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Inspection Time: A biomarker for cognitive decline ☆

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ABSTRACT

Inspection Time (IT) is a psychophysical speed measure that has been linked to a range of cognitive abilities with results finding that shorter IT is associated with superior performance in cognitive abilities. Following a recent suggestion by Nettelbeck and Wilson [Nettelbeck, T., & Wilson, C. (2004). The Flynn effect: Smarter not faster. Intelligence, 32, 85–93.] that IT might have promise as a biomarker for cognitive decline during old age, this study tested the predictive validity of IT (both absolute estimate and change through time) for future cognitive performance and cognitive decline. Elderly participants ($N = 124$) were assessed on predictors IT and alternative common biomarkers, and outcomes fluid reasoning, crystallised ability, perceptual speed and working memory, on three occasions over 18-months. Results confirmed that IT predicted future performance on fluid reasoning, perceptual speed and working memory and cognitive decline in two of these constructs. Most importantly, this study has established that short-term changes in IT predict future cognitive test performance in fluid reasoning, perceptual speed and working memory, independent of baseline IT. Findings are consistent with the proposition that IT is a valid biomarker and future research should investigate the predictive validity of IT for age-related outcomes such as dependence in daily functioning, nursing home placements and mortality.

Two recent papers have suggested that Inspection Time (IT) may have potential as a biological marker of the aging process (Nettelbeck & Wilson, 2004, 2005). This idea stems from an observation by Nettelbeck and Wilson (2004), that IT is stable across generations, unlike some other speed of processing tasks. They proposed therefore that IT measures some fundamental aspect of intelligence, independent from rising IQ (Flynn, 1999), and suggested that IT might provide a lead indicator or biomarker for cognitive decline with advancing age.

There are several attributes of the IT measure that make it a potential biological marker. First, slower IT has been linked to poorer performance on a range of cognitive abilities including fluid reasoning, visualisation, short-term memory, and omnibus IQ scores (Grudnik & Kranzler, 2001). Second, IT has been shown to decrease with maturation in children (Wilson, Nettelbeck, Turnbull, & Young, 1992) and slow during old age in cross-sectional research (Nettelbeck & Rabbitt, 1992). Third, IT is sensitive to age-associated disease with deficits in IT observed in patients with mild cognitive impairment (Bonney et al., 2006) and Alzheimer's Disease (Deary, Hunter, Langan, & Goodwin, 1991). Fourth, IT has low knowledge requirements, and can be assessed in a non-invasive, quick and reliable manner. Fifth, IT does not require a speeded motor response and thus is free from psychomotor confounding and does not lead to a speed–accuracy trade off, unlike most other speeded tasks.

To establish that IT is a valid biomarker for cognitive aging, it must be able to predict future test performance or decline in test performance on cognitive tasks (Birren & Fisher, 1992; Ingram, 1991) and it must do this more successfully than chronological age. Previous studies have established a strong link between IT and cognitive test performance in cross-sectional research. However, it is unclear whether slower IT is

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associated with poorer cognition in the future or decline in cognitive abilities over time. Moreover, Baker and Sprott (1988, p. 234) have argued that for biological markers of aging, "it is the rate of decline which can ultimately be more critical than the initial value". This suggests that abnormal decline in IT should predict poorer performance or decline in cognitive tests in the future. This study will test the predictive validity of IT by testing the following hypotheses. The first two hypotheses involve the prediction of cognitive abilities in the future: (1) people with slower IT scores at baseline will have poorer cognitive performance in the future, and (2) people whose IT increases over time will have more future problems in cognitive performance. The second two hypotheses involve the prediction of cognitive decline over time: (3) people with slower IT scores at baseline will decline more in cognitive performance over time and (4) people whose IT increases over time will also display declines in cognitive performance. IT was compared with three physiological measures (grip strength, blood pressure and visual acuity) that have been frequently explored as biomarkers (Anstey, Lord, & Smith, 1996) and linked to cognitive performance (Anstey & Smith, 1999; Baltes & Lindenberger, 1997; Elias, Robbins, Elias, & Streeten, 1998). While the association between physiological measures and cognitive aging may not be immediately obvious, it stems from the idea that physiological changes that occur with age provide a more accurate representation of the true 'age' of an individual (Birren & Cunningham, 1985) and that these physiological markers better predict cognitive function and decline than does chronological age.

