Genetics of Cognition: Outline of a Collaborative Twin Study

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A multidisciplinary collaborative study examining cognition in a large sample of twins is outlined. A common experimental protocol and design is used in The Netherlands, Australia and Japan to measure cognitive ability using traditional IQ measures (i.e., psychometric IQ), processing speed (e.g., reaction time [RT] and inspection time [IT]), and working memory (e.g., spatial span, delayed response [DR] performance). The main aim is to investigate the genetic covariation among these cognitive phenotypes in order to use the correlated biological markers in future linkage and association analyses to detect quantitative-trait loci (QTLs). We outline the study and methodology, and report results from our preliminary analyses that examines the heritability of processing speed and working memory indices, and their phenotypic correlation with IQ. Heritability of Full Scale IQ was 87% in the Netherlands, 83% in Australia, and 71% in Japan. Heritability estimates for processing speed and working memory indices ranged from 33-64%. Associations of IQ with RT and IT (–0.28 to –0.36) replicated previous findings with those of higher cognitive ability showing faster speed of processing. Similarly, significant correlations were indicated between IQ and the spatial span working memory task (storage [0.31], executive processing [0.37]) and the DR working memory task (0.25), with those of higher cognitive ability showing better memory performance. These analyses establish the heritability of the processing speed and working memory measures to be used in our collaborative twin study of cognition, and support the findings that individual differences in processing speed and working memory may underlie individual differences in psychometric IQ.

There is a wealth of evidence for a significant and substantial genetic influence on cognition (Bouchard & McGue, 1981; Boomsma, 1993; Chipuer et al., 1990; Devlin et al., 1997; Plomin & Petrill, 1997; McClearn et al., 1997). However, cognitive ability has primarily been measured by intelligence tests designed to assay a broad range of cognitive functions, and very little can be inferred about genetic influences on the underlying biological processes. To advance understanding of the genetic basis of intellectual functioning, genetic studies need to capitalize on tasks developed by experimental psychologists that probe specific cognitive functions, and electrophysiological measures employed by psychophysiologists that reflect how information is processed in the brain.

The present study measures two key elements of cognition — speed of processing and working memory capacity. Processing speed is a basic cognitive ability that reflects the general rate at which one can complete a task including the speed of perceiving, encoding, response selection and memory retrieval. Working memory is the ability to temporarily maintain and manipulate information in a limited capacity system (Baddeley, 1986; Baddeley & Hitch, 1974), allowing us to attend to events, maintain them, and integrate them with past experience to guide correct performance. Both these basic abilities play a significant role in higher level functioning including comprehension, reasoning, planning and learning (Baddeley, 1992), and undergo change in normal child development and adult aging (Carpenter et al., 1990; Kail, 1992; Salthouse, 1996; Fry & Hale 1996). It is a reasonable hypothesis, therefore, that genetic variability in these basic abilities may explain some of the substantial genetic variability in general cognitive ability.

The relationship between processing speed and general cognitive ability as measured by psychometric IQ has been extensively studied over the past 30–40 years (e.g., Jensen, 1982, 1987; Vernon, 1993; Nettelbeck, 1987; Kranzler & Jensen, 1989; Deary & Stough, 1996). The general finding is that processing speed performance on tasks that make minimal demands on higher-order cognitive functions is reliably correlated with psychometric IQ. A commonly used measure of processing speed, reaction time (RT), is consistently shown to be inversely related to IQ and when several RT measures are combined, up to 50% of the vari-

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ance in IQ scores can be explained (Vernon, 1989). However, RT encompasses a number of different subprocesses the speed of which can show substantial individual differences, and these can be measured using separate indices of processing speed. For example, inspection time (IT) is a measure of perceptual processing — the minimum time the brain needs for simple visual discrimination or to make an accurate judgement when stimuli are visible for a very brief period. It does not involve a speeded response. It is moderately correlated with IQ and the correlation has been found to be stronger with measures of performance IQ ("fluid" intelligence) than with verbal IQ ("crystallized" intelligence) (Deary, 1993).

The speed of other processes can be probed by psychophysiological measures, such as the latency of the event related potential (ERP) — P3 (or P300). P3 latency is found to have a significant negative correlation with cognitive ability (e.g., Egan et al., 1992; McGarry-Roberts et al., 1992; Polich & Martin, 1992) and the strength of the correlation seems to depend on the type and amount of processing required (e.g., Houlihan et al., 1998). Whereas, P3 latency reflects early stimulus updating, the onset of another ERP, called the lateralized readiness potential (LRP) (Coles, 1989) reflects the time the brain needs to select an appropriate motor response. Division of the LRP in a stimulus locked and a response locked part further allows the separation of individual differences in the speed of processing up to the LRP and that between the LRP and overt responses (Osman, Moore & Ulrich, 1995). While speed of processing indices are inter-correlated different patterns of genetic and environmental associations across task are indicated (Ho et al., 1988) suggesting that there may not be a single processing speed mechanism influencing intelligence but rather several different component processes (e.g., speed of perceptual processing, speed of short term memory rehearsal).

