

# **THE ASSOCIATION OF AVIATION MEDICAL EXAMINERS**



**PROFESSOR PATRICK RABBITT**

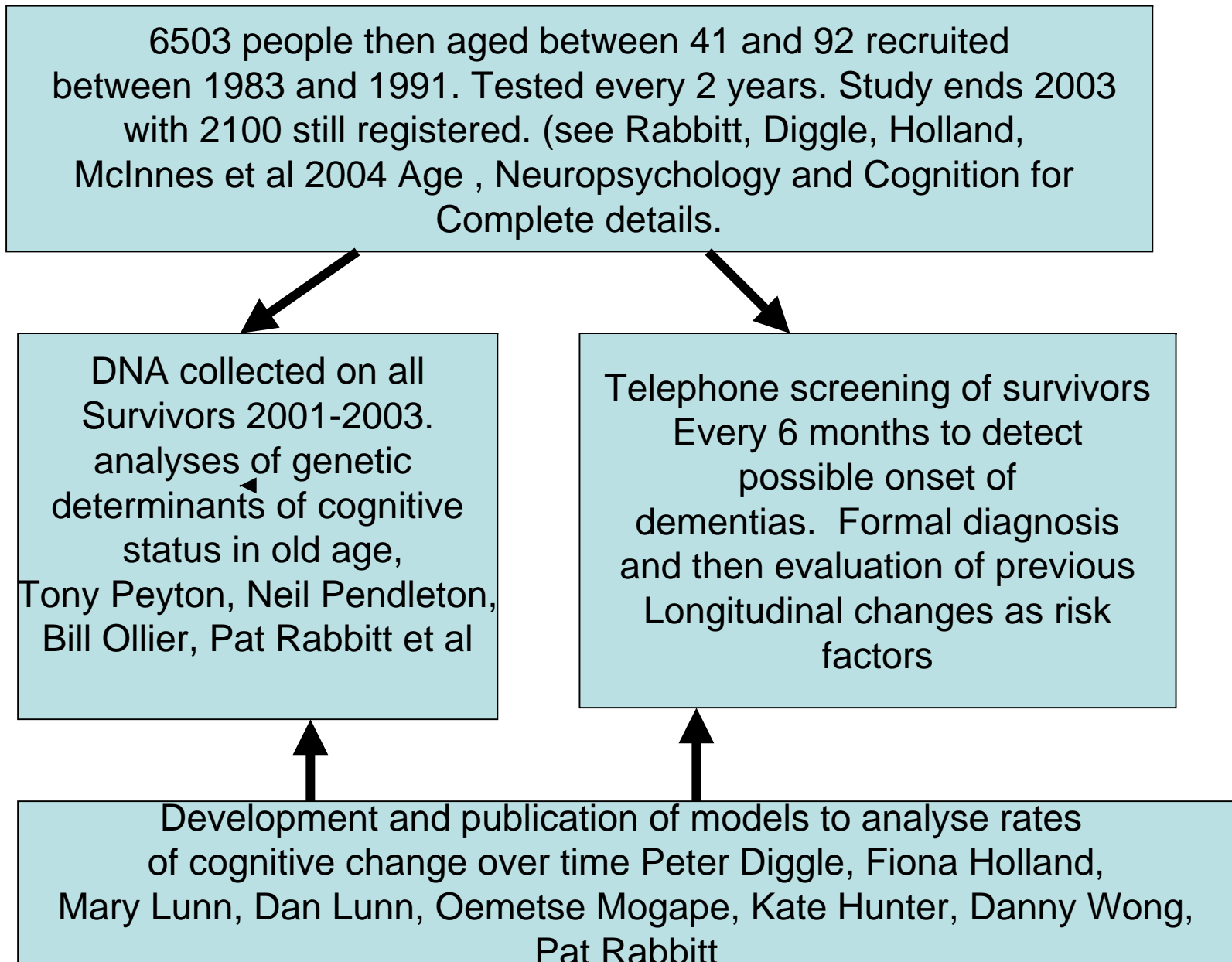
Emeritus Professor of Psychology, Oxford

# Assessing risk factors for accidents in individuals without symptoms

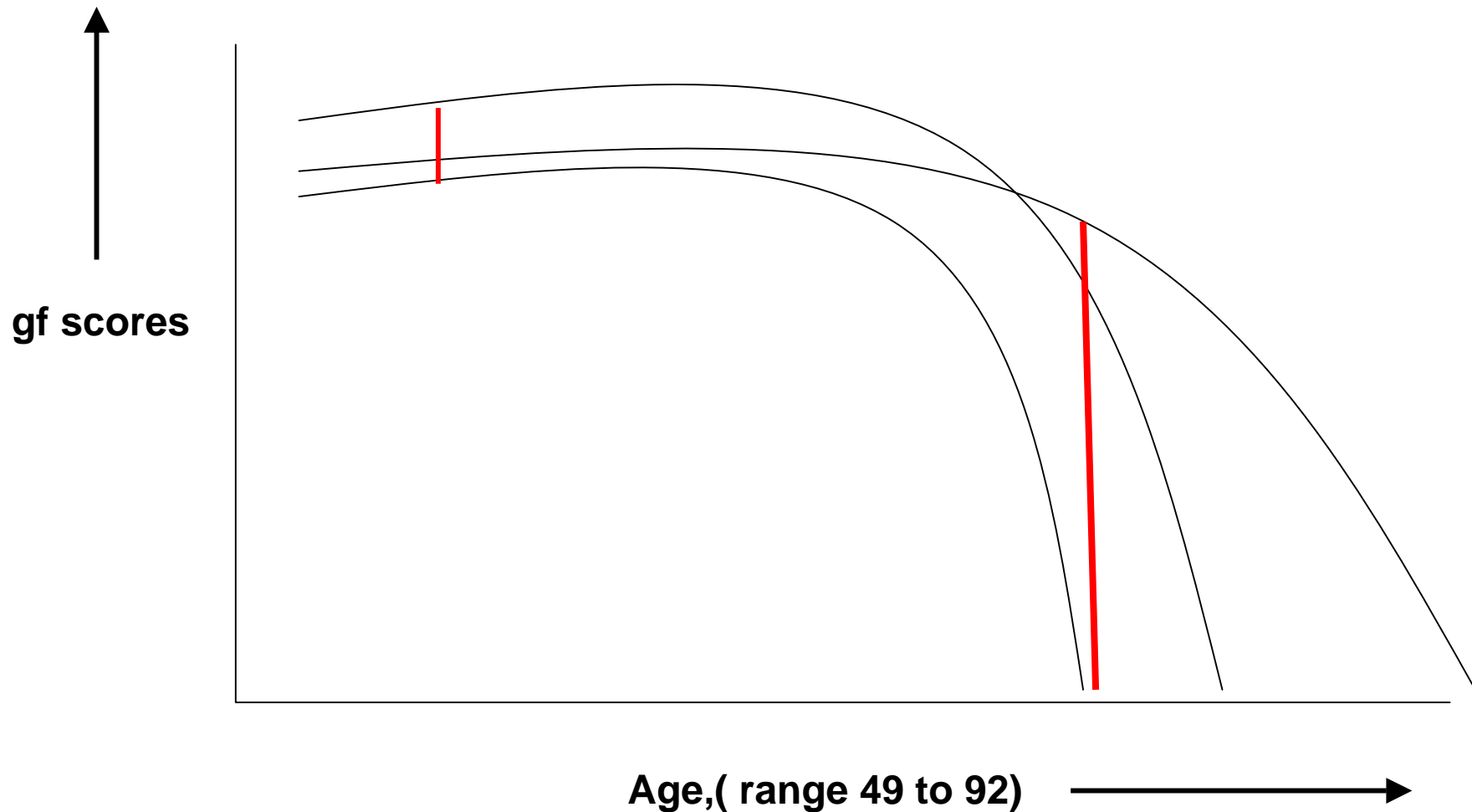
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(University of Oxford)

