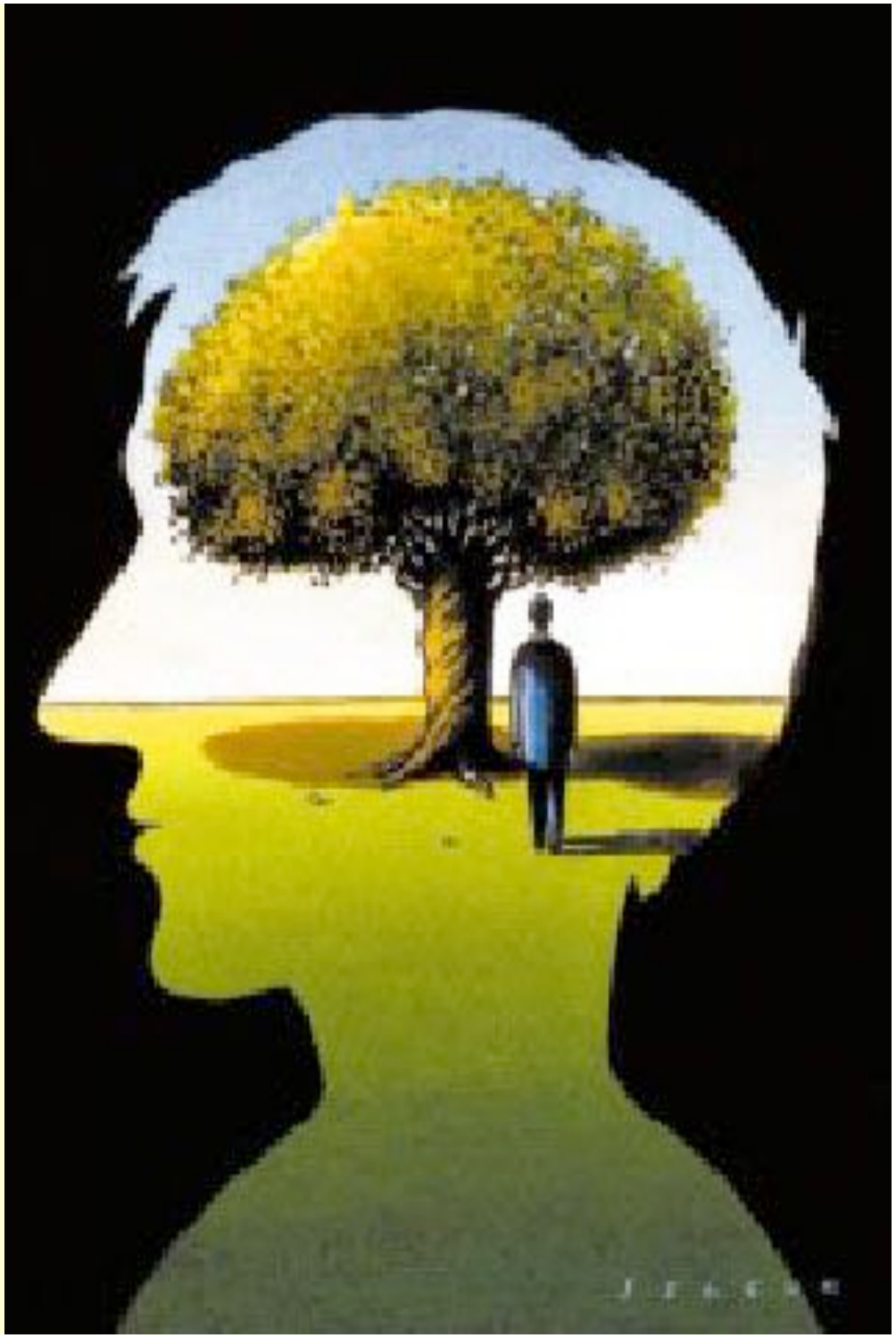
BRAIN RESERVE

Merci
de
votre accueil



BRAIN RESERVE

1. Origins of the concept

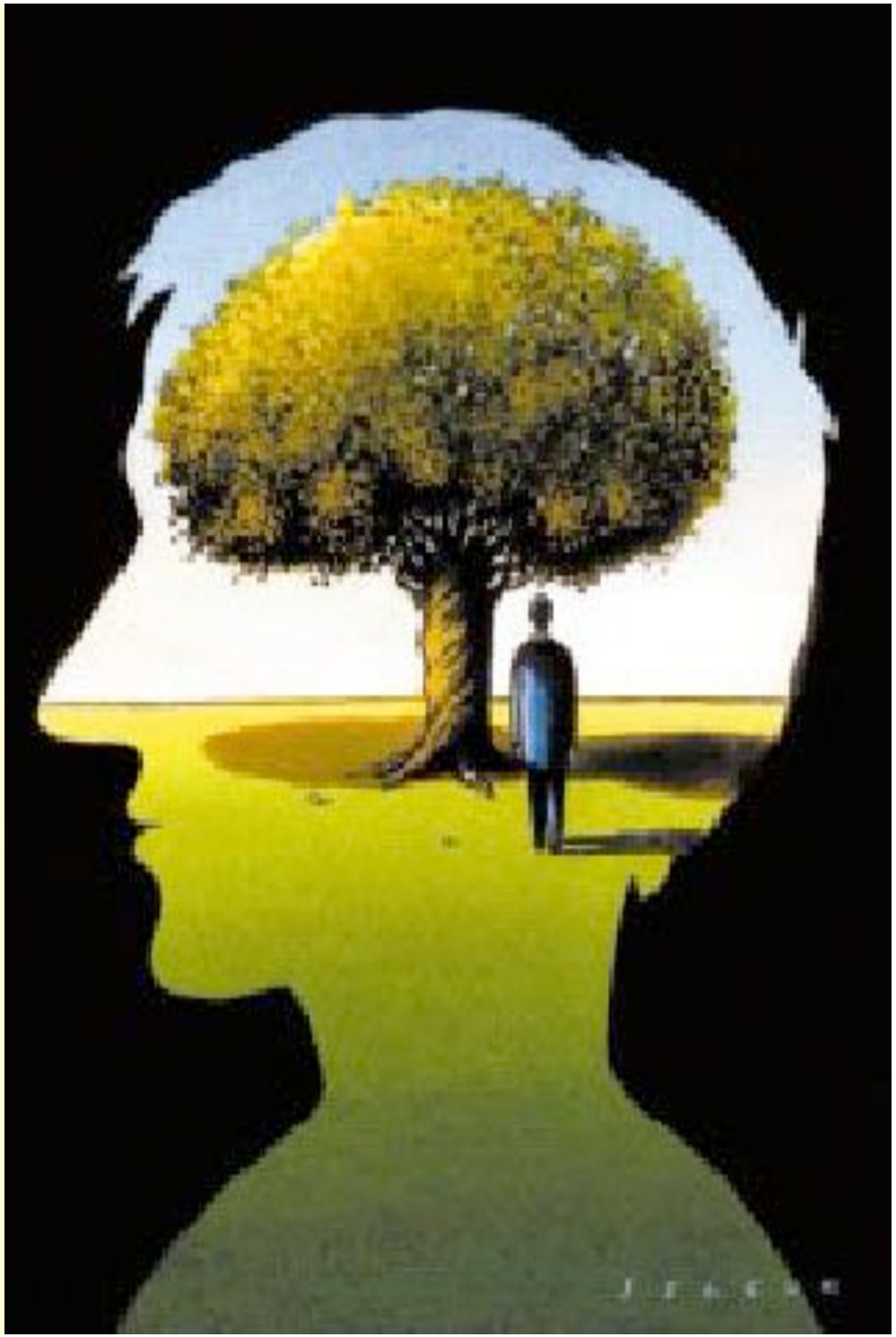
2. A life long process
   - From childhood
   - To adulthood