Initial research into the relationship between memory processing and general cognitive ability investigated short-term memory but more recently the focus has shifted to features of working memory, and in particular the limits of working memory capacity which meet both the processing and storage demands of a given task (Baddeley, 1986; Just & Carpenter, 1992). Baddeley & Hitch (in Baddeley, 1986) propose a model with a frontal lobe executive that selects the main processing goals, selectively focuses sensory attention, plans the overall strategy and, most importantly, controls two slave systems responsible for the encoding and temporary storage of either visual material (the visuospatial sketchpad), or verbal material (the phonological loop). Accumulating evidence suggests that individual differences in working memory and in general fluid intelligence are significantly related to one another with studies repeatedly showing performance on working memory span tasks to predict reasoning ability, comprehension, and other higher mental processes (Daneman & Merikle, 1996; Kyllonen & Christal, 1990; Necka, 1992). Moreover not only is working memory highly correlated with reasoning ability but processing speed is moderately correlated to working memory span (Kyllonen & Christal, 1990). Memory span tasks are thought to reflect something that is fundamentally important to higher level cognition. One suggestion is that those a with high working memory span have more limited-capacity attention resources available than those with a low working memory span, and therefore, individual differences in working memory capacity will have implications for tasks requiring controlled effortful processing (Engle et al., 1999).

A diverse body of research suggests that the prefrontal cortex and the various posterior regions to which it is networked may be the critical brain structure mediating individual differences in working memory and general fluid intelligence (e.g., Goldman-Rakic, 1987; 1992; Miller, 2000; Petrides, 1995; Fuster, 1997). Human brain-imaging studies show that the prefrontal cortex and its anatomical connections are highly activated during the performance of working memory and psychometric tasks (Duncan et al., 2000) and other research shows that lesions to the prefrontal cortex impair working memory performance (e.g., Fuster, 1991; D'Esposito & Postle, 1999). Research demonstrating that the prefrontal cortex is necessary for working memory has used a delayed response task that requires memory of target stimulus location during a delay. Prefrontal cortex neurons fire more frequently during the delay period whereas parietal neurons in monkey brains fire earlier and more frequently in response to target stimulus presentation (e.g., Chafee & Goldman-Rakic, 1998). Recent psychophysiological investigations indicate individual differences in working memory brain electrical activity. Using an n-back spatial working memory task, in which P3 amplitude is decreased under high working memory load, P3 amplitude is significantly larger in those of high ability suggesting they are better able to focus attention under greater working memory demands (Gevins & Smith, 2000). Similarly, the slow wave during the delay interval in delay tasks provides information on memory rehearsal and retrieval (Ruchkin et al., 1995; Geffen et al., 1997), and task-related shifts in EEG coherence (Petsche, 1997) and theta synchronisation are suggested as a putative index of working memory function, specifically with regard to the encoding of new information (Klimesch, 1999).

The present study describes a tripartite collaboration between laboratories in The Netherlands, Australia and Japan to develop a common protocol to study cognition in a large twin sample. The primary aim is to identify genetic variants that influence individual differences in general cognitive ability through "lower level" indices of processing speed and working memory using both performance and electrophysiological measures. In this paper we provide a detailed outline of the study and methodology and provide a description of the combined twin sample studied thus far. As a preliminary analysis we examine the heritability of performance indices of processing speed and working memory, and examine their phenotypic correlation with IQ.

Method

Participants

Participants are located through the Netherlands Twin Registry, the Brisbane Adolescent Twin Registry, and the Keio Twin Registry. Participants in the Netherlands and Australia have previously participated in a twin study of

cardiovascular risk factors and naevus (mole) development (Zhu et al., 1999) respectively. Zygosity is determined by questionnaire and by typing independent highly polymorphic DNA markers. All participants are required to have normal or corrected vision, no history of head injuries, neurological or psychiatric conditions. Written, informed consent is obtained from participants, and their parents if applicable (i.e., under 18).

Research Protocol

Table 1 lists the tasks and indices used in the three participating countries to measure cognitive ability in their respective twin samples. Tasks are grouped into three main categories — psychometric IQ, processing speed, and working memory. ERPs/EEG are recorded during several tasks (oddball, Ericksen flanker, delayed response (DR)) in addition to performance measures. A common protocol is clearly evident with a large overlap of tasks used across countries resulting in a significant number of common indices of mental ability with local additions.

In the Netherlands and Australia, co-twins usually attend together but are tested separately in parallel sessions with the total testing time being 4.5 (Netherlands) or 3.5 (Australia) hours. In Japan, participants are tested separately on the RT, IT and DR tasks, and for resting EEG. For all other measures, participants are tested in a group of 5–6 individuals (co-twins tested in separate groups) with 4–5 groups being tested in parallel and rotating around the different sessions. Both single and group sessions are 3–4 hrs long and are run independently of each other and therefore each twin pair is tested over a 1–3 year period. All participants receive some payment for participating (Netherlands — transport costs and 50 NLG, Australia — $20–$35AUD is given as a reward for accuracy on the DR task, Japan — 4000 yen).

Psychometric Intelligence

In this paper psychometric IQ is assessed using the WAIS in the Netherlands, the MAB, which correlates highly with the WAIS (Jackson, 1984), is used in Australia, and in Japan the Kyodai NX intelligence scale is used.

Wechsler Adult Intelligence Scale (WAIS). The WAIS (Wechsler, 1981) and the revised version of the WAIS (WAIS-R) are the standard neuropsychological instruments for the assessment of general cognitive ability in individuals 16 years and over and has been translated into Dutch and Japanese. The test comprises 11 sub-tests, six verbal (information, digit span, vocabulary, arithmetic, comprehension, similarities) and five performance (picture completion, picture arrangement, block design, object assembly, digit symbol) from which are derived 11 standardised sub-test scores and three composite scores including a full scale (i.e., total) score and a verbal and performance score. Participants were administered the test according to standard procedures.

