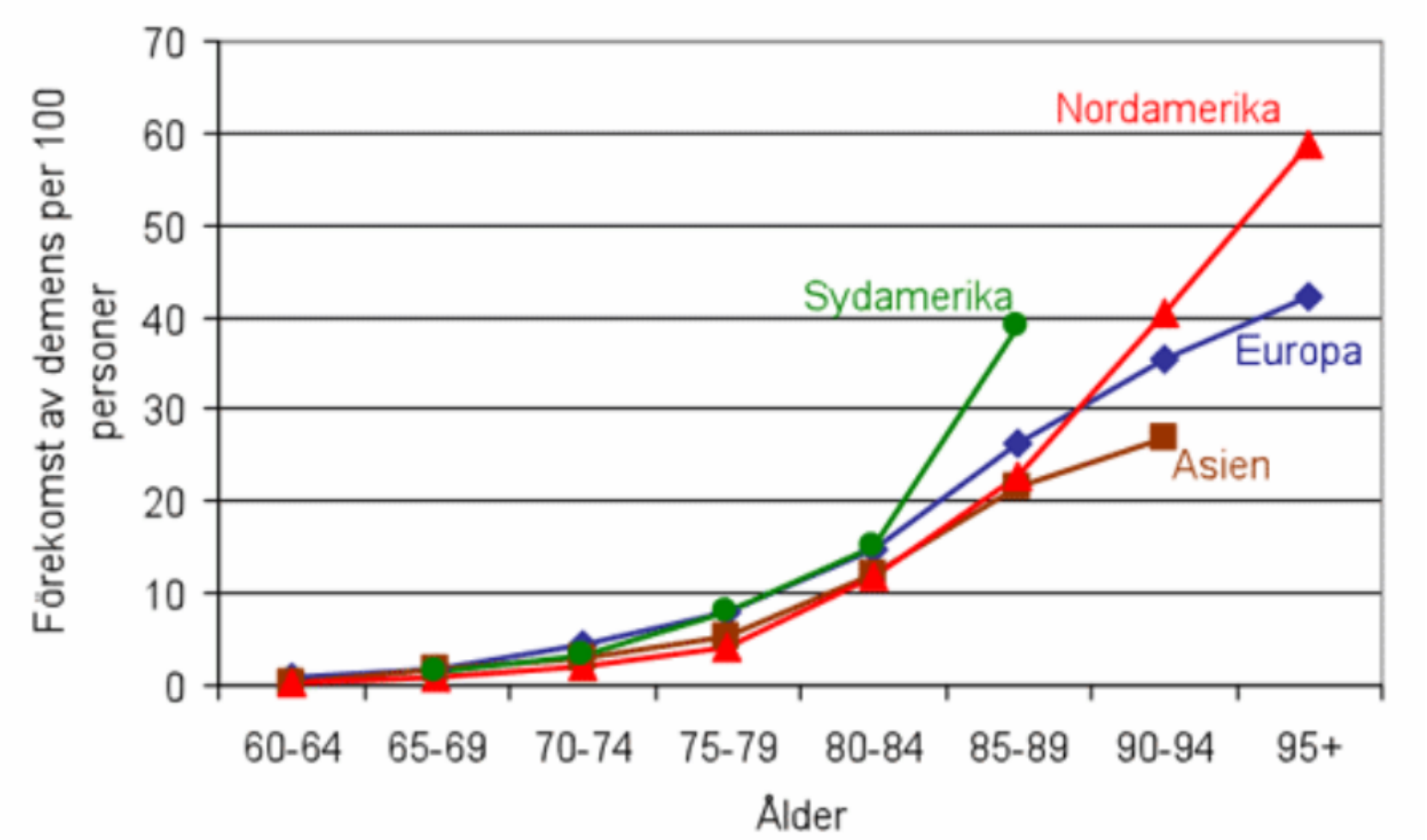
Ökad risk med stigande ålder

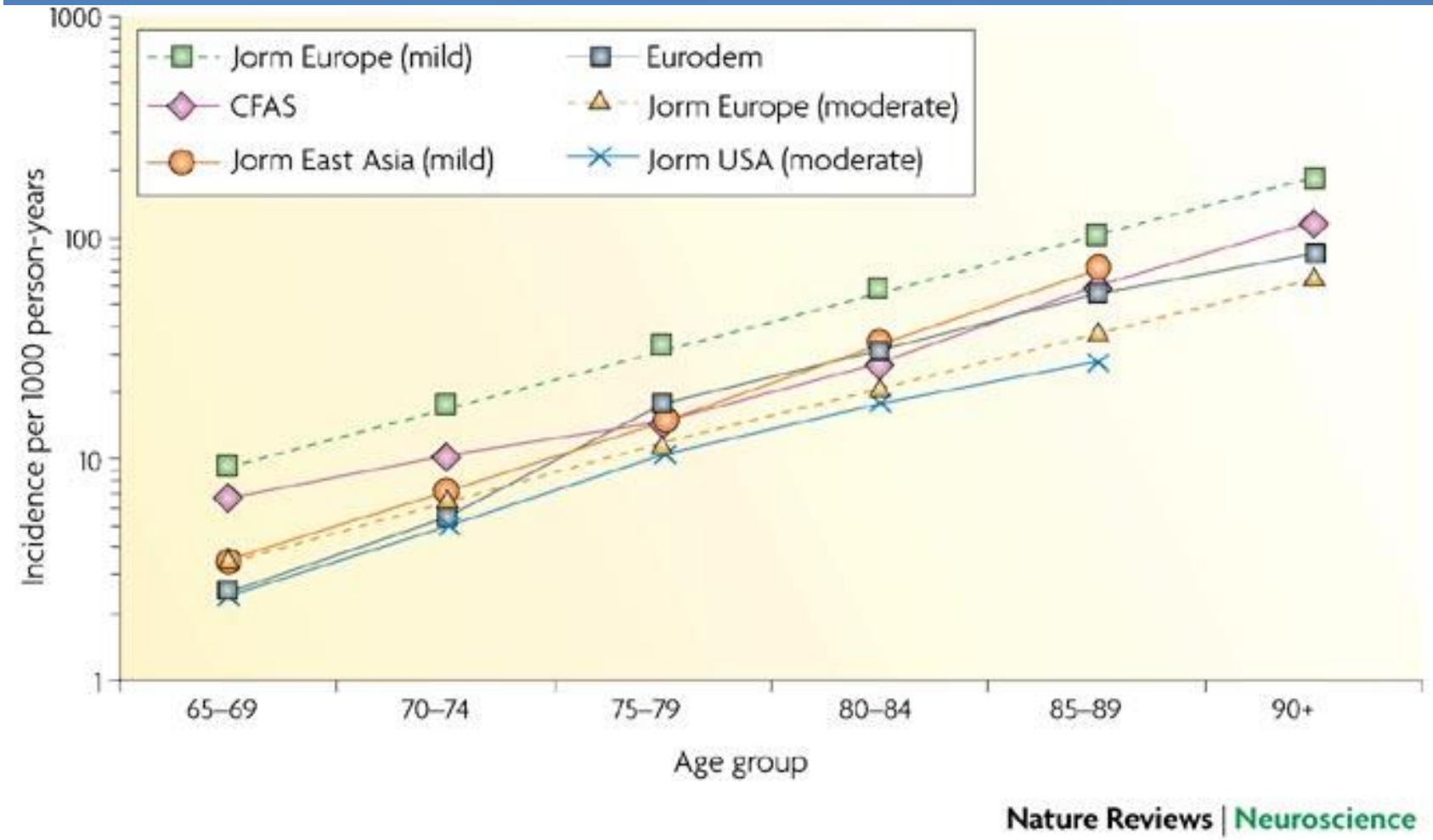


von Strauss E, et.al.: Nosology and epidemiology- Occurrence. In: The Swedish Council on Technology Assessment in Health Care (Eds.) Dementia – etiology and epidemiology. A systematic review.

ADA-GERO

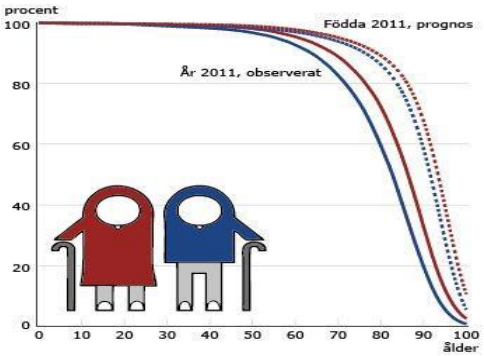
Incidence rates of dementia

in the UK compared with meta-analysis results in Europe and worldwide



Brayne *Nature Reviews Neuroscience* **8**, 233–239 (March 2007) | doi:10.1038/nrn2091

UNIVERSITY OF GOTHENBURG



Ett pris för den rektangulariserade överlevnadskurvan ??

En motbild ?

Fredag 10 november 2000

101-åring firade i hembygdsgården

■ I många år var Bror Andersson hembygdsföreningen i Hovslätt. Han var med och bildade föreningen och fungerade som dess kassör i hela 42 år.

När Bror på torsdagen fyllde 101 år blev det självklart ett besök i hembygdsgården.

– Det tillsammans med vännerna i "Samtal kring kaffet". Ett gäng glada pensionärer som under Margareta Kilands ledning träffas varannan vecka för att dela minnesbilder och framtidsyner.

– Bror har så mycket att dela med sig av, säger Margareta.

Hör dåligt gör Bror men huvudet är med.

– Överkroppen är inte gammal, säger födelsedagsbarnet. Jag minns bra.

Just den här dagen är samtalsämnena gamla skolminnen och vad mamma har betytt för deltagarna kring kaffebordet.

Bror deltar i samtalet, det blir mycket skratt och gemensamma minnen. Han, precis som de andra, har varit Hovslätt trogen nästan hela livet. På ett eller annat sätt.

Tårta, blommor och lite lagom uppvaktning blir det självklart också. Det är inte varje dag man har en 101-åring att fira!