3. Impact of brain reserve on AD symptoms, signs and evolution

4. Exploration of brain reserve

5. Brain interventions in healthy ageing adults

6. Need of more research on this topic



Discrepancy between pathological and clinical expressions of AD

Neuropathologic criteria used for the AD diagnoses	Nb of patients . AD lesions ⊕	Nb of normal individuals . Clinics ∅ . AD lesions ⊕	% of normal individuals . Clinics ∅ . AD lesions ⊕
Khachaturian	1,009	122	12%
National Institute on Aging/Reagan Institute	1,704	320	19%
Consortium to Establish a Registry for Alzheimer's Disease	1,835	265	14%

ROE CM et al Neurology 2007; 68: 223-8

BRAIN RESERVE and DEMENTIA

Main question:

AT AUTOPSY

10 to 40% of individuals with

brain exceeding

pathological criteria for Alzheimer Disease (AD)

showed

NO ANTE MORTEM COGNITIVE IMPAIRMENT

KATZMAN R et al Ann Neurol 1988; 23: 138-44
VALENZUELA MJ et al Psychol Med 2006; 26: 441-54

BRAIN RESERVE and DEMENTIA

Does some form of reserve
protect the brain from expressing pathology?

NO DIRECT RELATIONSHIPS

between

- BRAIN DAMAGE SEVERITY

and

- CLINICAL MANIFESTATION OF SYMPTOMS

RAMI L et al Neurobiology Aging 2007, doi: 10.1016/j. neurobiologyaging.2007.10.008
BOYLE PA et al Neurology 2008; 70: 1534-42

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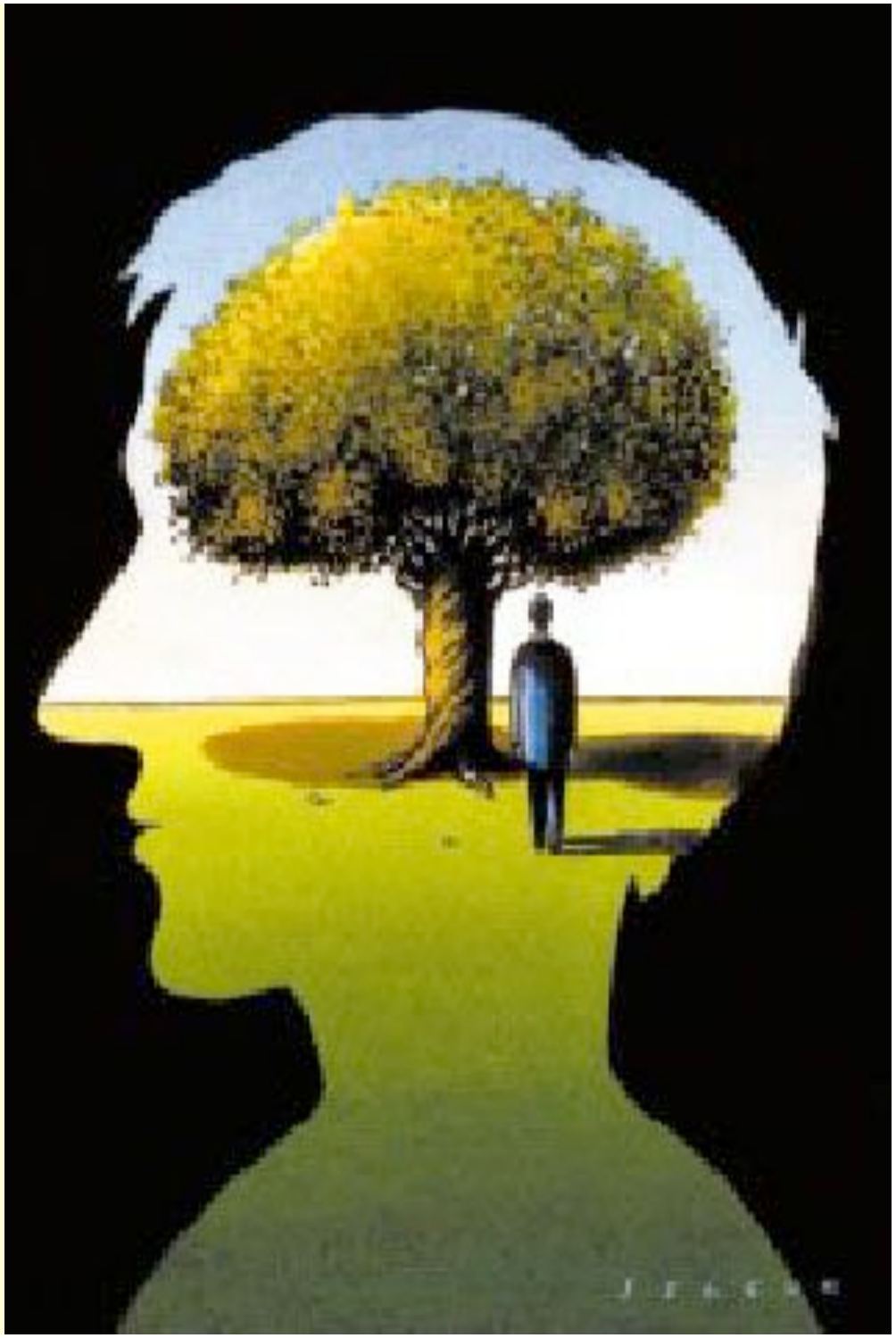

EARLY-LIFE RISK FACTORS for ALZHEIMER DISEASE (AD)

Supposed risk factors	Possible mechanisms
Intra-uterine development	*Undernutrition in utero* *Low birth weight*

BORENSTEIN AR et al Alzheimer Dis Assoc Disord 2006; 20: 63-72

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Early brain development	*Fetal life and 2 first years of life* *(93% of the brain development at 6)*

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Early life body growth	*Height* *→ highest cognitive scores*