Multidimensional Aptitude Battery. The MAB (Jackson, 1998) is a test of general intellectual ability that is modeled after the WAIS-R. It includes five verbal (Information, Comprehension, Arithmetic, Similarities, Vocabulary) and five performance (Digit Symbol, Picture Completion, Spatial, Picture Arrangement, Object Assembly) sub-tests and is designed for assessment of both adults and adolescents age 16 and older. Correlations with the WAIS-R for verbal, performance and full scale are 0.82, 0.65 and 0.91 respectively (Jackson, 1984). The test is computer administered and employs multiple-choice items with the participant identifying the best answer from five choices, and a total of 7 minutes is allowed for each sub-test. Standardised scores for each sub-test and verbal, perfor-

Table 1

Tasks (and Measures) Recorded by Each Country to Assess Mental Ability.

	Netherlands	Australia	Japan
Psychometric intelligence	WAIS (5 verbal & 4 performance sub-tests)	MAB (3 verbal & 2 performance sub-tests); WAIS-R (digit symbol subtest); National Adult Reading Test; Schonell Graded Word Fluency Test.	WAIS (2 verbal & 2 performance sub-tests), Ravens Matrices, Japanese Intelligence Test (vocabulary, verbal reasoning, mental rotation, paperfolding), Kanji knowledge, 4 card problem solving task, Vandenberg's 3D Mental Rotation task
Processing Speed	SRT (reaction time), Choice RT (reaction time, efficiency), IT (inspection time), Oddball task (P3latency)	Choice RT (reaction time, efficiency), IT (inspection time)	Choice RT (reaction time, efficiency), IT (inspection time)
Working Memory	DR task (accuracy, slow wave amplitude, P3 amplitude, P3 latency, EEG measures — frequency, power, coherence, and (de-) synchronisation), Sternberg digit span (accuracy, RT slope), Ericksen Flanker task (onset lateralised readiness potential)	DR task (accuracy, slow wave amplitude, P3 amplitude, P3 latency, EEG measures — frequency, power, coherence and (de-) synchronistaion)	DR task (accuracy, slow wave amplitude, P3 amplitude, P3 latency, EEG measures — frequency, power, coherence and (de-) synchronistaion), Verbal & spatial working memory span tasks (accuracy);

mance, and full-scale IQ scores are derived. In this study three verbal sub-tests (Information, Arithmetic, Vocabulary) and two performance (Spatial, Object Assembly) sub-tests are administered.

Kyodai NX intelligence scale. This is a standardised test widely used in Japan to assess psychometric IQ. It is a pencil and paper type test comprising four sub-tests each with 12 items, and is administered in a group situation. As well as standardised scores for each sub-test, composite scores of Verbal and Spatial abilities are derived from the Sentence Making and Verbal Reasoning, and Mental Rotation and Paper Folding sub-tests respectively. A Full scale IQ score is derived form the Verbal and Spatial abilities score.

Processing Speed & Working Memory

Processing speed is measured as reaction time (RT) during tasks of varying difficulty, and inspection time (IT). In these first analyses RT data are available for simple RT from the Netherlands and choice RT from Australia. An identical IT task is used in all 3 countries with sufficient data available from the Netherlands and Australia. As the software program is the same there is excellent standardisation of the giving of instructions, the stimuli and number of trials presented, and the processing and computation of the various speed indices. Similarly, the DR task is used at all testing sites with the same software or task routines being used, as well as task instructions and parameters being standardised across country. DR data are available for the Australian sample and spatial working memory span data from the Japanese sample.

Simple reaction time (SRT) task. In this task each trial is started by pressing a home key, which, after a 750 ms inter-trial interval, initiates the presentation of a 500ms visual warning stimulus (a plus sign) on the center of the screen. A variable blank interval separates the warning signal offset from the presentation of a visual reaction stimulus. The reaction stimulus represents either one digit from the set {1,2,3,4,5,6} or one letter from the set {A,B,C,D,E,F}, both requiring right-key responses. The reaction stimulus disappears as soon as the participant responds, or when a maximum time of 600ms has expired. After each trial subjects receive feedback in the form of the words 'correct', 'wrong', 'too early', 'too late' on the center of the screen. Mean decision time (DT), movement time (MT) and reaction time (RT) are calculated from the correct trials. In these analyses mean RT is used.

Choice reaction time task. This task consists of a standard series of spatially compatible choice RT tasks in which a horizontal line of 8 water taps is displayed at all times (adapted from Smith & Stanley (1983); Luciano et al., in press a). On each trial, drips appear below one of the taps and the participant's task is to switch the tap off by pressing the corresponding key on the computer keyboard. If the wrong key is pressed, the tap continues to drip, and is only switched off when the correct key is pressed. The left-most tap is controlled by the Z key, the second from the left, the X, and so on across to the / key controlling the rightmost tap. The response-stimulus interval is varied randomly between 750 and 1500ms. Processing load is manipulated by increasing the number of stimulus alternatives, so that blocks of 2 (48 trials), 4 and 8 (96 trials each) choice RT are presented. The dripping taps motif is used to set the task in a pseudo-games setting with participants urged to minimise water loss. For all conditions, eight taps appear on the monitor; those taps in use for the 2- and 4-choice conditions are made salient by brightening their colour. Mean RT and SD is computed for each of the 2, 4, and 8 choice conditions (from correct responses within 150–2000ms), and efficiency of responding, which takes into account both speed and accuracy, is derived from Shannon and Weaver's (1949) information theory. In this preliminary analysis mean RT for the 8-choice condition is reported.

