Alzheimer's Disease and Language

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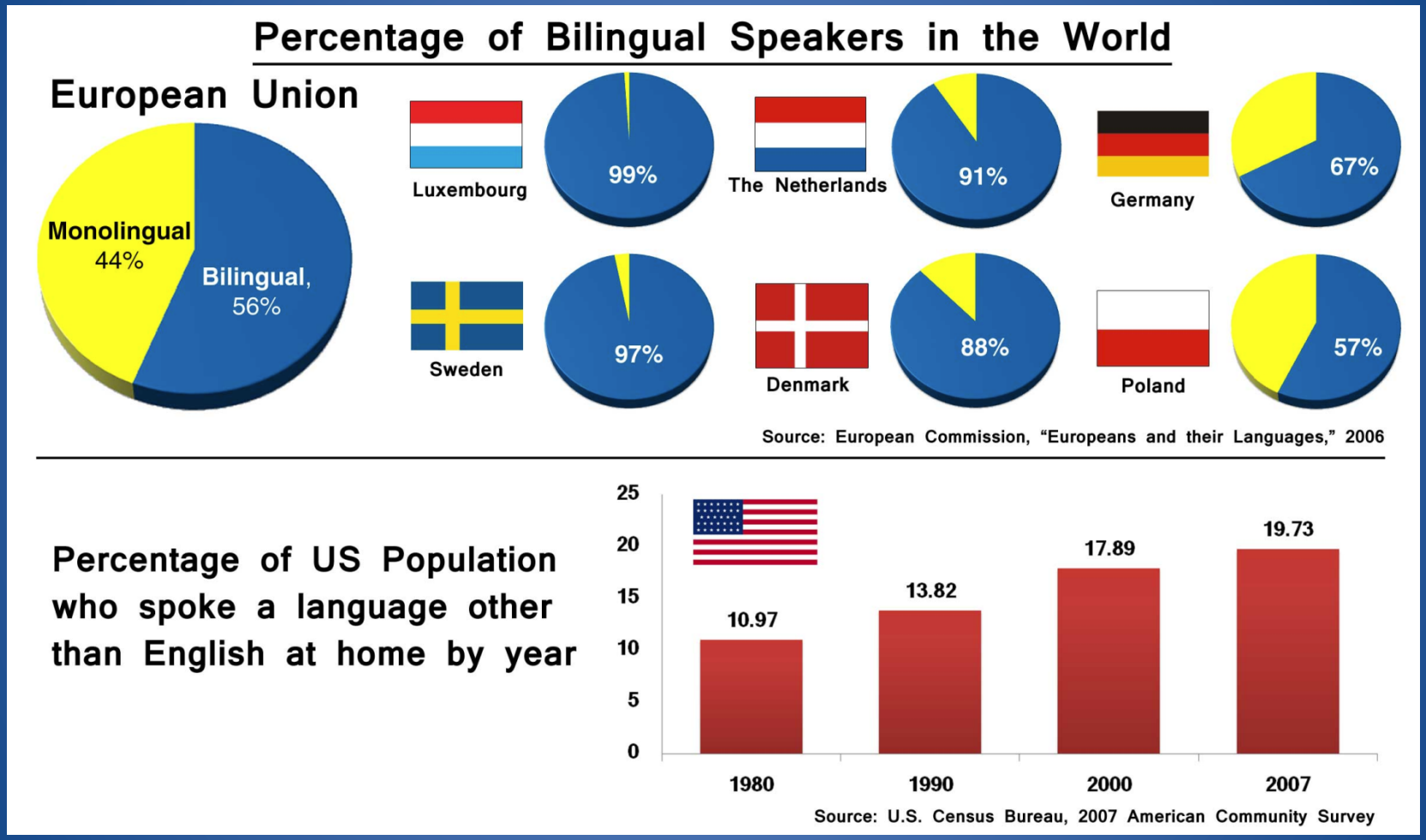
Outline

- Effects of bilingualism on the brain
- Language deficits in MCI and AD dementia
- Presentation of AD dementia in bilinguals
- Bilingualism and the risk of AD
- Bilingualism as a factor in cognitive reserve

