# Bilingualism : Consequences for the progression of MCI MCI conference, Miami Beach, January, 2018

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# Recent suggested protective factors for AD

**(based on animal or population studies, not RCT's)**

Rheumatoid arthritis

Use of NSAIDs

Nutrition:anti-oxidants (fruit juice) , red wine

Nutrition-flavenoids - blueberries

low homocysteine, (high folate, B6, B12 intake)

Mediterannean diet (low fat)

Cold water fish diet (omega fatty acids)

Use of Estrogen since menopause

More exercise (Larson, Ann. Int Med., 2006)

Education

Mental stimulation, professional (complex) work

Leisure activities

Bilingualism

## There are two ways to modify dementia clinical onset:
**(Both aim to explain disjunctions between degree of brain damage and its outcome)**

1. Increase Brain reserve capacity prenatal to childhood

- Genetic protective factors, early nutrition, etc. affect synapse count, brain size, etc. These increase "brain reserve capacity".
  - When synapses are depleted beyond a critical threshhold, symptoms occur.

2. Build Cognitive reserve

•Environmental factors: education, stimulating environment, occupation -affect active cognitive reserve.

•Greater flexibility and efficiency increase tolerance for pathology, affect critical threshhold for symptoms to occur

•Biological mechanism not yet clear.

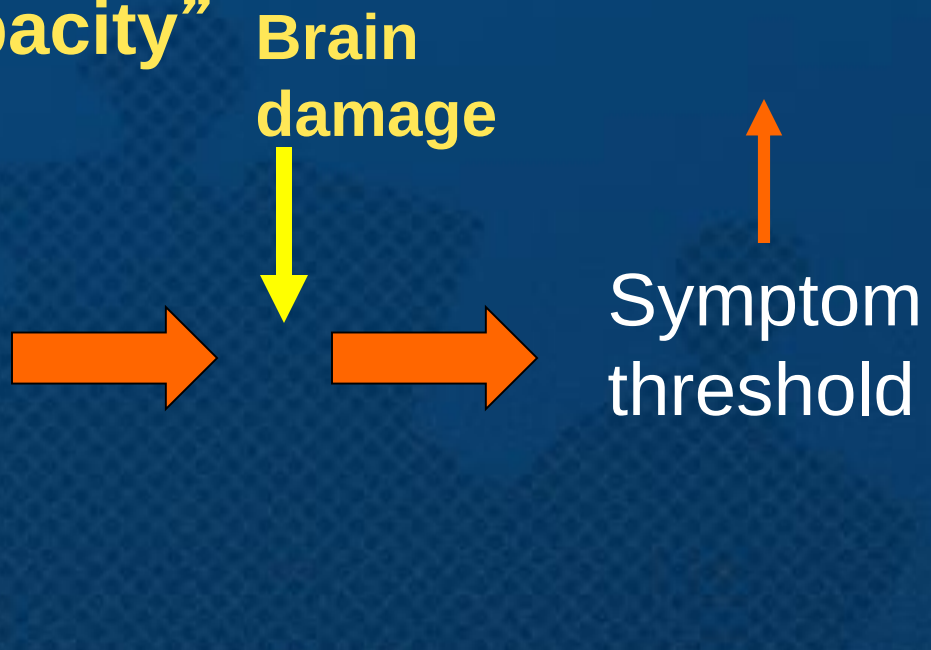
["What is cognitive reserve? Theory and research application of the reserve concept" [Stern, J Int Neuropschol,2002;8(3):448-460];

[Bartres-Faz and Arenaza-Urquijo, 2011]

# Evidence for brain reserve capacity-building the hardware of the brain

**“Brain reserve capacity”**

- Brain size
- Head circumference
- Neuronal count
- Synaptic count
- Cortical thickness
- Dendritic branching




- These are surrogates and measures for brain reserve capacity.

- pre-natal > post-natal > lifetime

# Evidence for Cognitive reserve "proxies" and acquired factors-all these delay onset of dementia or are associated with less dementia

- socioeconomic status
- income
- occupation
- education/literacy
- I.Q.
- Executive cognitive functions
- leisure activities
- Bilingualism (?)

# Modelling active cognitive reserve

- CR Implementation may involve two forms:
  - Neural reserve (different networks, greater capacity)
  - Neural compensation ( use of different processes in the presence of pathology)
- May or may not be reflected in greater number of synapses in certain individuals.
- Modifies effect of damage needed to produce deficits(eg.,AD)
- There may be overlap between cognitive reserve and brain reserve.

# Education and the prevalence of dementia and Alzheimer's disease

**[Katzman, Neurology,1993;43:13-20]**

Shanghai survey-1993

"lack of education is a major risk factor for..prevalence of dementia"

-Illiterates had twice the prevalence of dementia as educated individuals.

-subsequent similar effect in multiple studies around the world
-reflected in both prevalence and incidence of dementia
-reflected in strictly AD diagnoses, and in cognitive decline rates
-There is a "dose-response to education"

# Occupation and incident AD

- relationship found in 3 population studies
  [Kivipelto,Jorm,Helmer]
- relationship absent in 2 others

↑ (or explained by education)

- multiple other studies have found links
  - AD with lower SES

# Leisure activities promote CR, decrease AD incidence

Sweden longitudinal study [Kungsholma] [Pratiglioru et al, Lancet,2000;355: 1315-1319,Wang et al, Am J. Epidemiology,2002;155]

- Extensive social network is protective vs incident dementia
- Engagement in activities - social, mental, is protective vs incident dementia

# Imaging evidence for Cognitive Reserve

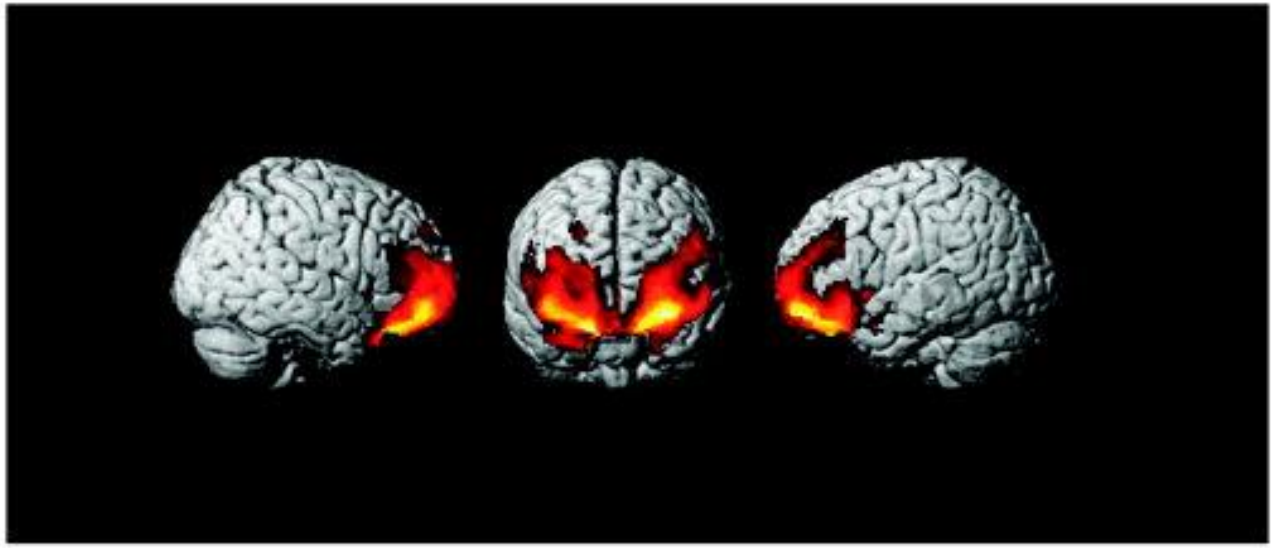
- Resting CBF affected by education, occupation, leisure
- Altered activation pattern correlates
- AD amyloid load [PIB] evidence for CR

# Cognitive reserve hypothesis: Pittsburgh compound B and fluorodeoxyglucose positron emission tomography in relation to education in mild Alzheimer's disease [Kemppainen et al.,Ann Neurol,2008;63:112-118]

- 12 high education, 13 low education AD patients in FInland
- same severity of dementia (MMSE = 26)
- FDG PET, [11C] PIB PET
- High educated group had increased PIB in lateral frontal cortex vs. low educated.
- High educated had lower glucose metabolism in TP cortex.

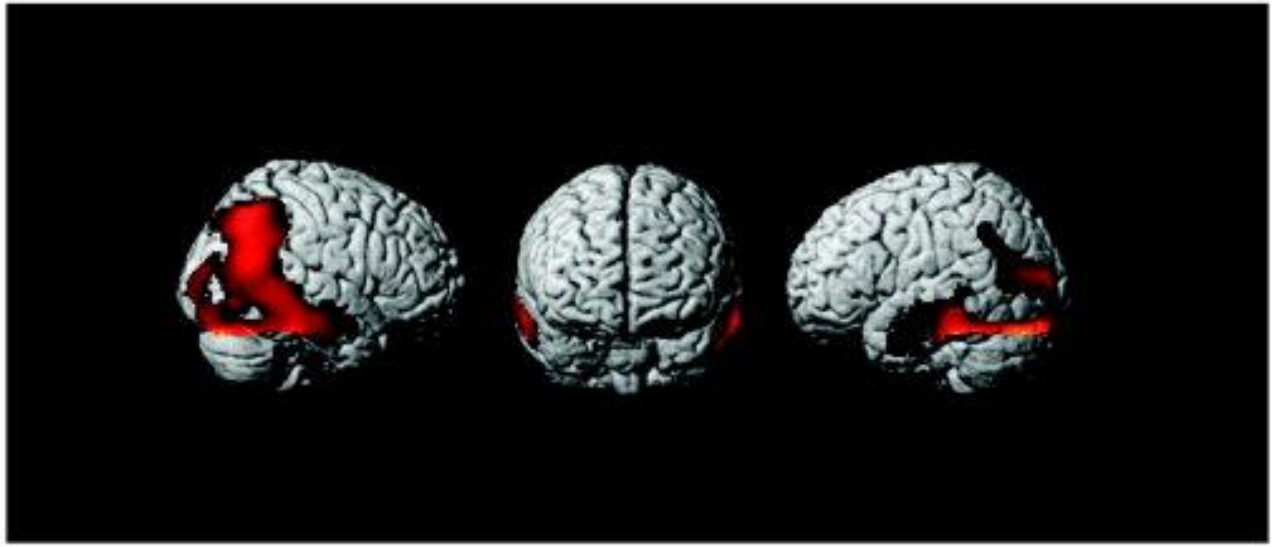
# Significant differences between High and Low Ed groups

PIB
High>
Low



FDG

High<
Low



# Does cognitive reserve affect just software, or also hardware?

Rats raised in enriched environment had thicker cerebral cortices, and performed better on cognitive tests. [Markhan et al, Neuron Glia Biol, 2004;1:351-63]

- Increase in hippocampus, ERC, BG.
- Neurons, synapses, dendritic arborization.