BORENSTEIN AR et al Alzheimer Dis Assoc Disord 2006; 20: 63-72

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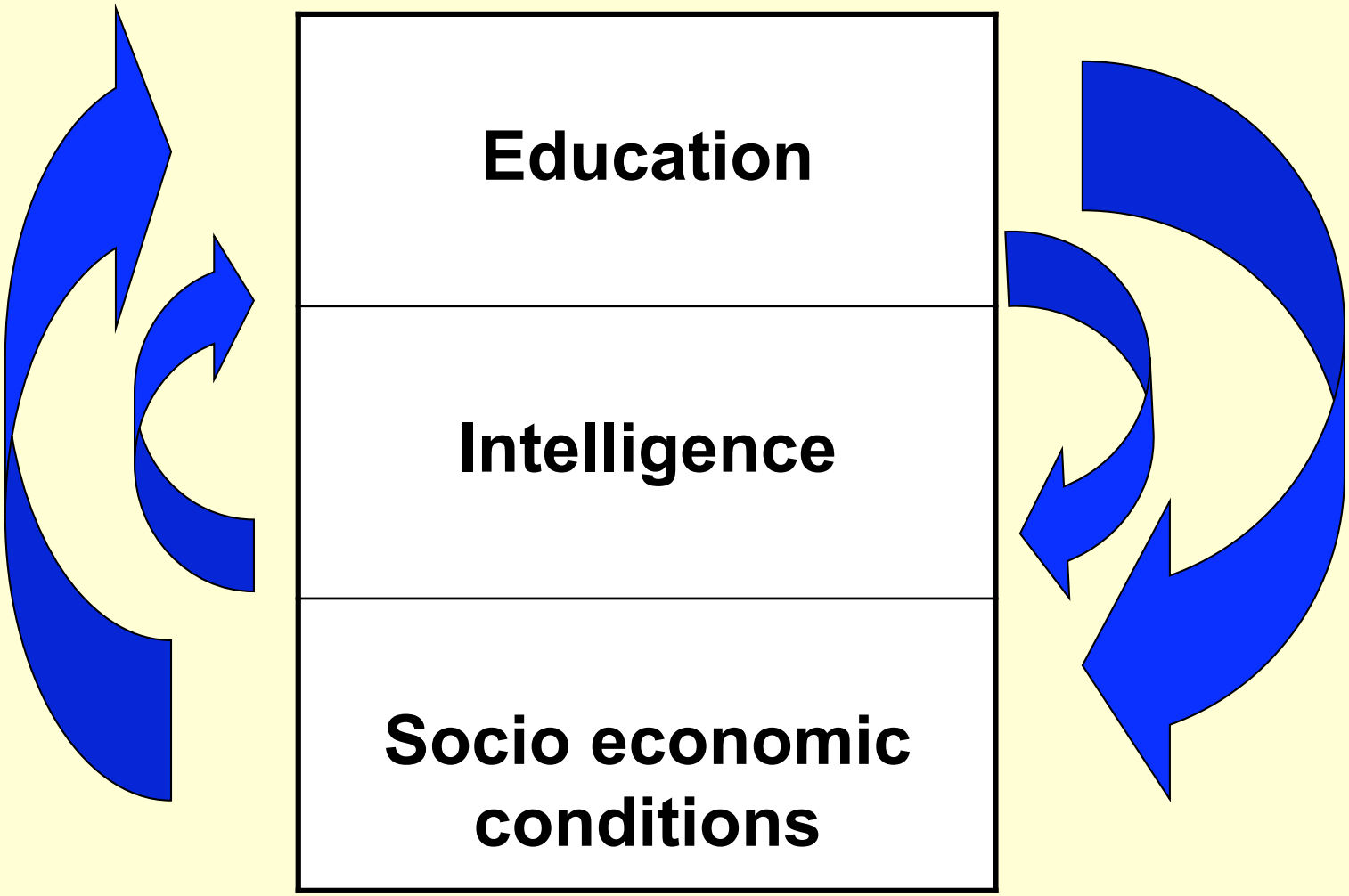
Early brain development	*Fetal life and 2 first years of life* *(93% of the brain development at 6)*
Early life body growth	*Height* *→ highest cognitive scores*
Early-life socio economic conditions	*Strong association with* *paternal social class and poverty*

BORENSTEIN AR et al Alzheimer Dis Assoc Disord 2006; 20: 63-72

EARLY-LIFE RISK FACTORS for ALZHEIMER DISEASE (AD)



BORENSTEIN AR et al Alzheimer Dis Assoc Disord 2006; 20: 63-72
Mc DONALD I J Clin Exp Neuropsychol 2007; 39: 127-41

HIGH EDUCATION and DEMENTIA

Meta-analysis of 15 selected longitudinal studies on a total of 629 published studies between 1984 and 2004

5/15 No protective effect	10/15 Protective effect

In persons with HIGH vs. low education, the risk of incidental dementia ⬇ 47%

But the heterogeneity in this analysis was signifigant p =.0063

VALENZUELA MJ et al Psychol Med 2006; 26: 441-54

HIGH INTELLIGENCE and DEMENTIA

Meta-analysis of 2 selected longitudinal studies on a total of 629 published studies between 1984 and 2004

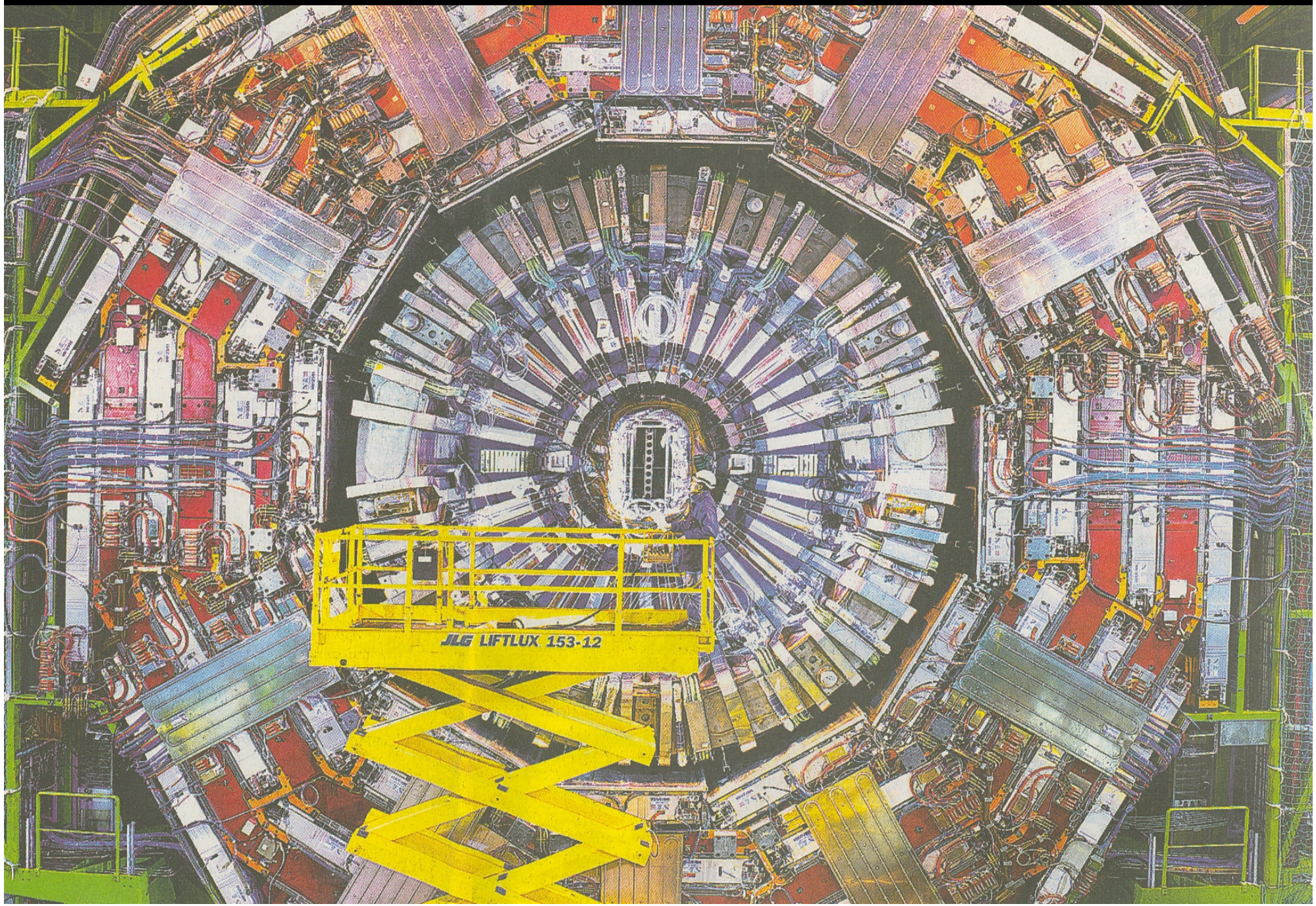
0/2	2/2
No protective effect	**Protective effect**