Bilingualism: demographics



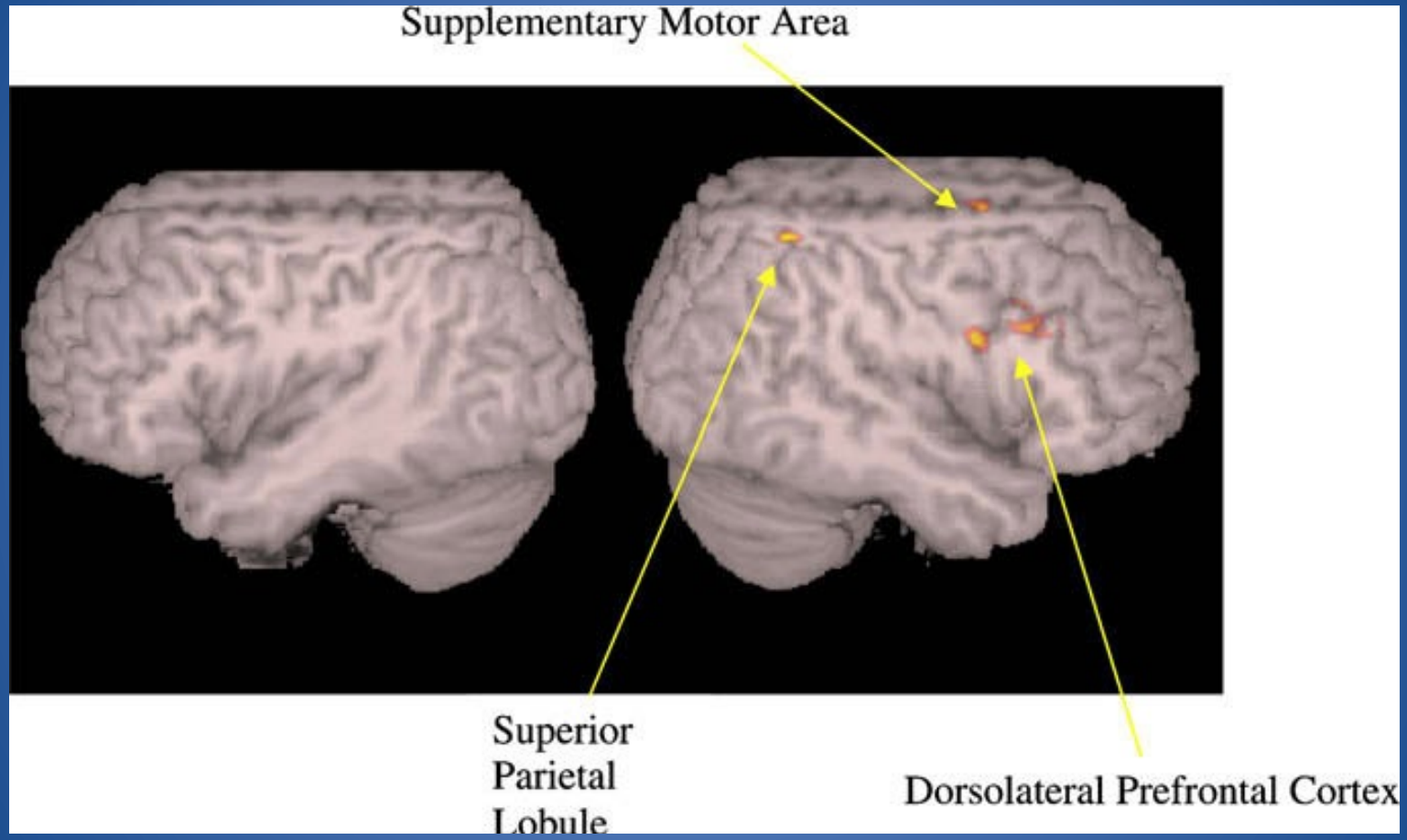
Marian and Shook, 2012

Bilingualism and language processing

- There is evidence of joint activation of languages at all times
- Joint activation creates an attentional problem: the bilingual speaker must select the correct language from competing options and inhibit the non-target language
- Language switching accompanied by activation of dorsolateral prefrontal cortex (DLPFC) – a brain area important for executive control

Hernandez 2009

Brain areas involved in language switching



Hernandez 2009

Effects of bilingualism on cognitive testing

- On picture-naming tasks, bilinguals are slower and less accurate than monolinguals, even in their first and dominant language
- Bilinguals are slower in semantic fluency task ("Tell me as many animals as you can in a minute")
- Bilinguals showed better executive control than monolinguals
- Bilinguals showed better episodic memory recall (Schroeder 2012)

Bialystok 2012

There is evidence for both cognitive advantages and disadvantages in bilingual adults

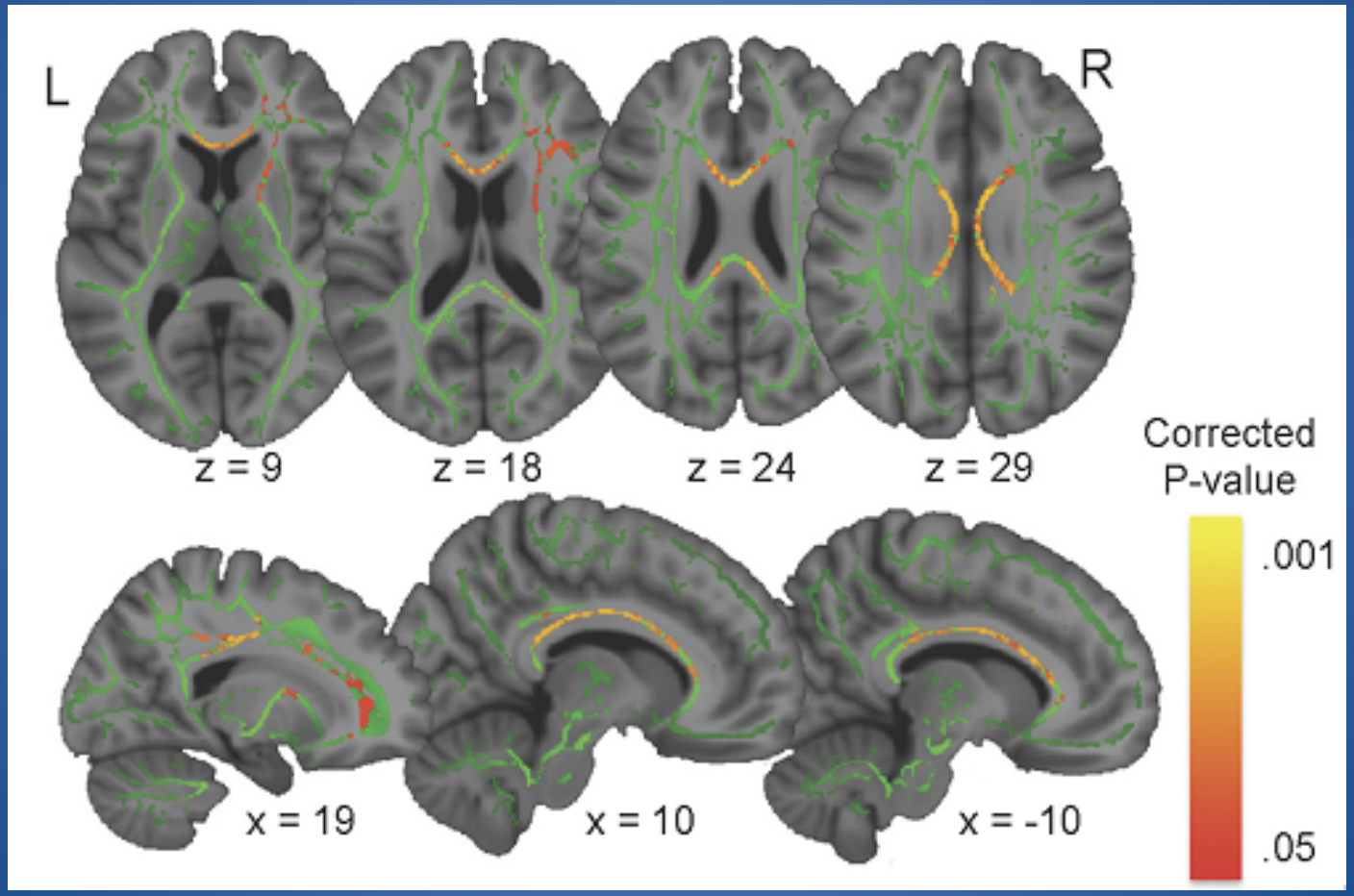
Areas of disadvantage for bilinguals	Areas of advantage for bilinguals
Vocabulary	Executive control
Picture naming	Episodic memory
Semantic fluency	