Inspection time task. (Smith & Stanley, 1983; Luciano et al., in press b) In this task the stimulus, a pi figure, is presented on a monitor at a viewing distance of approx. 0.5m. The stimulus consists of two vertical lines, 22mm and 27mm in length, which are joined at the top by a horizontal line 12mm long. The longer line appears on the left or the right equiprobably. Duration of the stimulus is variable, ranging from 14.2 to 2000ms. Following presentation of the stimulus, a mask consisting of two vertical lines 37mm long, shaped as lightening bolts, is presented for 300ms. The participant is required to judge which one of two lines is the longest by pressing either the left or right arrow keys on the keyboard. Each trial begins with the presentation of a central fixation spot (1s duration) along with a beep (presented at fixation onset for 100ms), followed by a blank screen for100ms and then the pi figure. Following the participant's response the screen is blanked for 750ms, before the next trial is presented producing an effect response-stimulus interval of approximately 2s. The task is presented as a pseudo-computer game with the two lines described as worms that quickly burrow into the ground, the object of the game being to identify the longer worm in order to catch the most fish. Feedback in the form of a fish appears at the lower left-hand side of the screen following every 5 correct judgements. Demonstration trials are provided prior to recording and the importance of accuracy and not speed of response is stressed. A PEST procedure (Taylor & Creelman, 1967) is used to vary stimulus duration, which is defined by screen refresh rate, across trials, based on accuracy of the participant's previous response. The task terminates when either 110 trials are presented or the PEST estimates become consistent. IT is estimated by fitting a cumulative normal curve to accuracy as a function of stimulus duration with a parameter for guessing included. The measure used in these analyses is the standard deviation of the curve

Delayed response task. In this task (Geffen et al., 1997) participants are required to focus on a black fixation spot (0.5° visual angle), in the center of a computer screen and use their peripheral vision to note the location of a 'target' soccer ball (1.5° visual angle), flashed briefly (150ms) on the screen, 250ms after fixation onset, and on an annulus (9.25° radius) from the fixation point. After a delay of several seconds (1 or 4s), signaled by the disappearance of the fixation, participants show they have remembered the soccer ball's location by lifting their hand, resting on a 5 x 5 cm response pad placed centrally in front of them, and touching the position on the touch sensitive screen with a pencil

shaped pointer. Responses are required to be prompt (150–1500ms post fixation offset) and within a 2° radius of the target centre. Australian participants received a monetary reward dependent on performance ($20–35) — 2 to 10c per correct trial (graded on pointing accuracy) with incorrect trials incurring a penalty of 5c. After each trial, feedback was shown on the screen showing the amount of money won.

Randomly interspersed with the memory trials are an equal number of sensory trials in which the peripheral target remains present throughout the delay and response interval (i.e., identical to memory trials except that target position does not have to be remembered). On 50% of both memory and sensory trials, a distractor identical to the target is briefly (150ms) presented peripherally, 300–700ms after target onset. Distractors occur on the same 9.25° annulus but not within a 15° radius of the preceding target. Following training and practice on the task participants complete a total of 432 (6 blocks of 72 trials in Australia and Japan) or 240 trials (2 blocks of 120 trials in the Netherlands). Accuracy of response is measured by the percentage of correct trials and position accuracy — distance (in mm) between target center and screen touch point. Speed measures include response initiation (RI) — latency from fixation offset to break of hand contact with the response pad, and movement time (MT) — latency from RI to screen touch time. Overall performance is measured as the amount of money won and is the performance measure used in these analyses.

Working memory span task. A variant of the spatial span task to assess working memory was adapted from Shah and Miyake (1996) and used for the Japanese sample. It was modified for group administration with stimuli projected on a screen in the front of the room. The primary task is to recall the position of an open circle presented in a 5 x 5 square matrix of dots with the restriction that consecutive circles do not appear in the same row or column. The memory set ranges from 2–5 circles and participants recall the position of the circles in the set by checking the appropriate position on a grid on a response sheet at the end of each trial, after instruction from the experimenter. The secondary task is to indicate whether a letter presented has correct or mirror-imaged orientation (50:50 probability). A small set of correct or mirror-imaged letters (F, J, L, P, R) are used and each letter can be presented in one of seven possible orientations (in 45 degree increments, not including upright). A total of 5 trials are presented. The number of circles remembered constitute a measure of spatial memory span and the number of sentences or letters identified correctly is a measure of spatial executive processing.

Statistical Analyses

To obtain a heritability estimate, the proportion of variance associated with genetic and environmental factors was estimated by fitting univariate models using the Mx program (Neale, 1997). Maximum likelihood estimates of correlations for each zygosity group were computed with means constrained to be equal but with separate male and female means specified to account for any sex effects. To distinguish between the possible mechanisms by which familial likeness may arise, the variance and covariance terms in the empirical base model were re-parameterized in terms of three broad causes of variation, two of which (additive genetic influences "A," and common environment "C") make family members more alike than random pairs of individuals, and one of which (unique environmental experiences, including error, "E") makes MZ twins and siblings different. The fit of the ACE, AE, CE and E models was evaluated using the chi-square test and the Akaike Information Criteria (Neale & Cardon, 1992).

Results

Table 2 specifies the sample after the first two years of this collaborative study, which comprises 2129 participants, including 378 MZ males, 540 MZ females, 208 DZ males, 312 DZ females and 368 DZ opposite sex twin pairs. 290

Table 2

Number of Participants Tested In Each Country[a].

	Netherlands		Australia	Japan
Participants	Young adults	Older adults		
Males	167	132	412	213
Females	197	168	447	393
Mean age (± *SD*)	25.8 (± 2.94)	50.7 (± 6.89)	16.3 (± 0.49)	19.9 (± 3.5)
Age Range	18.8–36.0	40.6–70.8	15.4–19.2	14–29
MZ males	46	44	168	120
MZ females	48	52	184	256
DZ males	36	18	96	58
DZ females	54	50	106	102
DZ opposite sex	52	42	204	70
One co-twin of pair	18	15	—	—
Siblings of twin pairs	110	79	101	—

[a] participants tested to 30 June 2000

siblings of twin pairs are also included which greatly increases power to detect both genetic and shared environmental effects provided age effects on the mean are properly regressed out and there is no substantial G and age interaction (Posthuma & Boomsma, 2000).

