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ORIGINAL RESEARCH

Genetic Influences on Five Measures of Processing Speed and Their Covariation with General Cognitive Ability in the Elderly: The Older Australian Twins Study

Teresa Lee · Miriam A. Mosing · Julie D. Henry · Julian N. Trollor · Andrea Lammel · David Ames · Nicholas G. Martin · Margaret J. Wright · Perminder S. Sachdev

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Abstract Processing speed (PS) is one of the basic elements of cognitive functions and has been regarded as a "common mechanism" which mediates general cognitive decline in aging. The present study of Australian twins (117 monozygotic pairs, 98 dizygotic pairs, and 42 single twins aged 65 years and over), estimated the genetic influences in five measures of PS: Digit Symbol Coding (DS), Trail Making Test A (TMTA), Stroop color naming and word reading (Stroop), Simple Reaction Time (SRT) and Complex Reaction Time (CRT); and their covariation with general cognitive ability (GCA): reasoning, problem-solving, and memory. Additive genetic factors explained 62% of the variance in DS, 42% in TMTA, 57% in Stroop, and 48% and 35% in SRT and CRT, respectively. Quantitative genetic modeling showed that all of the covariation between the five PS measures and GCA could be explained by one common genetic factor, while the covariation between the PS measures was partly explained by non-shared environmental as well as genetic influences. The genetic correlation among the PS measures was strongest for DS and TMTA, and between the PS measures and GCA was strongest for DS. These findings suggest that the different PS measures, as well as GCA were to a large extent influenced by the same set of genes and that the relationship between PS and GCA is entirely due to shared-genetic influences.

Keywords Genetic · Environmental · Twins · Aging · Processing speed · General cognitive ability

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T. Lee · J. N. Trollor · A. Lammel · P. S. Sachdev
Brain and Aging Research Program, School of Psychiatry, Faculty of Medicine, University of New South Wales, Sydney, NSW, Australia

T. Lee (✉) · P. S. Sachdev
Neuropsychiatric Institute, Euroa Centre, Prince of Wales Hospital, Randwick, Sydney, NSW, Australia
e-mail: teresa.lee@unsw.edu.au

M. A. Mosing · N. G. Martin · M. J. Wright
Genetic Epidemiology Laboratory, Queensland Institute of Medical Research, Brisbane, QLD, Australia

M. A. Mosing · J. D. Henry · N. G. Martin · M. J. Wright
School of Psychology, University of Queensland, Brisbane, QLD, Australia

J. N. Trollor
Intellectual Disability Mental Health, School of Psychiatry, Faculty of Medicine, University of New South Wales, Sydney, NSW, Australia

D. Ames
National Aging Research Institute, University of Melbourne, Melbourne, VIC, Australia

Introduction

Behavioral slowing has long been considered a main feature of aging (Birren and Fisher 1995). Normal aging is characterized by reductions in information processing speed (PS), which has been shown to peak in the early twenties, and then decline by approximately 20% by the age of 40, and by 40–60% by the age of 80 (Christensen and Kumar 2003). PS is usually measured by performance on timed psychomotor and visuomotor tasks, and it reflects the "the general rate at which one can complete a task including the speed of perceiving, encoding, response selection and memory retrieval" (Wright et al. 2001, p. 48). PS is considered to play a key role in virtually all higher level cognitive functions, including comprehension, reasoning, planning, and learning (Baddeley 1986).

Age-related changes in PS are thought to mediate age-associated declines in performance in complex cognitive tasks such as memory and reasoning (Salthouse 1996; Finkel et al. 2009), and general cognitive ability (Deary et al. 2010). However, it has also been argued that cognitive aging is associated with the ability to use effective control strategies, as well as theoretical models linking aging most strongly to diminished executive control (West 1996). Still others have associated cognitive aging with a reduction in attentional capacity, a decline in the neural integrity of the cognitive system, or a decrement in cognitive inhibition (Zimprich et al. 2008). Several studies have used measures of PS to study the relationship between PS and other cognitive abilities (Crowe et al. 1999; Deary et al. 2010), and most studies have incorporated PS measures with measures from other cognitive domains to form a cognitive factor in their investigations into the relationship between PS and general cognitive abilities (Finkel et al. 1995a; Pedersen et al. 1992; Plomin et al. 1994; Reynolds et al. 2005), but the genetic relationship between different measures of PS and general cognitive ability (without incorporating PS) has largely not been examined.

Salthouse (2000) has divided measures of PS that have traditionally been used in psychological research into six distinct domains. "Decision speed" is the time to respond to tests of moderately complex content. "Perceptual speed" is the speed of responding in tests with simple content, usually involving paper-and-pencil tests. "Psychomotor speed" can be measured by relatively simple tasks such as finger tapping, whereas "reaction time" (RT) refers to measures such as choice reaction time with visual stimuli and manual keyboard responses. "Psychophysical speed" is the decision accuracy with briefly presented visual or auditory stimuli, such as inspection time. Lastly, "time course of internal responses" includes speed as indexed via psychophysiological assessments, such as the latency of particular components of event-related potentials.