# University of Manchester Longitudinal study of Cognitive Change



When practice and drop-out effects have been taken into consideration it is apparent that as a sample ages, so variance between its members steadily increases. (Rabbitt, Diggle et al 2001; 2004)

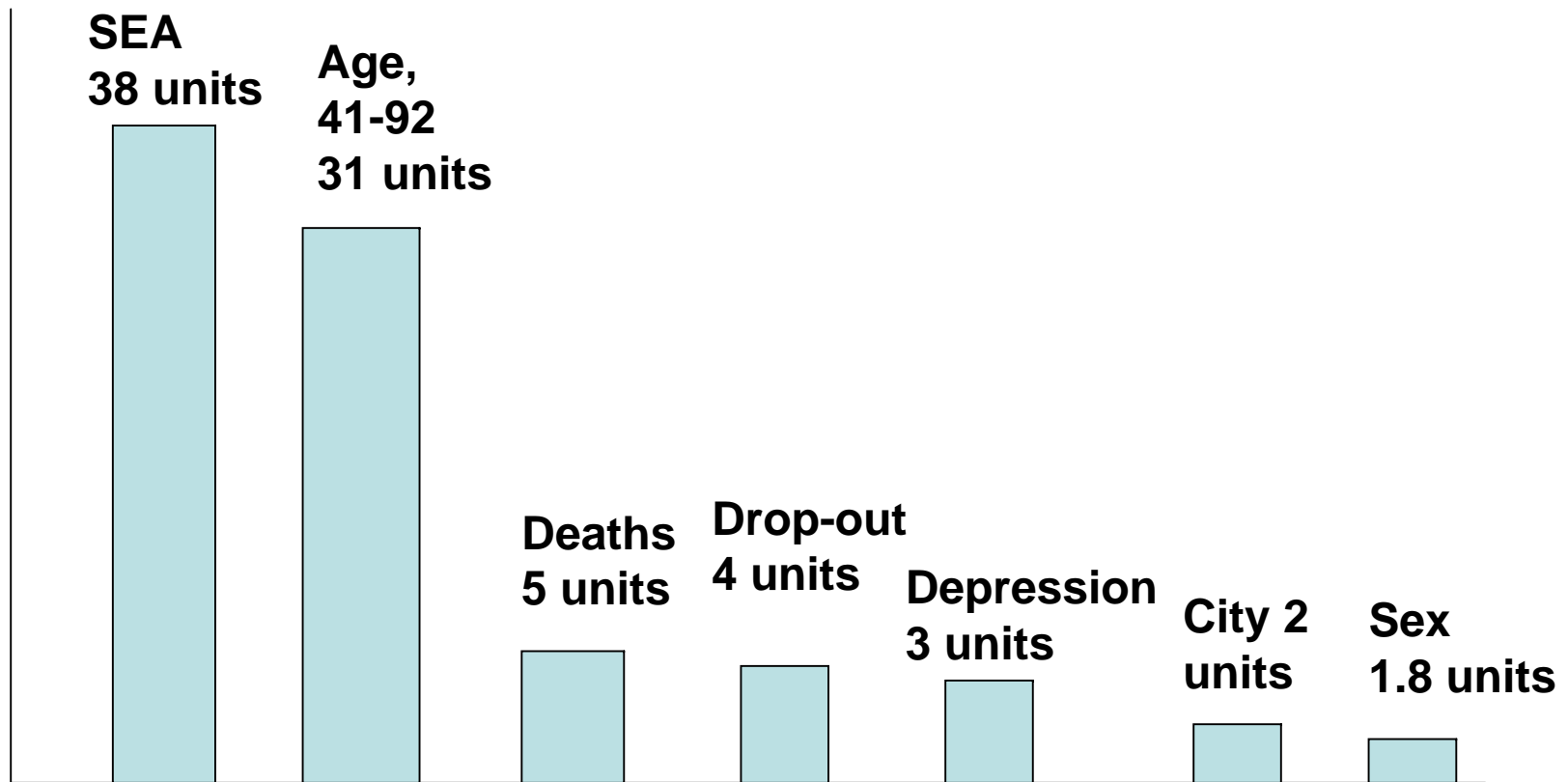


This means that people  
change at different rates

The issue is what factors speed or  
slow cognitive changes.

Obviously very many factors affect the sizes of age-related differences between people.

It is easy, but not very illuminating, to compare the variance **between** individuals due to different factors at a single time-point (Cross-sectional data (N = 5304 aged 49-92))



Units are **ranges** of AH4-1 intelligence test scores associated with each factor

# But cross-sectional comparisons are inadequate

We need longitudinal studies in which  
the same people are followed up over  
long periods of time.

A main goal of longitudinal studies is to determine the relative contributions of **the very large numbers of factors** that contribute to this variance in rates of change-trajectories of change.

- Genetic
- Socio-Economic Advantage.
- **Health**
- **Depression**
- Lifetime level of intellectual Ability
- Lifestyle
- Etc



A slightly different question is  
“what behavioural measures are  
the most sensitive indices of  
cognitive changes ?

Put another way: “which cognitive  
abilities change first ? “ And “Do  
changes in some abilities drive  
changes in others “ ?

