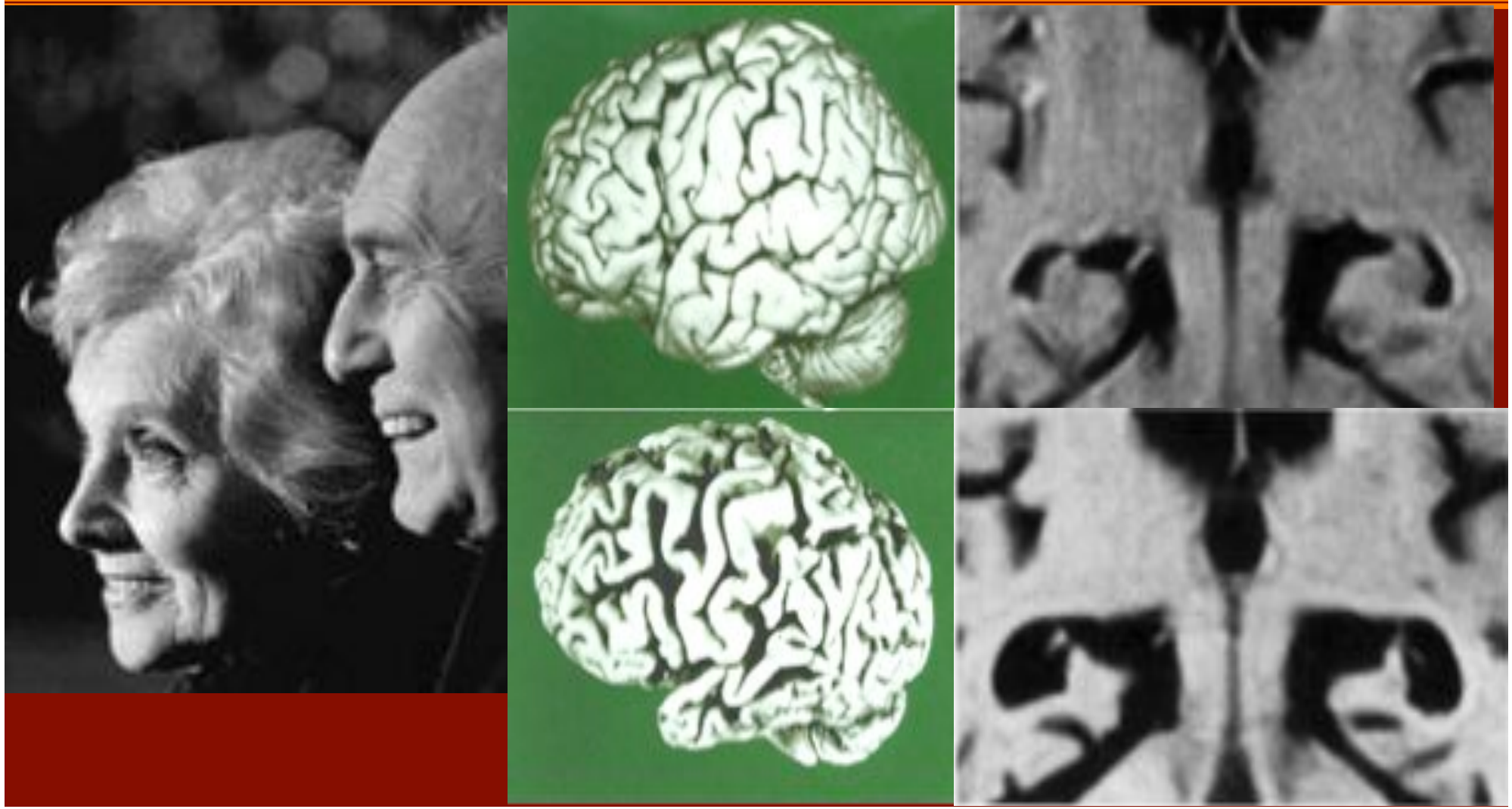
Zerebrale Altersveränderungen

Reinhold Schmidt, Klinische Abteilung für spezielle Neurologie



Zerebrale Altersveränderungen

Was ist Altern ?

- Zeit seit der Geburt
- Kein einzelner biologischer Marker
- Altersveränderungen im statistischen Sinn:

  Anatomische und physiologische Veränderungen die im Laufe des Lebens auftreten, die Mehrheit von Personen erfassen und keine signifikante akute Behinderung hervorrufen.

„Gewöhnliches Altern“

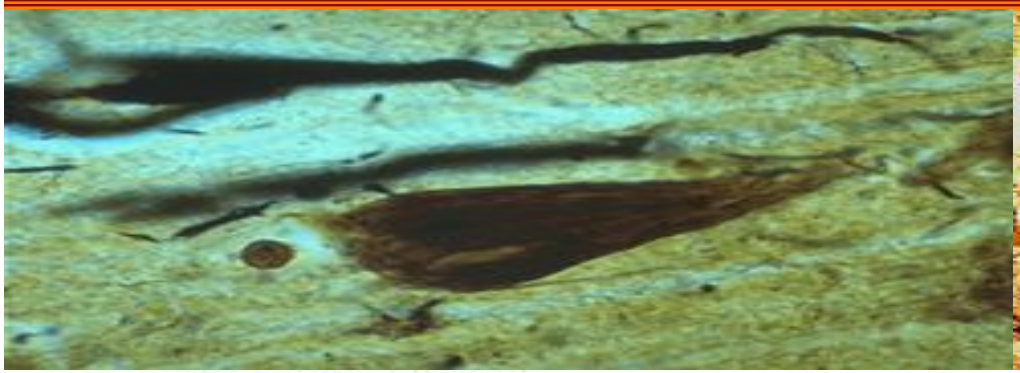
Anhäufung physiologischer Veränderungen die die Mehrheit der Population in einem bestimmten Lebensalter aufweist