In persons with HIGH vs. low premorbid IQ, the risk of incidental dementia ⬇ 42%

Heterogeneity in this analysis was NON signifigant p =.73

VALENZUELA MJ et al Psychol Med 2006; 26: 441-54

COMPLEX OCCUPATION and DEMENTIA



COMPLEX / HIGH OCCUPATION and DEMENTIA

Meta-analysis of 12 selected longitudinal studies on a total of 629 published studies between 1984 and 2004

3/12	9/12
No protective effect	**Protective effect**

In persons with high vs. low complex occupation the risk of incidental dementia ⬇ 44%

Heterogeneity in this analysis was NON signifigant p =.062

Being in charge of a number of people in one's life was independently protective against dementia rather than job!

VALENZUELA MJ et al Psychol Med 2006; 26: 441-54


Mentally stimulating leisure activities

Mentally stimulating leisure activities and DEMENTIA

Meta-analysis of 4 selected longitudinal studies
on a total of 629 published studies
between 1984 and 2004

0/4	4/4
No protective effect	**Protective effect**

In persons with HIGH vs. low complex leisures activities, the risk of dementia
⬇ 50%

Results controlled for a number of relevant co-variates,
including age, general health, education and occupation

Heterogeneity in this analysis was NON signifigant p =.73

VALENZUELA MJ et al Psychol Med 2006; 26: 441-54

Negative life events and cognitive performance

428 participants:

- **Tests of episodic memory, attention and psychomotor speed**
- **Endorsed the presence and severity of 24 life events**

At the individual-event level, individuals who

1) **Experienced the injury or illness of a friend during the past year and rated the event as having a real impact on their lifes**