ANETTE SVENSSON

Tillbaka i hembygdsparken. *Med blommor, tårta och gamla minnen firade Bror Andersson i Hovslätt på torsdagen sin 101-årsdag. I hembygdsparken med vännerna som träffas för "Samtal kring kaffet".*

Foto: Anette Svensson

Vården riskerar kollapsa när allt fler blir demenа

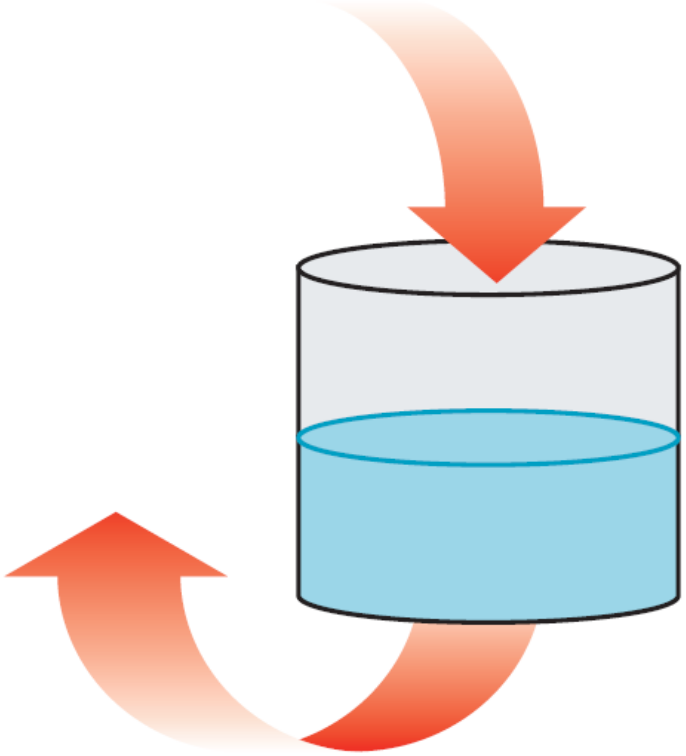
PUBLICERAD 2016-03-15

Foto: Jessica Gow/TT

Det stadigt ökande antalet demenssjuka kan orsaka kaos i sjukvården. Varningen kommer från en internationell forskargrupp som publicerar en omfattande rapport i medicintidskriften The Lancet Neurology på tisdagen, skriver Ekot på Sveriges radio.

ADA-GERO

Incidence: proportion of new dementia cases



Prevalence: proportion of people with dementia

Mortality: proportion of people who die

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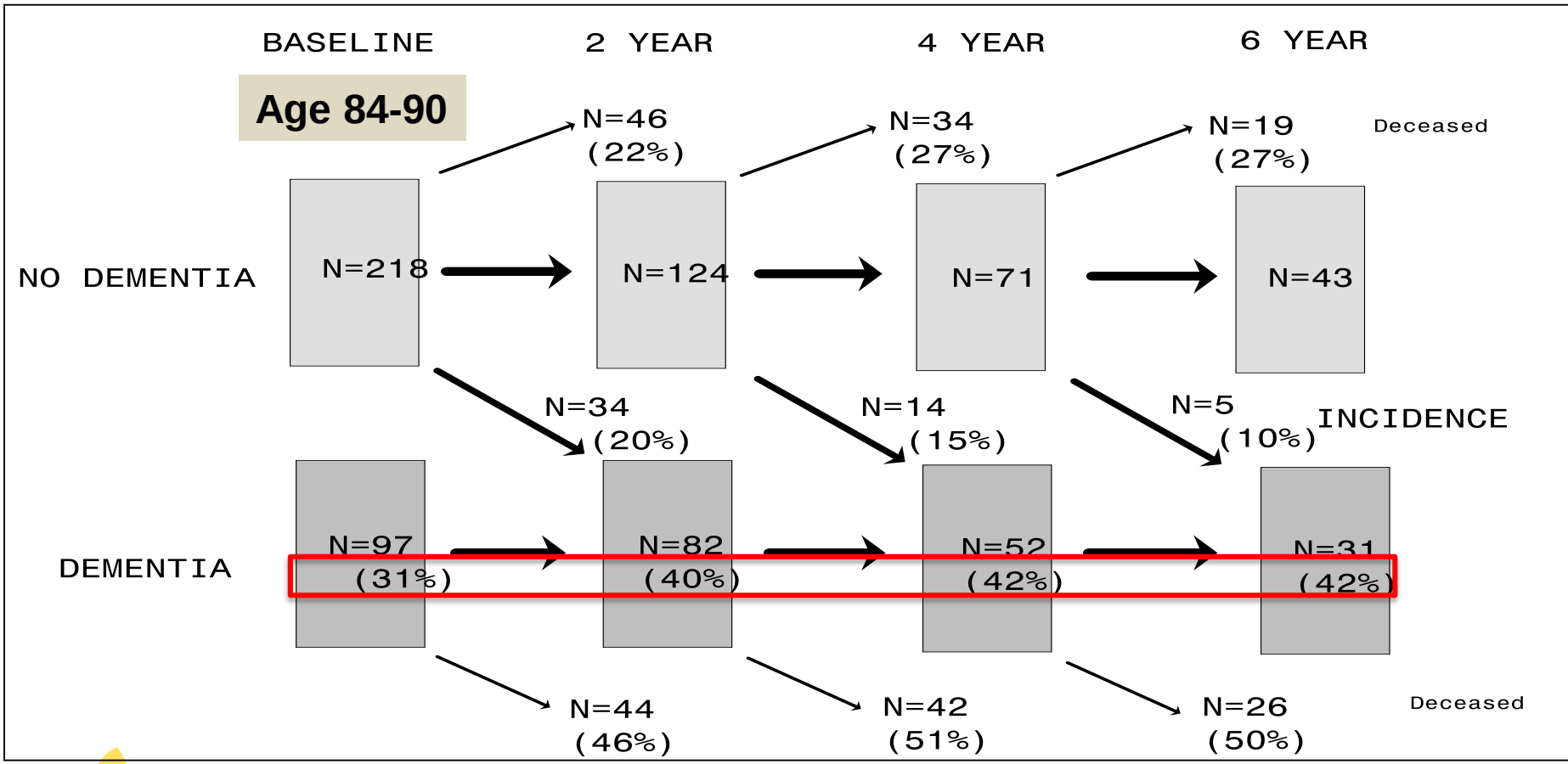
INTERNATIONAL JOURNAL OF GERIATRIC PSYCHIATRY, VOL. 12: 53–59 (1997)

EARLY COGNITIVE MARKERS OF THE INCIDENCE OF DEMENTIA AND MORTALITY: A LONGITUDINAL POPULATION-BASED STUDY OF THE OLDEST OLD

BOO JOHANSSON
Institute of Gerontology, University College of Health Sciences, Jönköping, Sweden
STEVEN H. ZARIT
Gerontology Center, College of Health and Human Development, The Pennsylvania State University, USA.

ABSTRACT

This study examines whether cognitive markers at prior examinations are indicative of subsequent dementia and mortality. The sample was composed of subjects aged 84–90 at baseline who were reexamined three times over a 6-year period on a comprehensive biobehavioral battery. Dementia was evaluated at each examination using DSM–III-R criteria. Results indicated that incident cases of dementia had lower cognitive scores both 2 and 4 years prior to diagnosis, compared to non-demented survivors. Evidence for terminal decline was also found, as people who subsequently died also had lower cognitive performance at prior examinations, compared to non-demented survivors. The findings suggest that mild cognitive dysfunction is an important clinical finding among the oldest old and may herald either the onset of dementia or mortality.



ADA-GERO

Förekomst av demenssjukdom resp. "icke-demens"

Ålder 95 = **52 %** (män 37,3; kvinnor 55,5%)

Börjesson et al, 204

Ålder 100 = **51%** **25%** **inga tecken på demens**

Andersen Ranberg,2001

ORIGINAL ARTICLE

Role of Genes and Environments for Explaining Alzheimer Disease

Margaret Gatz, PhD; Chandra A. Reynolds, PhD; Laura Fratiglioni, MD, PhD; Boo Johansson, PhD; James A. Mortimer, PhD; Stig Berg, PhD; Amy Fiske, PhD; Nancy L. Pedersen, PhD

Context: Twin studies using selected samples have shown high heritability for Alzheimer disease (AD).

Objective: To evaluate genetic and environmental influences on AD in a fully ascertained population of older twins, including like- and unlike-sex pairs.

Design: Five-group quantitative genetic model: male monozygotic twins, female monozygotic twins, male dizygotic twins, female dizygotic twins, and unlike-sex twins.

Setting and Participants: All twins in the Swedish Twin Registry aged 65 years and older. The study included 11 884 twin pairs, among whom were 392 pairs in which 1 or both members had AD.

Main Outcome Measures: All individuals were screened for cognitive dysfunction. Suspected cases of dementia and their co-twins received complete clinical diagnostic evaluations for AD. Estimates of heritability, shared environmental influences, and nonshared environmental influences, adjusting for age, were derived from the twin data.

Results: Heritability for AD was estimated to be 58% in the full model and 79% in the best-fitting model, with the balance of variation explained by nonshared environmental influences. There were no significant differences between men and women in prevalence or heritability after controlling for age. Within pairs concordant for AD, intrapair difference in age at onset was significantly greater in dizygotic than in monozygotic pairs, suggesting genetic influences on timing of the disease.

Conclusions: In the largest twin study to date, we confirmed that heritability for AD is high and that the same genetic factors are influential for both men and women. However, nongenetic risk factors also play an important role and might be the focus for interventions to reduce disease risk or delay disease onset.