Adult marmoset monkeys- similar changes in dendrites, synapse growth. [Kozorovitsky et al, PNAS,2005;102:`7478-82]

# NOTE- Cognitive reserve in dementia carries a price! Higher CR means more rapid later decline in AD

[Stern et al,Neurology,1999;53: 1942-57]

- pts with higher CR have later onset AD symptoms
- their AD = higher pathology burden
- therefore they decline more rapidly
- higher mortality rate in advanced AD

[Geerlings,Psychol.Med,1999;29: 1219-1226]

# Education delays accelerated decline on a memory test in persons who develop dementia

**[Hall et al., Neurology,2007;69:1657-1664]**

-117 individuals (Bronx Aging Study) with new onset dementia. Change in memory prior to the diagnosis on SRT annually.

-32 subjects < 7 years education, 64s's with 8-11, 21 s's with >12 years.

-rate of decline before diagnosis of AD greatest for the high education group.

-suggests that this group had "more reserve" and therefore had more pathology leading to rapid decline.

# Education delays accelerated decline on a memory test in persons who develop dementia

**[Hall et al., Neurology,2007;69:1657-1664]**

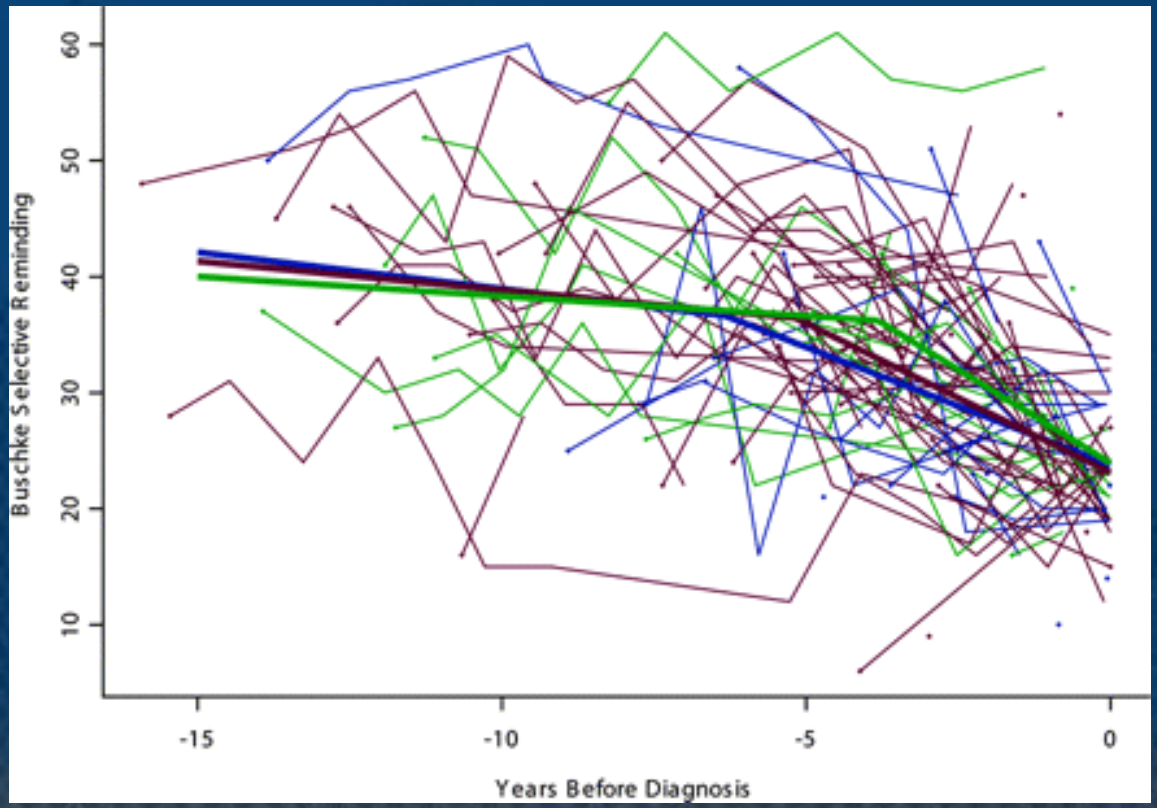



Figure Memory as measured by the Buschke Selective Reminding Test as a function of time to diagnosis of dementia and of education in 117 Bronx Aging Study participants who developed dementia

Narrow lines are the trajectories of the individual participants; broad lines are the average trajectories from the model described in the text and also described in table 2. Blue indicates less than 7 years education (32 Ss), red indicates 8 to 11 years (64 Ss), and green indicates 12 or more years education (21 Ss).

# How far does cognitive reserve go? Example of bilingualism

# What's good about bilingualism?

**Judith Kroll (2012)**

- More people in the world are bilingual than unilingual!
- Research shows that both languages in a bilingual's brain are active even if just using one language. The parallel activity of the two languages (in naming, reading, speaking, listening) is hypothesized to produce competition.
- A life of resolving cross-language competition may make you a "mental juggler"…so builds Cognitive Reserve

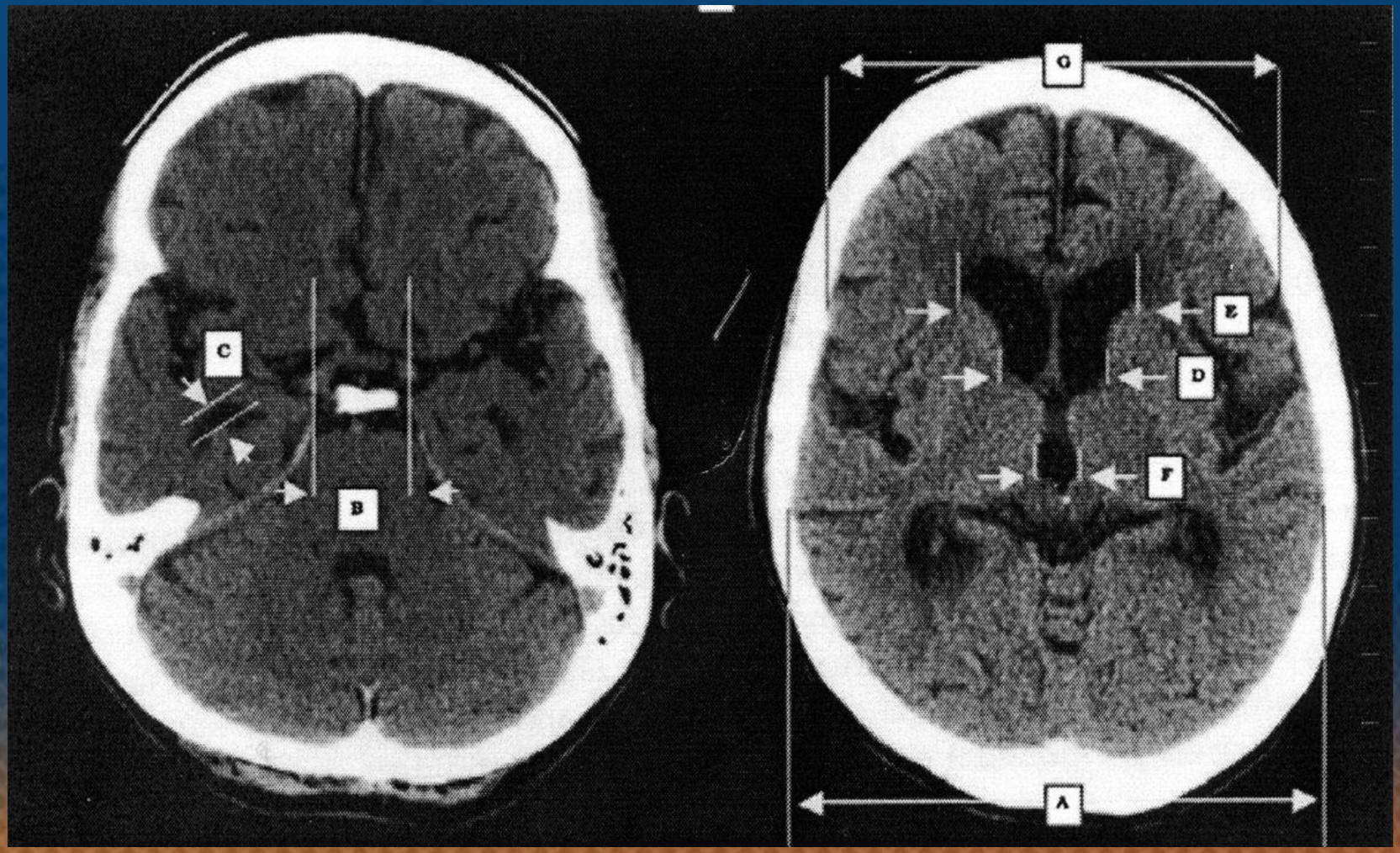
Abutalebi, Cappa: Bilingualism tunes the anterior cingulate cortex for conflict monitoring. So less activation of ACC during conflict monitoring.

# Some supporting evidence from CT measures

**"Bilingualism as a contributor to cognitive reserve: Evidence from brain atrophy in AD" Schweizer, Ware…Bialystok,** Cortex (2012), 48, 991-6

- 40 subjects with probable AD- 20 bilingual, 20 unilingual.
- Matched on education, MMSE, clock drawing.
- Actually had similar age of diagnosis! (77.3, 78.9).
- Seven linear measurements on axial CT slices (Evans ratio, temporal horn ratio, etc).
- If bilingualism is protective, then the brains of bilinguals should show greater atrophy in relevant areas, since their enhanced CR enables them to function at a higher level than would be predicted from their level of disease.
- the radial width of the temporal horn and the temporal horn ratio showed more atrophy in bilinguals, = more medial temporal atrophy. Other measures not significant
- Suggests bilinguals had more damage in MTL to produce same level of dementia, = greater cognitive reserve.