Effects of bilingualism on brain connectivity

- With brain aging there is reduced myelin, small vessel alterations, and reduced axonal structure/coherence as measured on DTI imaging
- Study of 28 healthy older adults (14 bilinguals, 14 monolinguals)
- Normal cognitive testing, matched for age and education
- On MRI brain DTI, bilinguals showed better maintenance of white matter integrity in the corpus callosum, superior longitudinal fasciculus, IFOF, and uncinate fasciculus

Luk 2011

Increased bihemispheric white matter connectivity in bilinguals



Luk 2011

Language deficits arising in AD

- AD is characterized by short term memory impairment: rapid forgetting, cues do not lead to improvement
- Language deficits in AD manifest as word-retrieval difficulties
- Language deficits tested as impaired object naming and verbal fluency (semantic worse than phonemic)
- Language deficits are due to impaired semantic memory (loss of knowledge of particular items or concepts and the associations between them)

Language deficits arising in AD

- In the initial stages of AD, the lexico-semantic system disintegrates progressively, whereas the phonological and syntactic systems remain relatively preserved
- As AD progresses, all levels of linguistic structure (phonology, morphology, syntax, lexicon, and semantics) deteriorate until a state of mutism results
- Logopenic primary progressive aphasia is often due to AD pathology and is characterized by hesitant, grammatically correct speech, spared language comprehension.

How does AD present in bilinguals?

From caregiver reports:

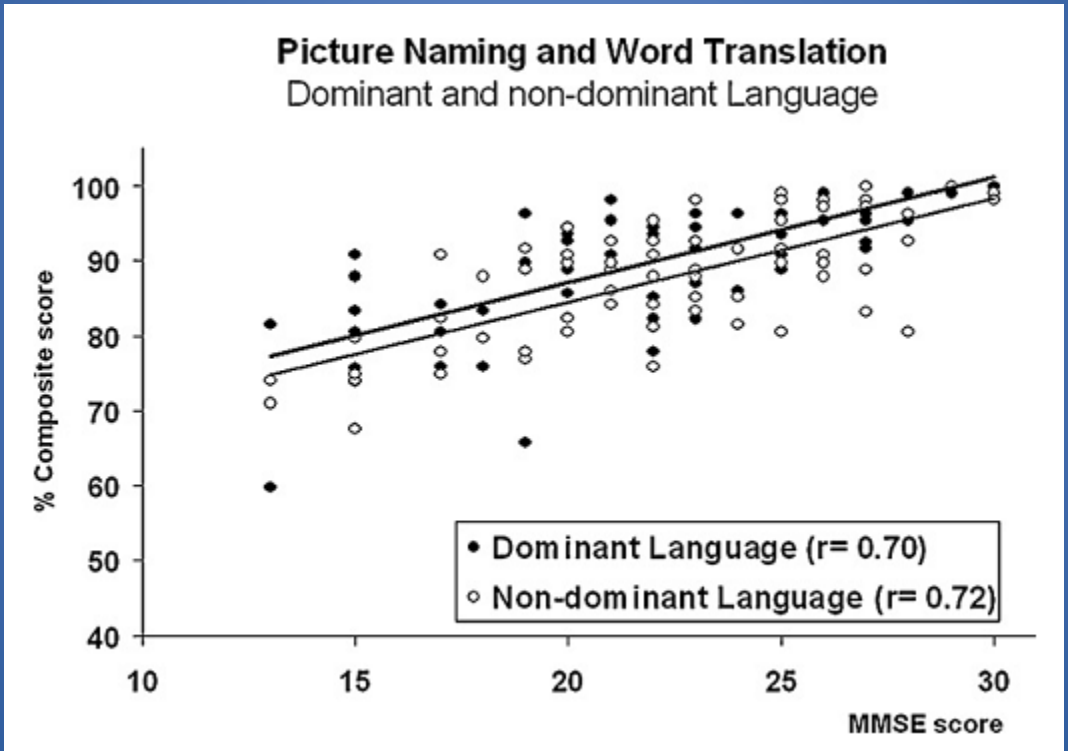
- Language mixing becomes problematic
- "Regression" to use L1 (first language)

Does AD differentially affect L1 or L2?

- In Catalan-Spanish bilinguals with AD, impairment was observed in both languages and in similar tests
- AD patients had fluent speech with word-finding difficulties, impaired comprehension of complex grammatical structures, and preserved automatic language (repetition, reading aloud).