The heritability of PS in the elderly is substantial, ranging from 58 to 85% (Pederson et al. 1992; Plomin et al. 1994; Swan et al. 1990; Lessov-Schlaggar et al. 2007; Swan and Carmelli 2002) and even higher for general cognitive ability, ranging from 60 to 90% (Finkel et al. 1995a; Lessov-Schlaggar et al. 2007; Pederson et al. 1992; Plomin et al. 1994; Reynolds et al. 2005; Swan et al. 1990; Swan and Carmelli 2002), with a reduction in genetic influences with advancing age (McClearn et al. 1997; Reynolds et al. 2005). A longitudinal study of the SATSA (Swedish Adoption and Twin Study of Aging) twins found a heritability of 80% for perceptual speed and 91% for a cognitive factor at age 65, but at age 80, heritability for cognitive ability (fluid ability, verbal, memory, perceptual speed) was 76% suggesting that environmental influences may increase steadily after age 65 (Reynolds et al. 2005). Most of these studies have measured perceptual speed using the Digit Symbol Coding test, either the standard paper-and-pencil format as in the National Heart Lung Blood Institute (NHLBI) studies (Swan et al. 1990; Swan and Carmelli 2002; Lessov-Schlaggar et al. 2007) or an oral version as in the studies involving SATSA twins (Perdersen et al. 1992; Plomin et al. 1994; Finkel et al. 1995a; McClearn et al. 1997; Reynolds et al. 2005). The Minnesota Twin Study of Adult Development and Aging (MTSADA) is the only study to have examined PS in elderly twins using RT tasks. While the heritability for movement time was 21%, no genetic influence was found for decision time (Finkel and McGue 2007).

The heritability estimates for PS are generally higher than those for memory. In the SATSA studies when memory was represented by Digit Span, Picture Memory, and Names and Faces test, the heritability estimates were approximately 50% and below (Pederson et al. 1992; Plomin et al. 1994; Finkel et al. 1995a, b; McClearn et al. 1997). However, higher heritability estimates (39–76%) were reported in the Longitudinal Study of Aging in Danish Twins (LSADT), which used a composite score of Digit Span and word recall (McGue and Christensen 2001, 2002, 2007). Using word recall, text recall, and Figural Memory tests, the MTSADA studies reported heritability estimates of 55% (Finkel and McGue 1993), and a similar heritability of 59% for Digit Span, text recall, and Figural Memory (Finkel et al. 1995b).

Twin studies in the elderly, similar to those in younger twin samples (Ho et al. 1988; Neubauer et al. 2000; Spinath and Borkenau 2000), show that the phenotypic relationship between PS and general cognitive ability is largely due to a common genetic factor. For example, Finkel and Pedersen (2000) showed in the SATSA twins that 70% of genetic variance in a cognitive factor (composed of four domains) was shared with perceptual speed. They then later reported that a substantial proportion of the genetic influence on both fluid intelligence and a cognitive ability factor was accounted for by genetic influence on perceptual speed (Finkel and Pedersen 2004). More recently, a longitudinal analysis of the same cognitive factor indicated that when speed variance was controlled for, the genetic variance for general cognitive ability decreased steadily with age, but much slower compared to the estimates uncorrected for PS (Finkel et al. 2009). Genetic influences on the longitudinal changes in PS were considered not only to have contributed to, but also to "drive" the genetic influences on longitudinal changes in memory and spatial abilities.

The present study is the first Australian study on cognitive functioning in elderly twins, aged 65 and above. We aimed to confirm the previous findings of PS in elderly twins, to extend them by examining the genetic and environmental influences on five measures of PS, and to

examine their relationship with general cognitive abilities (GCA). To date, there has been no other study in the elderly which has explored the genetic covariation among multiple PS measures and their covariation with general cognitive ability. We included three "perceptual speed" measures, and two "reaction time" measures, and computed a measure of general cognitive ability (GCA) using the first principal component score from a verbal reasoning test, a visuo-spatial problem-solving test, and a memory composite (derived from three episodic memory tests). The specific aims of the study were first, to estimate the heritability of each of the five PS measures and GCA in older individuals; second, to investigate the genetic and environmental influences on the covariation between the five PS measures; and third, to disentangle the genetic and environmental influences on the covariation between the PS measures with GCA.

Methods

Methodology of the Older Australian Twins Study (OATS), has previously been described in detail (Sachdev et al. 2009), and is summarized here. Monozygotic (MZ) and Dizygotic (DZ) twin pairs aged 65 or older were enrolled at one of the three study centers, each from the three eastern states of Australia. They were sourced from the Australian Twin Registry, media release, and newspaper advertisements. The inclusion criteria were: ability to consent to participate, have a consenting co-twin, having completed some education in English, and being of at least low average intelligence (IQ $\geq$ 80). Exclusion criteria were life-threatening illness, inadequate English to participate in assessment, and acute psychosis.