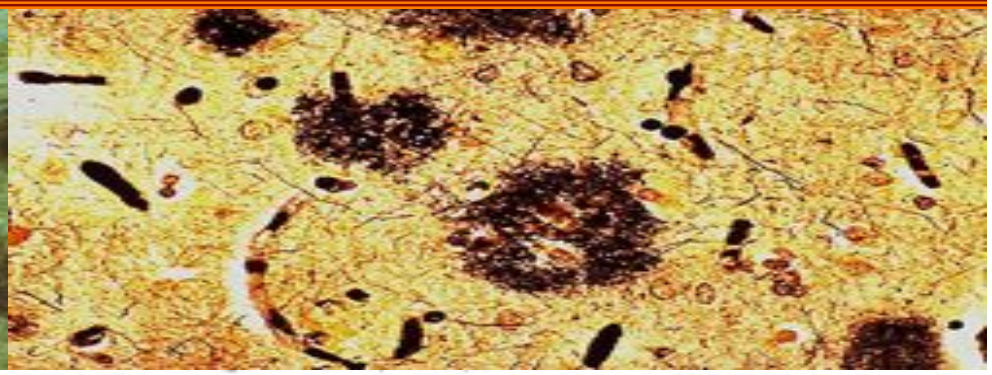
„Erfolgreiches Altern“

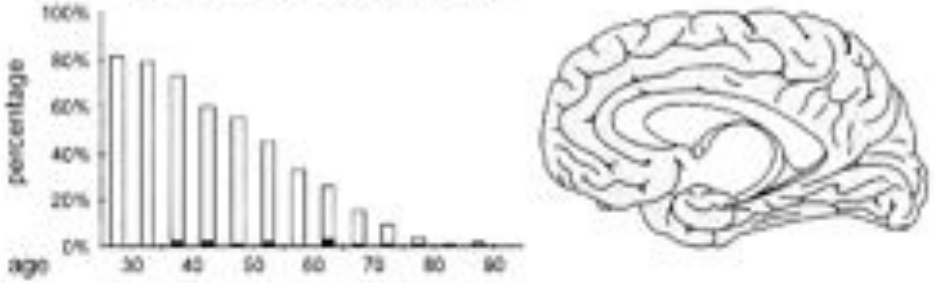
Vermeidung solcher Veränderungen

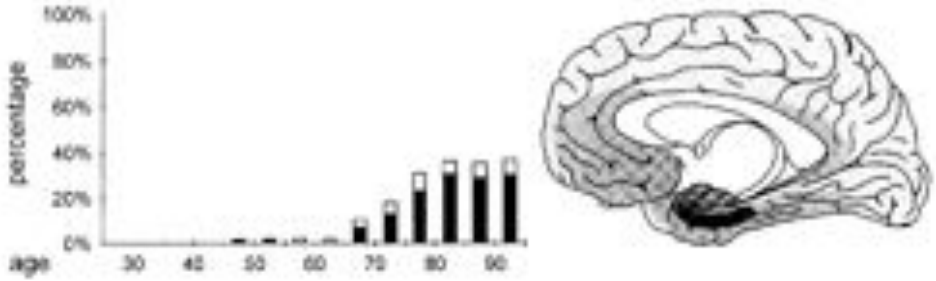
Zerebrale Altersveränderungen

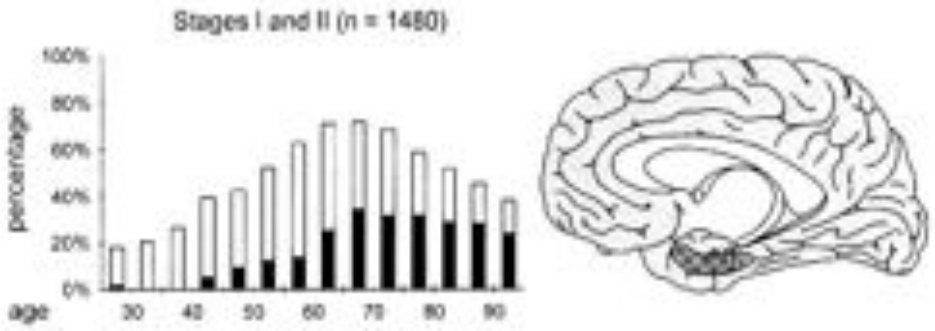
Welche morphologische Hirnveränderungen sind also per definitionem alters-assoziiert ?

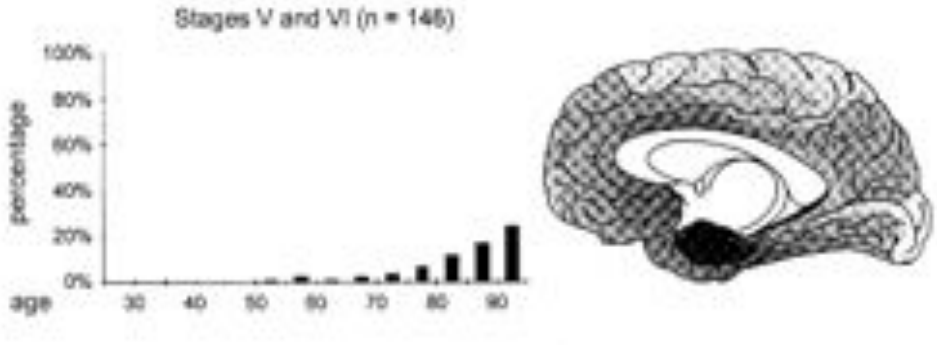






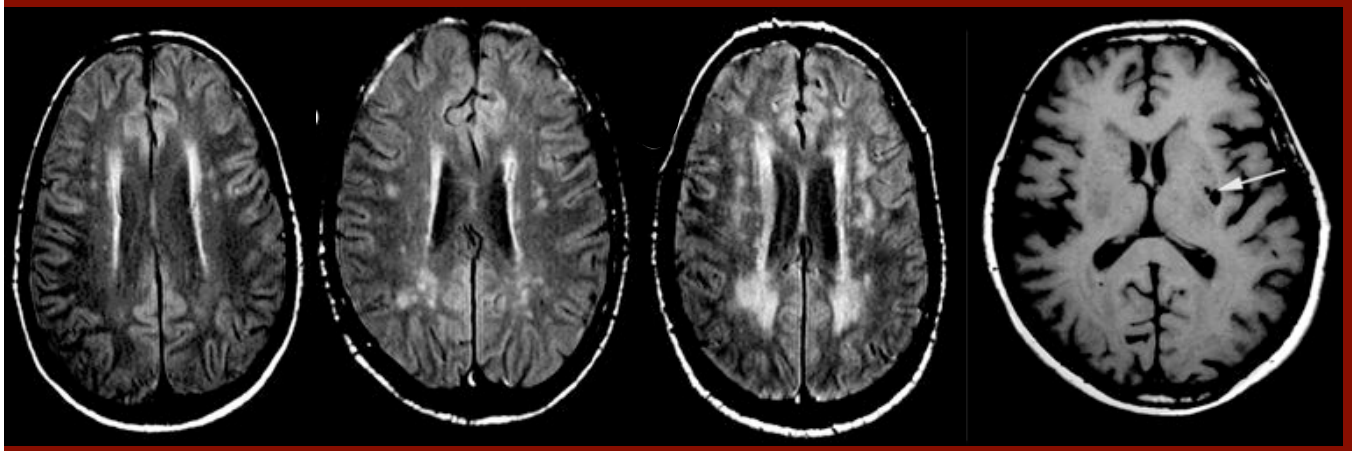


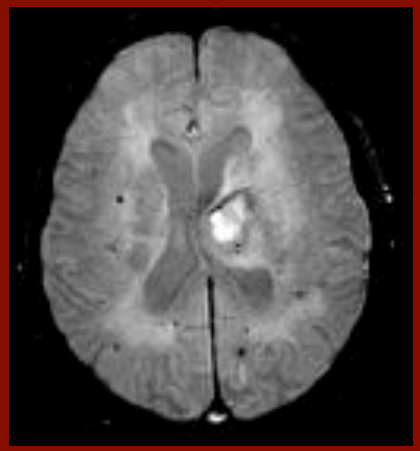




Zerebrale Altersveränderungen

Welche morphologische Hirnveränderungen sind also per definitionem alters-assoziiert ?