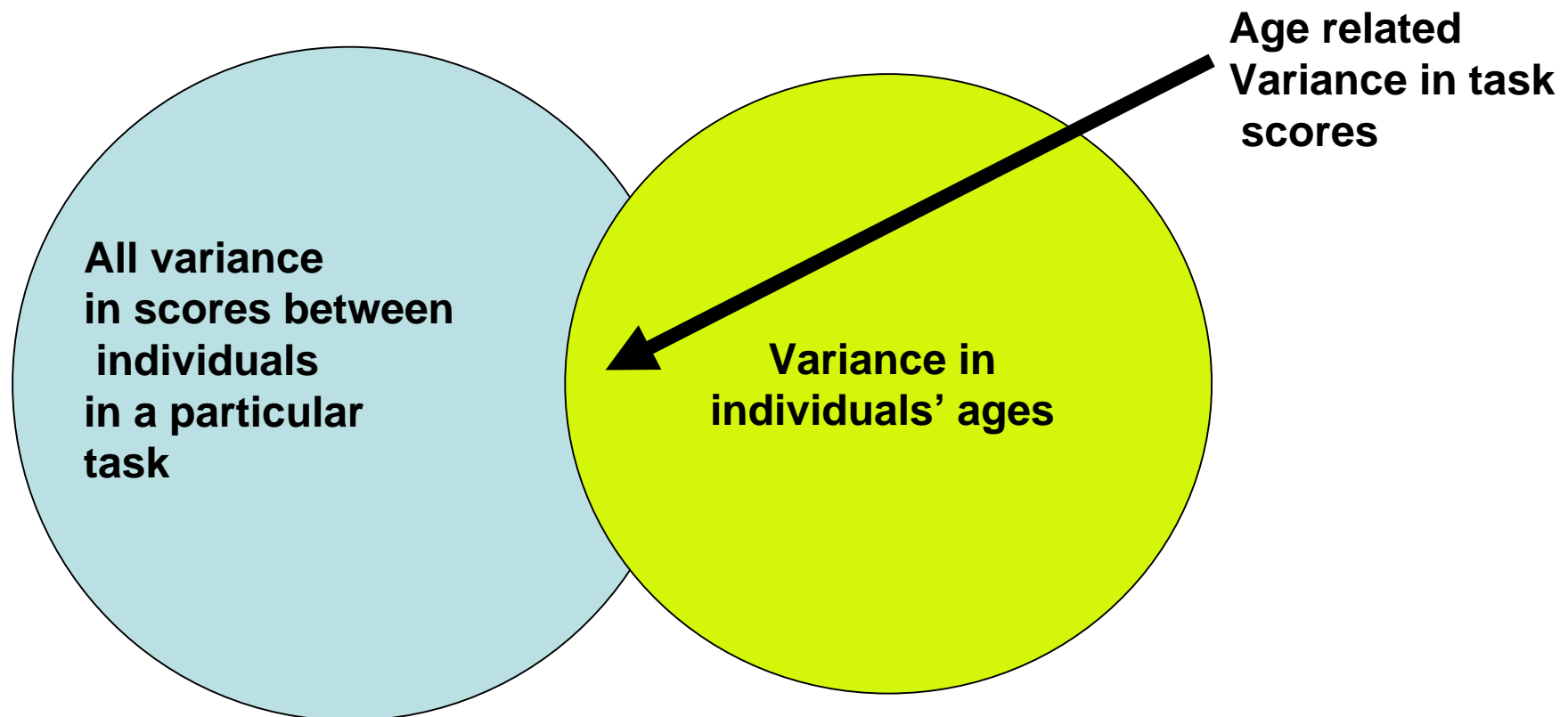
# Cognitive deficits

- The “standard theory” has been that the most sensitive behavioural index of age-related changes in all mental abilities is decision speed, measured in any of a variety of ways.
- Our work suggests that performance on brief (i.e. 10 min) pencil and paper “intelligence tests” is just as effective.

<b>Task</b>	<b>Correlation between Task Score and Calendar Age between 42 and 96 years</b>	<b>Percentage of the total variance between individuals due to all causes that is accounted for by differences in their Ages.</b>
AH4-1 intelligence test	-.366**	13.4%
AH4-2 intelligence test	-.453**	20.5%
Cattell Culture Fair Intelligence Test	-.436**	19.0%
Mill Hill A Vocabulary Test	-.026	.01%
Mill Hill B Vocabulary Test	-.048*	.02%
WAIS Vocabulary Test	-.169**	2.6%
Free Recall of 30 Words	-.323**	16.4%
Free Recall of 10 Words	-.297**	8.8%
Recognition Memory for 40 Pictures	-.247**	6.1%
Digit Span	-.194**	3.8%
Letter/Letter Coding	-.431**	18.5%
Visual Search Speed	-.347**	12.0%
Recall of Information about Imaginary people	-.293**	8.6%
Recall of Names of 12 Objects	-.377**	14.2%

# "Speed" explains nearly all age-related variance in all laboratory tasks, including working memory tasks

**By age-related variance:**  
we mean that part of the variance between individuals that is accounted for by differences in their ages



<b>Tasks</b>	<b>Age-related Var. by Cattell Intell. test Scores</b>	<b>Age-related variance by Let/Let Coding Speed</b>	<b>Age-related variance by Visual Search Speed.</b>
<b>AH4-1 intelligence test</b>	<b>100%</b>	<b>100%</b>	<b>93%</b>
<b>AH4-2 intelligence test</b>	<b>98%</b>	<b>96%</b>	<b>88%</b>
<b>Cattell intelligence test</b>	<b>-----</b>	<b>99%</b>	<b>81%</b>
<b>Free-Recall of 30 words</b>	<b>91%</b>	<b>93%</b>	<b>80%</b>
<b>Free-recall of 10 words</b>	<b>86%</b>	<b>88%</b>	<b>73%</b>
<b>Recognition memory for 40 pictures</b>	<b>95%</b>	<b>96%</b>	<b>83%</b>
<b>Cumulative Learning of 15 nouns</b>	<b>92%</b>	<b>93%</b>	<b>81%</b>
<b>Digit Span</b>	<b>94%</b>	<b>98%</b>	<b>100%</b>
<b>Letter/Letter Coding Speed</b>	<b>99%</b>	<b>----</b>	<b>92%</b>
<b>Visual Search Speed</b>	<b>93%</b>	<b>99%</b>	<b>-----</b>
<b>Recall of 3 items of Information about each of 5 people</b>	<b>88%</b>	<b>85%</b>	<b>65%</b>
<b>Recall of Names of 12 common objects</b>	<b>86%</b>	<b>88%</b>	<b>76%</b>

Differences in people's ages between 49 and 92 years account for relatively little of the variance between them in performance on most cognitive tests

Figures of 4% to 20% are typical.

Tests of speed and of gf seem to be much more age-sensitive than others.

Performance on tests of Speed or gf accounts for almost **all** age-related variance in most other cognitive tests.

- This means that, on almost all laboratory tasks, elderly people perform just like slow young people, or like people of any age with low IQ test scores.
- It has led to suggestions that “global slowing” or global changes in gf account for **all** of the observed age-related changes in performance.
- Perfect and Maylor “the dull hypothesis”

# Unfortunately

- Each of these rather global factors tends to be a strong statistical proxy for all of the others.
- Their effects often interact in counterintuitive ways.
- The measurement indices available for many of them are very much weaker, and very much less specific than we might like to suppose.

# For example....Intelligence

- Intelligence at entry to a study predicts subsequent mortality and so, as we have seen, rate of cognitive change (taking into account factors strongly associated with intelligence such as Socio-economic advantage, health-record, depression and amount of physical activity and social involvement weakens this relationship but it still persists).