Participants

The sample consisted of 477 twin individuals (67.7% female), including 119 MZ pairs and 99 DZ pairs, plus 41 single twins, with a mean age of 70.7 and standard deviation (sd) of 5.2 (range 65–88). Their average years of education were 11 (*s.d.* = 3). Mean IQ, estimated from the NART (National Adult Reading Test), ranged from 70 to 129 (mean = 106.23, *s.d.* = 10.88), and the mean MMSE (Mini-Mental State Examination) score was 28.66 (*s.d.* = 1.43). Seventeen participants (3.6%) were of non-English speaking background (NESB), and all were able to complete the National Adult Reading Test (NART), with their estimated IQ ranging from 80 to 118. Six (of the 477) participants were reluctant to complete the NART, and their estimated IQs were obtained from the Barona Demographic Equation (1984), and ranged from 91 to 100. There was no overlap of participants who were NESB and those who refused to complete the NART.

The sample is representative of the Australian population. The over-representation of females (ratio of 2:1) is consistent with the trend of more females (55%) than males in the Australian population over 65 years of age, with two times as many females than males at the age of 85, reflecting female longevity (Australian Bureau of Statistics 2009). It is also consistent with other twin studies of older populations such as the SATSA and LSADT, with female participants comprising approximately 60–70% of the study samples. Our male and female participants on average received 11.9 and 10.6 years of education, respectively, which is only slightly higher than the average for those born in the 1930s (10.0 years, Kelley and Evans 1996). Only 3.6% of our participants were from a NESB, as compared to 21.3% in the Australian population who were 65 years and older in 2006 (AIHW 2007). As our inclusion criteria required participants to have adequate English to complete cognitive testing and the questionnaires, this might have reduced the number of people who were of NESB to participate in the study.

Co-twins from one state (Queensland) were assessed on the same day at the study center. In the other two states (New South Wales and Victoria) co-twins were assessed from 1 week to 6 months apart, either at the study center, a regional center, or the participant's home. Zygosity was determined by the participants' responses to a questionnaire about being a twin. For a sub-sample of the twins (N = 110) who participated in earlier studies when they were middle-aged and who have been recently genotyped with high-density SNP arrays for GWAS, correct zygosity assignment was ascertained to be greater than 99%. Informed written consent was obtained from all participants, and the study had the appropriate ethics approvals.

Measures

Participants were administered a comprehensive battery of cognitive tests to assess the following cognitive domains: estimated intelligence, concentration, attention, verbal memory, visual memory, frontal/executive functions, confrontation naming, visuo-spatial and constructional ability, and PS. The assessments were conducted by research psychologists who were trained by the first author to ensure consistency in administration and scoring of the test protocol across three sites. For the present study five PS measures were selected (described in detail below). These included three neuropsychological tests of perceptual speed: Trail Making Test A, Digit Symbol Coding, and Stroop color naming and word reading, which are commonly used, and, hence, allow for comparison of results with past and future

research, and two RT tests: Simple RT and Choice RT, which are also commonly used and represent an aspect of PS as distinct from other neuropsychological tests.

Processing speed

Digit Symbol Coding Test (DS) (Wechsler Adult Intelligence Scale-Third Edition, Wechsler 1997). Participants were given 120 s to quickly fill in the symbols corresponding to rows of printed numbers. The number of correctly paired symbols was the score for this task and was used as a measure of psychomotor and perceptual speed.

Trail Making Test A (TMTA) (Reitan and Wolfson 1985). Participants were required to quickly draw lines to connect a series of numbers consecutively. The time taken was recorded as a measure of psychomotor and perceptual speed.

Stroop Color and Word Test Parts 1 and 2 (Stroop1 and Stroop2) (Delis et al. 2001). This test was modified and presented as part of a computerized battery. In Stroop1, participants were required to quickly name the colors of a page of crosses printed in different colored ink. In Stroop2, participants were required to quickly read the names of colors printed on a page. The time taken to read all items was recorded to index perceptual speed. Both tasks were reasonably well correlated ($r = 0.60$). The time taken in naming and reading were combined to form one score (Stroop).

Simple Reaction Time (SRT) task. Participants were required to touch the computer screen as soon as they saw a yellow square. The stimuli were randomly presented at 1, 2, and 4 s intervals, six trials for each, 18 trials in total. The median response time for the 18 trials in milliseconds was used as the SRT hit reaction time score. The task was preceded by a familiarization trial to insure color recognition and correct usage of the touch pen.

Complex Reaction Time (CRT) task. Participants were presented with two squares simultaneously. They were instructed to touch the upper square if the two squares were the same color, and to touch the bottom square if the two squares were of a different color. There were a total of 20 trials, with the four types of trials randomly presented (five of each). The CRT hit reaction time score was the median response time (in milliseconds) for 20 trials. This task was preceded by one practice task with four trials.

Both the SRT and CRT tasks were from our in-house computerized test battery, developed as part of the neuropsychological assessment of the Sydney Memory and Aging Study (Sachdev et al. 2010). Each task was administered twice in the same session, with one block of 18 (SRT) and 20 (CRT) trials presented at the beginning of the cognitive test battery and one block at the end. The correlation between the median scores for the two SRT blocks and the two CRT blocks were high (0.71 and 0.80, respectively). The median scores of block 1 and block 2 were used to form one SRT and one CRT score.