	N	Age Range	WML (%)	Lacunes (%)
Rotterdam Scan Study	1077	60-90	92	19
Cardiovascular Health Study	3301	65-97	96	20
Atherosclerosis Risk in Communities Study	1920	55-72	86	9
Austrian Stroke Prevention Study (ASPS)	901	45-75	67	9

Table 1 Prevalence of cerebral microbleeds (CMB) among subjects without cerebrovascular disease

Reference	Cohort characteristics	Max. CMB size, mm	Age ± SD (range), y	% HTN	n	% CMB
Austrian Stroke Prevention Study		5	60 (44–79)	32	280	6.4
16	Healthy elderly individuals	NR	62 (55–77)	0	66	4.5
17	Patients with headache or vertigo, >60 y	NR	72 ± 8	31	65	7.7
18	Patients with headache or "dizziness"	NR	76 ± 7	33	55	7.3
19	Patients with headache or "dizziness"	NR	75 ± 8	34	59	8.5
20	Subjects "without a history of cerebrovascular disease"	10	56 ± 16	NR	1,718	3.7
21	Participants of a screening program for "asymptomatic brain diseases"	7	56 ± 8	46	209	7.7
22	Framingham Study Offspring and Cohort	9	64 ± 12	29	472	4.7
Total					2,924	4.7

HTN = hypertension; NR = not reported.

Pathologische Befunde bei Demenz

Morphological diagnosis	(A)		(B)	
	n	%	n	%
"Pure" AD (CERAD pos., Braak V–VI)	623	41.5	432	52.0
Alzheimer type path. (plaque, limbic, NFT/SD) (26/53/28, 12/22/24)	107	7.1	58	7.0
AD+CVD (lacunar state, old/acute infarcts old, AH-sclerosis (129/66/37/4, 97/18/41/11)	236	15.7	167	20.1
AD+cerebral hemorrhage (CAA)	44	2.9	17	2.0
Lewy body variant AD/Diff. LB disease (33/33, 22/7)	66	4.4	29	3.5
AD+Parkinson pathologies, PD, Incid. LBD, SN lesions (51/14/8, 21/14/8)	73	4.8	43	5.2
MIX type dementia, (AD+MIE, +SAE, +SID) (39/22/7, 12/7/1)	68	4.6	20	2.4
AD+other pathologies (tumors, MS, MSA, etc.)	39	2.6	13	1.6
Alzheimer pathology total	1256	83.7	779	93.9
Vascular dementia (MIE, SAE, SID) (61/79/22, 5/6/6)	162	10.8	17	2.0
Other disorders (Huntington disease, FTD, CJD, others)	67	4.5	28	3.4
Nothing abnormal beyond age	15	1.0	6	0.7
Non-Alzheimer pathologies	244	16.3	51	6.1
Total	1500	100.0	830	100.0

Zerebrale Altersveränderungen

Die komplexe Interaktion von primär degenerativen und vaskulären Prozessen zeigt sich nicht nur Imagingstudien sondern auch in pathologischen Studien

Alzheimerpathologie + Infarkt erhöht Demenzrisiko 6 X

Alzheimerpathologie + LB-pathologie erhöht Demenzrisiko 10 x

Alzheimerpathologie + Infarkt + LB-pathologie erhöht Demenzrisiko 16 x

Zerebrale Altersveränderungen

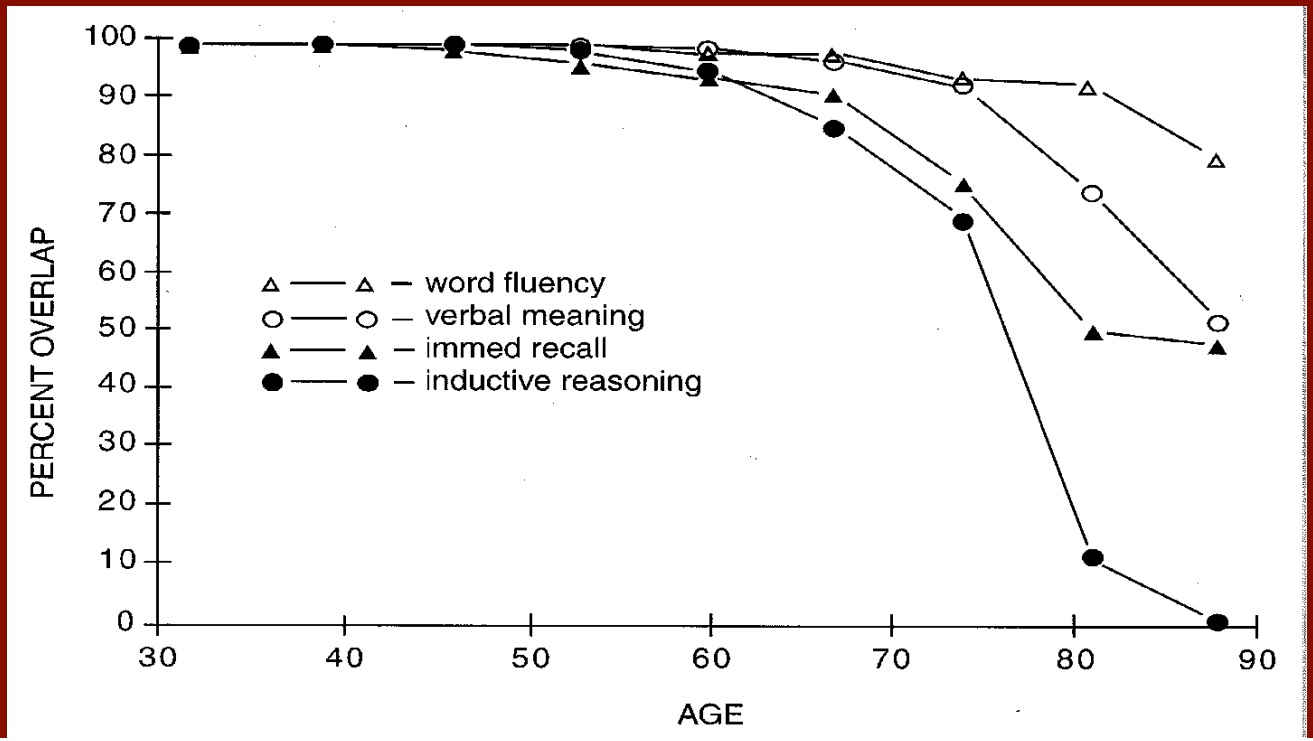
Wenn wir nun also primär degenerative Veränderungen und „vaskuläre" Läsionen im Alter endemisch sind, was passiert mit der Kognition ?