Costa, 2012

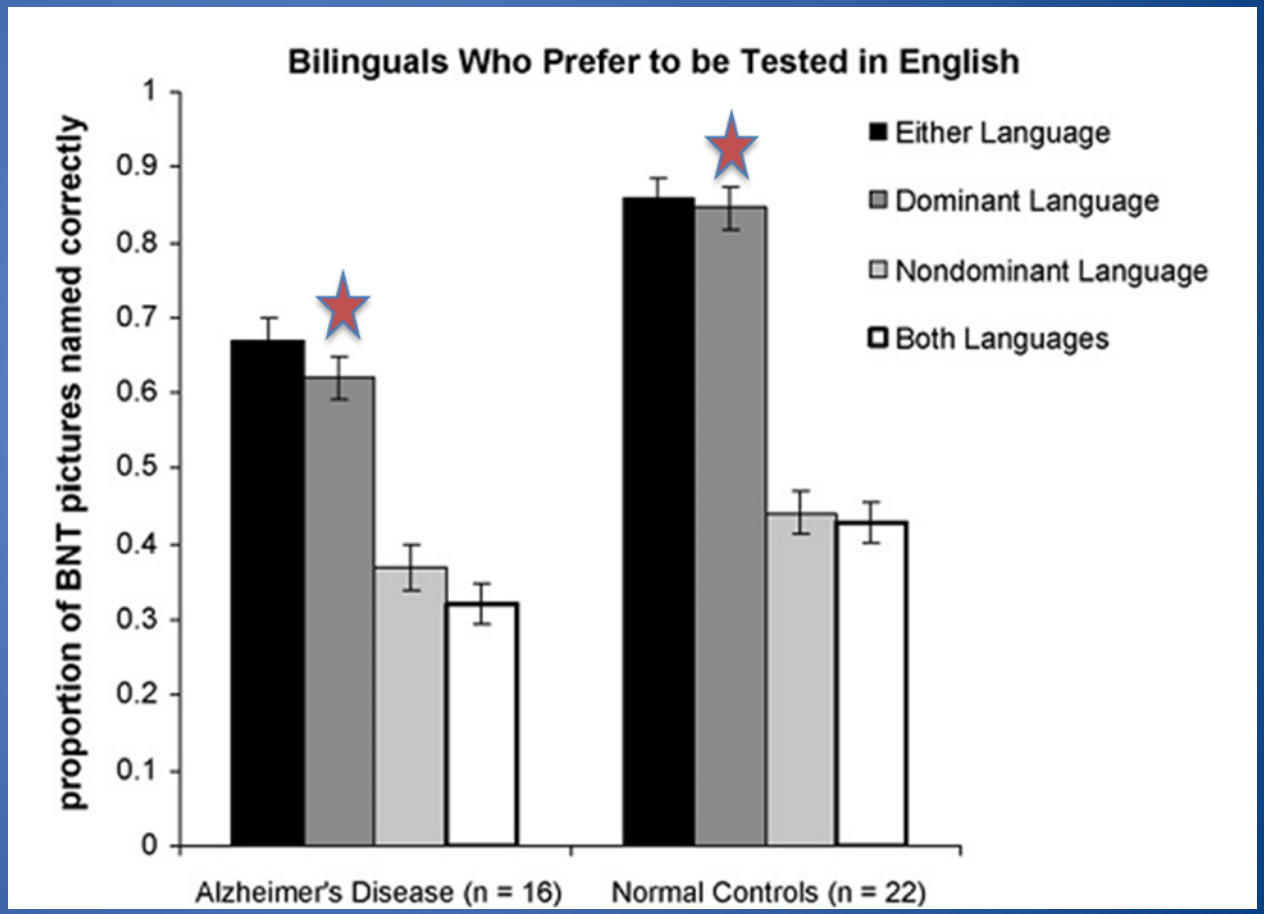
Both languages decline to a similar extent as dementia progresses



Costa, 2012

Hypothesis: Persons with dementia regress to use primarily their first language L1

- Study of Spanish-English bilinguals with AD
- Larger reductions in picture naming occurred in dominant language in AD
- The greater vulnerability of the dominant language may be AD affecting the richer semantic representations in the dominant language



Gollan 2009

Decline in semantic fluency in both languages in bilingual AD patients

- 11 mild AD patients, Spanish-English bilinguals, compared to age, education, age of English acquisition – matched elderly controls
- AD patients showed equivalent deficits in both languages on semantic task ("animals") and showed fewer semantic clusters ("insects," "farm animals," etc.)

	Controls		Alzheimer's Disease Patients	
	Mean	SD	Mean	SD
Phonemic				
Spanish	10.73	3.23	7.94	4.50
English	7.24	2.88	4.42	3.56
Semantic				
Spanish	15.55	6.09	8.09	3.56
English	11.18	3.82	5.09	2.55