   ➔ performed better

2) **Reported having less money to live on over the past year**

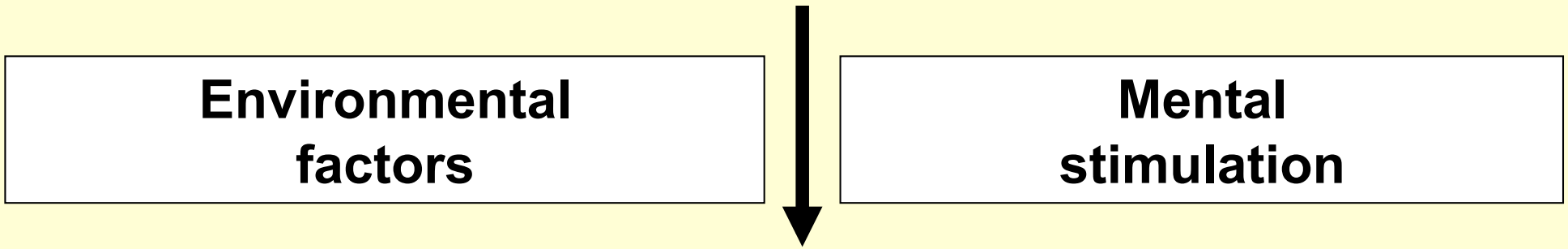
   ➔ performed more poorly

ROSNICK CB et al J Aging Health 2007; 19: 612-29

BRAIN PLASTICITY

Foundation of the
- Memory formation
- Learning process

Brain lifelong possibility of change and adjustment



BRAIN RESERVE concept

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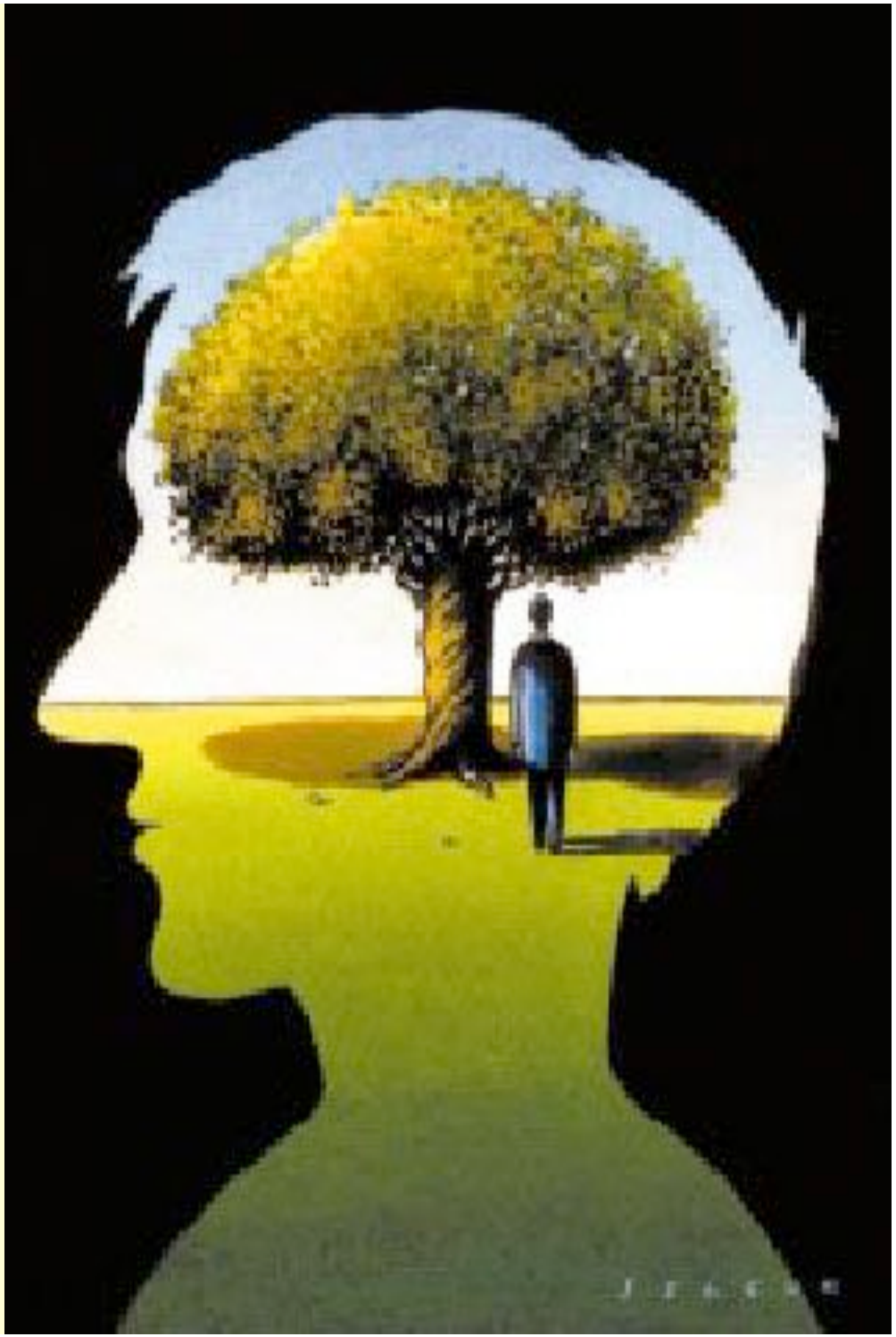

BRAIN RESERVE concept

The ability to tolerate
the age-related changes
and
the disease-related pathology
in the brain
without developing
clear clinical symptoms and signs

FRATIGLIONI L et al J Alzheimer Dis 2007; 12: 11-22

Brain reserve hypothesis in dementia

High education,

adult-life occupational work complexity,

as well as

a mentally and socially integrated

lifestyle in late life

could postpone

the onset of clinical dementia and AD

FRATIGLIONI L et al J Alzheimer Dis 2007; 12: 11-22

Dementia in highly educated patients

3.5 year follow-up study of 670 patients with AD categorized according to their educational level:

- **Low (≤ 8 years)**
- **Intermediate (≥ 9 and ≤ 12 years)**
- **High (≥ 13 years)**

Neuropsychological assessment: MMSE and Mattis DRS

Analyses were adjusted for age, gender, diabetes, hypertension and treatments

The most educated patients decline faster on neuropsychological tests than the lowest educated patients

BRUANDET A et al Dement Geriatr Cogn Disord 2008; 25: 74-80

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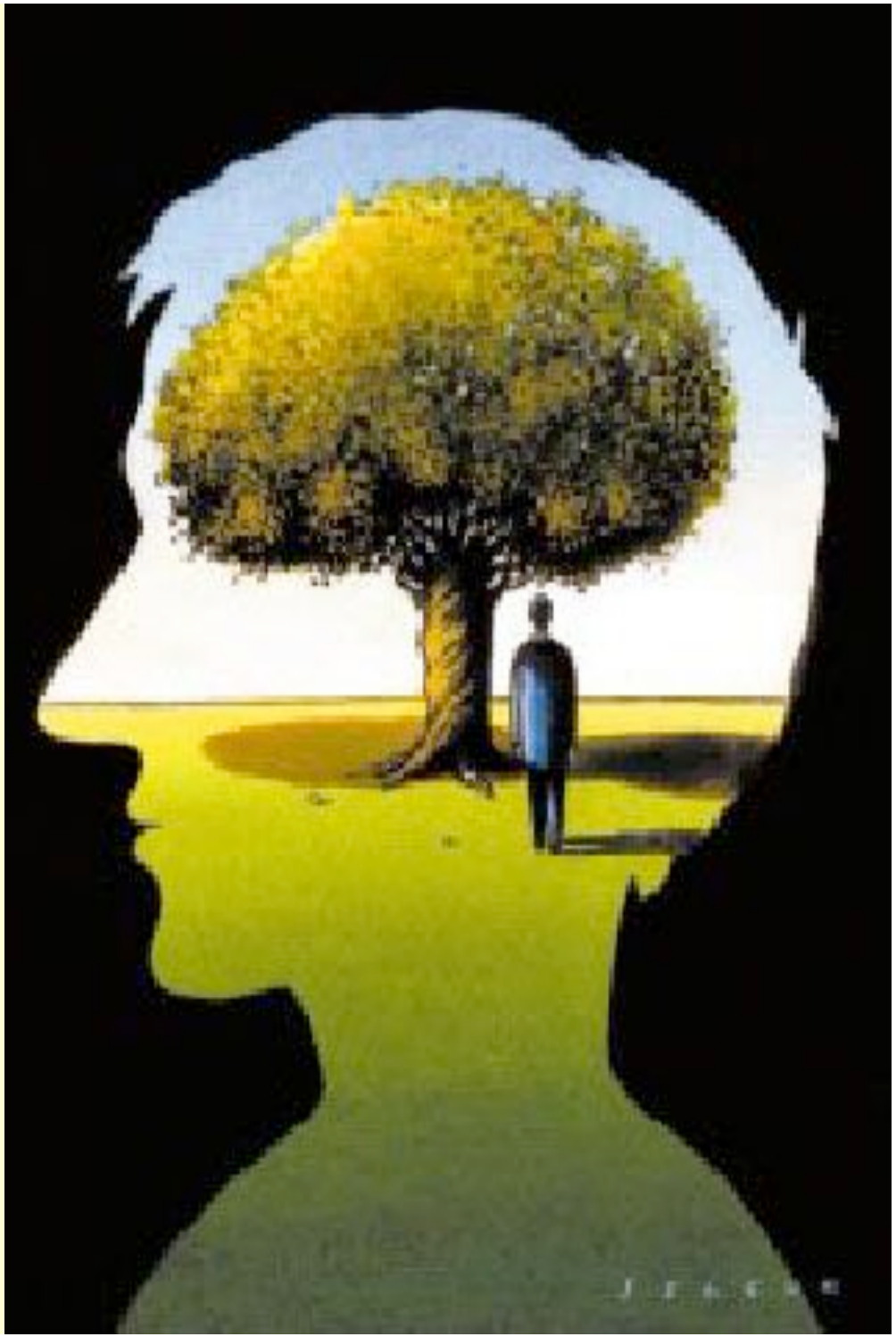