- Nicht alle Funktionen werden parallel eingeschränkt, manche werden überhaupt nicht eingeschränkt
- Es gibt starke individuelle Variationen kognitiver Leistung
- Daten über gesunde Hochbetagte werden erst gesammelt

Zerebrale Altersveränderungen

Kognition und Alter - Hauptbefunde

- Geringe Unterschiede im Vergleich zu jungen Personen bis etwa 60 Jahre
- Erst mit 75 bis 80 Jahren sind stärkere Funktionsverluste zu erwarten.
- Erst mit etwa 90 reicht der Funktionsverlust bis etwa 1 Standardabweichung der Leistung junger Personen
- Etwa die Hälfte aller 81-jährigen hält den Leistungsstandard über weitere 7 Jahre

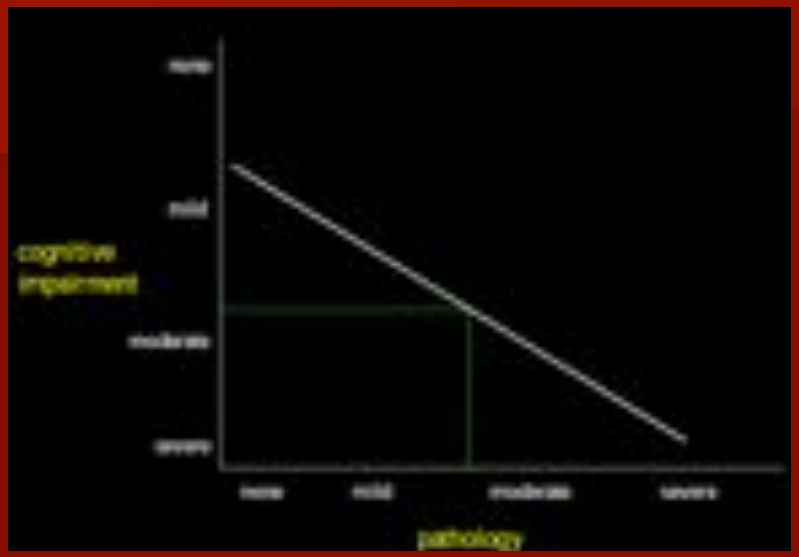


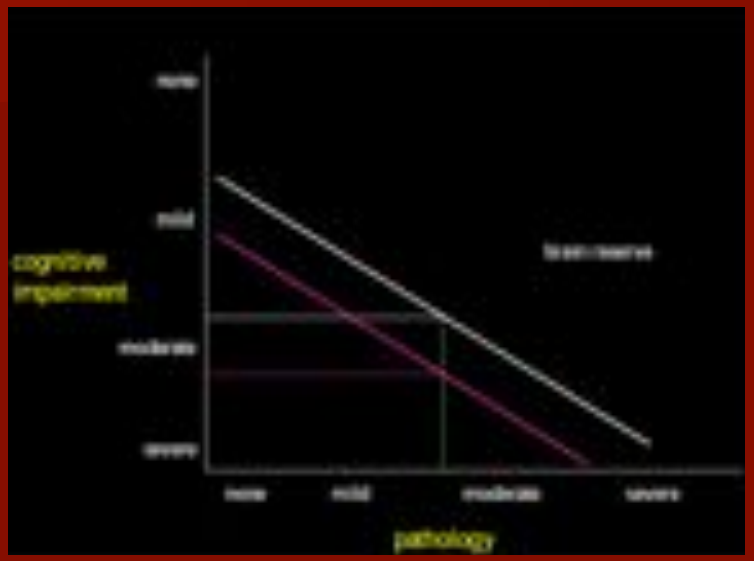
Zerebrale Altersveränderungen

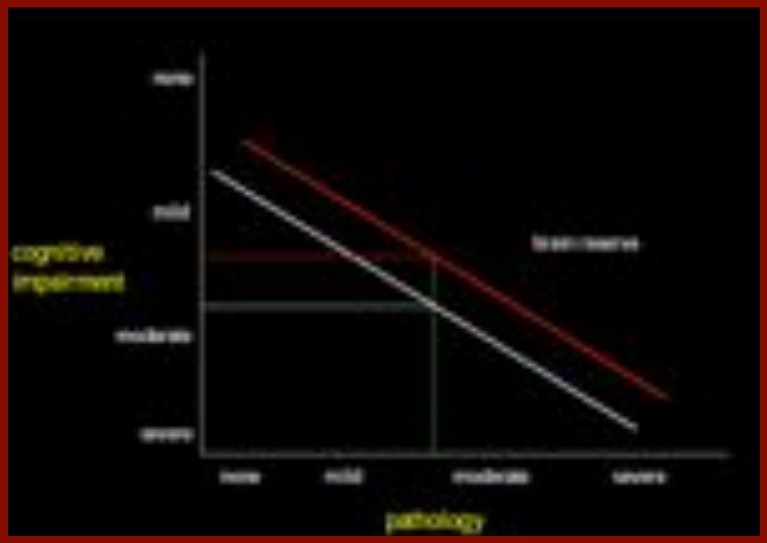
Wenn nun praktisch alle Menschen in höherem Lebensalter pathologische Hirnveränderungen haben, die mit kognitiven Störungen einhergehen können
Warum werden wir dann nicht alle dement ?