Bilingualism as a contributor to cognitive reserve: Evidence from brain atrophy in Alzheimer's disease
Schweizer, T. A. et al, Cortex (2012), 48, 991-996




Note: most measures are of medial temporal lobes

# Bilingualism as a contributor to cognitive reserve: Evidence from brain atrophy in Alzheimer's disease

Schweizer, T. A. et al, Cortex (2012), 48, 991-996

**Table 2 – Brain ratios and scores of monolingual and bilingual patients.**

| | Monolingual ($n = 20$) | | Bilingual ($n = 20$) | |
|---|---|---|---|---|
| | Mean | SD | Mean | SD |
| Bicaudate ratio | .17 | .03 | .18 | .05 |
| Huckman's number | 60.01 | 7.82 | 64.30 | 12.18 |
| Evans ratio | .36 | .05 | .35 | .07 |
| Suprasellar cistern ratio | .20 | .02 | .20 | .02 |
| Temporal horn ratio | .03*** | .01 | .05*** | .02 |
| Third ventricle ratio | .06** | .02 | .07** | .01 |
| Radial width of the temporal horn (rWTH) [a] | | | | |
| Left | 4.16*** | 1.09 | 7.23*** | 3.21 |
| Right | 4.04* | 1.56 | 6.48* | 3.64 |
| Largest | 4.69*** | 1.31 | 7.87*** | 3.53 |

*$p < .05$.
**$p < .01$.
***$p \leq .001$.
a $n = 19$/group.

# What do these studies mean?:

Authors conclude:

It is causation, not just association

How does bilingualism protect from dementia?

1. Could modify disease progress.
2. Stimulating activities could prevent hippocampal atrophy
3. Compensatory. Increase ability of brain to compensate for disease effects- most likely mechanism.

Key unanswered questions:

a) Do people who are bilingual thereby develop stronger brains, more connections, more cognitive reserve? Or

b) do people with better brains tend to become bilingual more than others?

**“Neuroanatomical evidence of multilingualism’s contribution to brain reserve and cognitive reserve in patients with mild cognitive impairment and Alzheimer Disease” (Duncan, Chertkow, Phiillips 2017)**

PURPOSE: Extend upon the work of Schweizer et al. (2012) using MRI derived cortical thickness measures and tissue density measures of brain atrophy in AD’s and also in MCI’s.

HYPOTHESIS: Brain reserve might show thicker cortices in all subjects in language areas. Cognitive reserve might show greater atrophy in matched AD bilinguals vs. monoliguals.

# Methods

- Research protocol MRIs  (1 mm slices). Cortical thickness and VBM (voxel based morphometry) measures were derived using machine driven algorithms developed at the MNI and JGH (Ad-Dab'bag et al. 2006, Nikelski et al. 2012)
- Subjects were matched within the AD & MCI groups based on age at time of scan and symptom severity.
- Regions of interest (ROI's) were selected to reflect areas involved in cognitive control (frontal areas, insula), memory (hippocampus & parahippocampal gyri) and language (temporal areas)
- .

# Subject Demographics

## AD Group:

| | Overall | Monolinguals | Multilinguals (2+ languages) |
|---|---|---|---|
| n (% female)√ | 36 (47%) | 18 (72%) | 18 (22%) |
| Age at scan* | 77.6 +/- 4.6 (69-84) | 78.3 +/- 4.6 (69-83) | 77.0 +/- 4.6 (69-84) |
| MMSE at scan* | 23.8 +/- 1.5 (22-26) | 23.6 +/- 1.3 (22-26) | 24.1 +/- 1.7 (22-26) |
| Education (yrs.) | 12.1 +/- 3.6 (7-22) | 11.9 +/- 3.3 (7-20) | 12.3 +/- 4.0 (7 -22) |
| Age at Dx | 76.8 +/- 4.5 (69-83) | 77.6 +/- 4.7 (69-83) | 76.1 +/- 4.3 (69-83) |
| % immigrants£ | 33.3% | 11.1% | 55.6% |

Note that Age at diagnosis and symptom onset is roughly same across groups

## MCI Group:

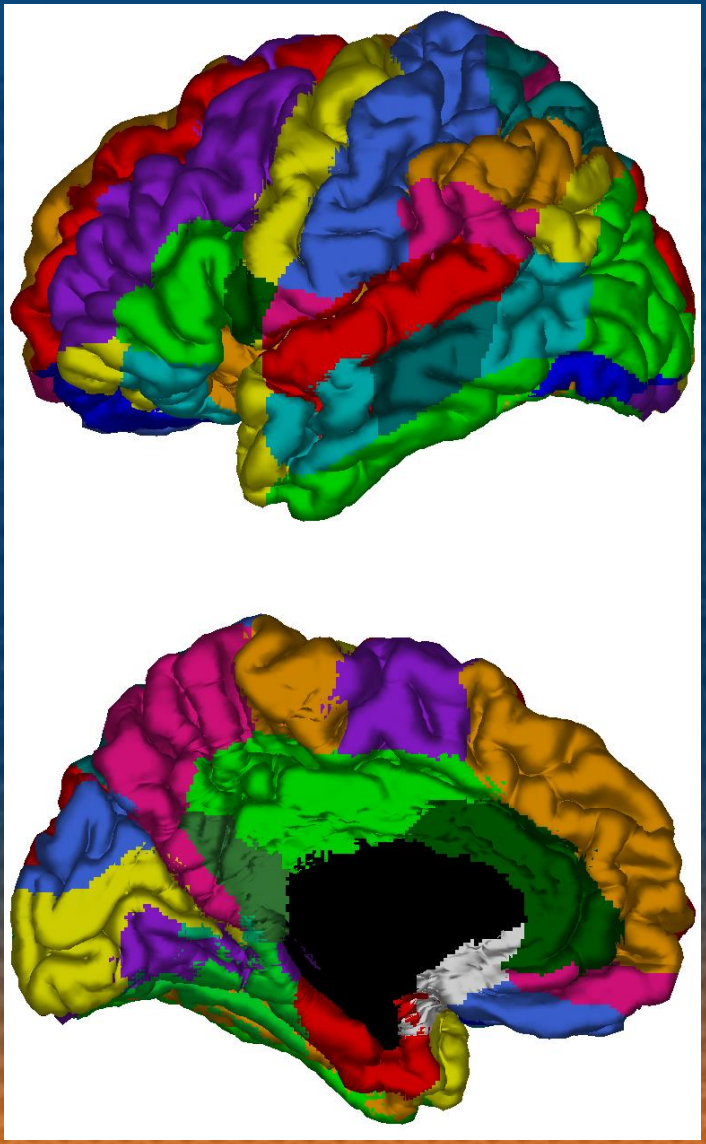
| | Overall | Monolinguals | Bilinguals | Multilinguals (3+ languages) |
|---|---|---|---|---|
| n (% female) | 87 (48%) | 46 (54%) | 22 (41%) | 19 (42%) |
| Age at scan* | 72.1 +/- 5.4 (55-79) | 72.5 +/- 4.9 (60-79) | 72.3 +/- 5.3 (59-79) | 71.2 +/- 6.8 (55-79) |
| MMSE at scan* | 28.0 +/- 1.5 (25-30) | 28.0 +/- 1.5 (25-30) | 28.5 +/- 1.4 (25-30) | 27.6 +/- 1.6 (25-30) |
| Education (yrs.) | 12.6 +/- 4.2 (7-25) | 12.6 +/- 3.8 (7-25) | 13.1 +/- 5.7 (4-25) | 12.2 +/- 3.2 (5-17) |
| Age at Symptom Onset | 67.8 +/- 6.5 (49-77) | 68.3 +/- 5.9 (49-77) | 68.2 +/- 6.0 (57-76) | 66.1 +/- 8.3 (49-77) |
| % immigrants£ | 40.2% | 23.9% | 45.5% | 73.7% |

√: proportion of females is significantly different between monolinguals & bilinguals (Continuity Corrected $\chi 2$: $p<0.01$)
*: Variables matched between linguistic groups
£: proportion of immigrants is significantly different between monolinguals & multilinguals (Continuity Corrected $\chi 2$: $p<0.05$)

Group means, standard errors, F-values, and *p*-values for demographic variables.

| | MCI | | | | | | | AD | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Monolingual (n=34) | | Multilingual (n=34) | | | | | Monolingual (n=13) | | Multilingual (n=13) | | | |
| | M | SE | M | SE | F | p | | M | SE | M | SE | F | p |
| **Age at scan** | 73.6 | 0.9 | 73.7 | 1 | 0.01 | 0.95 | | 78.5 | 1.5 | 78.0 | 1.5 | 0.06 | 0.81 |
| **MMSE at scan** | 26.7 | 0.4 | 27.6 | 0.3 | 2.16 | 0.15 | | 22.5 | 0.9 | 22.5 | 1.0 | 0.00 | 1.00 |
| **Scan to assessment (days)** | -18.5 | 12.3 | 10.7 | 25.4 | 0.36 | 0.55 | | 160.1 | 104.7 | 90.3 | 83.1 | 0.77 | 0.38 |
| **Education** | 12.5 | 0.7 | 12.3 | 0.7 | 0.05 | 0.83 | | 12.7 | 1.0 | 12.1 | 1.1 | 0.17 | 0.68 |
| **Age at symptom onset** | 68 | 1.1 | 67.8 | 1.3 | 0.02 | 0.90 | | 74.3 | 1.5 | 72.6 | 1.6 | 0.44 | 0.51 |
| **Age at diagnosis** | 71.5 | 0.9 | 72.2 | 1 | 0.28 | 0.60 | | 77.1 | 1.6 | 76.7 | 1.3 | 0.04 | 0.84 |
| | N | % | N | % | | | | N | % | N | % | | |
| **Women** | 17 | 50 | 15 | 41 | | | | 8 | 62 | 3 | 23 | | |
| **Immigrant** | 7 | 21 | 20 | 59 | | | | 2 | 15 | 7 | 54 | | |
| **Bilingual** | - | - | 18 | 53 | | | | - | - | 9 | 69 | | |

# Cortical thickness regions of interest (AAL method, 48 ROIs)



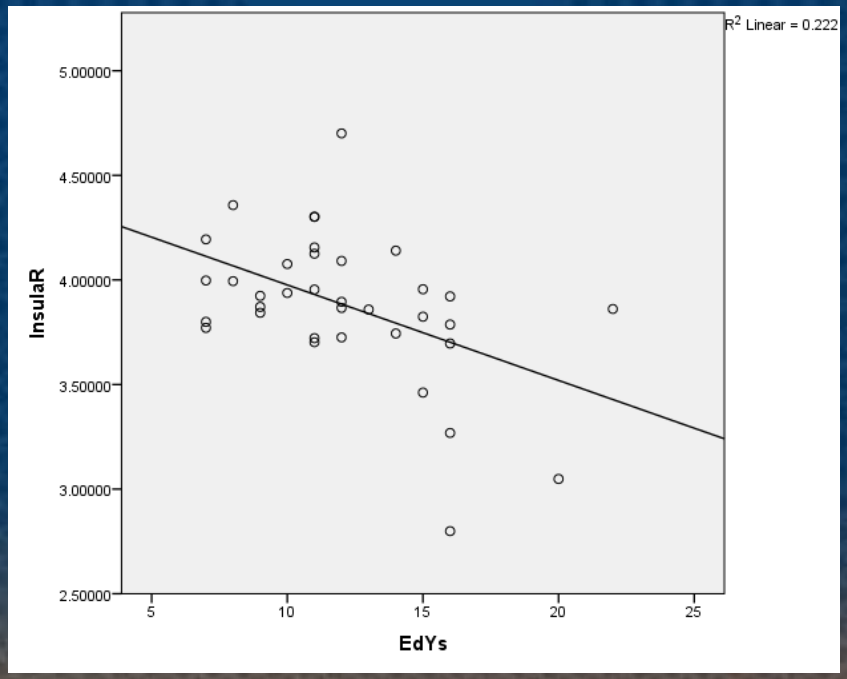
For each hemisphere, we assessed:

- Middle frontal gyrus
- Inferior frontal gyrus *(pars opercularis, triangularis)*
- Insula
- Anterior cingulate gyrus
- Parahippocampal gyrus
- Superior temporal gyrus
- Middle temporal gyrus *(anterior, middle, inferior)*
- Inferior temporal gyrus
- Temporal pole *(superior, middle)*

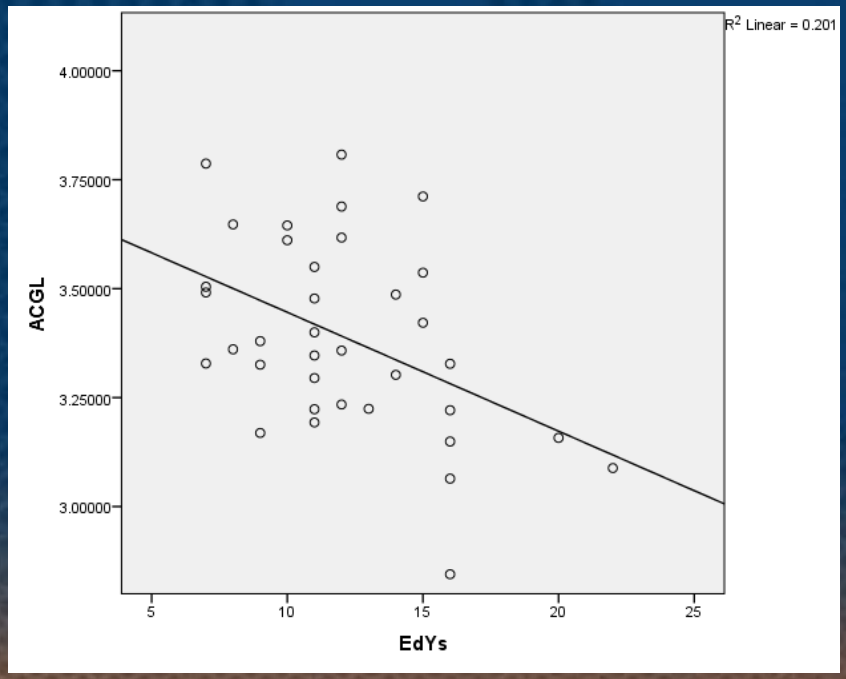
# Results support a CR for education in some areas

AD group: Education effects found:Cortical Thickness was found to be negatively correlated to education in two ROI's:

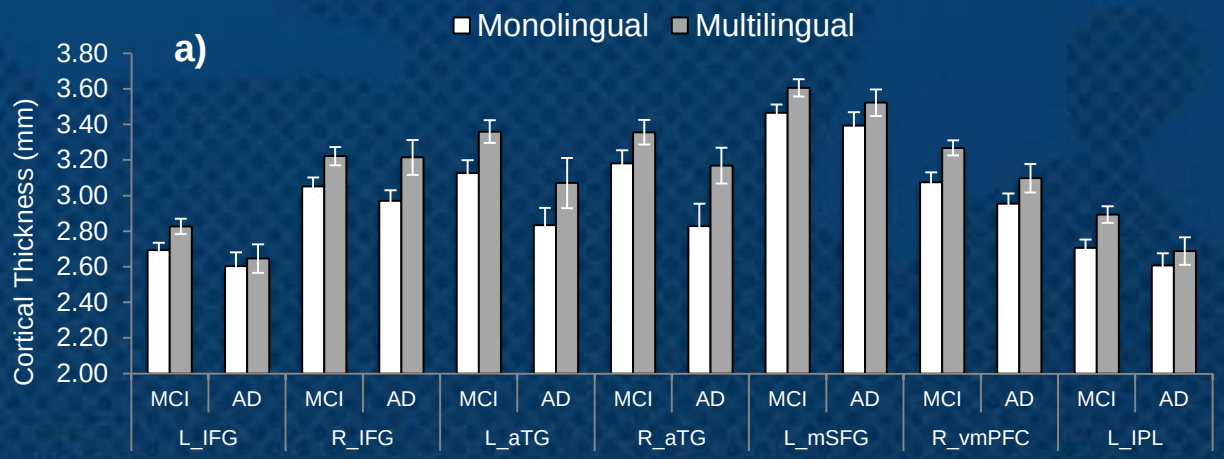
Right Insula (ß=-0.47, p=0.004)




Left Anterior Cingulate (ß=-0.45, p=0.006)

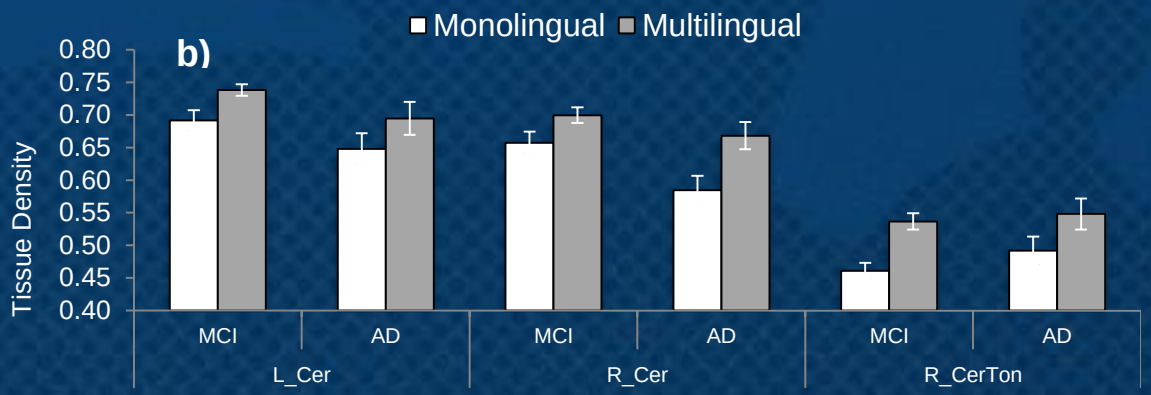


Bilinguals and Multilinguals have thicker cortices in many language regions:

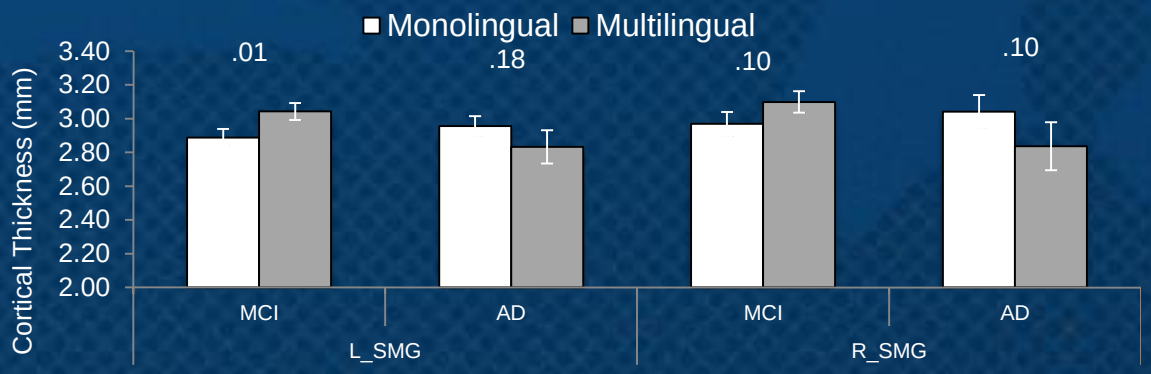



Effect seen in : left and right inferior frontal (and other frontal regions), right anterior middle temporal, left inferior parietal.

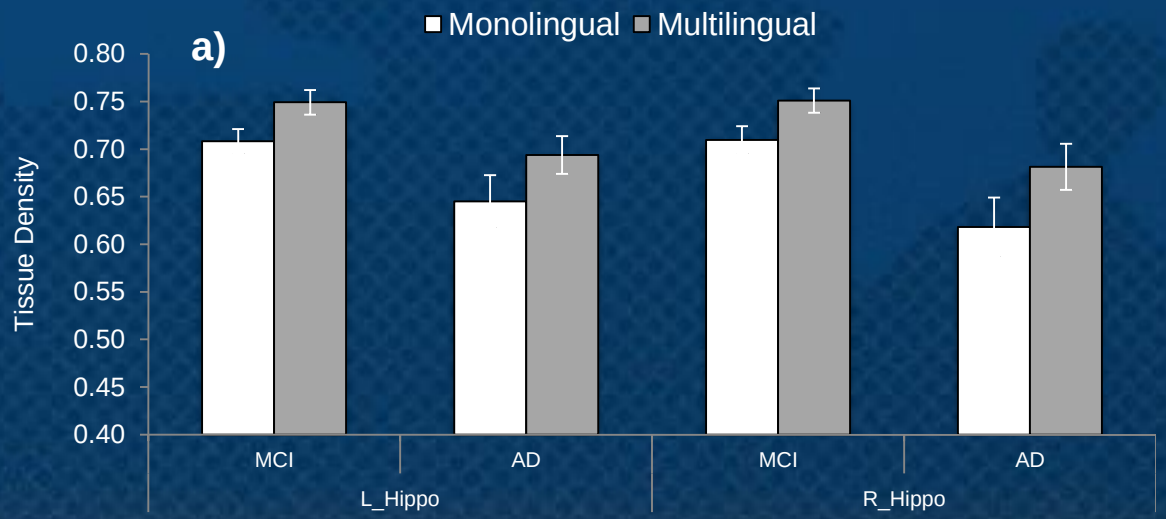
# Voxel –based morphometry also reveals areas with greater tissue density in cerebellum