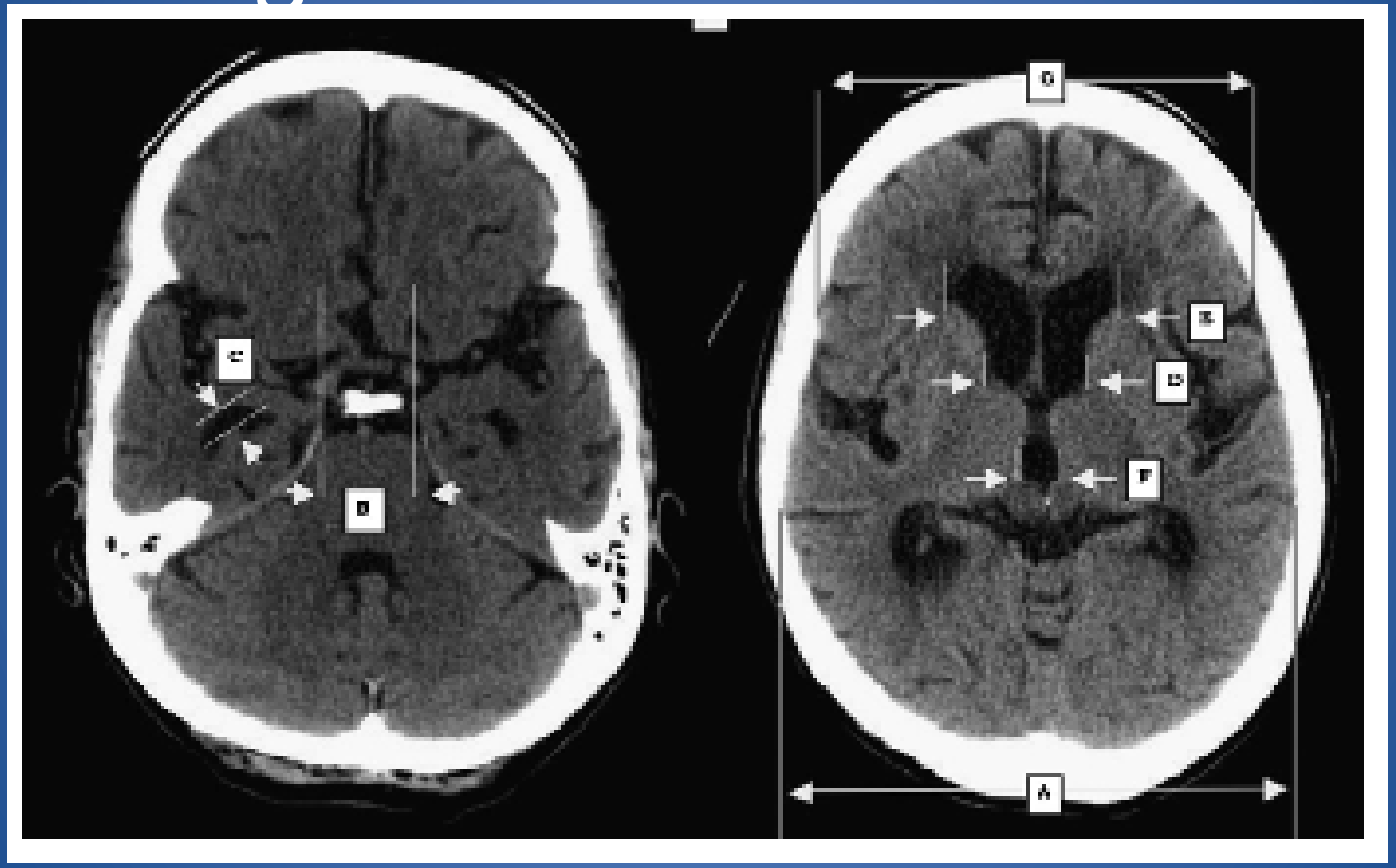
Salvatierra 2007

Effects of bilingualism on brain atrophy in patients with AD

- Study of 20 bilinguals, 20 monolinguals
- Mild AD, matched on stage of dementia
- Bilinguals showed greater temporal lobe atrophy: increased temporal horn ratio, third ventricle ratio, and radial width of the temporal horn
- This suggests that bilinguals required more cerebral atrophy to develop clinical symptoms

Schweizer et al, 2012

Worse temporal lobe atrophy in bilinguals with AD dementia



C: Temporal horn. D: 3rd ventricle.

Schweizer et al, 2012

Does bilingualism affect risk of developing Alzheimer's disease?

- Several studies with differing populations have examined the question
- Bilinguals and monolinguals may differ in numerous ways, apart from language
- Confounders include immigration status, education, socioeconomic status, access to medical care, cultural attitudes regarding dementia
- Bilingualism may impact risk of AD dementia, age of onset, rate of progression

Toronto: Bilingualism delays onset of dementia

- 184 patients referred to a Memory Clinic in Toronto
- 93 (51%) were bilingual (25 different languages, most common: Polish, Yiddish, German)
- Age of onset of was 4 years later in bilinguals
- Severity at initial visit and rate of decline similar
- Neither education (lower in bilinguals) nor occupational status (equal) accounts for the findings

Bialystok 2007

Mean value (and standard deviation) for descriptors for each language group

Language group	*N*	Age of onset	Age at first appointment	Years of education	MMSE at first appointment	Occupation status
Monolingual	91	**71.4 (9.6)**	**75.4 (9.3)**	**12.4 (3.8)**	**21.3 (6.4)**	**3.3 (1.5)**
Men	43	70.8 (9.5)	76.2 (9.1)	12.9 (4.8)	20.5 (6.8)	3.6 (1.5)
Women	48	71.9 (9.8)	74.7 (9.5)	11.9 (2.8)	22.0 (5.9)	3.0 (1.4)
Bilingual	93	**75.5 (8.5)**	**78.6 (8.4)**	**10.8 (4.2)**	**20.1 (7.1)**	**3.0 (1.6)**
Men	38	76.1 (5.9)	79.4 (6.3)	10.8 (4.8)	20.7 (7.5)	3.0 (1.7)
Women	55	75.1 (9.9)	78.1 (9.6)	10.7 (3.7)	19.6 (6.8)	3.1 (1.4)

Caveats to the Toronto study

- Very significant difference in immigrant %
- Monolinguals were 85% Canadian-born, bilinguals were 90% immigrant
- Majority of bilinguals were immigrants from Europe in the 1940s, with different cultural background and stressors

Montreal: Multilingualism, but not always bilingualism delays onset of AD

- 632 persons diagnosed with AD in Montreal
- In nonimmigrants, no difference in age of diagnosis between bilinguals (English/French) and monolinguals
- In immigrants, significant delay in diagnosis by increasing number of languages – monolinguals diagnosed 5, 6.4, 9.5 years earlier than speakers of 2,3, or 4+ languages.