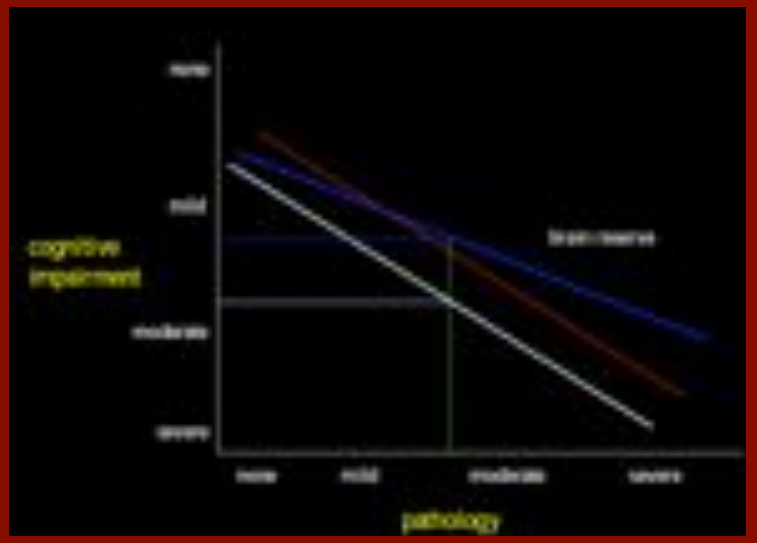
- Konzept der zerebralen Reserve
  - Hirnpathologie akkumuliert in Gehirnen mit unterschiedlicher Kapazität den ungünstigen Auswirkungen dieser Läsionen zu widerstehen
  - Nur relativ schwache Korrelation zwischen dem Ausmaß der Hirnpathologie und der kognitiven Leistungsfähigkeit

Additive negative, protektive oder interaktive Effekte









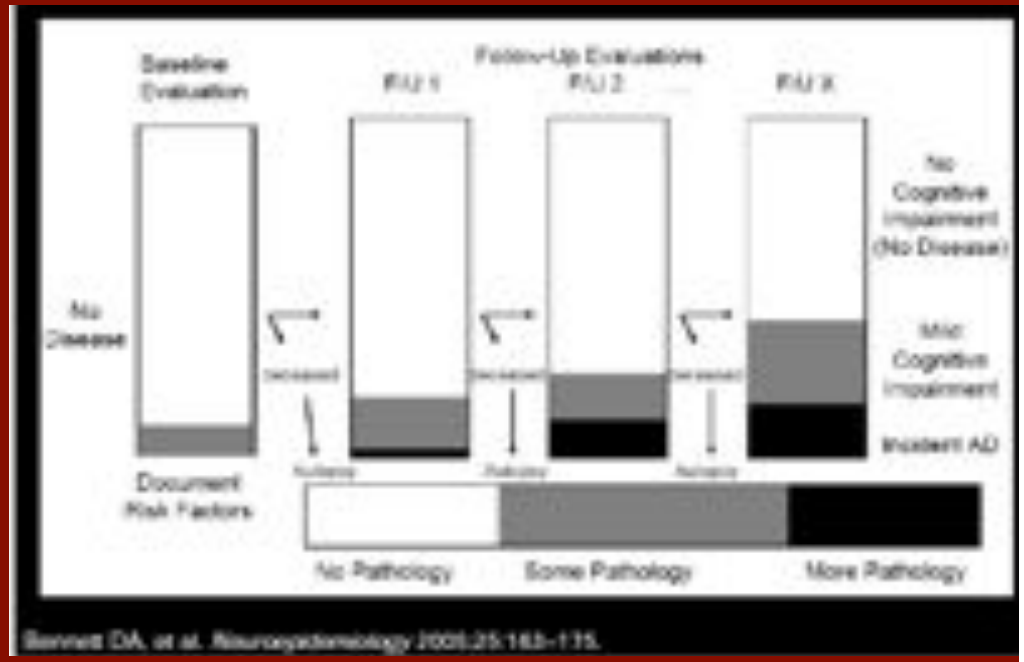
The Rush Memory and Aging Project

… because memories should last a lifetime

- Began enrollment in 1997
- > 1,200 residents from about 40 retirement communities and senior housing from across the Chicago area
- All agreed to annual cognitive and motor testing, and blood draw.
- All agreed to donate brain, spinal cord, muscle, and nerve at the time of death
- > 95% follow-up of survivors
- > 250 incident MCI and > 175 incident AD cases
- ~ 85% autopsy rate with > 250 autopsies to date

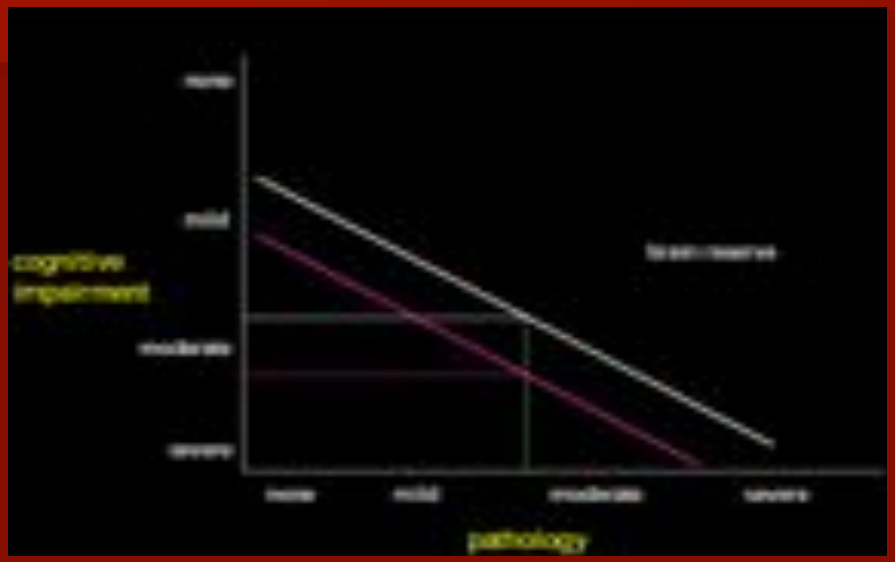
The Religious Orders Study

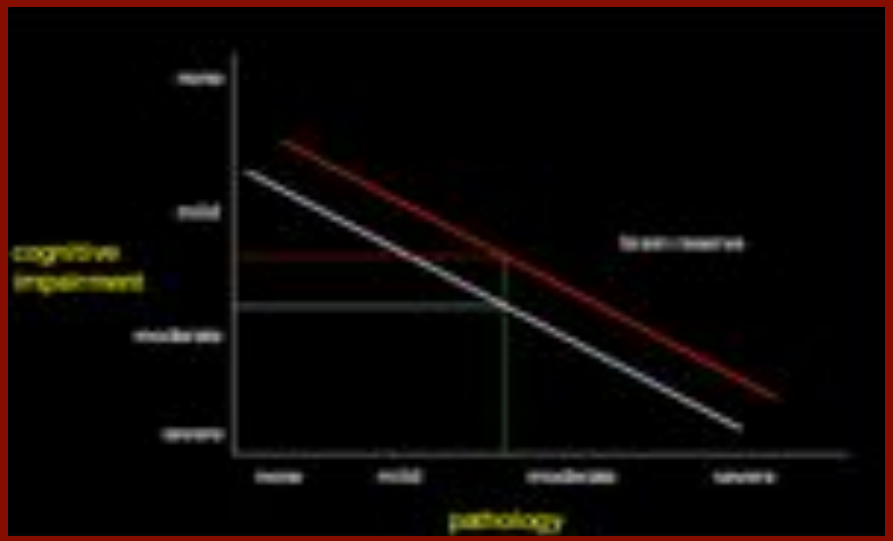
- Began enrollment in 1994
- > 1,100 older nuns, priests, and brothers without known dementia from across the U.S.
- All agreed to annual cognitive and motor testing
- All agreed to brain donation at the time of death
- > 95% follow-up of survivors
- > 350 incident MCI and > 250 incident AD cases
- ~ 95% autopsy rate with > 425 brain autopsies



Bennett DA, et al. Neuroepidemiology 2005;25:163–175.