Heritability of Indices

Heritability estimates for indices of psychometric IQ, and indices of processing speed, and working memory are shown in Figure 1. The best fitting model for the majority of measures is an AE model. For those measures for which an AE model is not the best fit non-significant $\Delta\chi^2$ for both AE and CE models indicated that there was insufficient power to distinguish between A and C as the primary cause of familial aggregation, possibly because both were present. A high heritability (71–87%) is indicated for psychometric IQ in all three countries. Heritability estimates for indices of processing speed and working memory are lower than those for IQ but are all moderately heritable, ranging from 33–64%.

For indices of processing speed a higher heritability estimate is indicated for choice RT (64% for the Australian sample), than for IT. A similar estimate of IT heritability is indicated for both the Dutch (40%) and Australian (36%) samples. For working memory the heritability estimates for the spatial span task (33% memory span, 48% executive processing) in the Japanese sample and the DR task (46%) in the Australian sample, are of similar magnitude.

Correlations with IQ

Correlations of full scale IQ (FIQ) with the various indices of processing speed and working memory are shown in Table 3, and range from 0.25 to 0.37. The correlations are all negative with the processing speed indices and positive with the working memory indices. The RT-IQ correlation is of the same magnitude for both the Dutch (–0.36) and Australian (–0.35) samples. Similarly, the correlation of IT with IQ is approximately the same for both countries, being –0.28 for the Netherlands and –0.33 for Australia, and these are of similar magnitude to the RT-IQ correlations. Correlations of IQ with working memory indices are also of similar magnitude across task and country. In the Japanese sample, IQ correlates 0.31 with spatial memory span and 0.37 with spatial executive processing, and in the Australian sample IQ correlates 0.25 with DR performance.

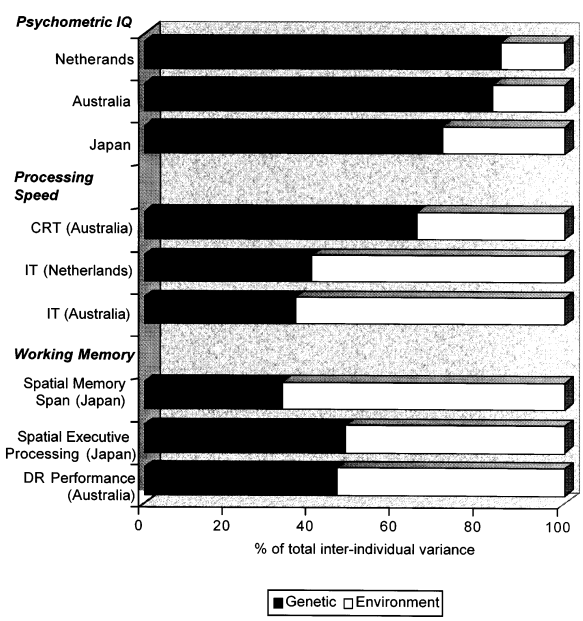

Figure 1

Heritability estimates of cognitive indices. The proportion of total variance explained by genetic and unique environmental factors is shown.

Discussion

This is one of the first collaborative studies to investigate the cognitive profile of genetically informative individuals using a common protocol comprising a broad range of performance and psychophysiological measures. The sharing of resources and expertise has ensured standardisation of protocols and many of the potential problems that limit the success or the pooling of data found in other studies have been overcome. Heritability estimates for psychometric IQ proved highly comparable across the three countries. They are higher than the estimates previously reported in twin studies (Plomin & Rende, 1991) and clearly re-confirm the importance of genetic influences in determining individual differences in cognitive ability. Two possible sources of these differences are speed of processing and working memory capacity.

Processing Speed

Confirming previous findings that those of higher ability process faster (e.g., Deary & Stough, 1996; Jensen, 1998) we found a consistent pattern of a moderate negative correlation of IQ with processing speed, lending additional support to a relationship between these measures. Correlations of IQ with simple and choice RT in the Dutch and Australian samples respectively, are moderate in magnitude, and are of similar magnitude to that reported in the literature (e.g., Jensen & Munro, 1979; Neubauer et al., 1997; Saccuzzo, Johnson & Guertin, 1994). Slightly

Table 3

Correlation of Processing Speed and Working Memory Indices with Standard Measures of Full Scale IQ (FIQ)

		FIQ Correlation (r)	No. of participants (N)	Country of sample
Processing Speed	Simple reaction time	–0.36**	531	Netherlands
	Choice reaction time	–0.38**	774	Australia
	Inspection time	–0.28**	603	Netherlands
	Inspection time	–0.33**	742	Australia
Working Memory	Spatial memory span	0.31**	468	Japan
	Spatial executive processing	0.37**	468	Japan
	Delayed–response performance	0.25**	774	Australia

** Correlation is significant at the 0.01 level (1-tailed)

stronger correlations are indicated for both simple and choice RT with IQ than for IT and IQ which may be due to RT tapping speed of decision time whereas IT taps speed of perceptual processing. IT is recorded in both the Netherlands and Australia using an identical task, and although different IQ tests are used the IT-IQ correlation is of similar magnitude. This finding that national origin has little effect on the magnitude of the speed–intelligence correlation has been found for RT in studies by Lynn and colleagues for Irish, Chinese, Korean, Hong Kong and British children (Chan et al., 1991; Lynn & Wilson, 1990; Ja-Song & Lynn, 1992; Lynn et al., 1991) but there have been no international studies involving the processing speed measure IT.