# In other words Intelligence is a marker for survival

- Conversely, **sudden declines** in intelligence, or in information processing speed, (i.e. over a 4 to 8 year period) are risk factors for mortality, pathology and further cognitive decline. (Rabbitt, Lunn & Wong, 2008 J of Gerontology in press)

# For example....Depression

- Depression has a significant effect on intelligence and on speeded performance
- This effect is marked, even at sub-clinical levels of depression (Rabbitt, Lunn, Ibrahim, McInness Psychological Medicine 2008).
- However it occurs partly because depression is associated with pathologies, particularly CVD, and is a risk factor for poor outcome.
- It also occurs because, in the elderly, and middle aged, depression is associated with poor self-maintenance and available support.
- Depression may be well worth considering as a potential index of loss of cognitive performance.

So, to turn back to intelligence and information processing speed sensitive markers for age-associated loss

- Since these measures do seem to be very sensitive to age, and also to the onset of pathologies, they are obvious choices as indices of impending risk in otherwise symptom-free individuals.
- Unsurprisingly nearly all behavioural indices of potential risk have been based on tests of information processing speed. With some, i.e. K Ball's "Useful Field of View " test, impressively strong predictions of car driving performance are claimed.

# Manchester Driving Study (funded by Dept of Transport)

- 500 individuals given tests of information processing speed (7); Ball's useful field of view test; tests of memory. Also "biological age markers" (Crf Anstey, Smith, Christiansen et al. such as Max expelled air volume; Balance and mobility; visual acuity (with and without glare) and hearing. Max Leg thrust.

# Measures of Driving Competence:

- Self-reports of driving competence and feelings of vulnerability.
- Assessments by driving instructors (200 out of 700 only).
- Previous accident records.

# Outcomes:

- No measures predicted Driving Instructors' ratings.
- No speed or memory measures predicted previous accident rates.
- The Ball "Useful Field of View" test did not predict previous accident rates/
- There were significant, but modest predictions of accident rates from Biological Measures (notably Balance).

# Tentative conclusions.

- The Manchester driving study found no evidence that either simple laboratory tests of speed and intelligence, or especially designed test batteries, such as Ball's, UFOV battery predicted driving skills.
- However there was evidence for modest predictions from tests of balance and max leg thrust.
- There are some mitigating factors: e.g. accidents are very rare events; driving is a very highly practised skill; people who are poor drivers tend to limit their driving exposure.

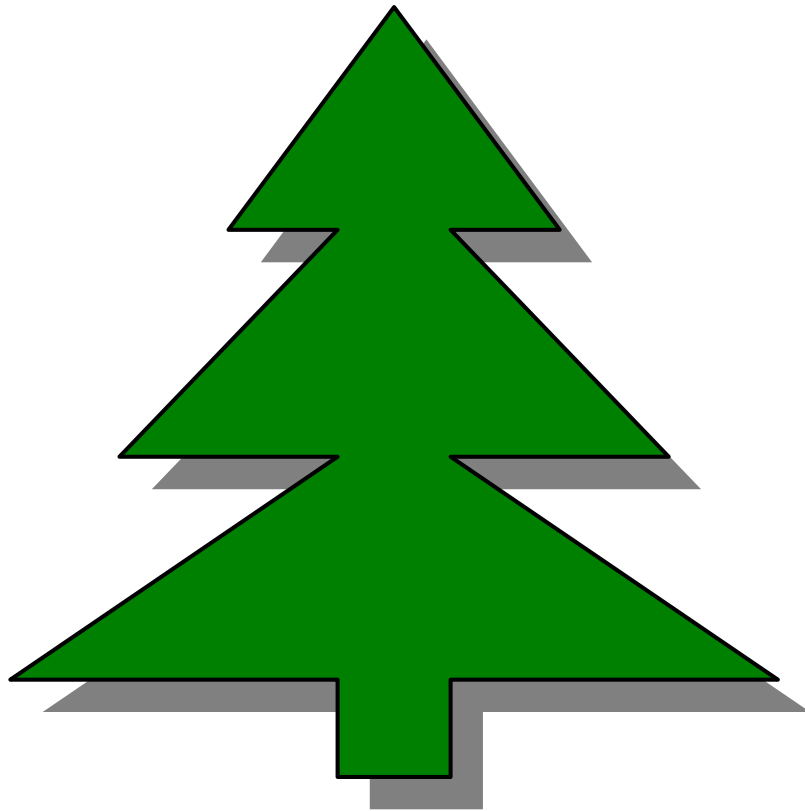
# Caution

- These data do not raise problems for other studies that have found robust relationships between performance in “real life” tasks and on complex simulators.

# Difficulties with Biological Markers

- So, of all the markers we tried, the biological markers seemed the most effective.
- However there are some logical problems in considering the functional significance of correlations between variables that change over time.

Where Calendar Age is concerned, markers that are **functionally totally unrelated** may show strong associations simply because they both act as “clocks” measuring the same elapsed time.



As “Tree-Bulk” increases



So scientists experience cognitive declines....

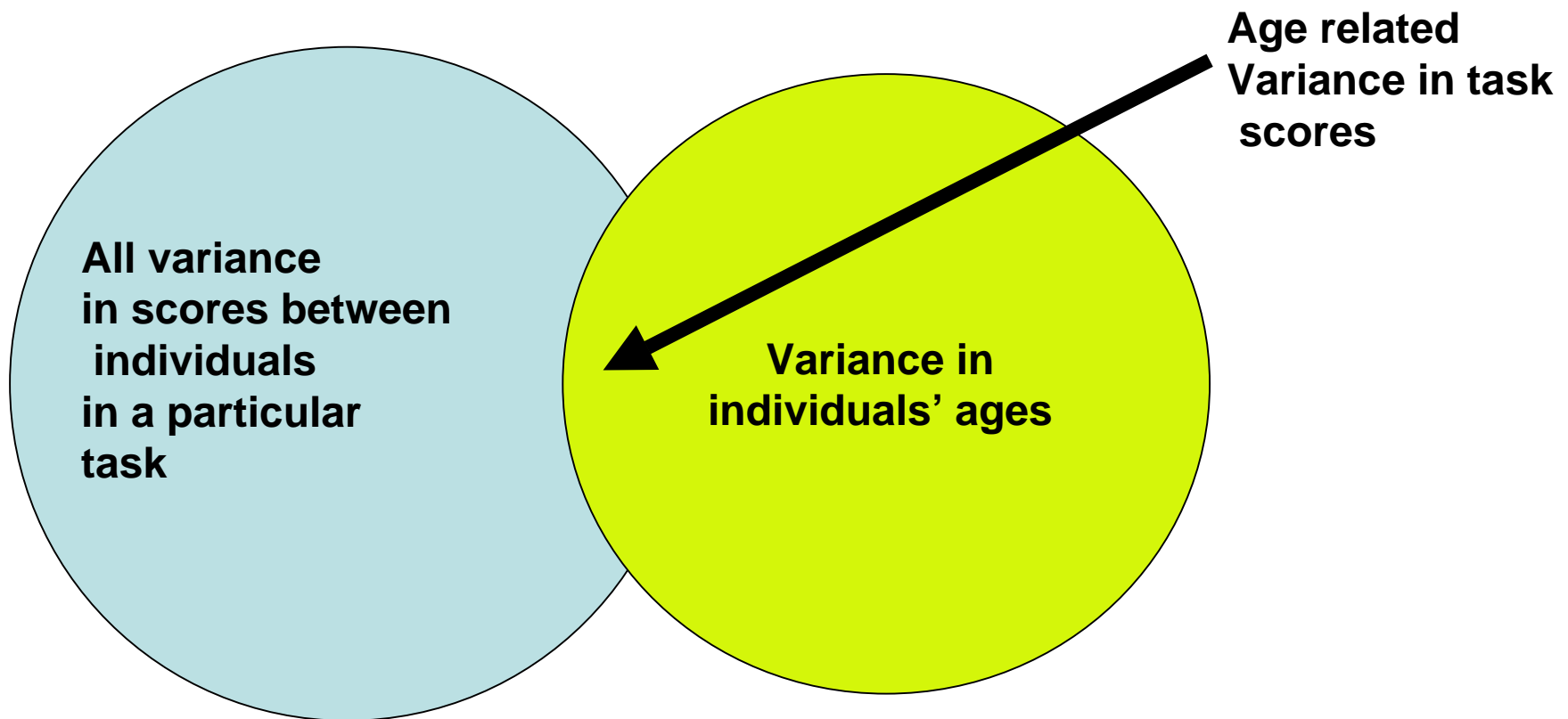
# **Examples of possible spurious functional relationships driven by synchronicity:**