Additiv wirkende Faktoren





- Neigung zu Dystress
- Einsamkeit
- Depression
- Riskofaktoren
- Kognitive Aktivitäten

Chronic distress and incidence of mild cognitive impairment

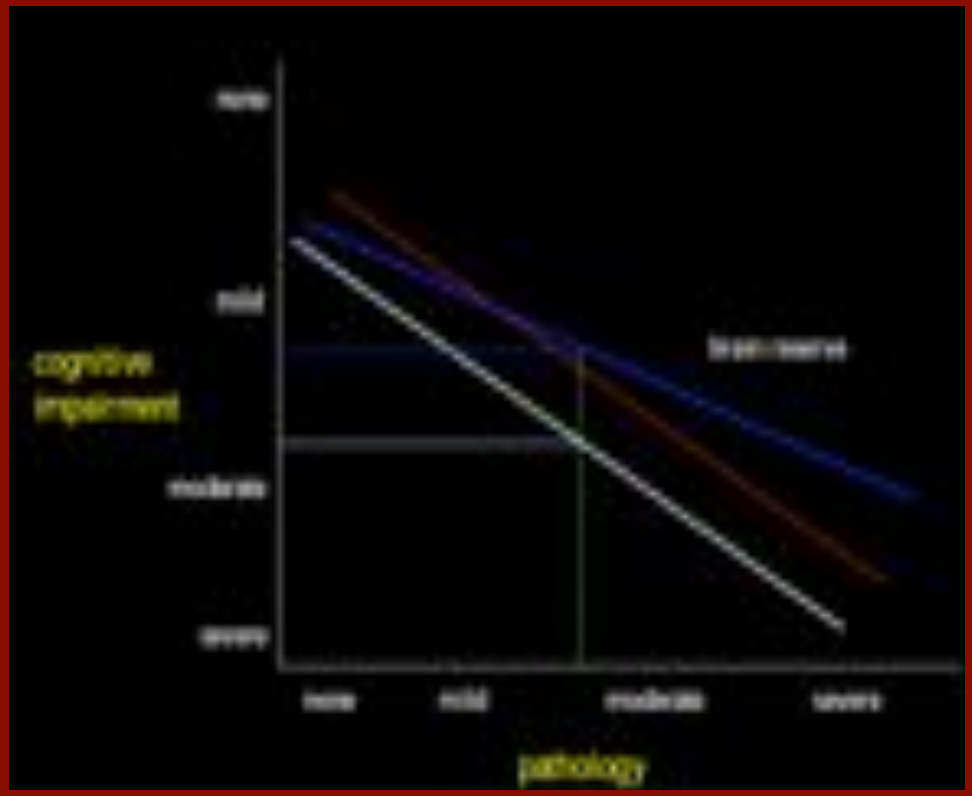
Wilson et al NEUROLOGY 2007;68:2085-2092

Von 1256 Personen der Religious Orders Study und des Rush MemoryAnd Aging Projects entwickelten in 12 Jahren 482 Personen MCIzu Stress neigende Personen zeigten um 40% häufiger MCI als Stress-resistente Personen unabhäng von depressiver Symptomatik.

Table 2 Descriptive information on persons who developed mild cognitive impairment (MCI) and those who did not*

Characteristic	Cohort	Incident MCI (n = 482)	No cognitive impairment (n = 774)	*p* Value
Age, y	Combined	78.1 (7.1)	76.0 (8.0)	<0.001
	RMAP	80.8 (7.1)	80.1 (7.6)	0.283
	ROS	76.5 (6.6)	71.5 (5.7)	<0.001
Education, y	Combined	16.9 (3.8)	16.3 (3.8)	0.006
	RMAP	14.4 (3.2)	14.5 (3.0)	0.835
	ROS	18.3 (3.3)	18.3 (3.4)	0.873
Women, %	Combined	70.3	70.9	0.821
	RMAP	76.3	72.9	0.395
	ROS	66.9	68.8	0.606
MMSE score	Combined	28.3 (1.7)	28.9 (1.3)	<0.001
	RMAP	28.0 (1.9)	28.6 (1.5)	<0.001
	ROS	28.4 (1.6)	29.2 (1.0)	<0.001
Distress score	Combined	16.3 (6.5)	15.2 (6.6)	0.004
	RMAP	15.3 (6.5)	14.6 (7.2)	0.213
	ROS	16.8 (6.4)	15.8 (5.9)	0.038
CES-D score	Combined	1.1 (1.6)	1.0 (1.5)	0.070
	RMAP	1.3 (1.8)	1.1 (1.6)	0.524
	ROS	1.0 (1.5)	0.8 (1.2)	0.038

Interaktive Effekte



- Zielstrebikeit
- Ausbildungsjahre
- Soziale Netzwerke

Loneliness and Risk of Alzheimer Disease

Robert S. Wilson, PhD; Kristin R. Krueger, PhD; Steven E. Arnold, MD; Julie A. Schneider, MD; Jeremiah F. Kelly, MD; Lisa L. Barnes, PhD; Yuxiao Tang, PhD; David A. Bennett, MD