The heritability estimate for RT is moderately high and corroborates previous findings that RT is significantly heritable (Rijsdijk et al., 1998; Vernon, 1989). To date there has been no attempt to examine whether individual differences in IT are genetically influenced. Our heritability estimates from the Dutch and Australian twin samples indicate IT is moderately heritable but that IT heritability is lower than that found by us for RT. Future work will examine the relationship between the RT and IT measures and whether the genetic variance in IT can be attributed to the same sources as the genetic variance of RT. We shall then extend these analyses further, incorporating all speed indices plus IQ measures to examine the genetic covariance among them. While multitask studies suggest that processing speed should be viewed as a general or task-independent construct (Vernon, 1993, Hale & Jansen, 1994) previous studies are restricted to only a few measures and have not considered the usefulness of using both performance and electrophysiological indices that probe several different components, and examining these in genetically informative individuals.

Working Memory

Our results show that those of higher cognitive ability have better working memory and confirm the importance of working memory in intellectual functioning. The correlation of IQ and spatial working memory span in the Japanese sample is of similar magnitude to that found previously for span tasks (e.g., Engle et al., 1999) and provides additional support for the association between memory span tasks and general cognitive ability. The relationship between DR working memory performance and IQ has not previously been examined. The correlation of IQ with DR performance is a little lower than that with spatial span, and this may reflect a difference between the working memory tasks but may also reflect the use of different IQ tests. Later analyses using the Japanese data, and using combined data from the three groups will be able to examine whether there are significant differences between the correlations.

Thus far there has been no attempt to examine whether individual differences in working memory functioning exhibits familial aggregation. The moderate heritability estimates for the spatial span and DR working memory tasks found in our analyses indicate that a significant part of the variance in working memory is due to genetic factors. Heritability estimates for spatial span (executive processing) in the Japanese sample, and DR performance in the Australian sample, are of similar magnitude. These estimates lie well within the wide range (16 to 66%) reported for various indices of short term memory (Finkel et al., 1995). The estimates are also similar to that found for one of our processing speed measures, IT, but lower than that indicated for RT.

One important avenue, not yet explored, is whether some of the variance in the psychophysiological DR working memory indices that capture the neural activation and utilisation of different brain regions, can be attributed to genetic factors, and whether they are related to psychometric IQ. These measures of brain activity provide us with the opportunity to examine whether individual differences are more pronounced in the anterior than posterior cortex, and whether differences can be attributed to genetic factors. If there is more variation across frontal areas than across parietal or temporal areas, this would provide some support for the notion that individual differences in working memory and general cognitive ability arise from individual variations in frontal lobe functioning.

In summary, we have provided a detailed outline of our multi-disciplinary collaborative study showing that a common experimental design used in The Netherlands, Australia and Japan provides comparable measures of processing speed, working memory and psychometric IQ. We have also highlighted the potential benefit of using several indices that probe different levels of processing and different specific processes. Our preliminary analyses show that the measures of processing speed (RT, IT) and working memory performance (memory span, DR performance) are associated with IQ and are moderately heritable. The next step is to examine the genetic and environmental covariation between general cognitive ability, processing speed, and working memory using quantitative genetic techniques. The finding of a common genetic factor mediating the relationship of IQ with indices of processing speed and working memory would support the few multivariate genetic analyses that indicate genetic overlap among specific cognitive abilities is considerable (Alarcon et al., 1998). A longer-term goal of our work is to use sib-pair linkage and association analysis to locate QTLs to gain some insight into whether common genes pleiotropically influence a series of cognitive traits, and to what extent there are genetic effects specific to each trait. As it is likely the QTLs will be of small effect size, the collection of multiple phenotypic measures from ultimately 1500 twin pairs, and combining the information from a number of genetically related measures will be essential to increase the possibility to detect QTLs for cognition.

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References

Alarcon, M., Plomin, R., Fulker, D.W., Corley, R., & DeFries, J.C. (1998). Molarity not modularity: multivariate genetic analysis of specific cognitive abilities in parents and their 16-year-old children in the Colorado adoption project. *Cognitive Development, 14*, 175–193.

Baddeley, A.D. (1986). *Working memory*. Oxford: Oxford University Press.

Baddeley, A.D. (1992). Working memory. *Science, 255*, 556–559.

Baddeley, A.D, & Hitch G. (1974). Working memory. In: G.A. Bower (Ed). *The Psychology of Learning and Motivation*, 47–89. New York: Academic Press.

Boomsma, D.I. (1993). Current status and future prospects in twin studies of the development of cognitive abilities, infancy to old age. In: T.J. Bouchard, & P. Propping (Eds). *Twins as a tool of Behavioral Genetics*, 67–82. Chichester: John Wiley & Sons.

Bouchard, T.J., & McGue, M. (1981). Familial studies of intelligence: A review. *Science, 212*, 1055–1059.

Carpenter, P.A., Just, M.A., & Shell, P. (1990). What one intelligence test measures: a theoretical account of the processing in the Raven Progressive Matrices Test. *Psychological Review, 97*, 404–431.

Chafee, M.V., & Goldman-Rakic, P.S. (1998). Matching patterns of activity in primate prefrontal area 8a and parietal area 7ip neurons during a spatial working memory task. *Journal of Neurophysiology, 79*, 2919–2940.

Chan, J.W.C., Eysenck, H.J., & Lynn, R. (1991). Reaction time and intelligence among Hong Kong children. *Perceptual Motor Skills, 72*, 427–433.

Chipuer, H.M., Rovine, M.J., & Plomin, R. (1990). LISREL modeling: Genetic and environmental influences on IQ revisited. *Intelligence, 14*, 11–29.

Coles, M.G. (1989). Modern mind-brain reading: Psychophysiology, physiology and cognition. *Psychophysiology, 26*(3), 251–269.