Arch Gen Psychiatry. 2006;63:168-174

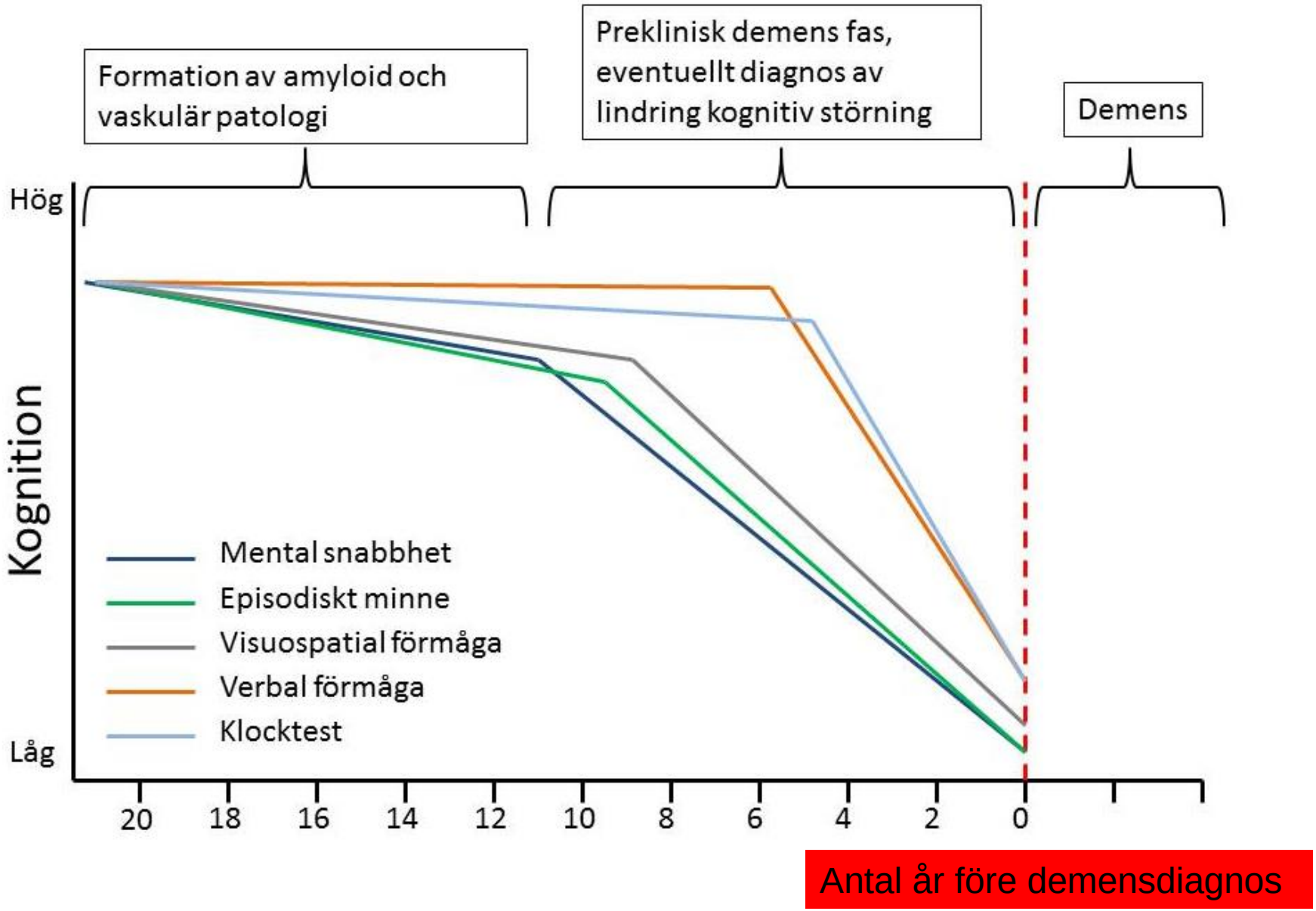
How Heritable Is Alzheimer's Disease Late in Life? Findings from Swedish Twins

Nancy L. Pedersen, PhD,[1,2] Margaret Gatz, PhD,[1,2] Stig Berg, PhD,[2,3] and Boo Johansson, PhD[3,4]

Although genetic effects are known to be important for early onset Alzheimer's disease, little is known about the importance of genetic effects for late-onset disease. Furthermore, previous studies are based on prevalent cases. Our purpose was to characterize the relative importance of genetic and environmental factors for incident Alzheimer's disease late in life, and to test for differences in the importance of genetic effects at different ages. A cohort of [illegible] twins 52 to 98 years of age who were without symptoms of dementia [illegible] incident dementia cases were detected through follow-up [illegible] cognitive testing or telephone screening followed by [illegible] psychologist, and nurse gave consensus diagnoses. During the follow[illegible] was diagnosed with Alzheimer's disease. Average age of onset was 83.9 years (standa[illegible], 6.5). Of the 26 monozygotic pairs in which at least one twin developed Alzheimer's disease, 5 were concordant (probandwise concordance, 32.2%). The concordance rate for dizygotic pairs was 8.7% (2 of 44 pairs). Structural model fitting indicated that 48% of the variation in liability to Alzheimer's disease could be attributed to genetic variation. Estimates did not differ significantly between twins younger than age 80 years and those older than age 80 years at baseline. Although these genetic estimates for incident disease are lower than those for prevalent disease, the importance of genetic factors for liability to Alzheimer's disease is considerable even late in life.

Ärftligheten för incident demens är hög även efter 80 – ung. 48%

Ann Neurol 2004;55:180–185


Formation av amyloid och vaskulär patologi
Preklinisk demens fas, eventuellt diagnos av lindring kognitiv störning
Demens
Hög
Kognition
Låg
Mental snabbhet
Episodiskt minne
Visuospatial förmåga
Verbal förmåga
Klocktest
20
18
16
14
12
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8
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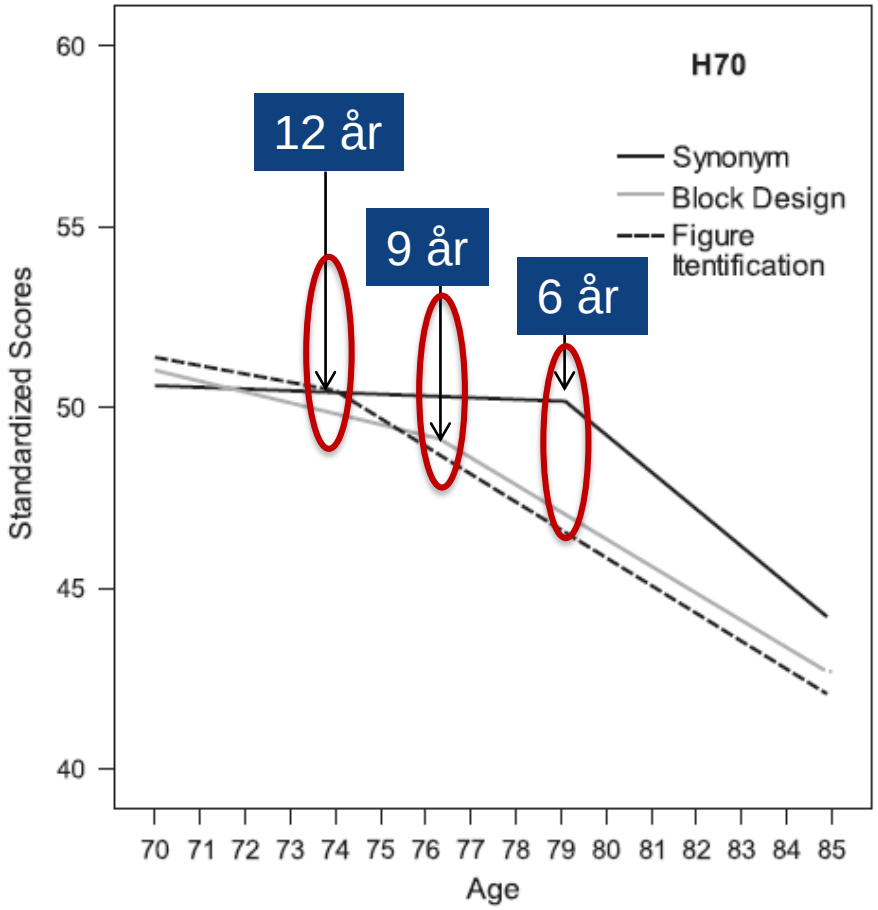
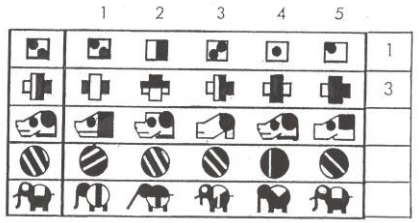
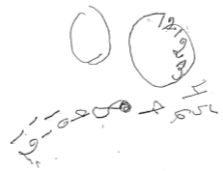
4
2
0
Antal år före demensdiagnos

Accelererad kognitiv försämring innan demensdiagnos







SE — antaga titta läsa finna göra

Fig. 1. Estimated average cognitive change trajectories before diagnosis of dementia for a prototypical individual diagnosed at age 85. The estimates are from the H70.

ADA-GERO

Journal of the International Neuropsychological Society (2011), **17**, 1–9.

doi:10.1017/S1355617710001372

Onset and Rate of Cognitive Change Before Dementia Diagnosis: Findings From Two Swedish Population-Based Longitudinal Studies

Valgeir Thorvaldsson,[1] Stuart W. S. MacDonald,[2,3] Laura Fratiglioni,[2] Bengt Winblad,[2] Miia Kivipelto,[2] Erika Jonsson Laukka,[2] Ingmar Skoog,[4] Simona Sacuiu,[4] Xinxin Guo,[4] Svante Östling,[4] Anne Börjesson-Hanson,[4] Deborah Gustafson,[4] Boo Johansson,[1] AND Lars Bäckman[2]

[1]Department of Psychology, University of Gothenburg, Gothenburg, Sweden
[2]Aging Research Center, Karolinska Institute, Stockholm, Sweden
[3]Department of Psychology, University of Victoria, Victoria, British Colombia, Canada
[4]Neuropsychiatric Epidemiology Unit, Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

(RECEIVED March 16, 2010; FINAL REVISION October 8, 2010; ACCEPTED October 8, 2010)

Abstract

We used data from two population-based longitudinal studies to estimate time of onset and rate of accelerated decline across cognitive domains before dementia diagnosis. The H70 includes an age-homogeneous sample (127 cases and 255 non-cases) initially assessed at age 70 with 12 follow-ups over 30 years. The Kungsholmen Project (KP) includes an age-heterogeneous sample (279 cases and 562 non-cases), with an average age of 82 years at initial assessment, and 4 follow-ups spanning 13 years. We fit mixed linear models to the data and determined placement of change points by a profile likelihood method. Results demonstrated onset of accelerated decline for fluid (speed, memory) *versus* crystallized (verbal, clock reading) abilities occurring approximately 10 and 5 years before diagnosis, respectively. Although decline before change points was greater for fluid abilities, acceleration was more pronounced for crystallized abilities after the change points. This suggests that onset and rate of acceleration vary systematically along the fluid-crystallized ability continuum. There is early onset in fluid abilities, but these changes are difficult to detect due to substantial age-related decline. Onset occurred later and acceleration was greater in crystallized abilities, suggesting that those markers may provide more valid identification of cases in later stages of the prodromal phase. (*JINS*, 2011, *17*, 000–000)

Change points identified 5-10 years before the onset of dementia

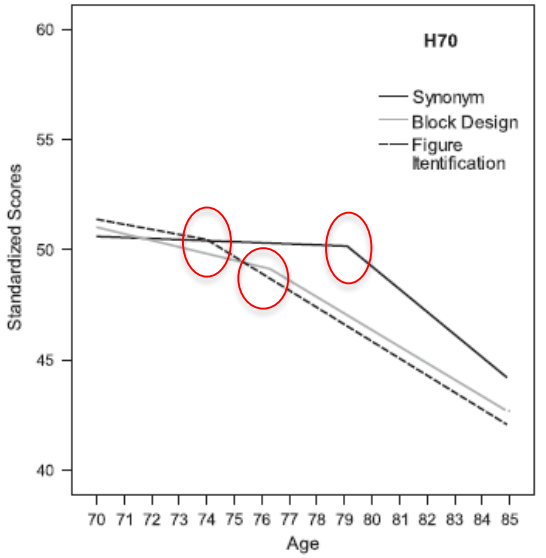


Fig. 1. Estimated average cognitive change trajectories before diagnosis of dementia for a prototypical individual diagnosed at age 85. The estimates are from the H70.