- **Changes in the brain affect intelligence but functionally unrelated cumulative mechanical damage to cochlea hair cells affects hearing.**
- **Changes in the lens and cornea affect vision but functionally unrelated changes in the brain affect Intelligence and Memory and driving performance.**
- **Joint/Skeletal problems affect balance but brain changes affect intelligence.**

So we need ways to test whether relationships between biological markers and performance reflect common functional changes rather than simply synchronicity.

# Speed” explains nearly all age-related variance in all laboratory tasks, including working memory tasks

**By age-related variance:**  
we mean that part of the variance between individuals that is accounted for by differences in their ages



# Lindenberger & Potter's (1998) Computation of Shared over simple Variance (Crf Baltes and Lindenberger, 1996).

Illustration of Balance accounting for Age Related variance in Stroop RT (N=600)

- (A) Simple Effects of Age = .303
- (B) Simple Effects of Balance = .311
- (C) Joint of Age & Balance = .332
- (D) Unique Age = (C) .332 – (B) .311 = .021
- (E) Shared Age = (A) .303 – (D) .021 = .282
- Shared/Simple effect = (D) .282/. (A) 303 = **93%**

Apply this kind of computation to compare effects of balance with those of gross neurophysiological measures of brain integrity.

One way to proceed is to see how gross age-related brain changes affects performance on cognitive tests.

- Raz and many others have shown relations between absolute brain volume in old age and cognitive performance on many tests.
- A different question is how age-related changes in brain volume account for age-related declines in cognitive performance.
- This can be extended to white matter hyperintensities and cerebral blood flow (Basilar and Carotid artery flow).

Note that the issue of functional causality is just as important when one is examining the effects of single markers of global neuropsychological status of the brain as when one is evaluating balance..

- For example if one is looking at the effects of white matter hyperintensity prevalence, and finds a correlation with scores on some particular task, then one does not know, without further evidence, whether one has detected a causal functional connection or merely a synchrony of independent changes.
- Some other unrelated brain change may be the true functional cause.
- A way to get around this is to take passage of time out of the equation by entering age as a co-predictor.

Note that what we are discussing here is **age-related** atrophy over the entire brain.

That is, the percentage loss of gross brain volume from young adult volume.  
(% of cerebro-spinal fluid volume adjusted for skull; size)

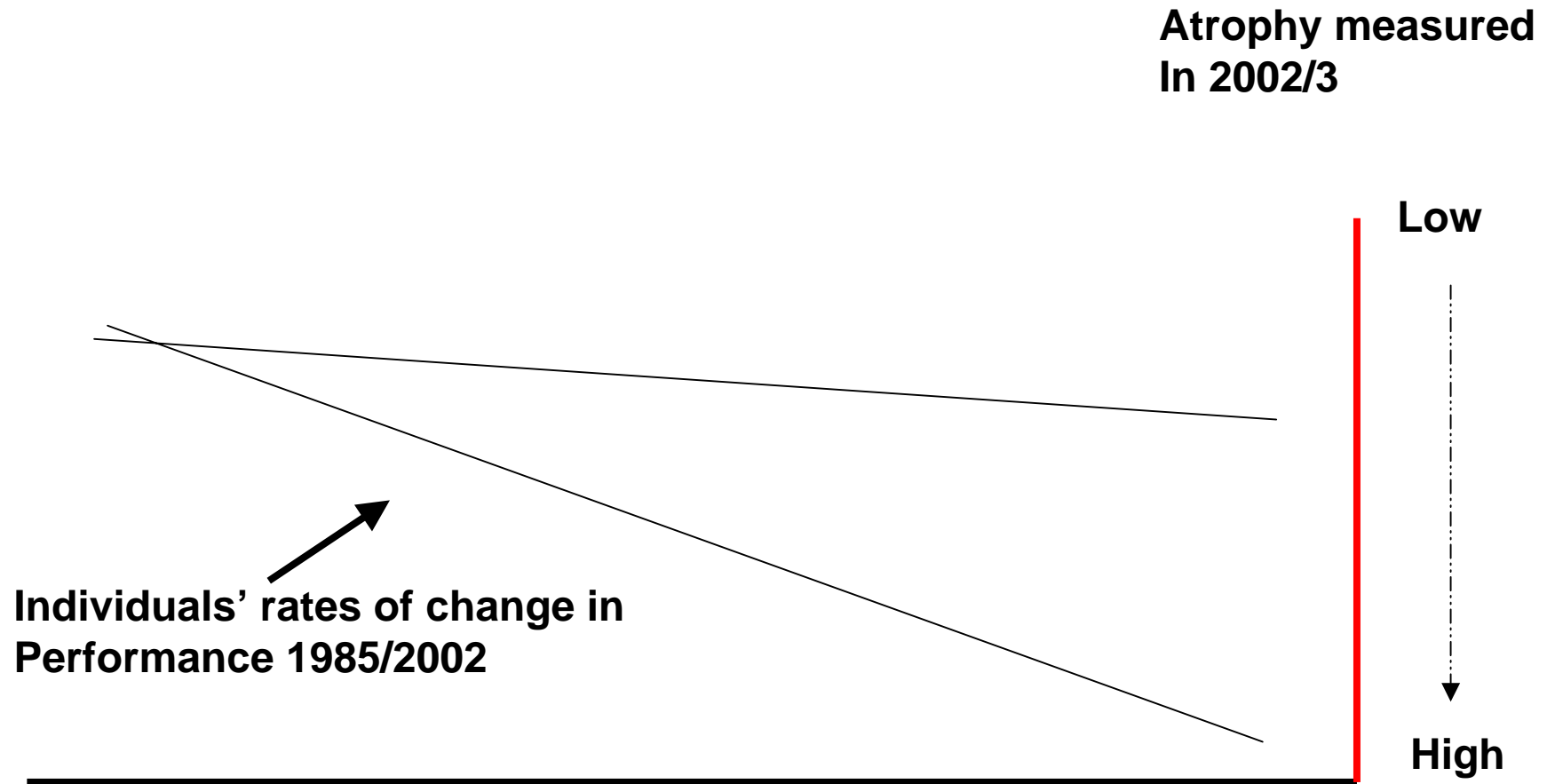
# Experiment

- 130 people aged from 62 to 85 years, who had been members of the 20 year longitudinal study, were brain scanned. Measures of brain atrophy, carotid and basilar artery blood flow, white matter lesions were obtained for 69 and grey matter thickness for 111.
- During the same 10 weeks they were given a battery of 3 intelligence tests, 2 tests of speed, 2 memory tasks and 3 “executive” tasks.