Chertkow 2010

Washington Heights: Bilingualism does not alter cognitive decline or dementia risk

- 1067 non-demented residents of Washington Heights, New York
- All were immigrants to U.S.A.
- Native Spanish-speakers, who had varying degrees of bilingualism
- Followed up to 23 years for development of dementia
- Greater level of bilingualism was associated with better initial performance on executive function and memory
- Bilingualism not associated with rate of change on cognitive tests
- Bilingualism not associated with risk of dementia

Zahodne 2014

Conflicting studies on effect of bilingualism on risk of dementia

Bilingualism is protective	Bilingualism is NOT protective
Bilinguals age of onset AD was 4 years later than monolinguals, n=184 (Bialystok 2007) ★	Non-immigrant Canadians in Montreal seeking assessment for AD, n=632 (Chertkow 2010) ★
Bilinguals age of onset AD was 5 years later than monolinguals, n=211 (Craik 2010)	Prospective, non-immigrant Japanese-Americans in Hawaii, n=236 (2299 total) (Crane 2009)
India: Bilinguals age of onset dementia 4.5 years later than monolinguals, n=648 (Alladi 2013)	Population-based study in Manitoba, no effect of bilingualism on prevalence or incidence of dementia, n=95 (990 total) (Yeung 2014)
Hispanics in San Diego, increasing degree of bilingualism correlated with later onset of AD, but only for those with education < 11 years, n=44 (Gollan 2011)	Population-based study in Manhattan, Hispanic immigrants, degree of bilingualism was not associated with incidence of dementia, n=282 (1067 total) (Zahodne 2014) ★
Luxembourg: Multilinguals had reduced risk of CIND than bilinguals, n=232 (Perquin 2013)	

Studies that did not find a protective effect of bilingualism on risk of AD

- Prospective
- Population-based
- More homogeneous participants
- Larger

Cognitive reserve

- Some factors allow a person to function within a normal cognitive range, despite the presence of brain pathology that would usually be associated with dementia
- Components of cognitive reserve:
  1. Education
  2. High occupational status
  3. Intelligence
  4. Mentally stimulating leisure activities
  5. Exercise
  6. Bilingualism?

Activity and experience can modify brain structure and function

- Brain reserve
  - arises from physical properties of the brain
  1. Size
  2. Neuronal count
  3. Synapse count
  4. Connectivity
  - A threshold model: once brain reserve is depleted past some fixed critical threshold specific deficits emerge

- Cognitive reserve – activities or experiences during life that can build brain reserve

How does cognitive reserve protect against dementia?

- Enhanced neural plasticity
- Compensatory use of alternative brain regions
- Enriched brain vasculature

How important is cognitive reserve?

- 30% of individuals who exceed pathologic criteria for AD at autopsy showed no signs of cognitive impairment during life

Valenzuela 2006

Cognitive reserve mediates link between pathology and memory performance

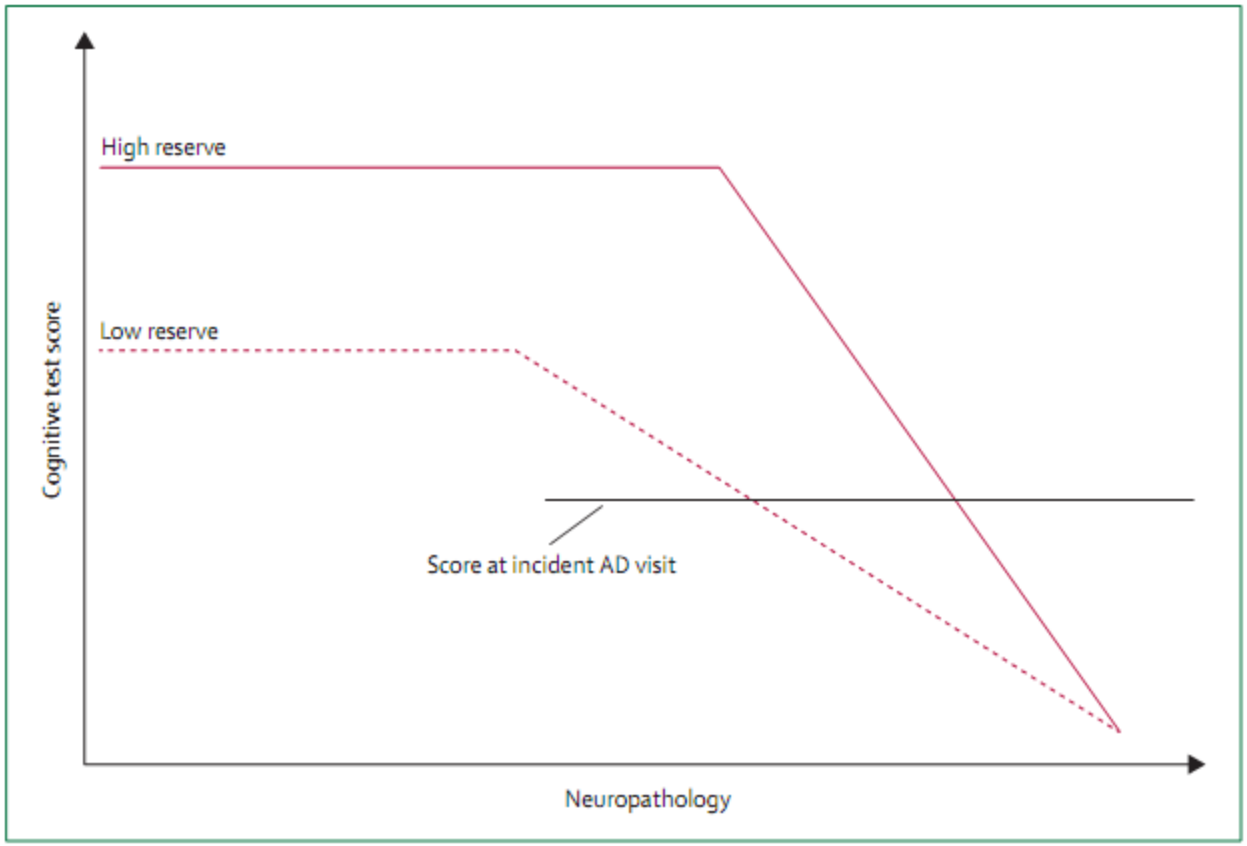
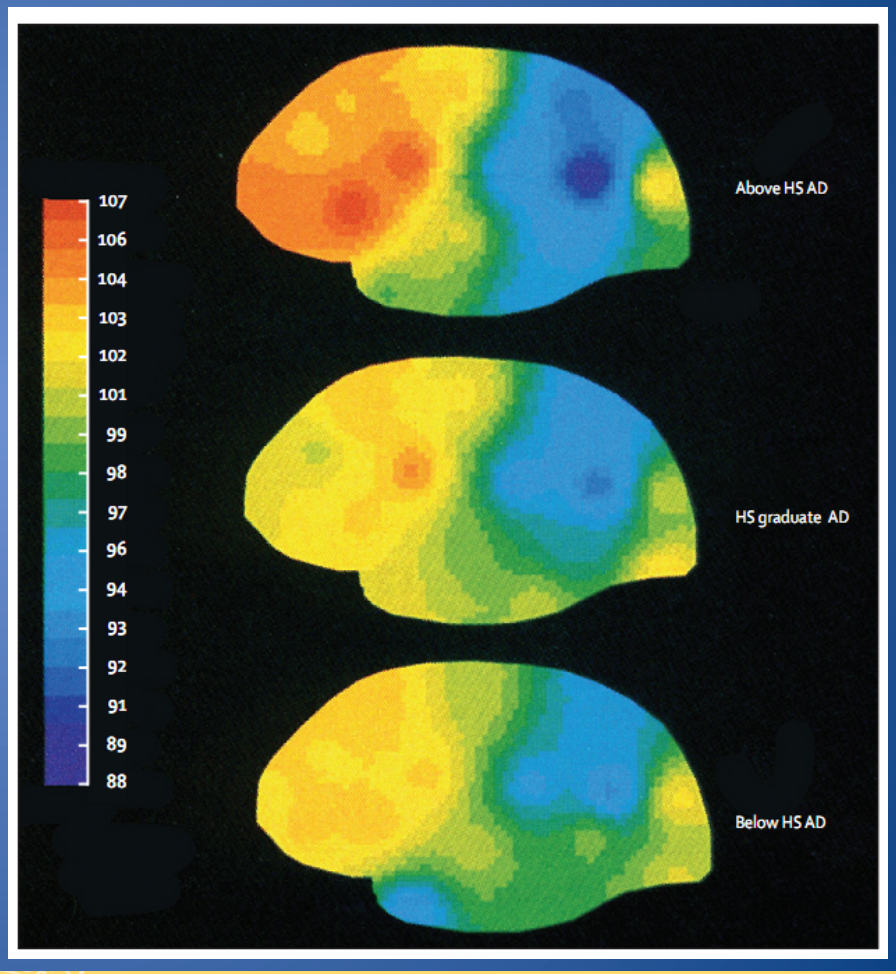