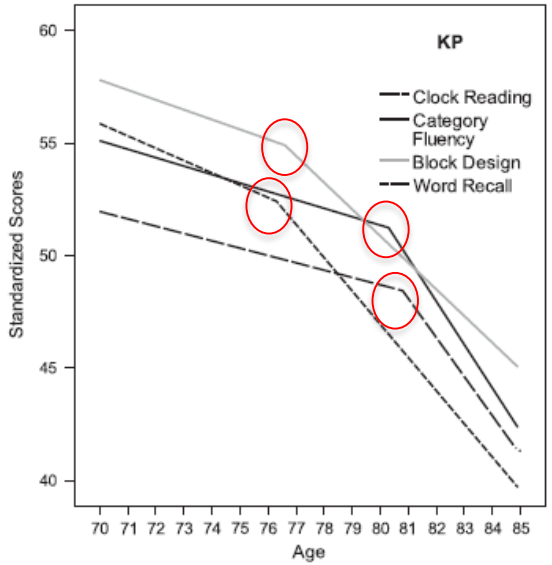


Fig. 2. Estimated average cognitive change trajectories before diagnosis of dementia for a prototypical individual diagnosed at age 85. The estimates are from the KP.

Physical Exercise at Midlife and Risk of Dementia Three Decades Later: A Population-Based Study of Swedish Twins

Ross Andel,[1] Michael Crowe,[2] Nancy L. Pedersen,[3,4] Laura Fratiglioni,[5] Boo Johansson,[6] and Margaret Gatz[3,4]

[1]School of Aging Studies and Florida Alzheimer's Disease Center, University of South Florida, Tampa.
[2]Department of Psychology, University of Alabama at Birmingham.
[3]Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden.
[4]Department of Psychology, University of Southern California, Los Angeles.
[5]Aging Research Center, Karolinska Institutet, Stockholm, Sweden.
[6]Department of Psychology, Göteborg University, Sweden.

Background. With the number of people with dementia increasing, identifying potential protective factors has become more important. We explored the association between physical exercise at midlife and subsequent risk of dementia among members of the HARMONY study.

Methods. Measures of exercise were obtained by the Swedish Twin Registry an average of 31 years prior to dementia assessment. Dementia was diagnosed using a two-stage procedure—screening for cognitive impairment followed by full clinical evaluation. We used two study designs: case–control analyses included 266 cases with dementia (176 had Alzheimer's disease) and 2870 controls; co-twin control analyses included 90 twin pairs discordant for dementia.

Results. In case–control analyses, controlling for age, sex, education, diet (eating fruits and vegetables), smoking, drinking alcohol, body mass index, and angina, light exercise such as gardening or walking and regular exercise involving sports were associated with reduced odds of dementia compared to hardly any exercise (odds ratio [OR] = 0.63, 95% confidence interval [CI], 0.43–0.91 for light exercise; OR = 0.34, 95% CI, 0.16–0.72 for regular exercise). Findings were similar for Alzheimer's disease alone. In co-twin control analyses, controlling for education, the association between higher levels of exercise and lower odds of dementia approached significance (OR = 0.50, 95% CI, 0.23–1.06; $p = .072$).

Conclusions. Exercise at midlife may reduce the odds of dementia in older adulthood, suggesting that exercise interventions should be explored as a potential strategy for delaying disease onset.

Key Words: Exercise—Dementia—Twins—Sweden.

Complexity of Work and Risk of Alzheimer Disease: A Population-Based Study of Swedish Twins

Ross Andel,[1] Michael Crowe,[2] Nancy L. Pedersen,[3,7] James Mortimer,[4] Eileen Crimmins,[5] Boo Johansson,[6] and Margaret Gatz[3,7]

Journal of Gerontology: PSYCHOLOGICAL SCIENCES
2003, Vol. 58B, No. 5, P249–P255

Does Participation in Leisure Activities Lead to Reduced Risk of Alzheimer's Disease? A Prospective Study of Swedish Twins

Michael Crowe,[1] Ross Andel,[2] Nancy L. Pedersen,[1,3] Boo Johansson,[4] and Margaret Gatz[1,3]

[1]Department of Psychology and [2]Leonard Davis School of Gerontology, University of Southern California.
[3]Department of Medical Epidemiology, Karolinska Institutet, Stockholm, Sweden.
[4]Department of Psychology, University of Göteborg, Sweden.

This study examined whether participation in leisure activities during early and middle adu[lthood] with reduced risk of Alzheimer's disease. The sample consisted of 107 same-sex twi[n pairs] and for whom information on leisure activities was self-reported more th[an 30] factor analysis of these activities yielded three activity fac[tors:] domestic activity. Matched-pair analyses compared [twins] for level of education. For the total sam[ple,] associated with lower risk of [dementia] intellectual–cultural [activities] men.

Journal of Gerontology: PSYCHOLOGICAL SCIENCES
2001, Vol. 56B, No. 5, P292–P300

Education and the Risk of Alzheimer's Disease: Findings From the Study of Dementia in Swedish Twins

Margaret Gatz,[1,2] Pia Svedberg,[2] Nancy L. Pedersen,[1,2] James A. Mortimer,[3] Stig Berg,[1,4] and Boo Johansson[4]

[1]Department of Psychology, University of Southern California, Los Angeles.
[2]Department of Medical Epidemiology, The Karolinska Institute, Stockholm, Sweden.
[3]Institute on Aging, University of South Florida, Tampa.
[4]Institute of Gerontology, Jönköping, Sweden.

The association between dementia and education was studied in 143 twin pairs discordant for dementia, using a matched-pair design, and in 221 dementia cases and 442 unrelated controls from the same twin registry, using a case-control design. Low education was defined as 6 years or less of schooling. Case-control analyses with prevalent cases showed low education to be a risk for Alzheimer's disease but not dementia in general. Low education did not significantly predict incident cases. In the matched-pairs analysis, which controls for genetic and other familial influences, differences in education between demented twins and twin partners were not statistically significant. However, for Alzheimer's disease, odds ratios resulting from matched pairs and case-control analyses were similar. Twins' comparative reports about intellectual involvement earlier in their lives suggest a long-standing difference on this dimension, with less involvement by the twin who became demented.

Livslång påverkan – bra och dålig

Kaskadmodellen (J. Birren)

Primärt / ”Normalt” åldrande

Sekundärt åldrande

sjukdomsrelaterat

Tertiärt åldrande - terminal nedgång

Psykisk snabbhet
Episodiskt minne
Exekutiv förmåga/ multi-tasking, logisk - spatial förmåga, verbal fluency

Kristalliserade/erfarenhets-baserade förmågor; språk - semantiskt minne

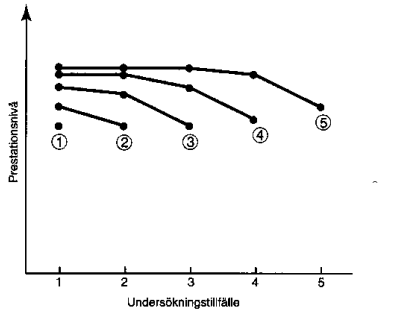
Global kognitiv nedgång =
alla domäner är påverkas

Tertiary aging

Avstånd från död

?

Terminal drop/decline
(*”tertiary aging”*)



1 Individer som medverkat vid tillfälle 1 men som avlidit innan tillfälle 2.
2 Individer som medverkat vid tillfälle 1 och 2, men som avlidit innan tillfälle 3.
3 Individer som medverkat vid tillfälle 1, 2 och 3 men som avlidit innan tillfälle 4.
4 Individer som medverkat vid tillfälle 1, 2, 3 och 4, men som avlidit innan tillfälle 5.
5 Individer som medverkat vid alla tillfällen.

Figur 6.10 Typfigur – "terminal decline". Kognitiv prestationsnivå, longitudinellt, för individer med olika överlevnad.