# Global brain atrophy predicts previous rate of age-related change

Rabbitt, Lunn & Ibrahim  
Neuropsychology 2007

Mary Lunn and Said Ibrahim used data gathered during longitudinal testing of all scanned participants to predict rates of change over the previous 17 years from current levels of atrophy. (Rabbitt, Lunn & Ibrahim, 2007, Neuropsychology)



The relative independent contributions of Age, atrophy and CF after variance associated with sex had been accounted for.

Test Group	Test	Beta for age given volume loss	Beta for volume loss given age	Beta for age given CBF	Beta for CBF given age
gf	Cattell CF	<b>-0.424*</b>	-0.054	<b>-0.441*</b>	0.049
	AH4-1	<b>-0.348*</b>	-0.222	<b>-0.417*</b>	0.207
	AH4-2	<b>-0.445*</b>	-0.058	<b>-0.441*</b>	0.149
Speed	L/D Code	-0.23	<b>-0.349*</b>	-0.142	<b>0.323**</b>
	VS	-0.25	<b>-0.225*</b>	-0.112	<b>0.261*</b>
Memory	PaP	<b>-0.303*</b>	-0.175	<b>-0.360*</b>	0.154
	OL	<b>-0.456*</b>	-0.123	<b>-0.498*</b>	0.095
Executive	Rey	<b>-0.436*</b>	-0.157	<b>-0.483*</b>	0.153
	Brixton	<b>0.281*</b>	0.229	<b>0.340*</b>	<b>-0.269*</b>
	C. Fluency	-0.342	<b>-0.342*</b>	<b>-0.309*</b>	0.201

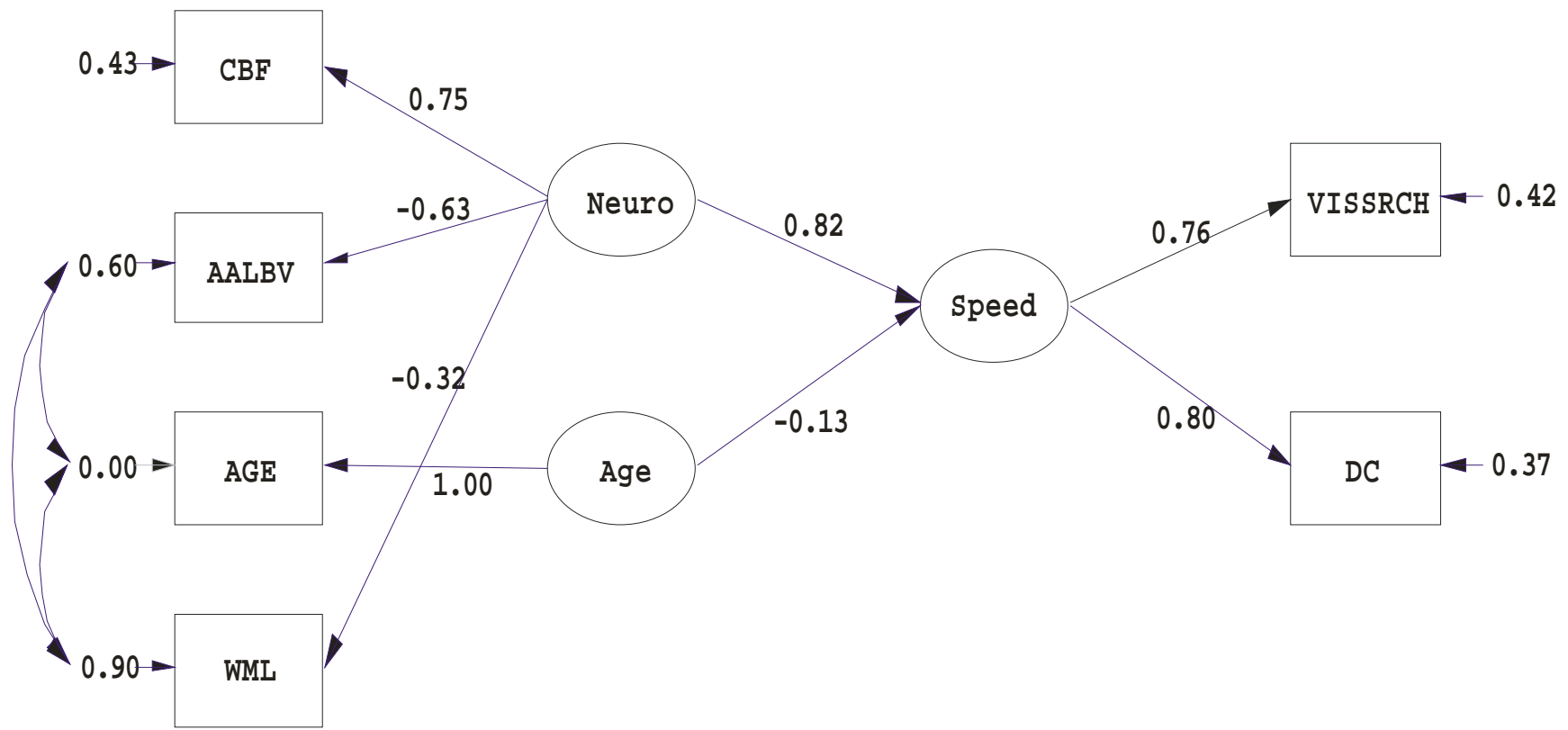
**Table 4: The proportion of age-related variance in test scores that are independently accounted for by atrophy and by CBF.**

<b>Test Group</b>	<b>Test</b>	<b>% age-related variance accounted for by loss of brain volume</b>	<b>% age-related variance accounted for by CBF</b>
<b>gf</b>	<b>CF</b>	<b>38.4%</b>	<b>10.3%</b>
	<b>AH4-1</b>	<b>60.7%</b>	<b>24.0%</b>
	<b>AH4-2</b>	<b>38.5%</b>	<b>18.8%</b>
<b>Speed</b>	<b>L/D Code</b>	<b>78.0%</b>	<b>36.3%</b>
	<b>VS</b>	<b>67.3%</b>	<b>33.7%</b>
<b>Memory</b>	<b>PaP</b>	<b>58.7%</b>	<b>21.8%</b>
	<b>OL</b>	<b>46.2%</b>	<b>13.4%</b>
<b>Executive</b>	<b>Rey</b>	<b>50.4%</b>	<b>18.0%</b>
	<b>Brixton</b>	<b>65.6%</b>	<b>32.5%</b>
	<b>C. Fluency</b>	<b>83.0%</b>	<b>28.6%</b>

# Using SEMs to examine relationships between Age, Speed Memory, Intelligence and Vocabulary

- **Dan Lunn, Oemetse Mogape et al**  
(Rabbitt, Mogape, Lunn et al *Neuropsychology* 2008)

Re-examine Age and Speed  
when gross brain changes are also  
considered.