General cognitive ability (GCA)

A GCA score was formed from the First Principal Component (FPC) for Similarities, Block Design, and a Memory composite scores (see below). If one of these three scores was missing it was imputed. The percentage of variance explained by the FPC was 61.8%, with loadings of Similarities, Block Design and Memory of 0.80, 0.77, and 0.79, respectively.

The *Similarities* subtest (from WAIS-III, Wechsler 1997) required the abstraction of the similarity of common objects or concepts. The correlation between performance on this test and the average Full Scale IQ of five age groups representing the age range of the participants was high (0.83, WAIS-III WMS-III Technical Manual 1997). Performance on this test reflected verbal and reasoning ability, the latter of which was considered a typical marker of fluid intelligence (Zimprich et al. 2008).

The *Block Design* subtest (from WAIS-R, Wechsler 1981). The participant was asked to construct models using blocks to match the geometric patterns printed on the stimulus booklet. The average correlation between performance on this test and the average Full Scale IQs of five age groups representing the age range of the participants was moderately high (0.64, WAIS-III WMS-III Technical Manual 1997). Performance on this test represents visuospatial and problem-solving abilities, and this subtest has usually been included as a fluid intelligence measure in research.

A composite measure for *episodic memory* was obtained from three sources: (1) immediate and delayed recall of Story A (correlation = 0.86 in this study) of the Logical Memory subtest from the Wechsler Memory Scale-Revised (Wechsler 1987), (2) the number of words recalled at the last of five trials, delayed recall, and total learning scores from the Rey Auditory Verbal Learning Test (RAVLT, Rey 1964), (3) Benton Visual Retention Test (multiple choice format, Sivan and Spreen 1996). The episodic memory measure was obtained by averaging the z scores of the Logical memory and the RAVLT, and then combining the mean of the z scores of these two composites with the z score of Benton Visual Retention Test (BVRT). The correlations between these measures in our study ranged from 0.76 to 0.90. These three tests were included in our episodic memory measure because they represent different modalities of episodic memory—verbal and visual, free recall and recognition memory.

Cognitive screening

The *National Adult Reading Test* (NART) (Nelson and Willison 1991) required oral reading of 50 phonetically irregular words. From the error scores, an equivalent IQ score could be derived which has been shown to be a valid estimate of intelligence (Crawford et al. 2001). Two participants who scored below the cut-off score of 80 were excluded, plus a further two with missing data due to clerical error.

The *Mini Mental State Examination* (MMSE) (Folstein et al. 1975) provided a gross index of general cognitive function, and consisted of 30 items pertaining to orientation, attention, language, memory and constructional ability. The number of correct responses was scored and adjusted for age, years of education and NESB (Anderson et al. 2007). One participant who scored below 24 was excluded from the study.

Statistical analyses

The distributions of each of the test scores were examined and transformed using logarithmic (TMTA) or square-root functions (Stroop, SRT, CRT). DS did not require transformation. The PS scores for 18 participants that were greater than three standard deviations from the mean were winsorized (five in Stroop, six in SRT, and seven in CRT). In addition, the scores for Stroop, TMTA, SRT, and CRT were reversed so that higher values represented better performance for all measures, and all were transformed to z scores (with mean of zero and variance of one). For the GCA measure four outliers were deleted, one from each of Similarities, Block Design, RAVLT and BVRT, and seven participants whose scores on the BVRT fell outside three *s.d.* of the mean were winsorized.

Prior to genetic modeling, each of the variables was tested for equality of means, within twin pairs and across the two zygosity groups, as well as for equality of covariance. No significant difference was found in the variable means within twin pairs or across zygosity groups (all $p > 0.05$). Age had a significant effect on all PS measures as well as GCA, with z scores decreasing between 0.05 and 0.08 per year. Sex was significant for DS (males faster than females) and SRT (females faster than males). Age and sex were analyzed as fixed effect covariates for genetic modeling (in the Means model).

The classical twin design was used to estimate the genetic and environmental influences on the covariation between the traits. While MZ twins share all their genetic makeup, DZ twins only share half of their genes on average. The twin design uses this information on the genetic relatedness of twins and allows for the proportioning of variance into additive genetic (A) and environmental influences. Environmental factors are either shared between the twin pair (C), that is, the teachers, common friends, and family, or non-shared (E) (also including measurement error), reflecting experiences unique to one of the twins, such as, a car accident involving one of the twins but not the other. While C influences increases a twin pair's resemblance in one trait, E influences make the twins more different from each other. If the MZ twin correlation is larger than the DZ twin correlation, A influences are suggested, while a DZ correlation more than half the MZ correlation indicates shared environmental effects (C). An important assumption of the classical twin design is that MZ and DZ twins only differ in terms of genetic relatedness, that is, C influences are not different for MZ compared to DZ twins.