Example

Onset of terminal decline in cognitive abilities in individuals without dementia

V. Thorvaldsson, MSc
S.M. Hofer, PhD
S. Berg, PhD
I. Skoog, MD, PhD
S. Sacuiu, MD
B. Johansson, PhD

Address correspondence and reprint requests to Dr. Valgeir Thorvaldsson, Department of Psychology, Göteborg University, Box 500, SE-405 30 Göteborg, Sweden
valgeir.thorvaldsson@psy.gu.se

ABSTRACT

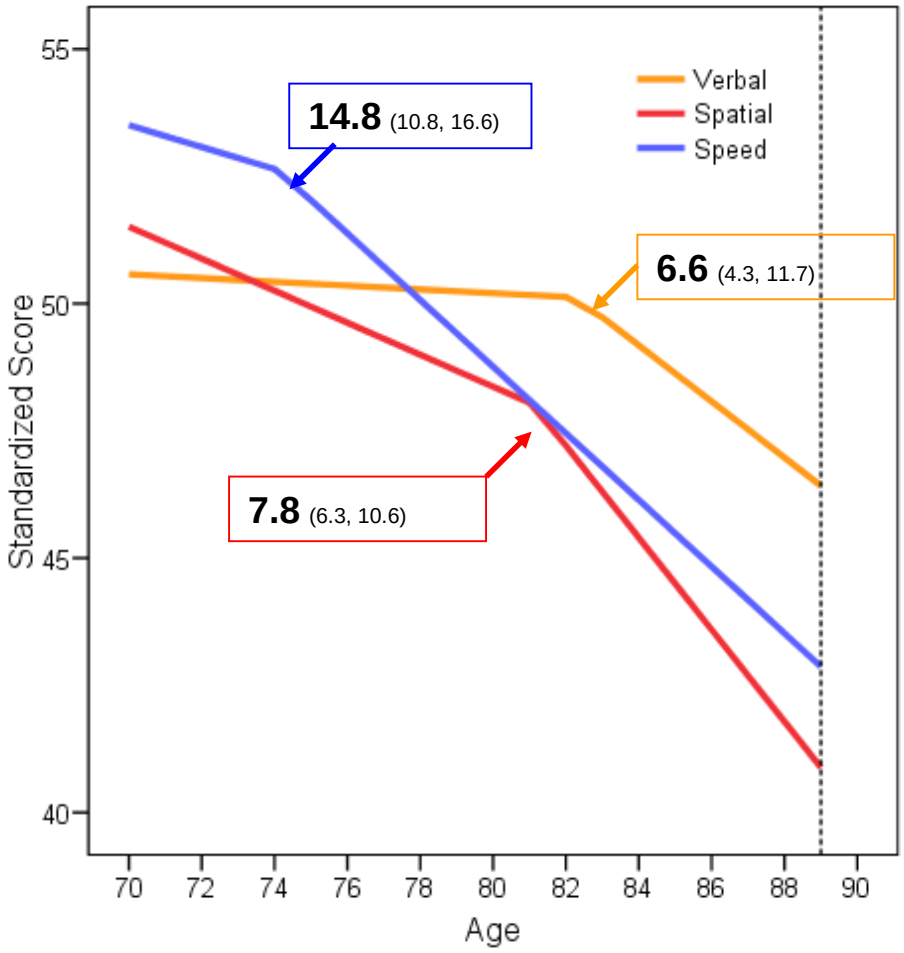
Objective: To identify time of onset and rate of mortality-related change (terminal decline) in cognitive abilities in later life.

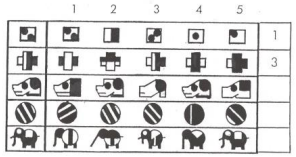
Method: The sample consisted of 288 individuals without dementia (born 1901–1902) drawn from the population of Göteborg, Sweden. Participants were followed from age 70 until death, with up to 12 measurement occasions on three cognitive abilities. Change-point analysis was performed using an automated piecewise linear mixed modeling approach to identify the inflection point indicating accelerated within-person change related to mortality. A profile likelihood method was used to identify the change point that best fit the data for each of three cognitive abilities.

Results: Onset of terminal decline was identified 6.6 years prior to death for verbal ability, 7.8 years for spatial ability, and 14.8 years for perceptual speed.

Conclusions: There is substantial acceleration in cognitive decline many years prior to death among individuals without dementia. Time of onset and rate of terminal decline vary considerably across cognitive abilities. *Neurology*® 2008;71:882–887

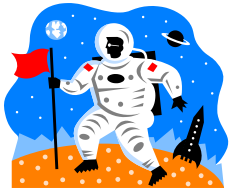
Tid innan död och accelererad kognitiv nedgång





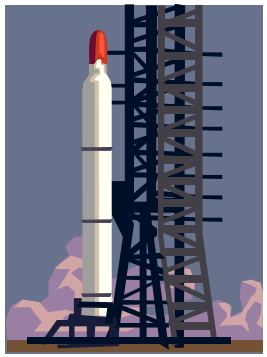
SE — antaga titta läsa finna göra

Thorvaldsson, V., Hofer, S. M., Berg, S., Skoog, I., Sacuiu, S., & Johansson, B. (2008). Onset of terminal decline in cognitive abilities in non-demented individuals. Neurology.

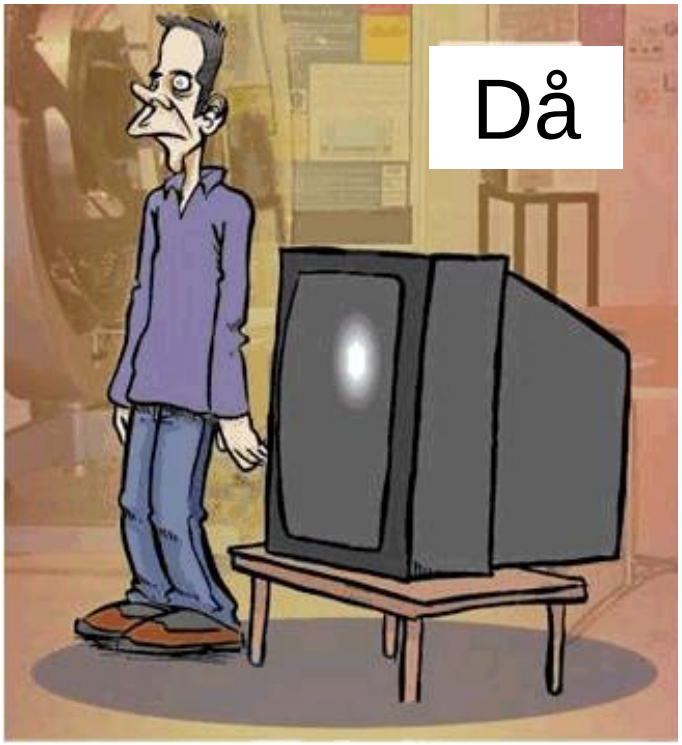


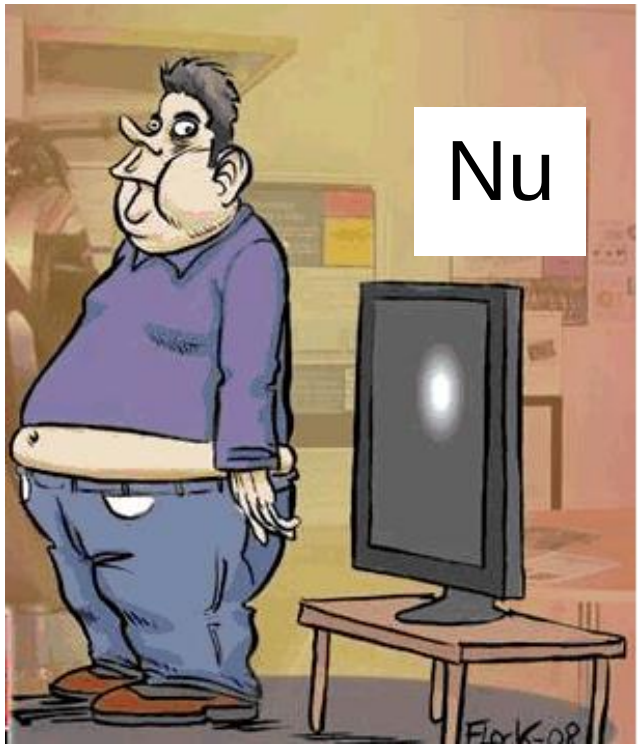
Generations och kohort effekter

samlat uttryck för att olika generationer / födelsekohorter ”exponerats” för skilda miljöbetingelser som påverkar överlevnad, hälsa, välbefinnande och funktion



Tiderna förändras och vi med tiden –
födelsekohortperspektiv på åldrande





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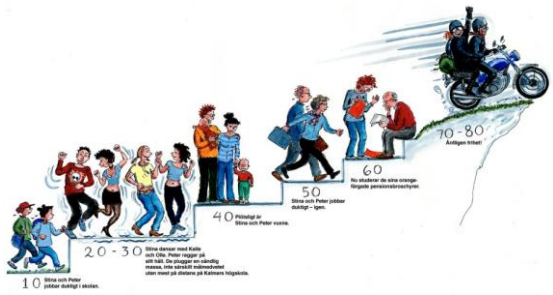
De nya äldre och det nya åldrandet

Rock ´n roll generationen är nu seniorer

70 is the new 50 – ”*hälsa och funktion*”

men

70 det nya 20 – ”*livsstil*”



ADA-GERO

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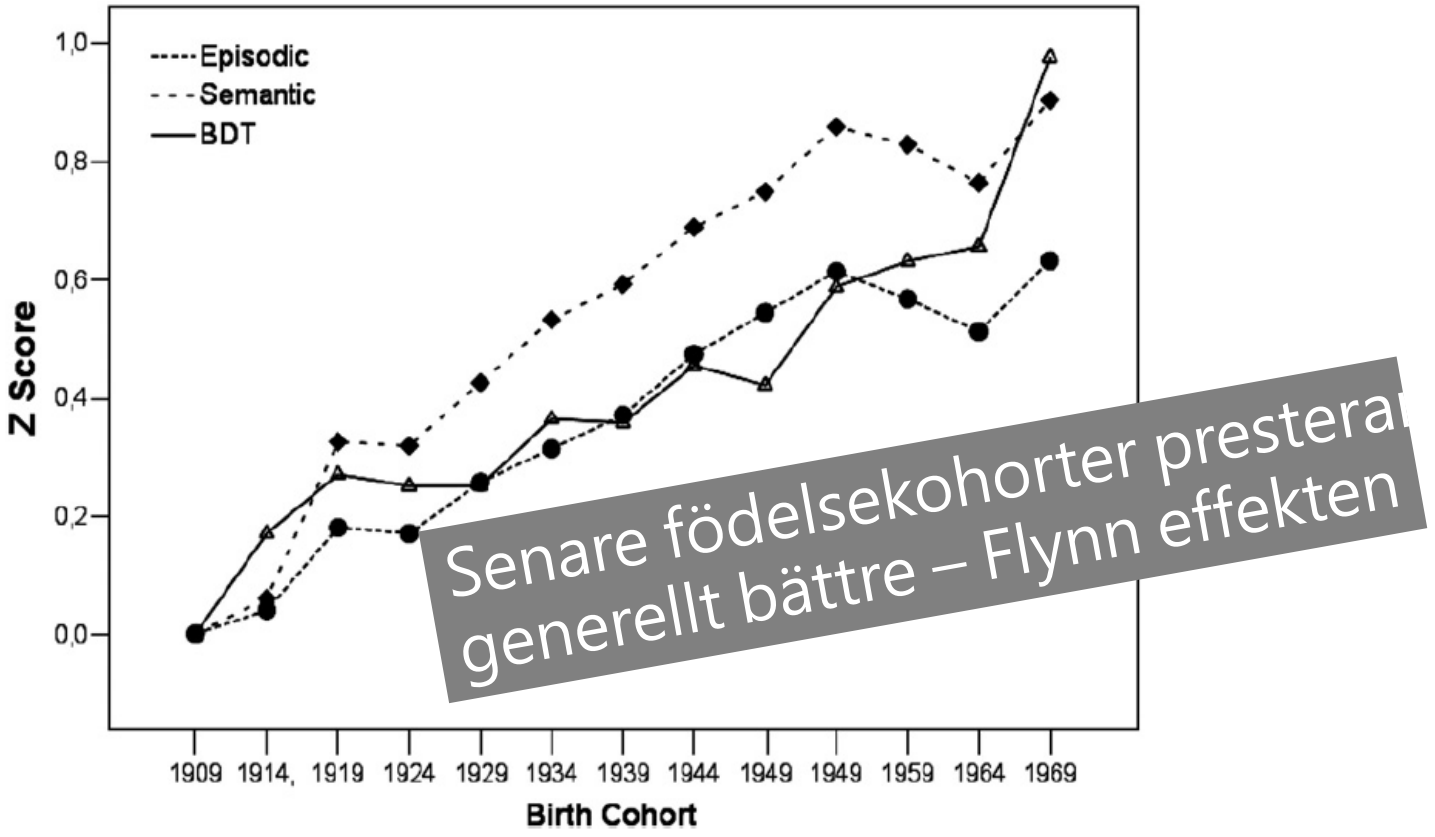
Födelsekohortperspektiv på åldrande och kognitiv funktion