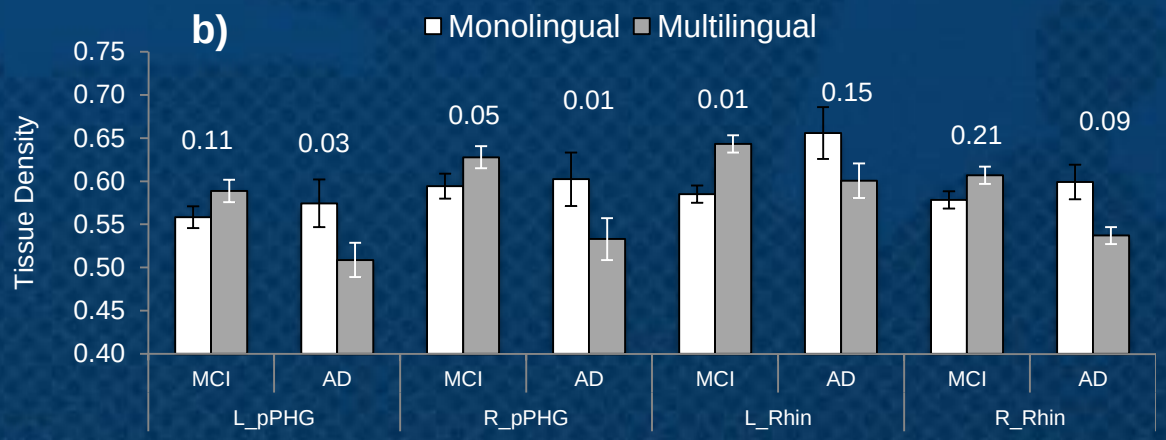
# Interaction between Language Group and Patient Group



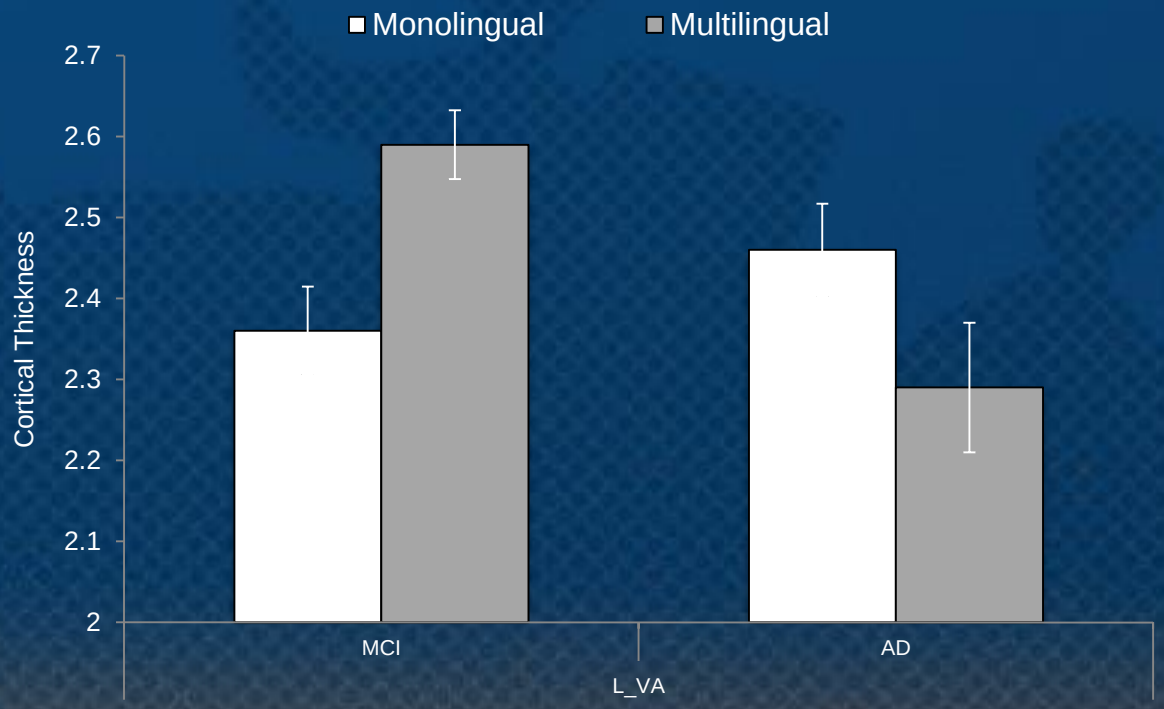

In the Supramarginal gyrus, MCI's show greater Ct for bilinguals (BR), and AD show greater atrophy for bilinguals (CR)


a)
Monolingual
Multilingual
Tissue Density
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
MCI
AD
MCI
AD
L_Hippo
R_Hippo

# Interaction in Parahippocampal regions: Bilinguals and Multilinguals have decreased tissue density compared to monolinguals:



# Interaction: Bilinguals and Multilinguals AD have thinner cortices in visual association regions:



**“Neuroanatomical evidence of multilingualism’s contribution to brain reserve and cognitive reserve in patients with mild cognitive impairment and Alzheimer Disease” (Duncan, Chertkow, Phiillips 2017)**

HYPOTHESIS:

1. Brain reserve might show thicker cortices/tissue density in all multilingual subjects in language areas. YES!
2. Cognitive reserve might show greater atrophy in matched AD bilinguals vs. monoliguals in regions susceptible to pathology. YES!

# Multilingualism and Age of onset of Dementia Study from a Memory Clinic in Hyderabad

Suvarna Alladi, Hyderabad, India



# Multilingualism in India

255 million speak at least two languages and 87.5 million speaking three or more

Urban Indians are more likely to be multi-lingual but as many as 136.7 million rural Indians speak at least two languages

Census India 2001

# 662 Memory Clinic patients in Hyderabad

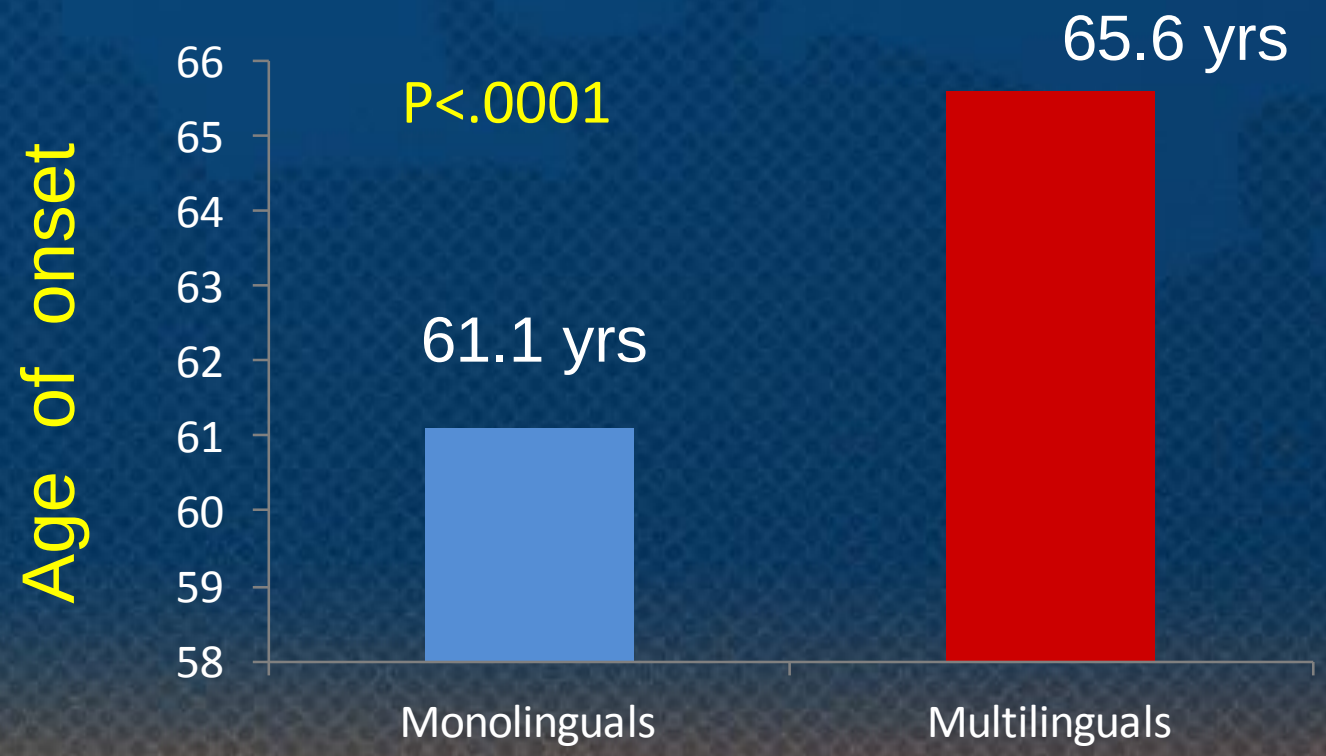
| | AD (n=240) | FTD (n=116) | VaD (n=189) | DLB (n=55) | Mixed Dementia (n=48) |
|---|---|---|---|---|---|
| Age of onset * (Mean) | 67.3 | 59.1 | 59.0 | 68.7 | 71.0 |
| Multilinguals (%) | 59.2 | 57.8 | 54.0 | 87.3 | 66.7 |
| Literates (%) | 87.1 | 84.5 | 77.2 | 94.5 | 93.8 |
| MMSE (Mean) | 17.3 | 19.2 | 17.8 | 19.1 | 17.8 |
| ACE-R | 51.0 | 57.5 | 51.2 | 56.7 | 52.0 |
| Family history (%) | 18.4 | 21.6 | 9.9 | 15.1 | 12.8 |