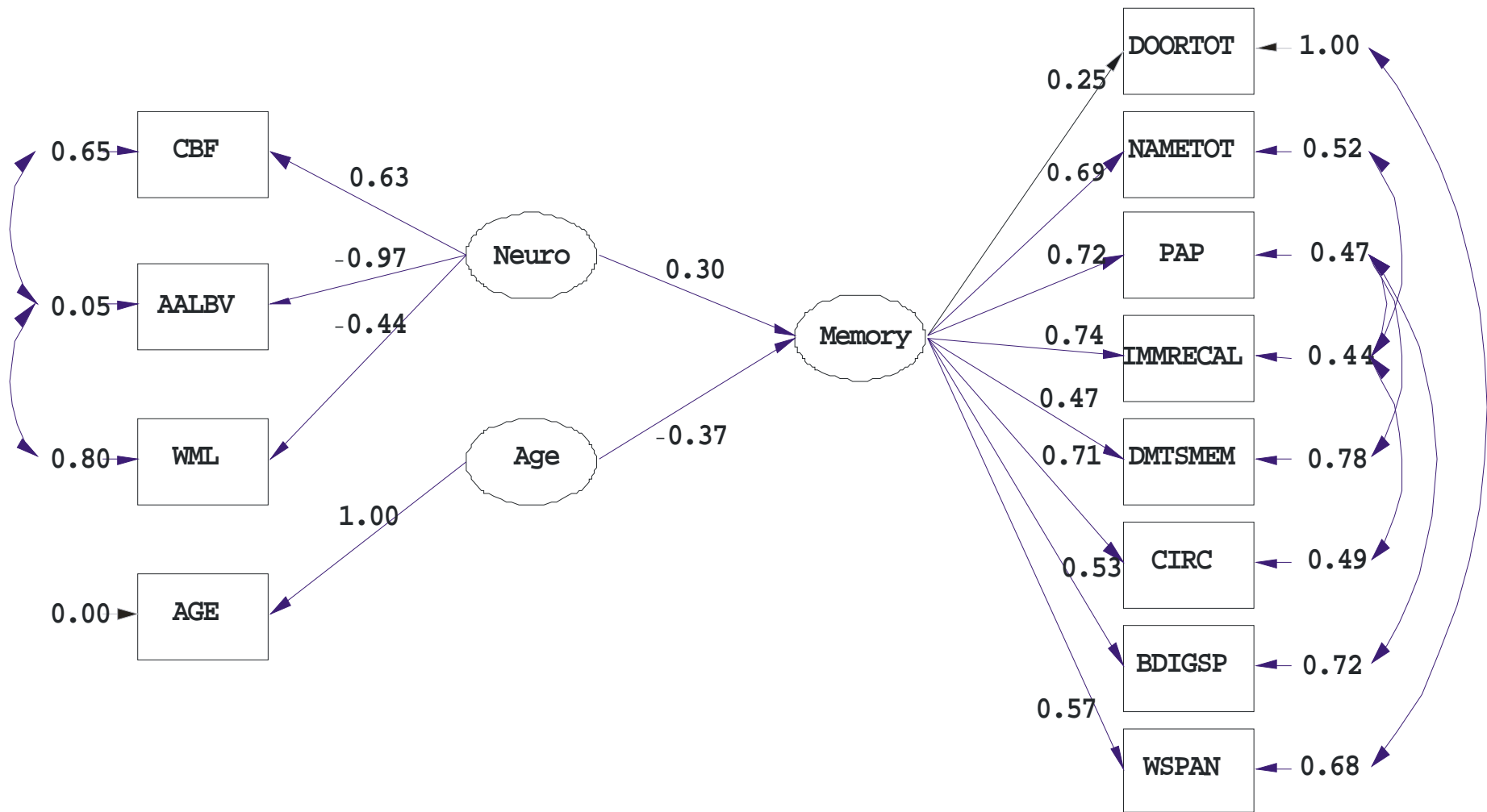
Chi-Square=2.54, df=4, P-value=0.63721, RMSEA=0.000

# The message:

- If individual differences in gross age-related losses of brain volume and in cerebral blood flow are taken into consideration **Calendar age**: i.e. a direct index of differences in life durations, is a crude index of differences in things that have happened to people in their lives, no longer predicts **any** significant proportion of individual differences in speed

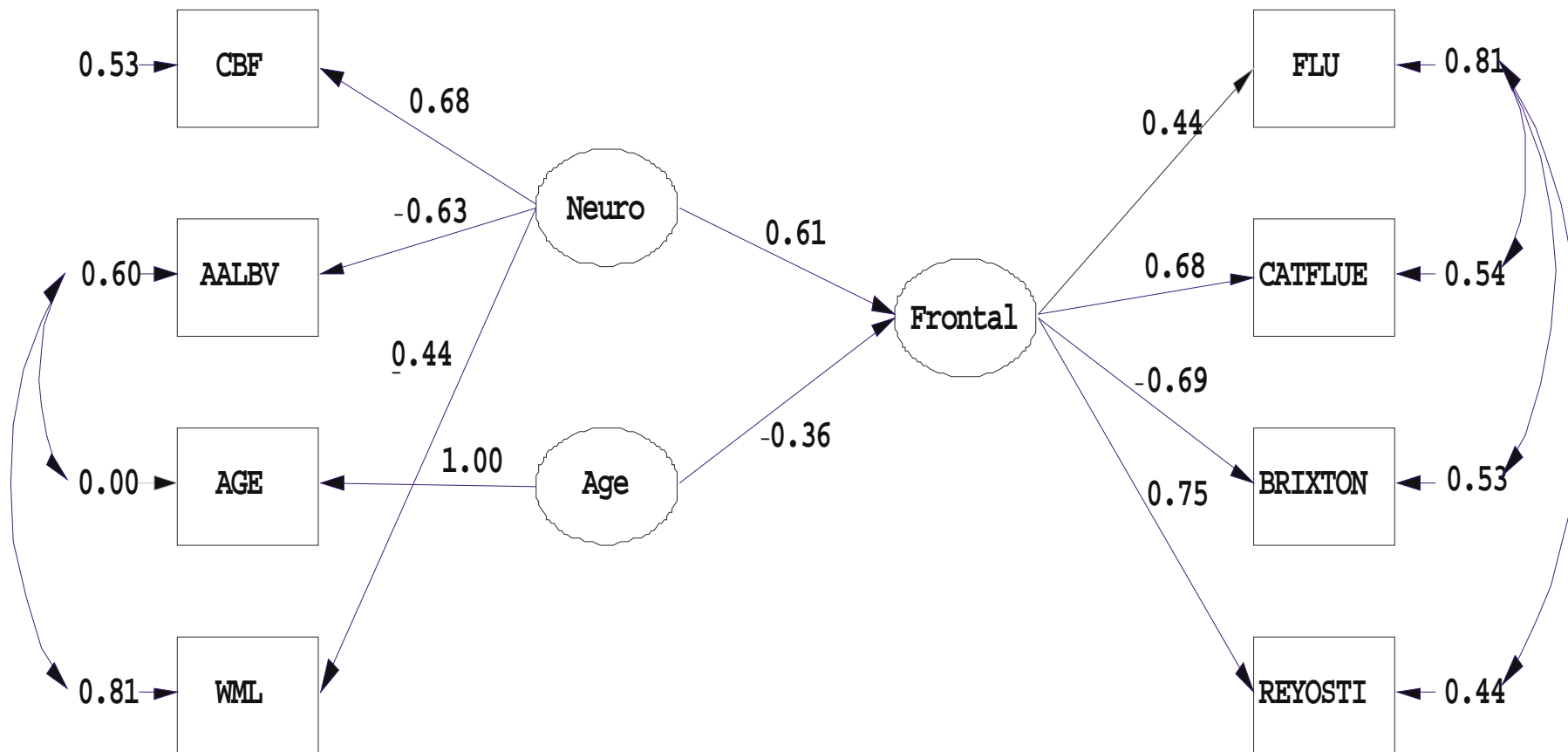
## What about Memory ?