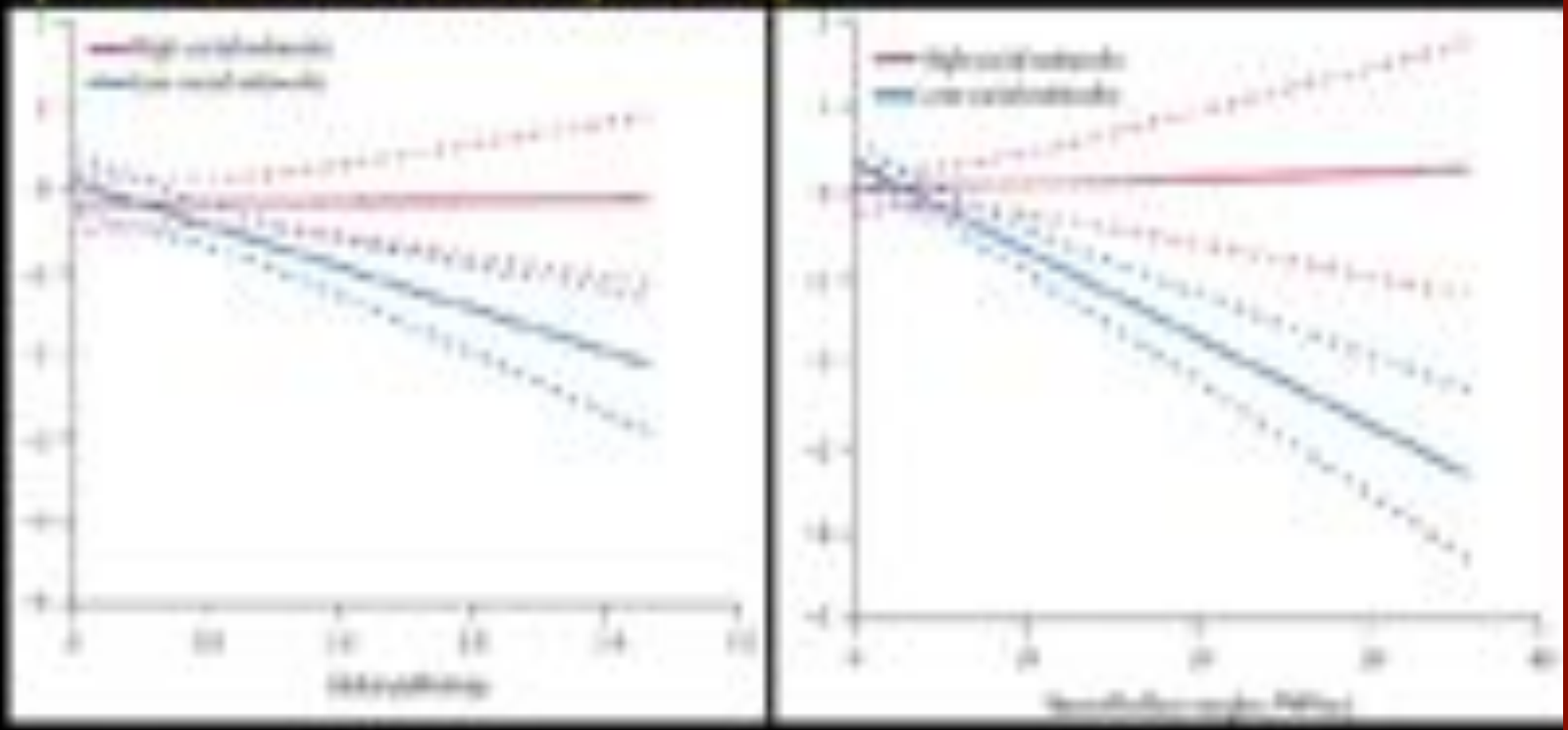
Table 1. Characteristics of Participants Who Did Not Develop AD and Those Who Did*

Characteristic	Participants Without AD (n = 716)	Participants With AD (n = 76)	*P* Value
Age at baseline, y	80.3 (7.1)	85.1 (5.9)	<.01
Educational achievement, y	14.5 (2.9)	14.8 (3.4)	.35
Female sex, %	77.2	61.8	<.01
African American race, %	6.0	4.0	.47
Income score	5.7	4.7	.03
MMSE score	28.2 (1.8)	25.8 (3.0)	<.01
Nine-item CES-D score	1.1 (1.5)	1.1 (1.7)	.97
Loneliness score	2.2 (0.6)	2.5 (0.6)	<.01
Social network size	7.0 (6.0)	6.4 (5.1)	.41
Social activity score	2.6 (0.6)	2.3 (0.5)	<.01
Cognitive activity score	3.2 (0.7)	2.8 (0.8)	<.01
Physical activity score	2.9 (3.4)	3.3 (4.2)	.42
Disability, %†	10.5	24.0	<.01
Vascular risk factors, %‡	79.5	85.5	.21
Vascular conditions, %‡	29.1	34.2	.35

Arch Gen Psychiat 2007

The effect of social networks on the relation between Alzheimer's disease pathology and level of cognitive function in old people: a longitudinal cohort study

Number of children, relatives (besides spouse and children) and other friends that they saw each month that they felt close to and at ease with and could talk to about private matters and could call upon for help