ADA-GERO

Kognitiv förmåga: En jämförelse mellan födelsekohorter

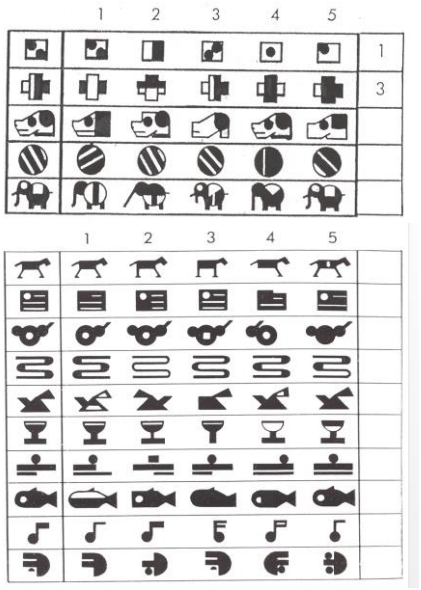
The BETULA Longitudinal Study



Senare födelsekohorter presterar generellt bättre – Flynn effekten

Fig. 3. Cumulative changes (*z*-scores) (1909–1969) on three cognitive factors (episodic memory, semantic memory, visuospatial ability) across birth cohorts.

Psif - Figurklassifikation



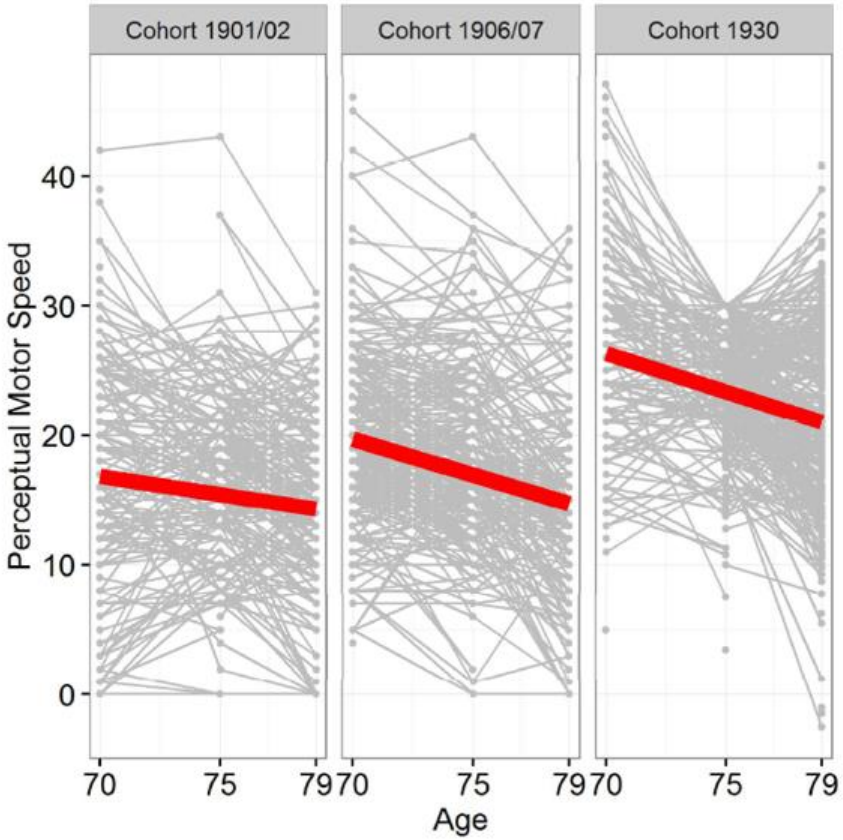


Figure 1. Examples of raw score trajectories for a perceptual motor speed performance in cohorts born 1901/02, 1906/07, and 1930 and examined at ages 70, 75, and 79 in the H70 study. The red lines refer to the estimated average change trajectories (Thorvaldsson, et al. 2017).

2017

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doi:10.1093/geronb/gbw125

OXFORD

Special Issue: Cognitive Aging: Original Research Report

Better Cognition in New Birth Cohorts of 70 Year Olds, But Greater Decline Thereafter

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Decision Editor: Nicole D. Anderson, PhD

Abstract

Objectives: To evaluate birth cohort differences in level of cognition and rate of change in old age.

Methods: Data were drawn from three population-based Swedish samples including age-homogenous cohorts born 1901/02, 1906/07, and 1930, and measured on the same cognitive tests at ages 70, 75, and 79 as part of the Gerontological and Geriatric Populations Studies in Gothenburg (H70). We fitted growth curve models to the data using a Bayesian framework and derived estimates and inferences from the marginal posterior distributions.

Results: We found moderate to large birth cohort effects in level of performance on all cognitive outcomes. Later born cohorts, however, showed steeper linear rate of decline on reasoning, spatial ability, and perceptual- and motor-speed, but not on picture recognition memory and verbal ability.

Discussion: These findings provide strong evidence for substantial birth cohort effects in cognition in older ages and emphasize the importance of life long environmental factors in shaping cognitive aging trajectories. Inferences from cognitive testing, and standardization of test scores, in elderly populations must take into account the substantial birth cohort differences.

- Strong evidence for substantial birth cohort effects in cognition in older ages
- Emphasize the importance of life-long environmental factors in shaping cognitive aging trajectories.
- Inferences from cognitive testing, and standardization of test scores, need to account for birth cohort differences.

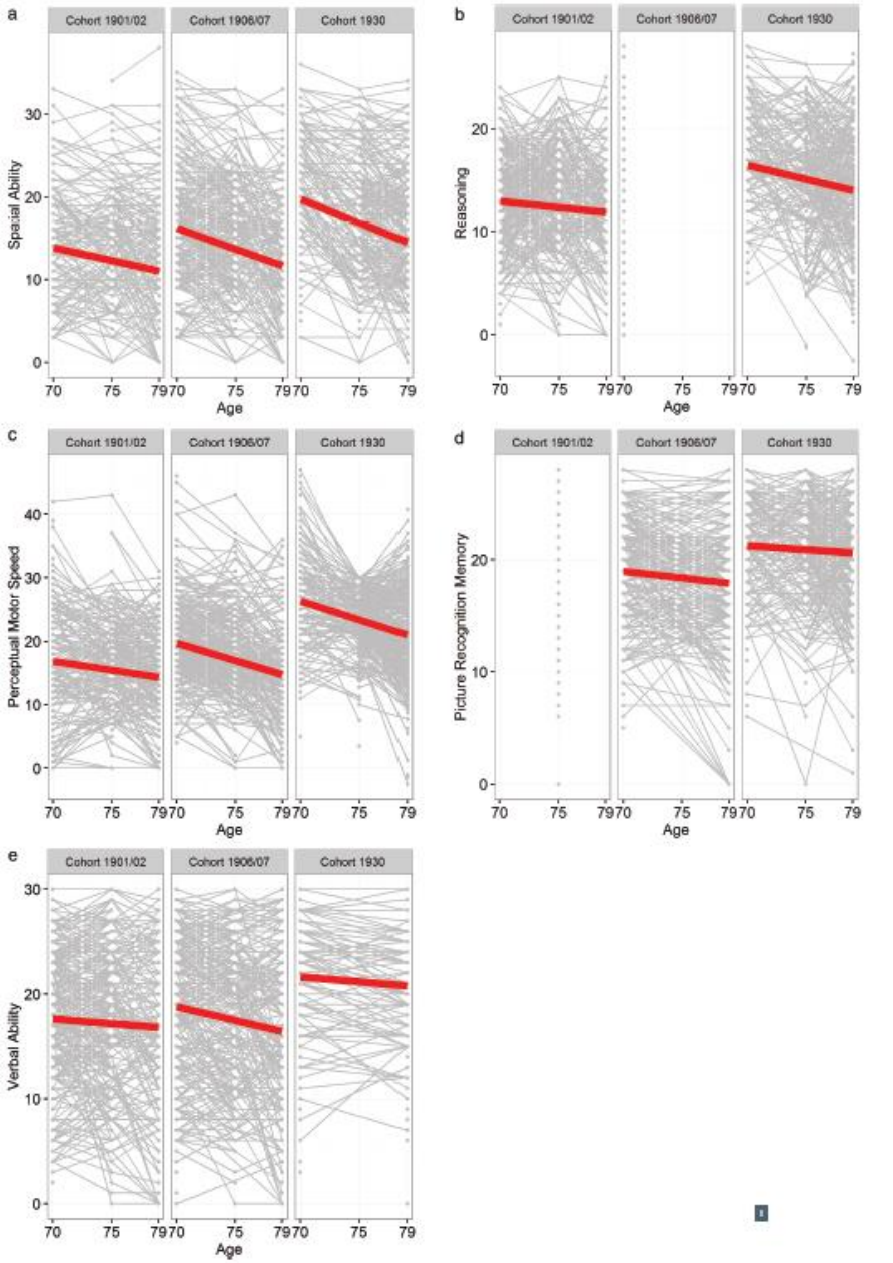


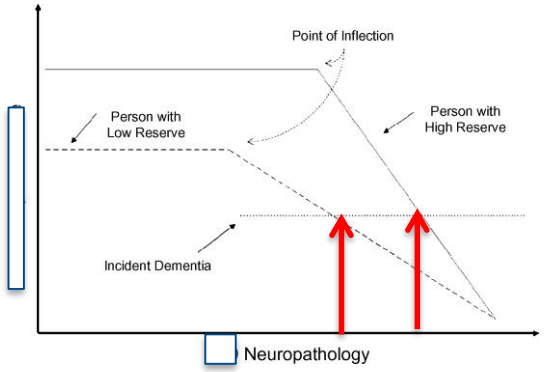
Figure 1. Raw score trajectories from all cognitive tests for cohorts born 1901/02, 1906/07, and 1930 and measured at ages 70, 75, and 79 as part of the H70 study. The bold/red lines refer to the estimated average change trajectories.