- We have seen that nearly all of that proportion of variance between individuals in behavioural tests of memory, that is associated with differences in their calendar ages, is accounted for by behavioural measures of speed.



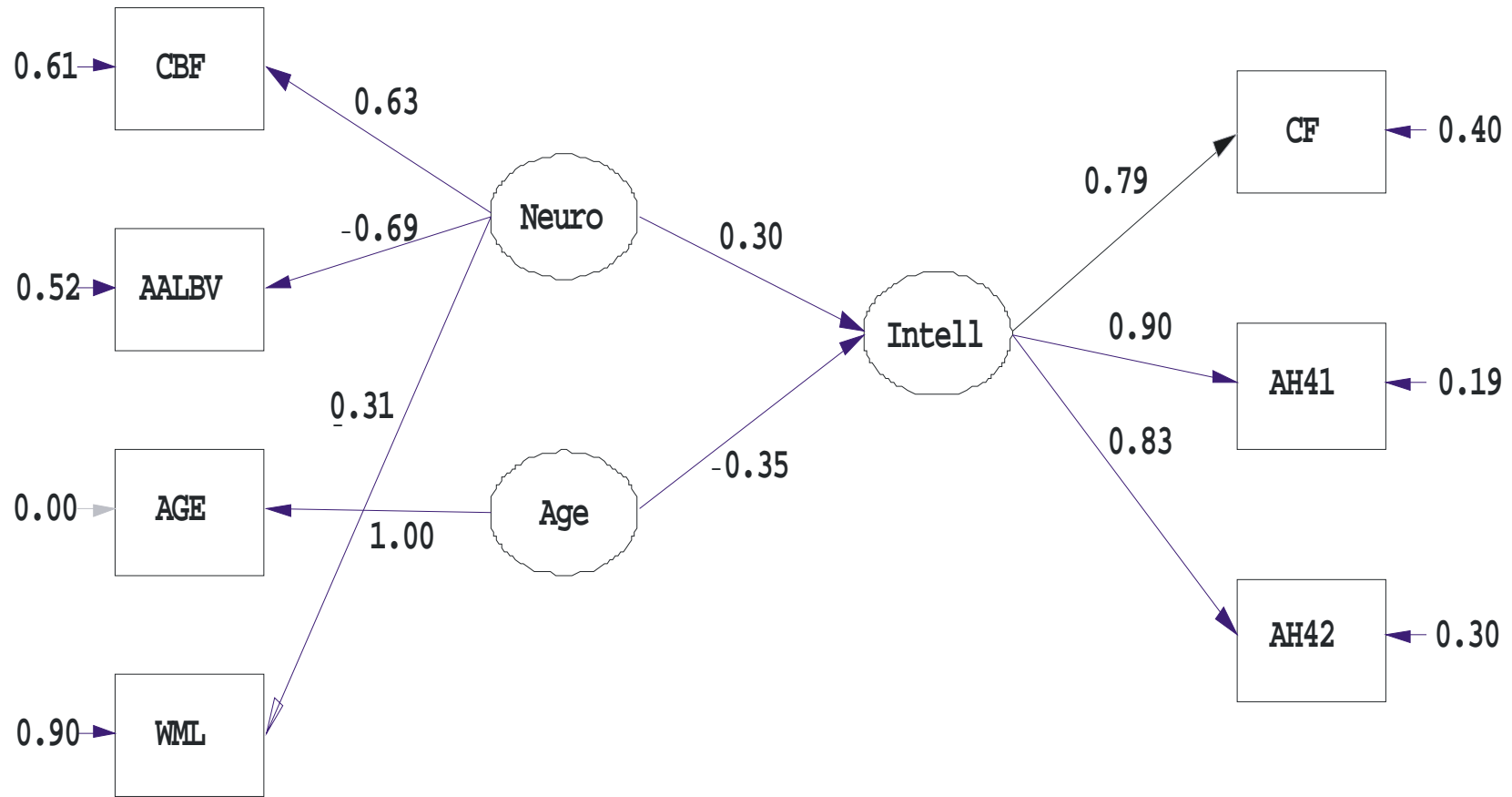
Chi-Square=51.92, df=40, P value=0.09811, RMSEA=0.048

# Age and Neuro as predictors of variance on Frontal Tasks



ChiSquare=15.49, df=12, P value=0.21592, RMSEA=0.047

# Age and Neuro as Predictors of Intelligence Test Scores



Chi\_Square=18.52, df=11, p value=0.07034, RMSEA=0.072

<b>Cognitive Performance Construct</b>	<b>Direct Effect of Age</b>	<b>Direct Effect of Neuro</b>
<b>Speed</b>	<b>NONE</b>	<b>Significant Substantial</b>
<b>Intelligence</b>	<b>Significant Modest</b>	<b>Significant Modest</b>
<b>Frontal</b>	<b>Significant Modest</b>	<b>Significant Modest</b>
<b>Memory</b>	<b>Significant Modest</b>	<b>Significant Modest</b>
<b>Vocabulary</b>	<b>NONE</b>	<b>Significant but very Little</b>

# Summary

- Balance appears to be a reasonably good marker for gross brain changes indexed by loss of volume, white matter lesions and cerebral blood flow.
- These gross brain changes are markers for performance changes.
- For speed gross brain changes account for \*all\* of that part of the variance between individuals that is accounted for by differences in their ages.

# A modest suggestion:

- The use of “biological markers” such as balance might be extended.
- Gross changes in brain neurophysiology, which can be easily and accurately measured, may prove to be very useful guides to past, and impending cognitive changes.

Thanks for your patience.