Daneman, M., & Merikle, P.M. (1996). Working memory and language comprehension: A meta-analysis. *Psychonomic Bulletin & Rreview, 3*, 422–433.

Deary, I.J. (1993). Inspection time and WAIS-R IQ subtypes: A confirmatory factor analysis study. *Intelligence, 17*, 223–236.

Deary, I.J., & Stough, C. (1996). Intelligence and inspection time. *American Psychologist, 51*, 599–608.

D'Esposito, M., & Postle, B.R. (1999). The dependence of span and delayed-response performance on prefrontal cortex. *Neuropsychologia, 37*, 1303–1315.

Devlin, B., Daniels M., Roeder K. (1997). The heritability of IQ. *Nature, 388*, 468–471.

Duncan, J., Seitz, R.J., Kolodny, J., Bor, D., Herzog, H., Ahmed, A., Newell, F.N., & Emslie, H. (2000). A neural basis for general intelligence. *Science, 289*, 457–460.

Egan, V.G., Chiswick, A., Brettle, R.P., & Goodwin, G.M. (1992). The Edinburgh cohort of HIV-positive drug users: The relationship between auditory P3 latency, cognitive function and self-rated mood. *Psychological Medicine, 23*, 613–622.

Engle, R.W., Tuholski, S., & Kane, M. (1999). Individual differences in working memory capacity and what they tell us about controlled attention, general fluid intelligence and functions of the prefrontal cortex. In: A. Miyake, & P. Shah (Eds). *Models of working memory: Mechanisms of active maintenance and executive control*, 102–134. Cambridge MA: Cambridge University Press.

Finkel, D., Pedersen, N., & McGue, M. (1995). Genetic influences on memory performance in adulthood: comparison of Minnesota and Swedish twin data. *Psychological Aging, 10*, 437–446.

Fuster, J.M. (1991). Role of prefrontal cortex in delay tasks: Evidence from reversible lesion and unit recording in the monkey. In H.S. Levin, H.M. Eisenberg & A.L. Benton (Eds). *Frontal lobe function and dysfunction*, 59–71. New Tork: Oxford University Press.

Fuster, J.M. (1997). *The prefrontal cortex: Anatomy, physiology, and neuropsychology of the frontal lobe* (3rd ed.). Philadelphia: Lippincott-Raven.

Fry, A.F., & Hale S. (1996). Processing speed, working memory, and fluid intelligence: Evidence for a developmental cascade. *Psychological Science, 7*, 237–241.

Geffen, G., Wright, M., Green, H., Gillespie, N., Smyth, D., Evens, D., & Geffen, L. (1997). Effects of memory load and distraction on performance and event-related slow potentials in a visuospatial working memory task. *Journal of Cognitive Neuroscience, 9*, 743–757.

Gevins, A., & Smith, M.E. (2000). Neurophysiological measures of working memory and individual differences in cognitive ability and cognitive style. *Cerebral Cortex, 10*, 829–839.

Goldman-Rakic, PS. (1987). Circuitry of the prefrontal cortex and the regulation of behavior by representational memory. In: F. Plum, V. Mountcastle (Eds). *Handbook of physiology Section 1 The nervous system vol. 5*, 373–417. Bthesda: American Physiological Society.

Goldman-Rakic, P.S. (1992). Working memory and the mind. *Scientific American, 267*, 110–117.

Hale, S., & Jansen, J. (1994). Global processing-time coefficients characterize individual and group differences in cognitive speed. *Psychological Science, 5*, 384–389.

Ho, H., Baker, L. A., & Decker, S. N. (1988). Covariation between intelligence and speed of cognitive processing: genetic and environmental influences. *Behavior Genetics, 18*(2), 247–261.

Houlihan, M., Stelmack, R., & Campbell, K. (1998). Intelligence and the effects of perceptual processing demands, task difficulty and processing speed on P300, reaction time and movement time. *Intelligence, 26*, 2–25.

Jackson, D. (1984). *Multidimensional Aptitude Battery – Manua*l. London: Research Psychologists Press.

Jackson, D. (1998). *Multidimensional Aptitude Battery-II – Manual.* Port Huron, MI: Sigma Assessment Systems.

Ja-Song, M., & Lynn, R. (1992). Reaction times and intelligence in Korean children. *The Journal of Psychology, 126*, 421–428.

Jensen, A.R. (1982). Reaction time and psychometric g. In: H.J. Eysenck (Ed). *A model for intelligence*, 93–132. Berlin: Springer.

Jensen, A.R. (1987). Individual differences in the Hick paradigm. In: P.A. Vernon (Ed). *Speed of Information-Processing and Intelligence*, 101–175. New Jersey: Ablex Publishing Corporation.

Jensen, A.R. (1998). *The g Factor: The Science of Mental Ability*. London: Praeger.

Jensen, A.R., & Munro, E. (1979). Reaction time, movement time, and intelligence. *Intelligence, 3*, 121–126.

Just, M.A., & Carpenter, P.A. (1992). A capacity theory of comprehension: Individual differences in working memory. *Psychological Review, 99*, 122–149.

Kail, R. (1992). Processing speed, speech rate, and memory. *Developmental Psychology, 28*, 899–904.

Klimesch, W. (1999). EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. *Brain Research Reviews, 29*, 169–195.

Kranzler, J.H., & Jensen, A.R. (1989). Inspection time and intelligence: A meta-analysis. *Intelligence, 13*, 329–347.

Kyllonen, P.C., & Christal, R.E. (1990). Reasoning ability is little more than working memory capacity? *Intelligence, 14*, 389–433.