The Lifetime of Experience Questionnaire (LEQ)

The following questions apply to the time in your life between 13 and 30 years of age

- **How many years of high school** (ie secondary school or grades after year 6) **did you complete?**
- **Did you gain an end of high school certificate (High School Certificate or ?)?**
- **Please specify what type(s) of training or study you attempted up until 30 years of age and for how long you were enrolled.**
- **How often were you seeing a member of your family or friend during this time?**
- **How often were you practicing or playing a musical instrument?**
- **How often would you practice or develop an artistic pastime (e.g. drawing, painting, writing, acting)?**
- **How often did you do any kind of physical exercise?**
- **How often did you read (material of any sort) for more than five minutes?**
- **How often would you practice speaking a second language?**
- **Did you travel to any of the following continents between the ages of 13-30?**

http://train.headstrongcognitive.comIleq.aspx

Brain volume decline in aging

Cross-sectional and longitudinal observation of
a volunteer sample of
362 nondemented adults aged 18 to 93 years

↓

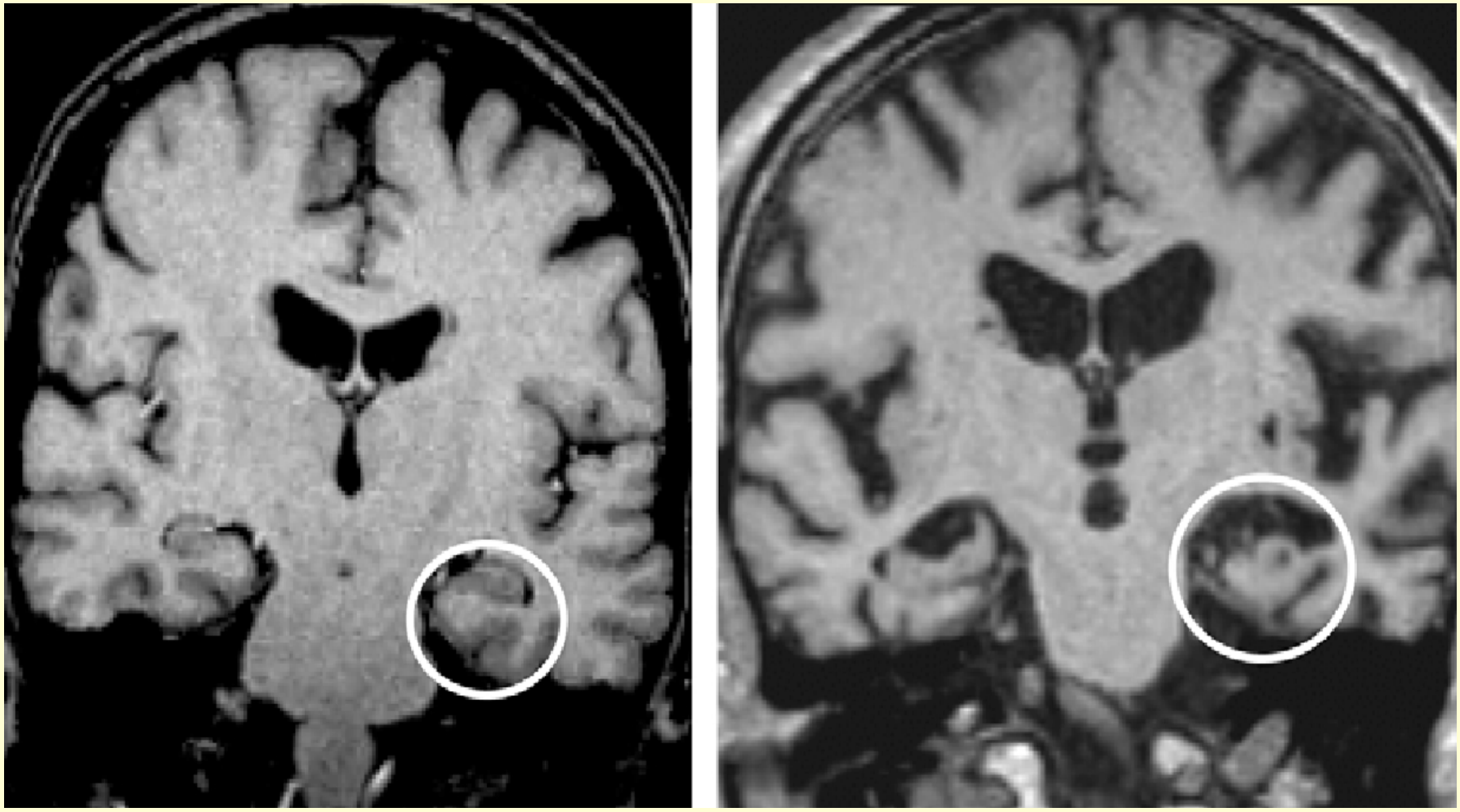
Whole-brain volume adjusted for head size
and change per year

↓

↓ 0.22% per year
between the ages of 20 and 80 years
with
accelerated decline in advanced aging

FOTENOS AF et al Arch Neurol 2008; 65: 113-20

Hippocampal Volume



Courtesy from Giovanni B FRISONI, Brescia, Italy

Cognitive reserve evaluation: Positron emission tomography (PET)

PET using [11C]PIB ⇨ Amyloid deposits

and 18F-fluorodeoxyglucose ⇨ Brain functioning
in 12 high- and 13 low-educated patients
with the same degree of cognitive deterioration

Compared with low-educated patients,
HIGH-educated patients showed:

1) More amyloid deposits
in the lateral frontal cortex

2) Lower glucose metabolic rate
in the temporo-parietal cortical regions

BRAIN RESERVE

KEMPPAINEN NM et al Ann Neurol 2008; 63: 112-8

BRAIN RESERVE EXPLORATION: Positron Emission Tomography (PET)

Healthy elders (compared with cognitively impaired)

Education, intellectual and social life activities

were inversely correlated with

regional brain metabolic activity

and/or

brain cerebral flow in

temporal, parieto-temporal and occipital regions

During cognitive tasks,

specific brain networks were differentially activated

ALEXENDER GE et al Am J Psychiatr 1997; 154: 165-72

PERNECZKY R et al J Neurol Neurosurg Psychiatr 2006; 77: 1060-3

SCARMEAS N et al Arch Neurol 2003;60. 359-65

SCARMEAS N et al Arch Neurol 2004; 61: 73-8

BRAIN RESERVE EXPLORATION: Positron Emission Tomography (PET)

During cognitive tasks,
compared with cognitively impaired,
healthy elders
activated
multiple, different and specific
brain networks

ALEXENDER GE et al Am J Psychiatr 1997; 154: 165-72
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SCARMEAS N et al Arch Neurol 2003;60. 359-65
SCARMEAS N et al Arch Neurol 2004; 61: 73-8

Imaging of brain haemodynamics: assessing cerebral perfusion

93 patients with mild Alzheimer's disease and
16 healthy controls
underwent 18-FDG-PET imaging of the brain