Different models were fitted to the data using the full information maximum likelihood (FIML) estimation in Mx (Neale et al. 2002; Neale 2005), making use of both paired and unpaired twins, the latter contributing to estimates of means and variances. In Maximum-Likelihood procedures, the -2LL (minus two times log-likelihood) statistics are compared between nested models (restricted model versus general model) to assess the difference in model fit. A saturated (ACE) Cholesky decomposition was fitted first, estimating all parameters, and then progressively more restricted models were compared to the fit of the previous models. Subsequently, we also fitted two independent pathway models, allowing for one and two common genetic pathways, respectively. The genetic factor structure was determined with the help of a varimax rotation of the genetic correlations obtained from the best fitting Cholesky model using SAS System for Windows (SAS Institute Inc. 1999–2001). As we were mainly interested in the genetic influences on the covariation between the variables, we only applied the independent pathway model and retained the environmental influences as a Cholesky. The Akaike's Information Criterion (AIC, Akaike 1987) was used to compare model fit of the two independent pathway models (as they were not nested). The AIC reflects not only the parsimony of the model but also the goodness of fit (the lower the AIC value, the better the model fit).

Results

The final sample consisted of 472 individuals: 117 MZ pairs, 98 DZ pairs and 42 single twins (Table 1). Availability of data differed for the five PS and GCA measures. Missing data was due to technical failure with computerized testing at one study site, and a minority due to participants' visual problems or their reluctance to use the computer. Table 2 shows the phenotypic correlations between the PS variables and with GCA. The correlations

Table 1 Means and standard deviations of processing speed variables and general cognitive ability (*GCA*) for total sample, MZ and DZ twins, male and females

N:	DS (no. correct) 466 Mean (s.d.)	TMTA (s) 470 Mean (s.d.)	STROOP (s) 336 Mean (s.d.)	SRT (milliseconds) 328 Mean (s.d.)	CRT (milliseconds) 328 Mean (s.d.)	GCA (IQ) 442 Mean (s.d.)
Total	56.08 (13.13)	38.24 (12.91)	24.65 (5.29)	533.14 (122.38)	879.99 (152.91)	100.11(14.98)
MZ (179–253)	55.72 (12.82)	38.05 (13.09)	24.53 (5.44)	533.05 (117.84)	873.70 (128.22)	98.86 (14.77)
DZ (137–217)	56.48 (13.49)	38.47 (12.72)	24.80 (5.06)	533.26 (128.50)	888.22 (180.33)	101.37 (15.19)
M (95–149)	52.42 (12.28)	40.56 (13.96)	25.60 (5.50)	507.46 (121.60)	876.22 (147.06)	100.84 (14.84)
F (301–317)	57.79 (13.18)	37.16 (12.27)	24.22 (5.15)	544.18 (121.32)	881.62 (155.66)	99.61 (15.08)

MZ monozygotic, *DZ* dizygotic, *DS* Digit Symbol, *M* male, *F* female, *TMTA* Trail Making Test A, *STROOP* Stroop color word test, *SRT* simple reaction time, *CRT* complex reaction time, *GCA* general cognitive ability IQ equivalent, *s.d.* standard deviation. Data from 441, 442, and 440–468 individuals were available for Similarities, Block Design and the memory composite respectively for forming GCA

Table 2 Phenotypic correlations with significance level and twin correlations with 95% confidence intervals for monozygotic (MZ) and dizygotic (DZ) twin pairs for each variable corrected for sex and age

	DS	TMTA	Stroop	SRT	CRT	GCA
Phenotypic correlations						
DS		0.56*	0.59*	0.27*	0.43*	0.44*
TMTA			0.43*	0.21*	0.39*	0.34*
Stroop				0.39*	0.55*	0.39*
SRT					0.60*	0.30*
CRT						0.34*
Twin correlations						
MZ (81–118)	0.58 (0.45–0.69)	0.41 (0.25–0.55)	0.55 (0.38–0.68)	0.41 (0.21–0.57)	0.36 (.16–.53)	0.74 (0.64–0.81)
DZ (61–98)	0.24 (0.04–0.42)	0.16 (−0.05–.34)	0.27 (0.02–0.49)	0.31 (0.07–0.52)	0.17 (−0.09–0.41)	0.26 (0.06–0.44)

DS Digit Symbol, *TMTA* Trail Making Test A, *Stroop* Stroop color naming and reading, *RT* simple reaction time, *CRT* complex reaction time, *GCA* general cognitive ability

* Significant at 0.01 level (2-tailed)

among the PS variables ranged from 0.21 to 0.59 and between the PS variables and GCA from 0.30 to 0.44. All the correlations were significant at the $p < 0.01$ level.

Genetic modeling

Twin correlations for MZ and DZ twins for each of the phenotypes are displayed in Table 2. The overall pattern of twin correlations showed a trend for genetic influences, with MZ correlations being larger than the DZ twin correlations for all variables.

An ACE Cholesky decomposition was modeled first, with the five PS variables (DS, TMTA, Stroop, SRT, and CRT) and GCA as the last variable. All shared environmental factors (C) could be removed without a significant deterioration in model fit (Table 3). Two independent (AE) pathway models, allowing for one and two common genetic pathways respectively, fitted the data more parsimoniously (no significant decrease in model fit) compared to the reduced (as well as the original) Cholesky decomposition. The AIC indicated that the independent model allowing for two common genetic factors was the most parsimonious. This model is shown in Fig. 1, with the non-significant pathways ($p > 0.05$) retained for completeness and shown as dashed lines. Estimates of the E influences with confidence intervals (as Cholesky decomposition) are shown in Table 4a.