* $P<0.05$

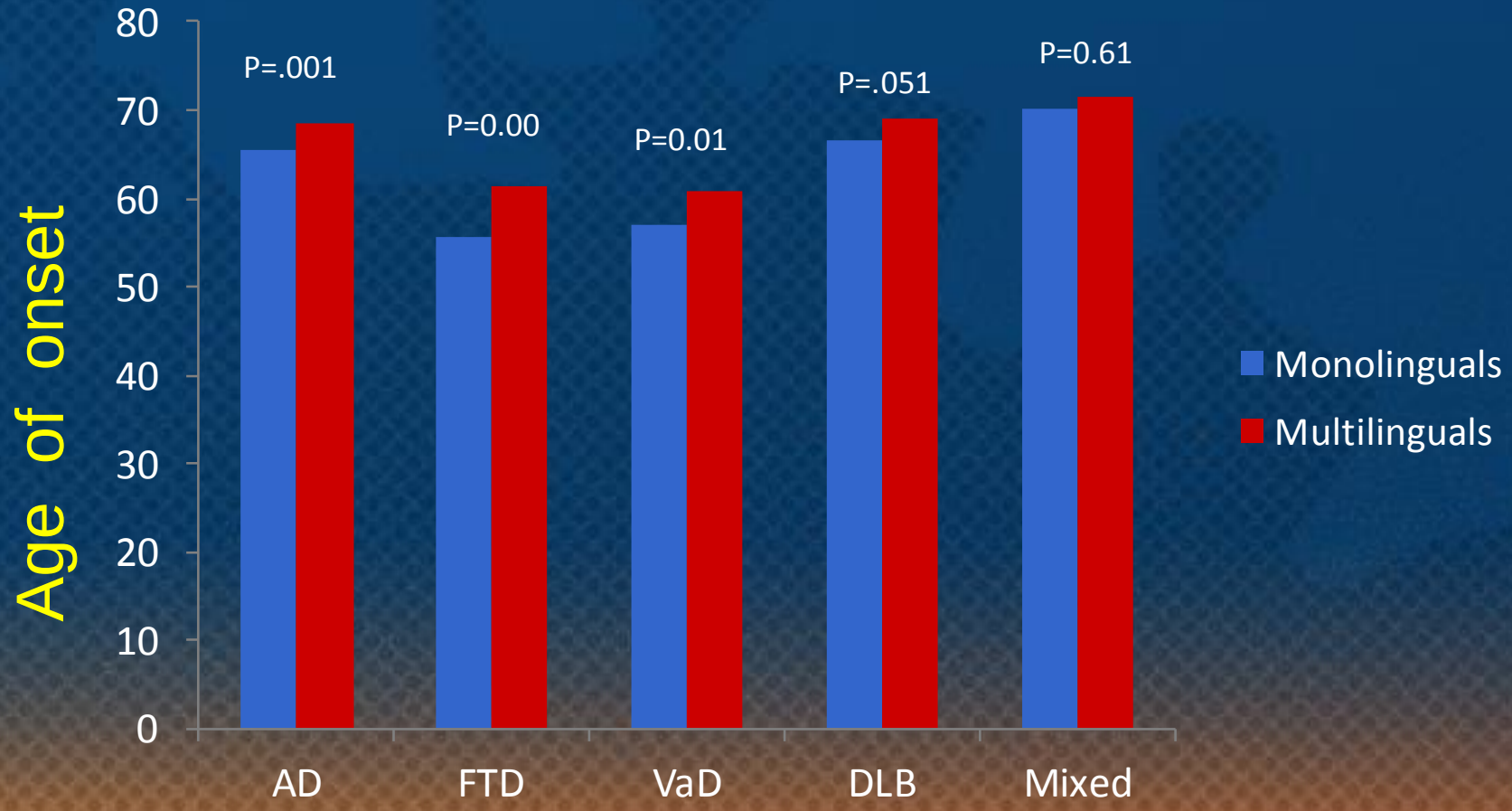
# Multilingual cohort in the Hyderabad cohort were "older, had larger proportion of men, were more educated, urban dwellers and higher skill levels in their occupation"

| | Monolinguals | Multilinguals | P value |
|---|---|---|---|
| Age at presentation | 63.4 | 68.1 | .000 |
| Age at onset | 61.1 | 65.6 | .000 |
| Gender- Male % | 32 | 68 | .000 |
| Literacy % | 68.9 | 95.4 | .008 |
| Urban vs Rural % | 61% :39 | 82.3:17.7 | .03 |
| Years of Education (yrs) | 5.9 (5.1) | 12.9 (4.9) | .000 |
| Occupation %<br>•Elementary<br>•Service workers<br>•Associate professionals<br>•Legislators<br>•Professionals | <br>4.2<br>48.9<br>2.6<br>.5<br>43.7 | <br>1.6<br>56.9<br>6.8<br>17.4<br>17.4 | .000 |

# Multilingualism and age of onset of dementia



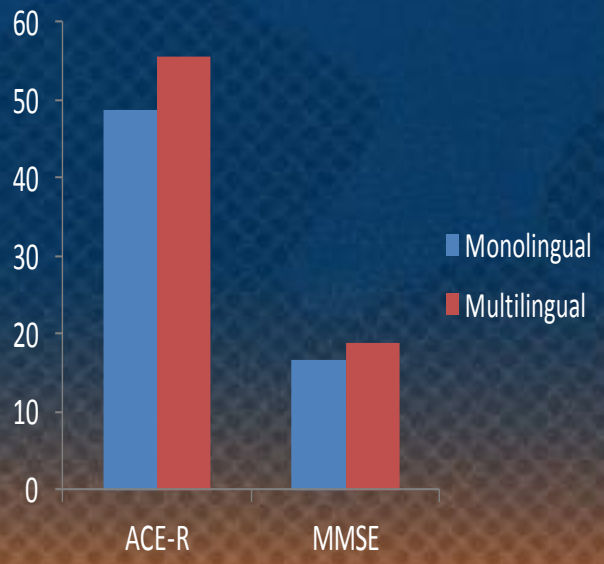
# Multilingualism and Dementia Subtypes



# Multilingualism and Severity of dementia

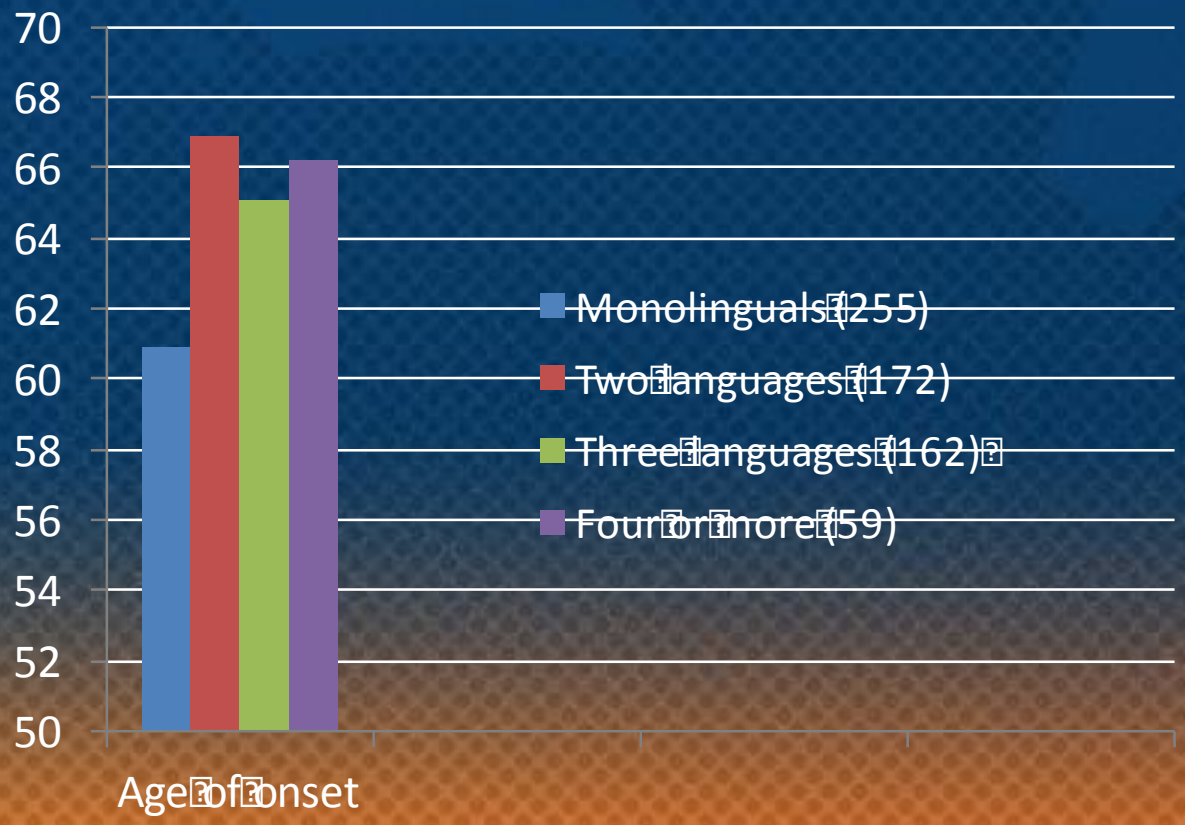
Multilinguals had higher scores on ACE-R, MMSE and CDR compared to Monolinguals

| | Mono | Multi | P value |
|---|---|---|---|
| MMSE | 16.7 (7.5) | 18.9 (8.0) | .000 ** |
| ACE-R | 48.6 (23.3) | 55.5 (24.7) | .000 ** |
| CDR<br>•Mild<br>•Moderate<br>•Severe | <br>36%<br>50%<br>45% | <br>64%<br>50%<br>55% | <br>.001** |
| Family History | 14.5% | 16.9% | .56 ns |
| Duration of illness | 2.13 | 2.35 | .124 ns |

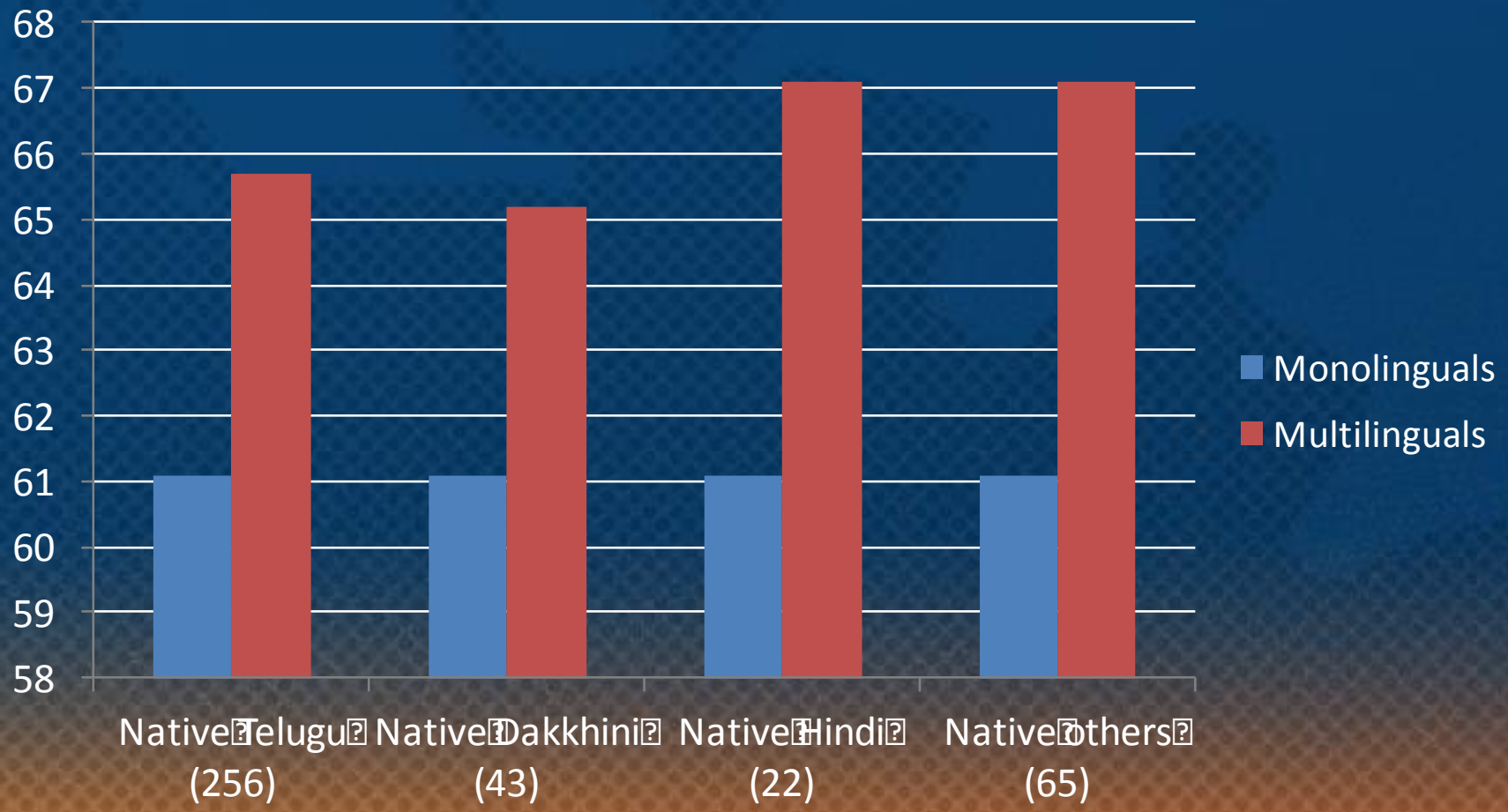


# Does the number of languages known matter

**No difference in age of onset between bilinguals and multilinguals**



# Does the native language matter- Not in the Hyderabad cohort



# Other factors associated with age of onset of dementia

Education

Rural vs Urban dwelling

Stroke

Dementia subtype

No effect of family history, vascular risk factors, gender and occupational status