Kognitiv reserv

- Skilda förutsättningar att **klara/bemästra/hantera** neurobiologiskt åldrande och åldersrelaterade neuropatologiska förändringar *(Stern, 1999)*
- Utbildning,, intellektuell ”träning”, SES mm – indikatorer för kognitiv reserv
- Individer med högre kognitiv reserv med neuropatologiska förändringar som indikerar pre-klinisk demens / MCI ..
  - har lägre risk att utveckla demenssjukdom

    och/eller

  - visar demenssymtom senare



- än de med lägre kognitiv reserv med likartartade neuropatologiska förändringar

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Kognitiv prestation mellan 70-79 års ålder: En jämförelse mellan tre födelsekohorter (nivå och förändring)


Birth Cohort Differences in Fluid Cognition in Old Age: Comparisons of Trends in Levels and Change Trajectories Over 30 Years in Three Population-Based Samples

Spatial ability

Reasoning

1930

1905/06

1901/02

1930

1901/02

Birth cohort 1901
Birth cohort 1906
Birth cohort 1930

Cognitive measure

20
18
16
14
12
10

70
75
80

Age

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Kognitiv förändring – en kohortjämförelse

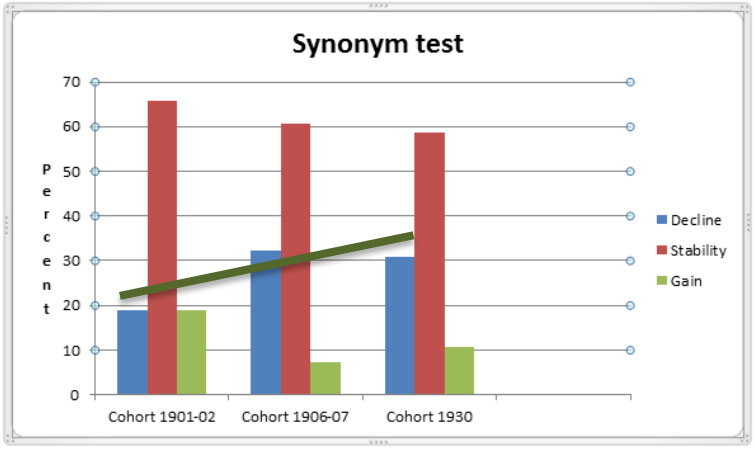

Figure 1 Proportions of participants in each cohort showing cognitive decline, stability or gain from 70 to 79 years on the synonym test.

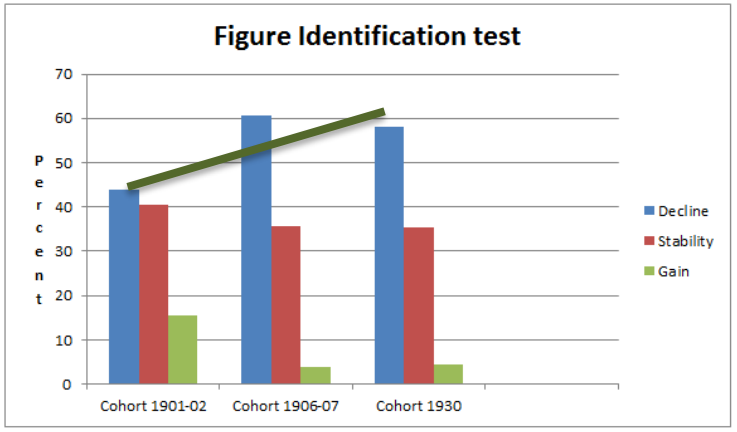

Figure 3 Proportions of participants in each cohort showing cognitive decline, stability or gain from 70 to 79 years on the figure identification test.

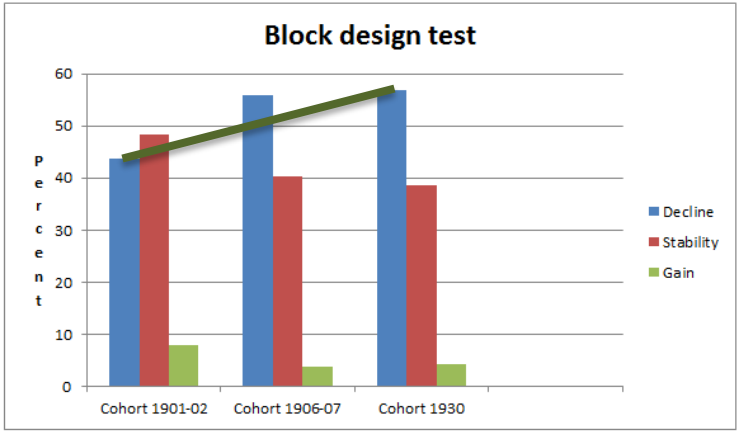

Figure 2 Proportions of participants in each cohort showing cognitive decline, stability or gain from 70 to 79 years on the block design test.

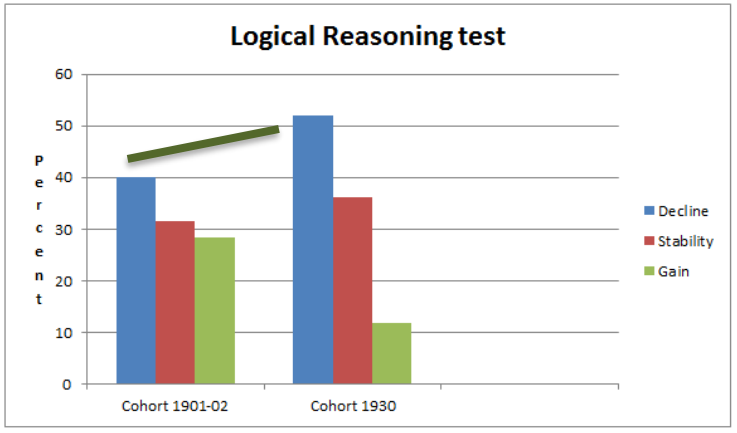

Figure 4 Proportions of participants in each cohort showing cognitive decline, stability or gain from 70 to 79 years on the logical reasoning test.

Äldre födelsekohorter – mindre nedgång 70-79. Större andel stabila eller t.o.m förbättrade.

Kohortskillnader – mindre selektivt urval som överlever till högre ålder och/eller kognitiv reserv

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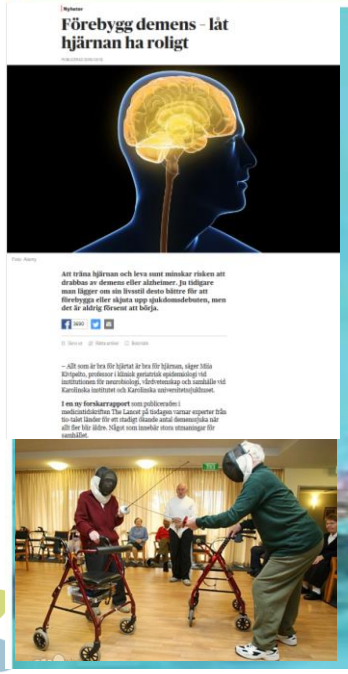
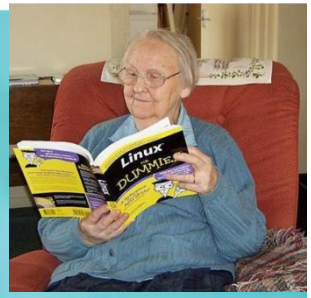
Vad gör vi och vad kan vi göra?

Use it or loose it?

Inga garantier men

Ökat stöd för samband mellan förändring i fysisk, kognitiv och social aktivitet och kognitiv funktion