Heritability estimates from this model for the five PS measures were 0.62 (DS), 0.42 (TMT), 0.57 (Stroop), 0.48 (SRT), and 0.35 (CRT), and 0.74 for GCA. A common genetic factor (A1) influenced all five PS variables as well as GCA, explaining a large amount of variance in (44% DS, 21% TMTA, 37% Stroop, 13% SRT, 27% CRT and 33% GCA) and covariance between the variables. In addition, for DS, TMTA and SRT another 7%, 2% and 8%, respectively were due to a second genetic (A2) factor, with a significant specific genetic factor accounting for 20% of the total variance in Stroop. For GCA, 41% of the variance was due to a specific genetic factor, indicating that approximately half of the genetic variance ($h^2 = 0.74$) in GCA was due to genes shared with the PS variables. CRT was the only PS variable influenced by the common genetic

Table 3 Model fitting results for the six variables with the best fitting model in *bold*

Multivariate model fitting results	AIC	−2LL	df	Δ −2LL	Δ df	*p* Value
Cholesky decomposition-ACE model	972.80	5174.81	2105			
Cholesky decomposition-AE model	939.20	5183.20	2122	8.39	17	0.96
Independent pathway model-1 common genetic factor (AE)	933.47	5195.47	2131	12.27	9	0.20
Independent pathway model-2 common genetic factors (AE)	**931.70**	**5187.70**	**2128**	**4.50**	**6**	**0.61**
Omnibus drop of all E-factors shared with the PS variables	930.48	5196.48	2133	8.78	5	0.12

Model fit (−2LL) of the independent pathway models was compared to the Cholesky (AE), and the Aikaike's information criterion (*AIC*) was used to determine the most parsimonious independent pathway model

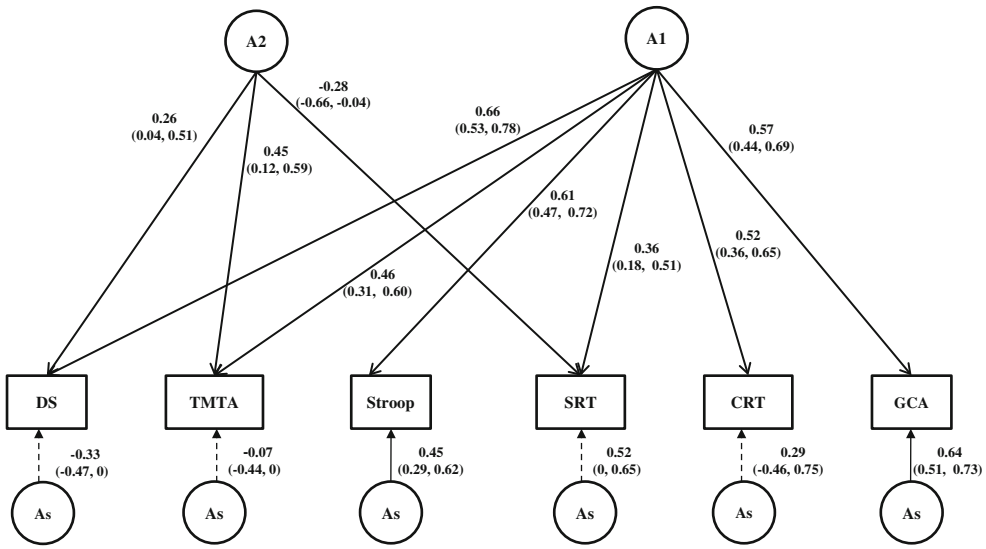

Fig. 1 Best fitting independent pathway model allowing for two common genetic pathways showing the relationship between DS, TMTA, Stroop, SRT, CRT, and GCA. To facilitate interpretation of the model, non-shared environmental (*E*) influences are shown in Table 4a. Non-significant pathways in the model ($p > 0.05$) were retained for completeness and are shown as *dashed lines*

Table 4 (a) Model fitting results for non-shared environmental (*E*) influences in the independent pathway model (two factors), and (b) genetic correlations of processing speed variables and general cognitive ability (*GCA*)

	DS	TMTA	Stroop	SRT	CRT	GCA
(a)						
E1	0.63 (0.55–0.72)	0.16 (0.04–0.29)	0.22 (0.10–0.34)	0.12 (−0.01–0.29)	0.10 (−0.04–0.26)	0.08 (−0.01–0.18)
E2		0.74 (0.66–0.82)	0.10 (0.00–.21)	0.14 (0.01–0.26)	0.12 (0.00–0.25)	0.04 (−0.04–0.12)
E3			0.60 (0.52–0.70)	0.17 (0.04–0.31)	0.24 (0.10–0.38)	−0.01 (−0.11–0.09)
E4				0.68 (0.58–0.78)	0.45 (0.34–0.55)	0.08 (−0.02–0.17)
E5					0.60 (0.54–0.67)	−0.06 (−0.16–0.03)
E6						0.50 (0.43–0.58)
(b)						
DS		0.82	0.67	0.31	0.68	0.58
TMTA			0.50	0.12	0.62	0.52
Stroop				0.40	0.75	0.51
SRT					0.49	0.32
CRT						0.47

(A1) factor alone (no other genetic influences), indicating that its genetic makeup was entirely shared with GCA.