The regression analysis showed
a marked inverse association between
- years of schooling and
- glucose metabolism
in the posterior temporo-occipital and precuneus in the left hemisphere

People with higher education
(higher brain reserve)
can cope with brain damage for a longer time

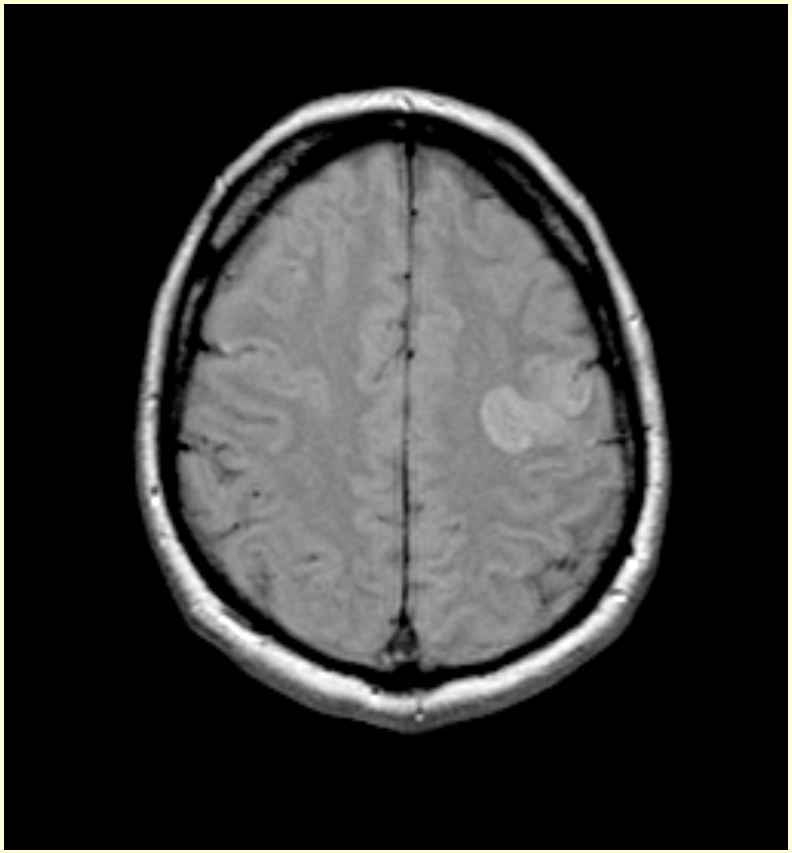
PERNECZKY R et al J Neurol Neurosurg Psychiatry 2006;77:1060-3


People with higher education
(higher brain reserve)
can cope with brain damage for a longer time

Severity of brain infarcts on cognitive decline

Cognitive reserve decreases the cognitive impact of vascular injury in the brain

Cardiovascular Health Study (population-based, longitudinal study of 3,660 people aged 65 y.)



ELKINS JS and al Neurology 2006; 67: 435-40

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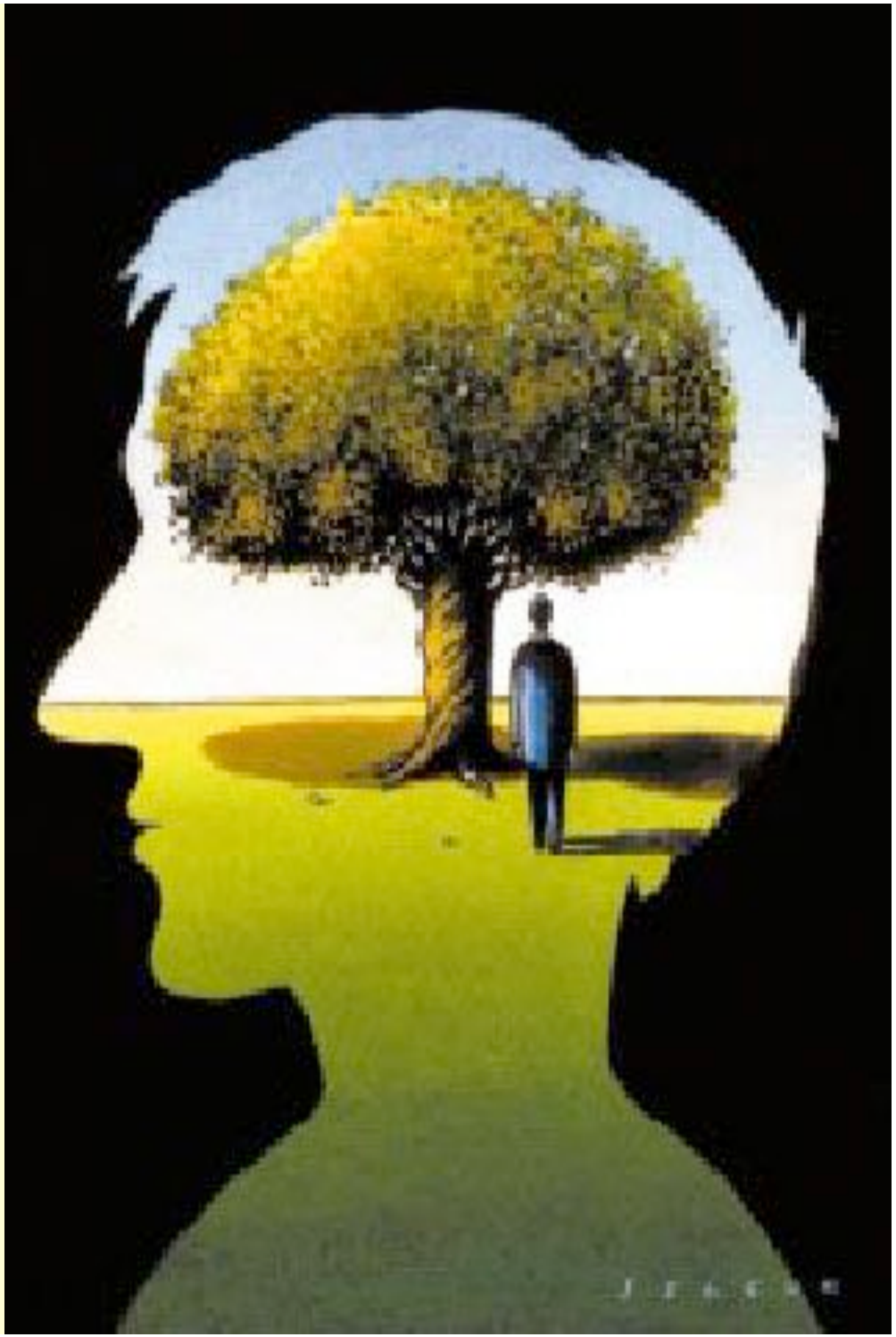

Risk factors for Alzheimer Disease

Two distinct sets of risk factors

The pathological trajectory

Accumulation of AD lesions over the life span at an increased rate

The clinical expression

Attainment of a critical threshold of « brain reserve » below which normal cognitive function cannot be sustained