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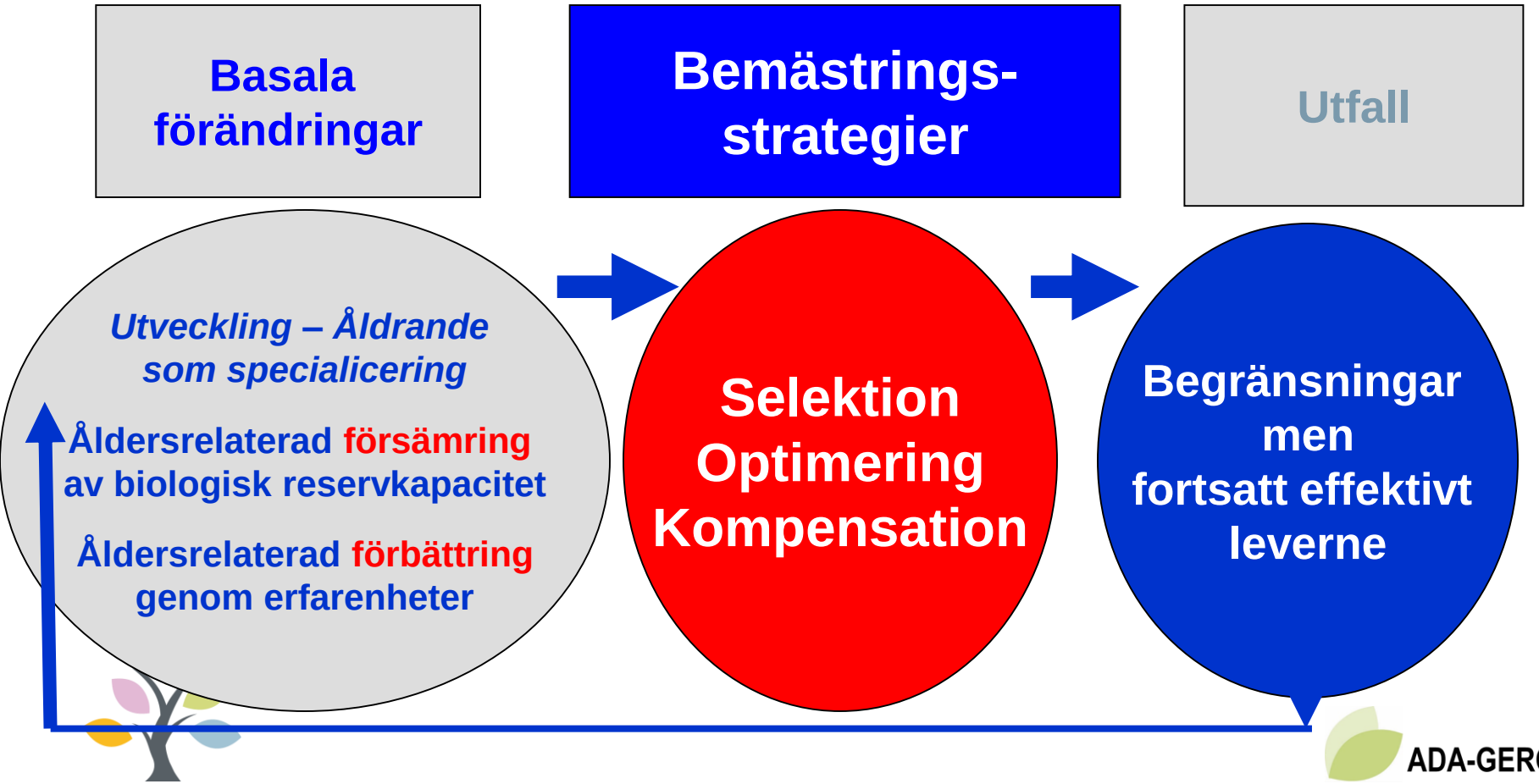
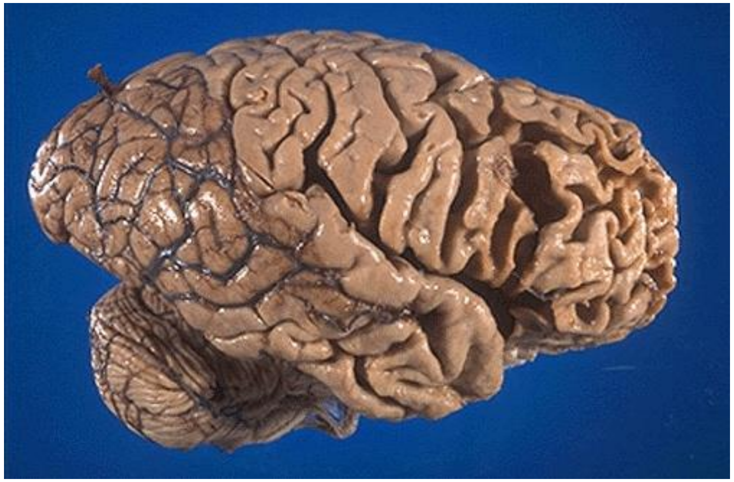
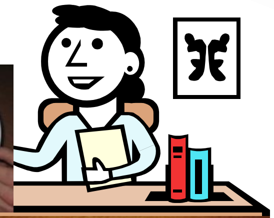
En kognitiv bemästringsmodell - SOC



ADA-GERO

Bedömning och kognitiv utredning





Mini Mental Test/MMT
(Efter Folstein MF et al. J Psychiatr Res 1975;12:189–198)

Testning skall ske utan tidspress eller distraherande moment och med värnande om patientens självkänsla. Vid nedsatt allmäntillstånd, sänkt vakenhetsgrad, grav hörselnedsättning, språksvårigheter eller andra faktorer som kan ge orättvisande resultat bör testningen uppskjutas eller ifrågasättas. Testresultatet ger en objektiv värdering av patientens kognitiva funktioner och kan ge vägledning vid utredning av demens eller demensliknande tillstånd. Vid screeningundersökningar har man använt gränsvärden runt 24 poäng för identifiering av kognitiva störningar. Man har ofta god hjälp av upprepad testning för att följa ett förlopp. Observera att demenssjukdom kan föreligga trots gott resultat vid MMT och att avsevärt poängavdrag vid MMT kan avspegla en depression eller konfusion med reversibel kognitiv svikt. CSK -98.

Uppgifterna i denna MMT-version är huvudsakligen formulerade enligt Svensk Förening för Kognitiva Sjukdomar (SFK). Stockholm feb 2000.

Patientbricka

Datum /

Patient: ....

Datum: .... Testansvarig: ....

Pat poäng	max poäng	
....	(5)	**ORIENTERING** Fråga patienten vad det är för: År. Årstid. Datum. Veckodag. Månad.
....	(5)	Fråga patienten var han/hon är ... Land. Län. Kommun (Stad). Sjukhus (Vårdcentral/Bostadsområde). Våningsplan.
....	(3)	**REGISTRERING** Nämn tre föremål (ex nyckel, tandborste, lampa). Be patienten repetera dem. Den första repetitionen avgör antalet poäng, men fortsätt repetera orden till patienten lärt sig dem (upp till 6 ggr). Antal försök som krävdes för inlärning: ....
....	(5)	**UPPMÄRKSAMHET OCH BERÄKNING** Be patienten börja vid 100 och dra ifrån 7, och sedan fortsätta dra ifrån 7 tills Du säger stopp (93-86-79-72-65). *Ett poäng för varje rätt svar.* Om patienten inte kan eller inte vill medverka ges 0 poäng. Be patienten bokstavera ordet "konst" baklänges. Om patienten gör fel men sedan fortsätter rätt, räkna antalet rätt (ex tsnok 5p, tsonk 3p). OBS! Vid förnyad testning av samma patient ska det alternativ som användes första gången användas.
....	(3)	**MINNE** Be patienten återge de tre ord du tidigare bad honom/henne lägga på minnet.
....	(2)	**SPRÅK** Pröva benämningsförmågan genom att peka på en klocka och fråga patienten vad det är. Gör samma sak med en penna.
....	(1)	Be patienten repetera: "INGA OM, MEN ELLER VARFÖR". Instruera/tala tydligt! Tillåt bara ett försök.
....	(3)	Utför 3-stegsuppmaning: Ge patienten ett blankt papper och säg tydligt: "Tag det här papperet i höger hand, vik det på mitten och lägg det i knät!" Ge ett poäng för varje riktigt utförd uppgift.
....	(1)	Visa patienten texten "BLUNDA" (se baksidan). Be patienten läsa texten och göra som det står. Ge bara poäng om patienten verkligen blundar.
....	(1)	Be patienten skriva en mening (längst ned på blankettens baksida). Diktera inte. Meningen måste innehålla subjekt och predikat och vara förståelig.
....	(1)	**SPATIAL FÖRMÅGA/KOPIERING** Be patienten rita av figuren på blankettens baksida. Alla 10 vinklarna skall finnas och överlappningen skall forma en fyrhörning. Tremor och rotation ignoreras.
....	(30)	**TOTAL POÄNGSUMMA**

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2015 IPA Junior Research Awards – Second Prize Winner

Trends of patient referral to a memory clinic and towards earlier diagnosis from 1985–2009

Timo Grimmer,[1] Stephanie Beringer,[1] Victoria Kehl,[2] Panagiotis Alexopoulos,[1] Aurel Busche,[1] Hans Förstl,[1] Oliver Goldhardt,[1] Bianca Natale,[1] Marion Ortner,[1] Henning Peters,[1] Lina Riedl,[1] Carola Roßmeier,[1] Wiebke Valentin,[1] Janine Diehl-Schmid[1] and Alexander Kurz[1]

[1] *Department of Psychiatry and Psychotherapy, Klinikum rechts der Isar der Technischen Universität München, Ismaninger Str. 22, 81675 Munich, Germany*
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ABSTRACT

Background: It may be assumed that increased public awareness of dementia due to Alzheimer's disease (AD) together with the availability of efficacious treatment will result in diagnostic evaluation at earlier stages of cognitive decline and diagnosis of dementia due to AD at earlier stages.

Methods: All persons that were examined at a university based memory clinic, in Germany, between 1985 and 2009 were included.

Results: In the 3,951 persons identified, linear regression analysis revealed a positive association between Mini Mental State Examination (MMSE) score and year of initial examination (yearIE) ($\beta = 0.266$; $p < 0.001$). In the 1,821 patients diagnosed with dementia due to AD, a positive association between MMSE score and yearIE ($\beta = 0.230$; $p < 0.001$) was revealed. MMSE scores were higher ($\beta = 0.195$; $p < 0.001$) after the introduction of cholinesterase inhibitors in Germany in 1997.

Conclusions: Diagnostic evaluation of individuals occurred at progressively earlier stages of cognitive decline. Dementia due to AD was diagnosed at progressively earlier stages, and this trend was associated with the availability of efficacious treatment. This is the first study on changes in patient referral and diagnosis based on a continuous 25 years period.

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Main Take Home Messages

ADA-GERO

Kaskadmodellen (J. Birren)

Med stigande ålder blir kronologisk ålder en allt sämre prediktor för kognitiv hälsa

Primärt / ”Normalt” åldrande

Sekundärt åldrande

sjukdomsrelaterat

Tertiärt åldrande -

terminal nedgång

Psykisk snabbhet
Episodiskt minne
Exekutiv förmåga/ multi-tasking, logisk - spatial förmåga, verbal fluency

Kristalliserade/erfarenhets-baserade förmågor; språk - semantiskt minne

Global kognitiv nedgång =
alla domäner är påverkas

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Ett gerontologiskt perspektiv

Samspelet mellan biologiska, psykologiska och sociala faktorer ger skilda förutsättningar för ett åldrande med bevarad eller sviktande kognitiv hälsa

ADA-GERO