The correlation between the five PS variables and GCA was entirely due to one common genetic factor (A1), with all non-shared environmental factors between the PS variables and GCA being non-significant (also when all dropped at the same time as shown in Table 3). This A1 factor also explained all the genetic covariance between Stroop and CRT and the other PS variables, while DS, TMTA and SRT were also influenced by a second common genetic factor (A2). As shown in Table 4a, non-shared environmental influences explained a significant part of the covariation between the PS variables. For example, the environmental factor (E4) accounted for 46% (0.68^2) of variance in SRT while also accounting for 20% of variance in CRT, though there was still another 36% specific to CRT.

Genetic correlations among the PS variables and GCA are shown in Table 4b. Genetic correlations between the PS variables were generally in the moderate range with the lowest genetic correlation between TMTA and SRT (0.12) and a high correlation between TMTA and DS (0.82). Notably the genetic correlations between SRT and the other four PS variables were low (0.12–0.49) especially compared with CRT (0.49–0.75). The genetic correlations between the PS variables and GCA ranged from 0.32 to 0.58, with the highest correlation between DS and GCA.

Discussion

The present study had three aims: We investigated the relative contribution of G and E influences on variance in PS and GCA (aim 1), as well as G and E influences on the covariation between the five PS measures (aim 2) and finally, we aimed to disentangle the G and E influences on the covariation between the PS measures and GCA (aim 3) in the elderly. The heritability of various aspects of PS was examined using five indicators of this construct: DS, TMTA, Stroop, SRT and CRT, utilizing the classical twin design. Genetic modeling revealed moderate to moderately high heritability for all the PS measures (35–62%). The remainder of the variance (38–65%) was explained by non-shared environmental factors, which included measurement error. The heritability of GCA, as represented by a composite score composed of measures of verbal reasoning, visuo-spatial problem-solving, and episodic memory, was high (74%). The covariation between the PS variables was to a large extent explained by genetic influences, with the remainder being due to non-shared environmental factors. CRT was the only PS variable sharing its entire genetic make-up with GCA. The genetic correlations among the PS variables ranged from 0.12 (between TMTA and SRT) to 0.82 (DS and TMTA), and DS also had the highest genetic correlation with GCA (0.58). Finally, the covariance between the five PS variable and GCA was entirely explained by one common genetic factor shared between the five PS variables and GCA.

The heritability estimate of DS was comparable with the findings from previous elderly twin studies. When examined in one of the NHLBI studies (Swan and Carmelli 2002), heritability of DS was 68% (mean age 71) which was similar to our finding of 62% (mean age 71). The MTSADA group had studied the genetic influences on intraindividual variability of Simple and Complex Reaction Time, in a slightly younger group (median age 62). Heritability of decision time and movement time was found to be low, and was considerably lower than the estimates of 48 and 35% for SRT and CRT, respectively in our study. This disparity is most likely due to the different aspects of RT examined, intraindividual variability in their study versus individual difference in the present study. To our knowledge, our study is the first to examine genetic influence in Trail Making Test A, Stroop color naming speed and word reading speed (as measures of PS) in elderly twins.

In examining the heritability of RT measures, Beaujean (2005) who reported on a meta-analysis of nine twin studies, and Neubauer et al. (2000) in their study of two elementary cognitive tasks of PS and intellectual abilities, found that heritability increased as the complexity of the task increases. Our findings do not support this, at least with the RT measures, as the heritability estimates of SRT and CRT were 48% and 35%, respectively. As CRT requires decision-making in responding, it would be considered the more complex of the two RT tasks and therefore, would be expected to have higher heritability compared to SRT. The heritability estimate of TMTA, which involved perceptual speed and motor speed, was 42%, was also slightly lower than that of SRT.

Our heritability estimate for GCA was not quite as high as those reported by the SATSA group, that is, approximately 80% (Pedersen et al. 1992; Plomin et al. 1994) for mean age of 65. In a longitudinal study, Reynolds et al. (2005) reported heritability of 91% for GCA at age 65, which was somewhat lower at age 80 (76%). Even so, the lower heritability estimate of GCA (74%) in the present study could be associated with the difference in measures included in GCA. PS variables were examined independently in our study, and were not included in the first principal component analysis used to form GCA, as in most of the previous SATSA studies described (Perdersen et al. 1992; Plomin et al. 1994; Finkel et al. 1995a; McClearn et al. 1997; Reynolds et al. 2005). By creating a GCA measure from other cognitive domains and excluding PS, the aim was not to confound or inflate the genetic overlap

between PS and GCA. Nevertheless, the association found between PS variables and GCA in our study, albeit not as strong as in other studies, would support the inclusion of PS in a higher-order, multi-factorial GCA.