Slowing or stopping the AD process

Enhancing the « Brain Reserve »

Two distinct preventive strategies

BORENSTEIN AR et al Alzheimer Dis Assoc Disord 2006; 20: 63-72

BRAIN RESERVE INTERVENTIONS

- **Delay the dementia onset**
- **Decrease the apparent prevalence of the disease**

- **Lead to personal benefits**
- **Increase general quality of life**
- **Favour self confidence and social engagement**

- **Lead to social and economic benefits**

VALENZUELA MJ et al Psychol Med 2006; 26: 441-54

BRAIN RESERVE INTERVENTIONS in HEALTHY ADULTS

Early post retirement behavioural programmes stimulating leisures activities

Complex problem solving

SCHAIE K Am Psychol 1994; 49: 304-13

Supra normative training of verbal memory

KLIEGL R et al Dev Psychol 1989; 26: 247-56

Cognitive training

BALL K et al JAMA 2002; 288: 2271-81

Memory-based mental exercises

VALENZUELA M et al Neurology 2001; 56: 592-8

↓

Stimulation of compensatory mechanisms
Activation of atypical brain networks
Enrichment of synapses and dendritic responses

BRAIN RESERVE INTERVENTIONS in HEALTHY ADULTS

Early post retirement behavioural programmes stimulating leisures activities

↓

Stimulation of compensatory mechanisms
Activation of atypical brain networks
Enrichment of synapses and dendritic responses

SEVERAL KEY QUESTIONS:

1. Length of the training?
2. What are the possible mechanisms of action?
3. Does the training in a specific task generalize to other tasks?
4. Does it produce long-lasting effects?

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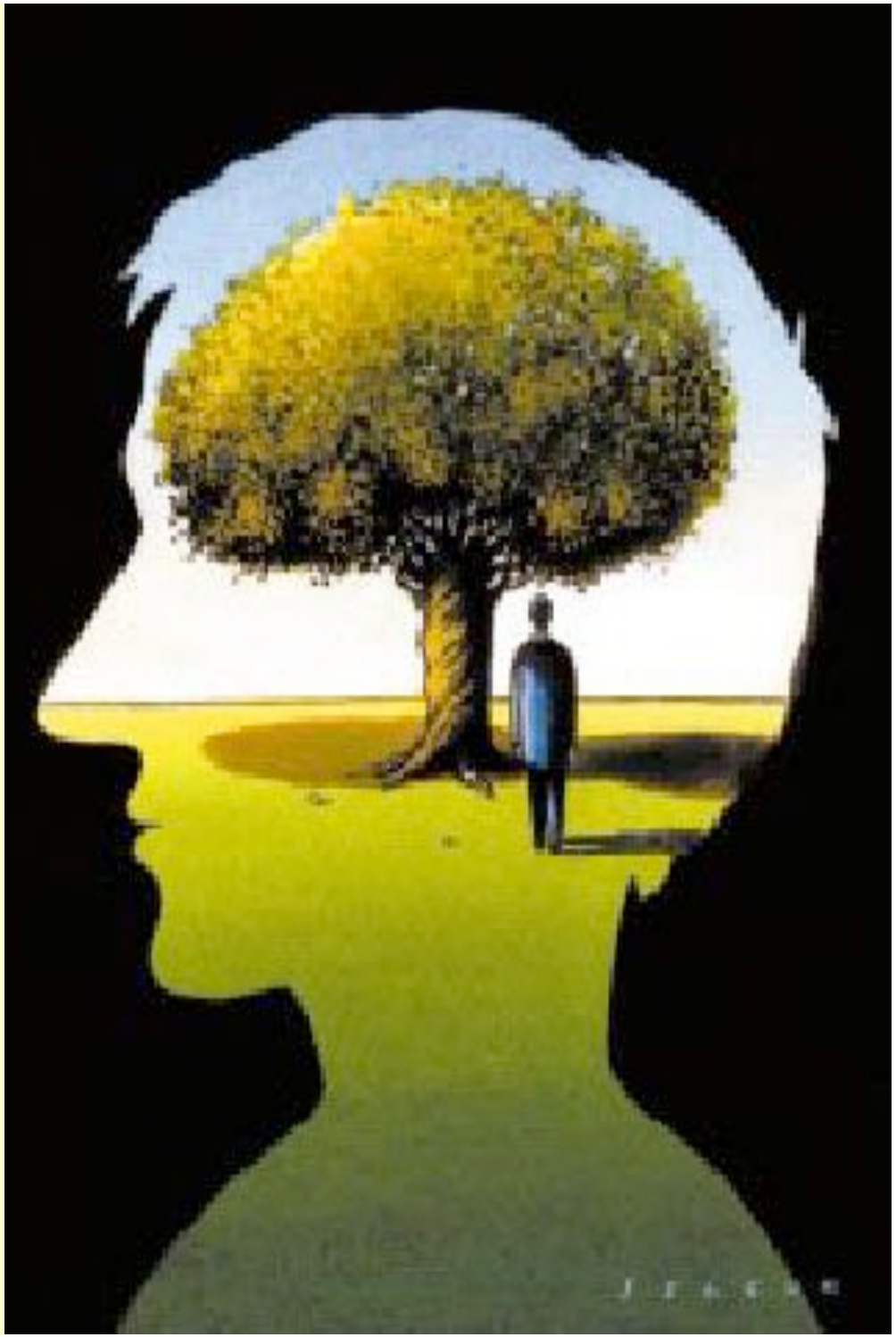

ALZHEIMER DISEASE (AD)

Results from
THE COMPLEX INTERPLAY
between
- GENETICS
- ENVIRONMENTAL EXPOSURE
experienced
THROUGHOUT THE LIFE COURSE

Increase in BRAIN RESERVE factors:
education, intelligence, socio economic conditions,
(height, brain weight and brain circumference)
may help to attenuate the predicted epidemic of AD

BORENSTEIN AR et al Alzheimer Dis Assoc Disord 2006; 20: 63-72

COMPLEX MENTAL ACTIVITIES and DEMENTIA

Meta-analysis of 22 studies based on data from over 29'000 individuals

Education	**OR: 0.53** [0.45-0.62]
Occupational complexity	**OR: 0.56** [0.49-0.65]
Cognitive lifestyles activities	**OR: 0.50** [0.42-0.61]
High mental activity during the whole life course	**OR: 0.54** [0.49-0.59]
High mental activity only during the adult life	**OR: 0.57** [0.41-0.67]

VALENZUELA M et al Current Opinion Psychiatr 2008; 21: 296-302

?

In fact, empirical test
may reveal that
higher behavioral brain reserve
<u>delays</u>
disease presentation
<u>rather than truly</u>
<u>decreases</u>
dementia incidence

?

VALENZUELA MJ et al Psychol Med 2006; 26: 441-54

BRAIN RESERVE

Many thanks for your attention