1. Participants

The sample (n=124) comprised individuals who completed the first three waves of data collection in the *Aging and Cognitive Change Study* in Adelaide (Australia) between 2003 and 2005. Participants were recruited via television, radio and print media and were required to be aged over 70 years, fluent in English and living independently in the community. All participants were screened for dementia using the Alzheimer's Disease Assessment Scale (ADAS-Cog<21 points, Weyer, Erzigkeit, Kanowski, Ihl, & Hadler, 1997). Baseline measurements were collected in 2003 (T_1), the second wave of data was collected 6-months later in 2004 (T_2) and the final wave was collected 12-months later in 2005 (T_3). The sample comprised 79 women (M=77.4 years, SD=4.5) and 45 men (M=76.9 years, SD=3.4), with an average of 11.8 years of formal education. This sample was highly educated compared with a representative sample of older Australian adults (see Anstey, Hofer, & Luszcz, 2003), and may therefore have represented an 'elite' group with respect to cognitive abilities.

2. Materials

2.1. Biomarkers

The IT task was computer-based. First, a warning cue (small cross, 5×5 mm) appeared for 520 ms. The target figure followed (two vertical lines, 10 mm and 21 mm long, connected at the top by a horizontal line of 17 mm; shorter line left or right with equal probability). This was presented for a short variable time followed by a flash mask (Evans & Nettelbeck, 1993) for a period of 375 ms. Participants were required to indicate whether the shorter line was on the left or right. Responses were made via the keyboard and the next item did not appear until a response was registered.

Three physiological measures were administered. These were Grip Strength (GS; in kg) measured by dynameter; Systolic Blood Pressure (SBP; mmHg) by automatic BP monitor Omron T5 model; and Visual Acuity (VA) measured binocularly from Snellen chart, with corrective glasses if applicable. VA was defined as the natural logarithm of the minimum size of letters that participants could read at a distance of 4 m.

Table 1
Descriptive statistics for biomarkers and cognitive tasks at each wave of data collection

	Wave 1		Wave 2		Wave 3		Average r-value[a]
Measure	$Mean_1$	SD_1	$Mean_2$	SD_2	$Mean_3$	SD_3	
Biomarkers							
IT (ms)	89.73	(32.32)	86.53	(27.34)	91.59	(29.76)	.66**
GS (kg)	19.18	(8.77)	19.33	(9.12)	19.07	(9.45)	.97**
SBP (mm Hg)	148.84	(23.50)	142.45	(20.44)	140.18	(19.84)	.63**
VA (log units)	1.79	(0.27)	1.77	(0.28)	1.82	(0.33)	.56**
Cognitive tasks							
RSPM	17.14	(4.65)	–	–	14.02	(4.31)	.69**
CCFT	23.94	(5.58)	–	–	23.81	(5.72)	.76**
CF	22.41	(7.04)	–	–	21.34	(9.20)	.67**
STW	54.02	(4.40)	–	–	53.53	(3.42)	.68**
INFO	28.63	(5.08)	–	–	28.67	(5.17)	.73**
SIM	22.59	(4.63)	–	–	23.02	(4.93)	.77**
DS	55.38	(13.03)	–	–	56.16	(13.40)	.90**
VM	32.97	(4.80)	–	–	32.81	(5.82)	.74**
RS	14.99	(8.89)	–	–	14.99	(8.85)	.58**

Note. IT = Inspection Time, GS = Grip Strength, SBP = Systolic Blood Pressure, VA = Visual Acuity, RSPM = Raven's Standard Progressive Matrices, CCFT = Cattell Culture Fair Test, CF = Concept Formation, STW = Spot-the-Word, INFO = Information, SIM = Similarities, DS = Digit Symbol, VM = Visual Matching, RS = Reading Span.

[a] Adjusted with Fisher's z-transformation.

* p<.05 (two-tailed), ** p<.01 (two-tailed).