# CONCLUSIONS IN HYDERABAD

Multilingualism was associated with a 4.5 year delay in onset of dementia compared with monolingualism in the Indian context suggesting a protective effect for normative and neighbourhood multilingualism in a nonimmigrant population

The protective effect of multilingualism was pronounced for almost all dementia subtypes, and for both degenerative and vascular etiologies .

The delay in initial symptom onset in multilinguals across dementia subtypes may be related to the protection from decline of attention and executive functions, as observed in healthy people and in normal ageing

# CONCLUSIONS

Beyond Bilingualism, there was no significant advantage for multilingualism in the Indian context

The pattern of language use and exposure in the predominantly trilingual Hyderabadi population is likely to have blurred the distinctions between bilinguals and multilinguals, thereby resulting in little difference in the amount of cognitive reserve acquired and age of onset of dementia symptoms

# The Montreal/McGill University study of Bilingualism, multilingualism and dementia

Chertkow, H., Whitehead, V., Phillips, N., Wolfson, C., Atherton, J., & Bergman, H. (2010). Multilingualism (but not always bilingualism) delays the onset of Alzheimer's disease - evidence from a bilingual community. *Alzheimer's Disease & Associated Disorder, 24,* 118–125.

# What we have in Montreal:

55% of the population are Francophones, 1/3 of them learn English usually from age 6

35% of the population are Anglophones, ¾ of them having learned French from age 8 (but their French is not as good)

10% of the population are allophones / immigrants, who have acquired one or two of the Canadian languages in teenage or adulthood.

They all present to our university –based Memory Clinic at the Jewish General Hospital of McGill University

## "Multilingualism (but not always bilingualism) delays the onset of AD"

**Chertkow et al, 2010 Alz. Dis. Assoc. Disord., 24, 118-125)**

- **Jewish General Hospital/McGill Memory Clinic in Montreal Canada-**
  - **large set of multilingual immigrants**
  - **Another large set of Canadian born subjects bilingual in French and English.**
  - **Also many unilingual English and French-speaking subjects.**
- Chart review of 632 patients seen between 1997 and 2006 in JGH/McGill Memory Clinic, with diagnosis of probable Alzheimer Disease
- All had age of dementia diagnosis documented
- Bilingual vs. unilingual vs. multilingual definition
- 143 had age of memory loss onset documented
- MRI assessment for volumetrics and cortical thickness

# Alzheimer's Disease: Mean values (and standard deviation) for demographic variables of multilinguals and unilinguals.

| Language Group | n | Age at Diagnosis Mean (SD) | Years of Education Mean (SD) | MMSE score Mean (SD) |
|---|---|---|---|---|
| Unilingual | 379 | 76.7 (7.8) | 10.9 (3.5) | 23.1 (3.9) |
| Men | 139 | 77.1 (7.0) | 11.1 (3.7) | 22.7 (4.0) |
| Women | 240 | 76.3 (8.1) | 10.8 (3.3) | 23.3 (3.8) |
| Multilingual | 253 | 77.6 (7.2) | 10.7 (3.8) | 22.9 (4.3) |
| Men | 122 | 78.1 (7.3) | 11.1 (4.2) | 23.5 (4.3) |
| Women | 131 | 76.9 (7.5) | 10.3 (3.4) | 22.4 (4.2) |

**% immigrants in each group – Unilinguals: 6%; Multilinguals: 53%**

Overall, no beneficial effect of multiple languages on Age at diagnosis of AD dementia

Chertkow, H., Whitehead, V., Phillips, N., Wolfson, C., Atherton, J., & Bergman, H. (2010). Multilingualism (but not always bilingualism) delays the onset of Alzheimer's disease - evidence from a bilingual community. *Alzheimer's Disease & Associated Disorder, 24,* 118–125.

# However, further analysis shows subtle effects, particularly for multiple languages

- Regression model of age at diagnosis by language status (uni vs. multilingual) showed a trend towards multilinguals being Dx'ed later (ß coeff: 1.4; p=0.06) and immigrants being Dx'ed earlier (ß coeff: -1.4; p=0.09).
- Amongst multilinguals, number of languages spoken correlated with age of diagnosis (Spearman r=0.14, p=0.026)
- Regression model of age of diagnosis by number of languages showed the more languages spoken, the later the diagnosis (ß coeff: 1.4; p=0.001).
- Post hoc analysis showed those who spoke 4+ languages were diagnosed 4 years later than uni- or bilinguals; trilinguals showed a trend towards being diagnosed later than uni- or bilinguals (1.9 yrs., $0.05 < p < 0.1$); there was no difference in age of diagnosis between uni- and bilinguals.

Chertkow, H., Whitehead, V., Phillips, N., & Bergman, H.
Bilingualism fails to delay the onset of Alzheimer Disease.

# Age of AD dementia diagnosis organized according to number of languages spoken.

| Number of Languages spoken | n | Age at Diagnosis | Years of Education | MMSE score at diagnosis |
|---|---|---|---|---|
| 1 | 379 | 76.7 (7.8) | 10.9 (3.5) | 23.1 (3.9) |
| 2 | 168 | 76.7 (7.8) | 10.7 (3.7) | 22.8 (4.3) |
| 3 | 67 | 78.6 (6.0) | 11.3 (4.2) | 23.1 (4.3) |
| $\geq$ 4 | 18 | 80.8 (5.5) | 9.1 (3.6) | 23.6 (2.7) |

# AD Dementia group - subgroup with reliable age of symptom onset data

- Age of symptom onset was reliably available in a subset of 143 cases
- Language status (uni vs. multilingual) did not delay age of symptom onset.
- As with age of diagnosis in the larger cohort, number of languages was significantly positively correlated with age of symptom onset (Spearman $r= 0.32$, $p.<0.02$).
- Further analyses showed 3+ languages delayed symptom onset by 5 years relative to uni- or bilinguals, who were not different from each other.

# AD Dementia Demographic information on subset of patients with age of symptom onset data.

| Language Group | n | Age at symptom onset | Age at Diagnosis | Years of Education | MMSE score at diagnosis |
|---|---|---|---|---|---|
| Unilingual | 89 | 71.5 (7.5) | 75.5 (7.3) | 10.5 (3.7) | 23.5 (4.1) |
| Multilingual | 54 | 72.5 (8.9) | 76.5 (8.0) | 11.2 (3.8) | 24.3 (2.4) |

# AD Dementia – the subset of "born in Canada" subjects

- A further analysis was done examining a subset of native English/French uni- and bilinguals (356 unilingual, 42 bilingual).
- Regression showed bilinguals being diagnosed **earlier** than uniinguals (ß coeff: -3.0; p=0.02).
- An analysis of decline after diagnosis in a subset of 154 cases (92 unilinguals, 62 multilinguals) did not show a difference in rate of decline.

# Demographic information on subset of English and French unilingual and bilingual patients.

| Language Group | n | Age at Diagnosis | Years of Education | MMSE score at diagnosis |
|---|---|---|---|---|
| Unilingual | 356 | 77.0 (7.6) | 11.1 (3.2) | 23.2 (3.8) |
| Bilingual | 42 | 74.4 (7.5) | 11.2 (3.9) | 22.9 (4.1) |

**But if you break down the population in terms of ethnicity (Anglophones, Francophones, Immigrants), you see that the effect of multiple languages only shows up in certain of the groups!**

## RESULTS – ORIGINS SUBGROUPS

**Age of Diagnosis of Alzheimer's disease organized according to number of languages spoken within Native Canadians whose mother tongue in English (Native English), Native Canadians whose mother tongue is French (Native French), and immigrants to Canada (Immigrants).**

| Number of Languages spoken | Native English | Native French | Immigrants |
|---|---|---|---|
| 1 | 78.0 (7.0) | 72.7 (9.1) | 71.4 (8.1) |
| [n] | [289] | [66] | [23] |
| 2 | 77.9 (7.5) | 75.9 (6.5) | 76.5 (8.2) |
| [n] | [62] | [24] | [81] |
| 3 | 79.8 (5.6) | 79.5 (2.5) | 77.8 (6.4) |
| [n] | [24] | [4] | [39] |
| ≥ 4 | 80.7 (3.2) | - | 80.9 (5.9) |
| [n] | [3] | - | [15] |

So why do unilingual anglophones not get AD at an earlier age, like the other groups?
Analysis shows it is not due to socioeconomic status

# Prodromal AD: Age at symptom onset

Individuals with amnestic Mild Cognitive Impairment (MCI) -either had Positive PIB PET amyoid scanning [Pittsburgh Compound B (PiB) PET scan which showed elevated PiB uptake ("PiB positive": Global SUVR ≤1.24).], OR had subsequent progression to AD dementia. , Termed "Prodromal AD" (n=30).