Figure 1: Hypothesised change in memory function over time in individuals with high and low cognitive reserve

Stern, 2012

Inverse relationship between education level and cerebral blood flow in AD

- 20 patients in each group, matched for clinical severity
- SPECT scans performed
- All groups showed typical parieto-temporal reduced CBF
- Highest educated group showed the lowed CBF, indicative of the greatest pathology



Stern 1992

Magnitude of cognitive reserve effects

- Meta-analysis of 29 studies involving over 29,000 persons
- Higher levels of education, mentally-stimulating occupation, higher premorbid IQ, and mentally-stimulating leisure activity reduced risk of dementia by 42-50%

Outcome: 01 Incident Dementia

Study (first-named author)	High activity (n/N)	Low activity (n/N)	OR (95% CI random)	Weight (%)	OR (95% CI random)
Education					
Hebert (1992)	34/362	42/149		2·6	0·26 (0·16–0·44)
Paykel (1994)	13/376	36/783		1·8	0·74 (0·39–1·42)
Bickel (1994)	7/84	27/230		1·1	0·68 (0·29–1·63)
Stern (1994)	37/329	69/264		3·1	0·36 (0·23–0·56)
Cobb (1995)	138/2033	37/267		3·5	0·45 (0·31–0·67)
Person (1996)	8/86	30/236		1·2	0·70 (0·31–1·60)
Schmand (1997)	59/949	93/1114		4·1	0·73 (0·52–1·02)
Evans (1997)	24/312	70/326		2·7	0·30 (0·19–0·50)
Elias (2000)	59/604	47/441		3·4	0·91 (0·61–1·36)
Ott (1999)	32/2386	68/2601		3·2	0·51 (0·33–0·77)
Ganguli (2000)	87/736	112/562		4·5	0·54 (0·40–0·73)
Scarmeas (2001)	82/866	130/922		4·6	0·64 (0·48–0·85)
Qiu (2001)	37/536	110/760		3·5	0·44 (0·30–0·65)
Fitzpatrick (2004)	323/2598	154/764		5·7	0·56 (0·46–0·69)
Tuokko (2003)	63/289	79/232		3·5	0·54 (0·37–0·80)
Occupation					
Bickel (1994)	10/153	24/159		1·4	0·39 (0·18–0·85)
Stern (1994)	17/201	71/327		2·2	0·33 (0·19–0·58)
Paykel (1994)	20/454	28/683		2·1	1·08 (0·60–1·94)
Evans (1997)	22/245	50/284		2·4	0·46 (0·27–0·79)
Schmand (1997)	29/682	111/1206		3·2	0·44 (0·29–0·67)
Schmand (1997)	36/668	110/1173		3·5	0·55 (0·37–0·81)
Jorm (1998)	7/178	6/86		0·7	0·55 (0·18–1·68)
Elias (2000)	46/467	63/607		3·4	0·94 (0·63–1·41)
Scarmeas (2001)	37/425	126/1013		3·6	0·67 (0·46–0·99)
Helmer (2001)	21/281	372/2669		2·9	0·50 (0·32–0·79)
Anttila (2004)	21/652	27/420		2·1	0·48 (0·27–0·87)
Karp (2004)	52/574	49/339		3·3	0·59 (0·39–0·89)
Premorbid IQ					
Schmand (1997)	62/1084	90/979		4·1	0·60 (0·43–0·84)
Elias (2000)	23/271	40/271		2·2	0·54 (0·31–0·92)
Leisure activity					
Fratiglioni (2000)	129/964	47/239		3·7	0·63 (0·44–0·91)
Scarmeas (2001)	77/891	130/881		4·5	0·55 (0·41–0·74)
Wang (2002)	37/338	86/394		3·3	0·44 (0·29–0·67)
Verghese (2003)	84/382	40/87		2·2	0·33 (0·20–0·54)
Total (95% CI)	1733/21456	2574/21468	◆	100·0	0·54 (0·49–0·59)