Luciano, M., Smith, G.A., Wright, M.J., Geffen, G.M., Geffen, L.B., & Martin, N.G. (in press a). Genetic influence on the relationship between choice reaction time and IQ: A twin study. *Moscow Journal of Psychology*.

Luciano, M., Smith, G.A., Wright, M.J., Geffen, G.M., Geffen, L.B., & Martin, N.G. (in press b). On the heritability of inspection time and its covariance with IQ: A twin study. *Intelligence*.

Lynn, R., & Wilson, R.G. (1990). Reaction times, movement times and intelligence among Irish nine year olds. *The Irish Journal of Psychology, 11*, 329–341.

Lynn, R., Chan, J.W.C., & Eysenck, H.J. (1991). Reaction times and intelligence in Chinese and British children. *Perceptual Motor Skills, 72*, 443–452.

McClearn, G.E., Johansson, B., Berg, S., Pedersen, N.L., Ahern, F., Petrill, S.A., & Plomin, R. (1997). Substantial genetic influence on cognitive abilities in twins 80 or more years old. *Science, 276*, 1560–1563.

McGarry-Roberts, P.A., Stelmack, R.M., & Campbell, K.B. (1992). Intelligence, reaction time, and event-related potentials. I*ntelligence, 16*, 289–313.

Miller, E.K. (2000). The prefrontal cortex and cognitive control. *Nature Reviews Neuroscience, 1*, 59–65.

Neale, M. (1997). *Statistical Modeling with Mx*. Richmond, VA 23298: Department of Psychiatry, Box 126 MCV.

Neale, M.C., Cardon, L.R. (1992). *Methodology for genetic studies of twins and families*. Dordrecht: Kluwer Academic Publisherst.

Necka, E. (1992). Cognitive analysis of intelligence: The significance of working memory processes. *Personality and Individual Differences, 13*, 1031–1046.

Nettlebeck, T. (1987). Inspection time and intelligence. In: P.A. Vernon (Ed). *Speed of information processing and intelligence*, 295–346. Norwood, NJ: Ablex.

Neubauer, A. C., Riemann, R., Mayer, R., & Angleitner, A. (1997). Intelligence and reaction time in the Hick, Sternberg, and Posner paradigms. *Personality and Individual Differences, 22*(6), 885–894.

Osman, A., Moore, C.M., & Urlich, R. (1995). Bisecting RT with lateralized readiness potentials: precue effects after LRP onset. *Acta-Psychologia, 9*(1-3), 111–127.

Petrides, M. (1995). Functional organization of the human frontal cortex for mnemonic processing – Evidence from neuroimaging studies. *Annals of New York Acadademy of Science, 769*, 85–96. Petsche, H. (1997). EEG coherence and mental activity. In: F. Angeleri, S. Butler, S. Giaquinto, J. Majakowski (Eds). *Analysis of the electrical activity of the brain*. Chichester: John Wiley and Sons.

Plomin, R., & Petrill, S.A. (1997). Genetics and intelligence: what's new? *Intelligence, 24*, 53–77.

Plomin, R., & Rende, R. (1991). Human Behavioural Genetics. *Annual review of psychology, 42*, 161–190.

Polich, J., & Martin, S. (1992). P300, cognitive capability, and personality: A correlational study of university undergraduates. *Personality and Individual Differences, 13*, 533–543.

Posthuma, D., & Boo*msma, D.I. (2000). A note on the statistical power in extended twin designs.* Behavior Genetics, 30, 147–158.

Rijsdijk, F. V., Vernon, P. A., & Boomsma, D. I. (1998). The genetic basis of the relation between speed-of-information-processing and IQ. *Behavioural Brain Research, 95*, 77–84.

Ruchkin, D.S., Canoune, H.L., Johnson, R., Jr., & Ritter, W. (1995). Working memory and preparation elicit different patterns of slow wave event related potentials. *Psychophysiology, 32*, 399–410.

Saccuzzo, D. P., Johnson, N. E., & Guertin, T. L. (1994). Information processing in gifted versus nongifted african american, latino, filipino, and white children: Speeded versus nonspeeded paradigms. *Intelligence, 19*, 219–243.

Salthouse, T.A. (1996). The processing-speed theory of adult age differences in cognition. *Psychological Review, 103*, 403–428.

Shah, P., & Miyake, A. (1996). The separability of working memory resources for spatial thinking and language processing; an individual differences approach. *Journal of Experimental Psychology: General, 125*, 4–27.

Shannon, C.E. & Weaver, W. (1949). *The Mathematical Theory of Communication*. Urbana, Ill: The University of Illinois Press.

Smith, G.A. & Stanley, G. (1983). Clocking g: Relating intelligence and measures of timed performance. *Intelligence, 7*, 353–368.

Taylor, M., & Creelman, T. (1967). PEST: Efficient estimate on probability function. *Journal of the Acoustical Society of America, 41*, 782–787.

Vernon, P.A. (1989). The heritability of measures of speed of information processing. *Personality and Individual Differences, 10*, 573–576.

Vernon, P.A. (1993). *Biological Approaches to the Study of Human Intelligence*. Norwood, NJ: Ablex.

Wechsler, D. (1981). *Manual for the Wechsler Intelligence Scale for Children (3rd ed.)*. New York: Psychological Corporation/Harcourt Brace and Company.

Zhu, G., Duffy, D.L., Eldridge, A., Grace, M., Mayne, C., O'Gorman, L., Aitken, J.F., Neale, M.C., Hayward, N.K., Green, A.C., & Martin, N.G. (1999). A major quantitative-trait locus for mole density is linked to the familial melanoma gene CDKN2A: A maximum-likelihood combined linkage and association analysis in twins and their sibs. *American Journal of Human Genetics, 65*, 483–492.