The phenotypic correlations among our PS measures were all significant. As expected, the correlations between the three perceptual speed measures were stronger than their correlations with the two RT measures. Similarly, the correlations between the two RT measures were stronger between themselves than with the three perceptual speed measures, and consistent with Deary et al. (2010), DS was the PS measure that was most strongly associated with GCA.

The covariation between the different PS measures was mainly due to genetic influences, with two common genetic pathways explaining all the genetic covariation, one (A1) influencing all five PS measures as well as GCA, while the other (A2) only influenced DS, TMTA and SRT. In addition, among the five PS measures, only Stroop was additionally influenced by a specific genetic factor. The strongest genetic correlation among the PS variables was between DS and TMTA (0.82) indicating that these two measures of PS are largely influenced by the same genes or the same set of genes. The DS test has been reported to be a complex task which involves psychomotor speed, ability to learn, working memory, motor persistence, attention and sustained attention, freedom from distraction, visuo-motor co-ordination and tracking, visual search, clerical speed and accuracy, and speed of processing (Crowe et al. 1999; Lezak et al. 2004). The TMTA measure involved psychomotor and processing speed, visual attention and sustained attention, visuo-motor scanning and tracking, and sequencing (Lezak et al. 2004; Tombaugh 2004). In addition, apart from speed there are other overlapping cognitive abilities in these two variables, which are associated with frontal and executive functions. Moderately high correlations (0.62–0.75) were also shown between DS and Stroop, DS and CRT, as well as CRT and TMTA, and CRT and Stroop. Of note is the finding of a negative path coefficient from the genetic factor A2 to SRT, suggesting there may be some genetic source of variation that operates in the opposite direction for SRT. These findings emphasize the relevance of separating and specifying different aspects of PS, and cautions against analyzing PS as a unitary construct.

The third aim of our study was to explore the G and E influences on the relationship between the different measures of PS and GCA. Results showed that all of the covariation between the five PS variables and GCA could be explained by shared genetic influences. Pedersen et al. (1994) reported similar findings with most (but not all) the covariation between the PS measures and general cognitive ability (including PS) being due to shared genetic influences. Approximately half of the genetic influence on GCA was shared with the PS measures in our study, which is lower compared to the SATSA studies with about 70% of genetic variance of the cognitive factor being shared with PS (Pedersen et al. 1994; Finkel and Pedersen 2000). However, this higher estimate is most likely due to the fact that the SATSA studies included a PS factor in their general cognitive ability measure, inflating the estimate of shared genetic influences. Our findings highlight the high genetic overlap between PS and GCA, and also emphasize the relevance of taking general cognitive abilities, such as memory and fluid intelligence, into account in the analysis of other cognitive domains.

This study represents the first Australian study of genetic influence on cognitive functions of the elderly, with a genetically informative sample of twins aged 65 and above. We confirmed the findings of previous studies conducted in other countries, and extended their findings by employing several measures of PS, and explored the genetic and environmental relationship between PS measures and verbal, non-verbal, and memory abilities (GCA). While the strength of this study is the use of multiple measures of PS to explore its relationship with GCA, there are several limitations. The relatively small sample size would have reduced the statistical power in our analyses, and as such, we were unable to examine the genetic influences on sex difference. In the present study we found that males were faster than females in DS, and females faster than males in SRT. This is inconsistent with previous studies where a female advantage has been demonstrated with DS (Majeres 1983; Snow and Weinstock 1990) and in older adults (MacDonald et al. 2003), and males have been shown to be faster than females in simple RT over all decades from age 40 to 90 (Bleecker et al. 1987), and at older ages (Der and Deary 2006). The reason for the disparity of findings in DS and SRT is unclear. It is possible that psychological factors such as motivation or impulsivity are involved, as least for SRT. Another explanation for the faster DS performance in the elderly males might be survival bias, i.e., elderly men in our study might represent a cognitively and physically more able group in the population.

Another limitation is the cross-sectional nature of our study. With longitudinal data, we would be able to examine individual difference in cognitive change, in the context of genetic effects, and to study the direction of causality. It would also be of interest to study the genetic and environmental relationships between PS and other cognitive domains, such as executive functions, which may mediate the phenotypic and genetic relationship between PS and GCA. Unique environmental influences play a substantial role in some PS measures, and should be investigated because of their potential for modification, and hence, contribution to successful aging.

In summary, our findings suggest that heritability of perceptual speed, as in DS and Stroop, is substantial, with

lower heritability for TMTA, SRT, and CRT. Heritability of GCA was the largest with 74% of variance explained by genetic influences. The majority of covariance between the five PS measures was explained by two common genetic factors, one shared between the PS measures and GCA and the other factor only influencing three of the PS measures (DS, TMTA, SRT), and one common genetic factor explained all the covariance between the PS and GCA measures. These findings suggest that the different PS measures, as well as GCA were to a large extent influenced by the same set of genes.

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