Test for heterogeneity $\chi^2 = 55{\cdot}62$, df=32, $p = 0{\cdot}006$
Test for overall effect $z = -12{\cdot}30$, $p < 0{\cdot}00001$

0·1 0·2 1 5 10
Favours protective Favours risk factor

Valenzuela 2006

Limitation in concept of cognitive reserve

Correlational in nature:

- Do individuals with high educational/ occupational attainment have genetically well-endowed brains which allow them to succeed in life and resist AD?
- Or does educational/occupational attainment lead to cognitive reserve and protect against dementia?

Bilingualism as a source of cognitive reserve

- Bilingualism is generally *not* due to an inherited brain characteristic
- Generally due to immigration or a difference between family language and language of school or workplace
- Thus bilingualism is an environmental factor that may produce cognitive reserve

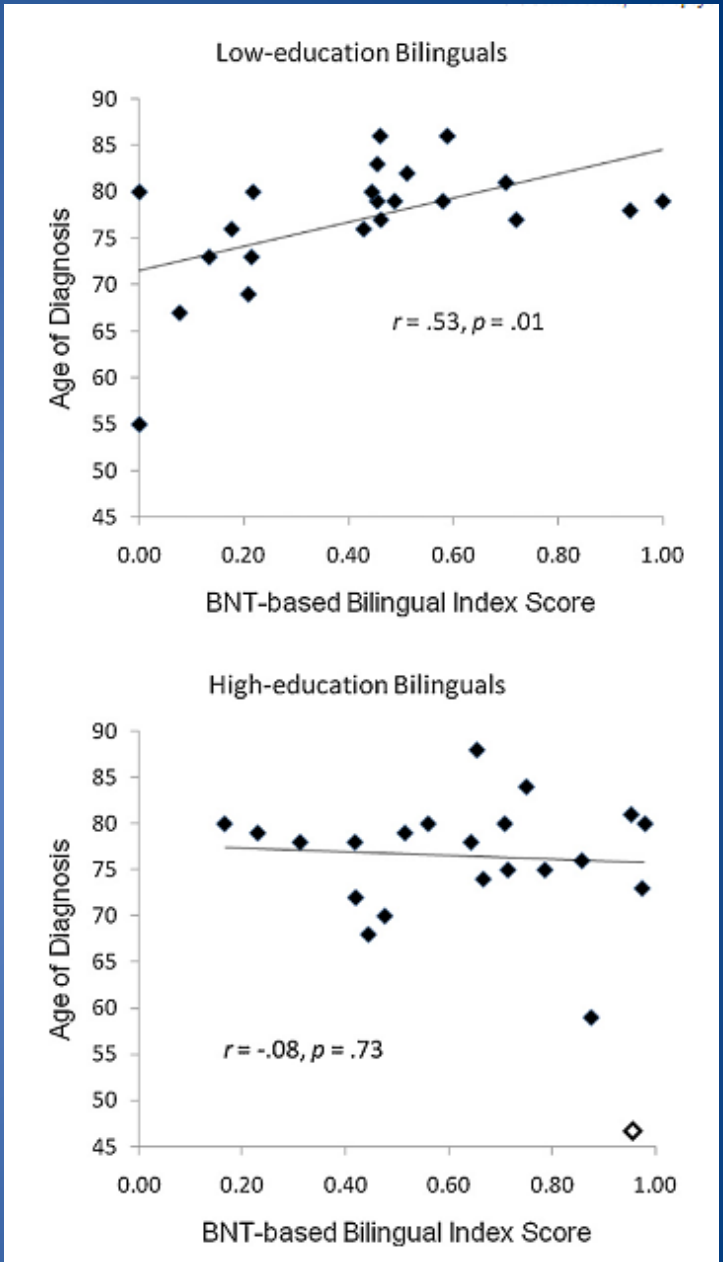
Is there evidence that bilingualism is a form of cognitive reserve?

- Executive function/control: Decision-making, inhibition, multi-tasking, logic
- Bilinguals show advantages in tests of executive control
- The continuous practice/experience of monitoring context for potential language switches and inhibiting the language not under active use builds the cognitive reserve in executive control

Bilingualism delays AD onset only in low-education persons

- 44 Spanish-English bilinguals diagnosed with AD
- Varying degrees of bilingualism based on Boston Naming Test
- Increasing degree of bilingualism was associated with later age of diagnosis, but only in those with 11 years of education or less
- Is there an upper limit on the amount of cognitive reserve that can accumulate?

Gollan 2011



Further questions

- Multilingualism?
- Level of bilingualism?
- Age of bilingualism?
- Similarity between languages?
- Is bilingualism additive with other forms of cognitive reserve, or is there a maximum which cannot be exceeded?

Conclusions

- Bilinguals show better memory and executive function than monolinguals throughout the lifespan
- When bilinguals develop AD, both languages decline
- Bilingualism, or especially multilingualism, may delay risk of AD

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