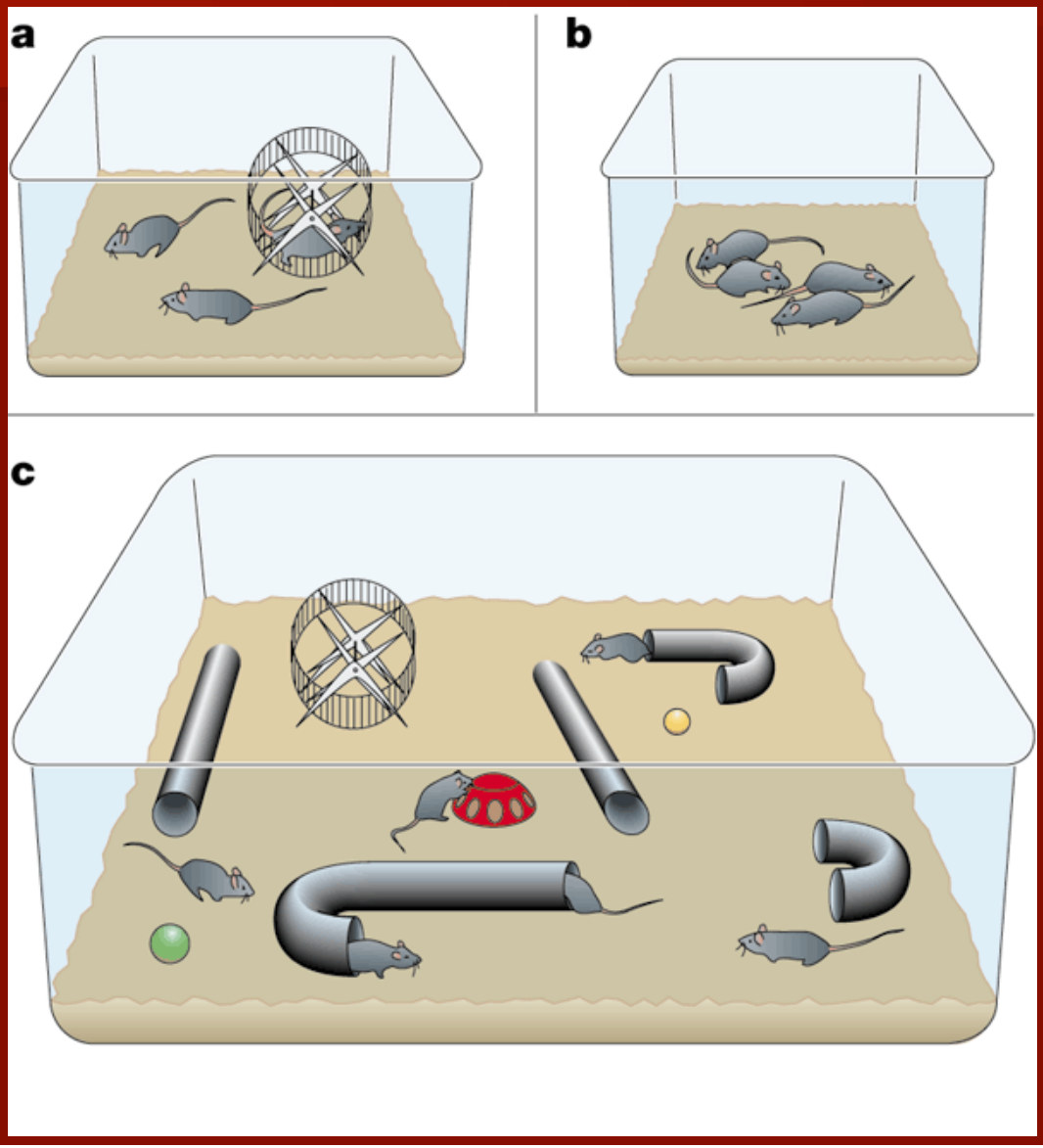


Bennett DA, et al. *Lancet Neurology* 2006;5:406-412

NEURAL CONSEQUENCES OF ENVIRONMENTAL ENRICHMENT

Henriette van Praag, Gerd Kempermann & Fred H. Gage

Nature Rev Neurosci 2000

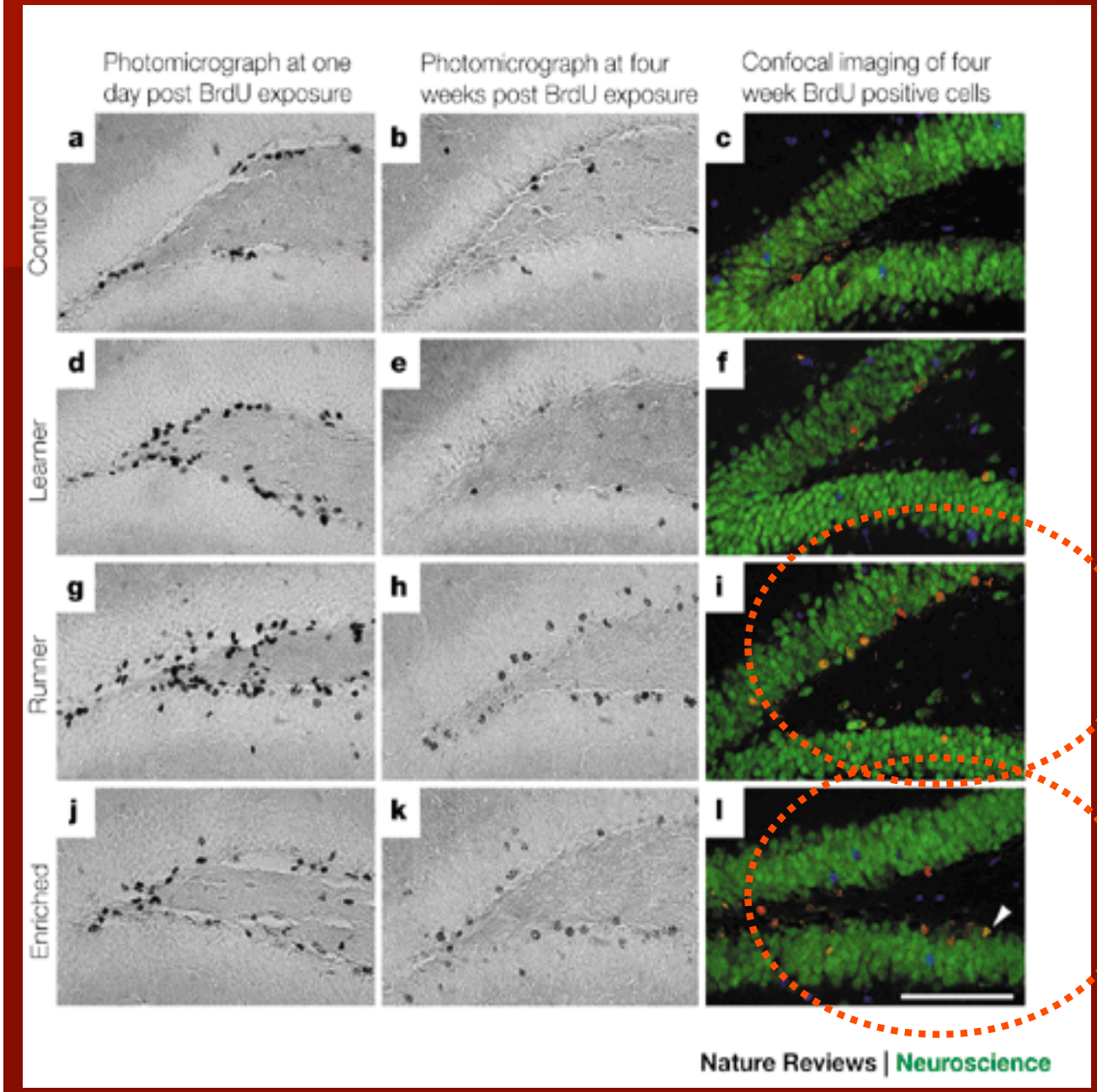


Living conditions in different experimental groups.

a | A cage containing a running wheel for voluntary physical exercise (48 x 26 cm)

b | A standard housing cage (30 x 18 cm).

c | Cage for an enriched environment (86 x 76 cm). Enrichment consisted of social interaction (14 mice in the cage), stimulation of exploratory behaviour with objects such as toys and a set of tunnels, and a running wheel for exercise



Effects of elements of enrichment, such as learning and exercise, on cell proliferation and neurogenesis in the dentate gyrus.

Both enrichment (**k**,**l**) and voluntary exercise (**h**, **i**) enhance the survival of newborn neurons. Learning did not affect cell survival (**e**,**f**), similar to controls (**b**,**c**). Confocal images of sections triple labelled for BrdU (red), NeuN (green, neuronal phenotype) and s100 (blue, selective for glia), show that relatively more cells become neurons in the running and enriched groups.