Distribution:
Progressed to AD: 23
PiB positive: 14
Both: 7

"Prodromal AD" demographics

| | Overall | Monolinguals | Multilinguals |
|---|---|---|---|
| n (% female) | 30 (43%) | 16 (31%) | 14 (57%) |
| Age at scan | 73.7 +/- 4.5 (63-79) | 73.8 +/- 4.8 (63-79) | 73.6 +/- 4.3 (64-79) |
| MMSE at scan | 27.9 +/- 1.4 (25-30) | 27.9 +/- 1.4 (25-30) | 27.9 +/- 1.5 (26-30) |
| Education (yrs.) | 13.3 +/- 4.3 (7-25) | 14.3 +/- 4.5 (7-25) | 12.1 +/- 3.8 (7 -22) |
| Age at Symptom Onset | 69.6 +/- 5.7 (56-77) | 70.2 +/- 5.0 (59-76) | 69.0 +/- 6.5 (56-77) |
| % immigrants | 26.7% | 18.8% | 35.7% |

Results show there Was no difference in Age of symptom Onset between Monolinguals and multilinguals

# What our language data shows:

In the overall group:

- We were unable to confirm that bilingual individuals had later onset of dementia diagnosis  OR later onset of symptom onset.
- Only those speaking 3 or more languages had any benefit
- Immigrants seem to develop dementia earlier than native born Canadians.

But in subgroups of immigrants and francophones, there WAS a protective effect of more languages

The unilingual Montreal anglophones are “protected” somehow

- NO evidence that it was higher socioeconomic status!
- Possibilities- ?nutrition  ?stress  ?genetics ?vascular risks? –ALL POSSIBLE

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Note

# Bilingualism as a protection against the onset of symptoms of dementia

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**Abstract**

This study examined the effect of lifelong bilingualism on maintaining cognitive functioning and delaying the onset of symptoms of dementia in old age. The sample was selected from the records of 228 patients referred to a Memory Clinic with cognitive complaints. The final sample consisted of 184 patients diagnosed with dementia, 51% of whom were bilingual. The bilinguals showed symptoms of dementia 4 years later than monolinguals, all other measures being equivalent. Additionally, the rate of decline in Mini-Mental State Examination (MMSE) scores over the 4 years subsequent to the diagnosis was the same for a subset of patients in the two groups, suggesting a shift in onset age with no change in rate of progression.


*Keywords:* Bilingualism; Cognitive reserve; Dementia

**Bialystok et al. (2007): Bilinguals' age of onset of symptoms 4.1 years later than unilinguals.**

# Problems with Bialystok et al:

- Did not distinguish between bilinguals (2 languages) and those who spoke more than two languages.
- Their multilingual elderly patients were 90% immigrants.
- Might immigrant vs. native affect dementia diagnosis point?
- Assessing the onset of memory loss is notoriously unreliable (Wolfson)
- Random point- when patient comes to a doctor to be diagnosed (cultural factors)
- Report used all "dementia cases" in Dr. Freedman's Memory Clinic at Baycrest in Toronto

# Follow up studies- Same findings for AD dementia

## ”Delaying the onset of AD: Bilingualism as a form of cognitive reserve”

## Craik, Bialystok, Freedman, Neurology, 2010

→

1. Assessed 109 unilingual and 102 bilingual ADs.
2. Found the same pattern: Bilingual patients diagnosed 4.3 years later (mean age 77 at diagnosis), with sympotom onset 5.1 years later than monolinguals (mean age 72 at diagnosis) .
3. Bilingualism  therefore= a strong form of cognitive reserve.

# More follow-ups from Toronto

## "The Effect of bilingualisim on Amnestic MCI"

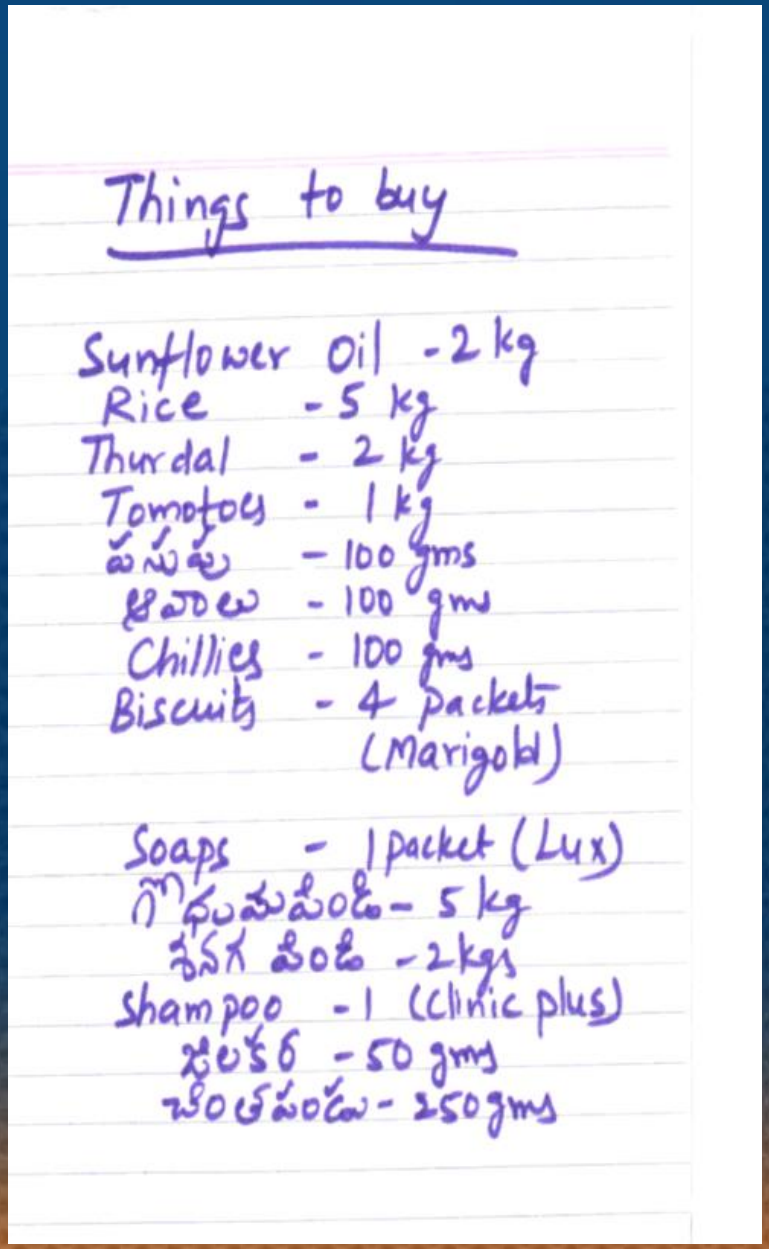
## Ossher, Bialystok, Craik, Murphy, Troyer

## J. Gerontology, Series B, (2012), vol 10.

- Examined age of amnestic MCI WITHOUT other domains involved (n=68), and WITH (n=43)
- Only patients with single domain amnestic MCI show an effect of bilingualism.
- Individuals recruited from ads, not assessed for age of onset of memory loss

Age: MCI without –unilingual 75, bilingual 79
MCI with – unilingual 76, bilingual 74.

Very open to many criticisms!




***Difference between Montreal and Hyderabad?: Day to day use of normative multilingualism in India***

# Conclusions

- Results in the MCI/ Prodromal AD subgroup : There is evidence for bilingualism building brain reserve –cortical thickness differences in language regions of brain.

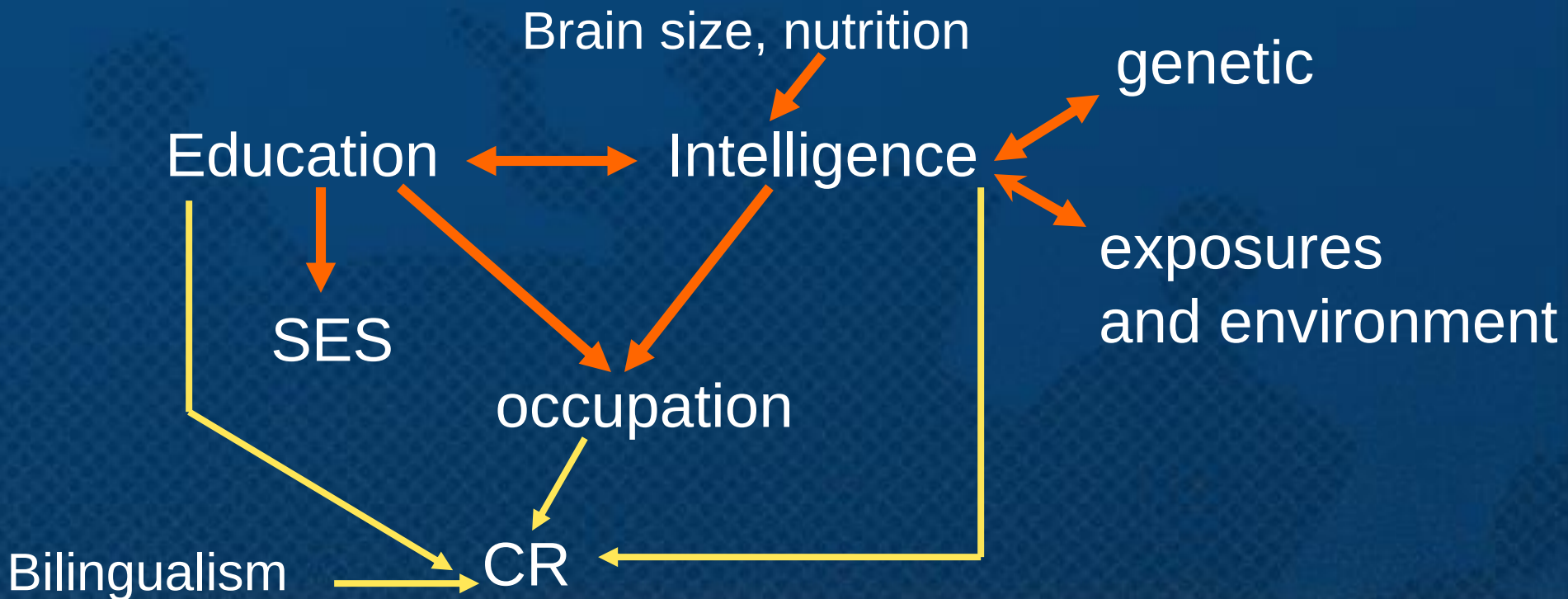
AD group supports cognitive reserve (CR) hypothesis for education = more atrophy for same symptom severity.

- Multilingual and sometimes bilingual AD subjects have 4 years later disease onset = cognitive reserve
- We replicated the CR results for bilingualism/multilingualism (greater atrophy at the same level of dementia severity in multilinguals).

Overall, the hypothesis of bilingualism contributing to cognitive reserve was partially supported.

- Results in the MCI group (more education = greater cortical thickness) are suggestive of education contributing to brain reserve and building thicker cortices! Women in this group were also found to have greater Ct than men.

# Conclusion from studies- CR is complex, contains Nature and Nurture factors




Cognitive reserve in each individual appears to be a complex phenomenon. Learning languages is ONE piece of the puzzle, ONE aspect of an individual's life which may be protective. It may play a bigger role in one cultural setting than another!

# Collaborators and my research team

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