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Neural correlates of cognitive efficiency

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Since its inception, experimental psychology has sought to account for individual differences in human performance. Some neuroimaging research, involving complex behavioral paradigms, has suggested that faster-performing individuals show greater neural activity than slower performers. Other research has suggested that faster-performing individuals show less neural activity than slower performers. To examine the neural basis of individual performance differences, we had participants perform a simple speeded-processing task during fMRI scanning. In some prefrontal cortical (PFC) brain regions, faster performers showed less cortical activity than slower performers while in other PFC and parietal regions they showed greater activity. Regional-causality analysis indicated that PFC exerted more influence over other brain regions for slower than for faster individuals. These results suggest that a critical determinant of individual performance differences is the efficiency of interactions between brain regions and that slower individuals may require more prefrontal executive control than faster individuals to perform successfully.

Keywords: Human brain; Functional MRI; Cognitive control; Executive control

The observation that some individuals consistently perform better than others across a broad range of tasks has led to a number of proposals suggesting that a limited set of fundamental abilities or processing resources govern performance across a broad range of cognitive tasks (Spearman, 1904; Kahneman, 1973; Norman and Bobrow, 1975; Vernon, 1983; Baddeley, 1986; Just and Carpenter, 1992). One such proposal has been that individuals differ in the efficiency with which fundamental cognitive operations are performed (Vernon, 1983). Cognitive efficiency theories suggest that, when cognitive operations can be performed quickly, resource allocation can be minimized and performance maximized.

Behavioral evidence for efficiency explanations of performance differences between individuals relies on measures of *processing speed* (e.g., Vernon, 1983), as indexed by relatively simple cognitive tasks that measure the time required to perform elementary cognitive operations. Examples of these tasks are the digit–symbol substitution test (DSST; Wechsler, 1981), letter cancellation, and digit–string comparison. Processing speed tasks are designed, on one hand, to be sufficiently simple so that individual reaction time (RT) differences may be reasonably attributed to the execution speed of a few elementary cognitive operations and not to differences in semantic knowledge or other strategies or abilities. On the other hand, they are designed to be sufficiently complex so as to require more than purely sensorimotor operations. These tasks, along with correlational and statistical control methods, have been used to test efficiency explanations of performance differences between healthy adults, between younger and older children, and between younger and older adults. They have also been used to study disease- and trauma-related performance changes. Results of these studies provide important clues about the role of processing efficiency in accounting for individual performance differences and suggest hypotheses regarding the neural substrate of individual differences in processing efficiency.

Efficiency explanations of developmental performance improvement have received support from analyses indicating systematic relationships between juvenile and adult reaction times across different cognitive tasks. In one study for instance, Kail (1986) had 8- to 21-year-old subjects perform mental rotation and picture matching tasks. He observed that age-

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related performance improvements on both kinds of tasks were well-described by an exponential function that accounted for as much as 85% of the variance. Similar results have been obtained with other kinds of tasks including letter-naming and memory search (e.g., Kail, 1988; 1991; Keating and Bobbitt, 1978). These authors have proposed that development of a global processing speed ability governs developmental improvements in cognitive task performance.

Such changes appear to be associated with development of PFC. In a review of developmental cognitive and physiological literatures, Gomez-Perez and colleagues (2003) observed coincident time-courses of age-related cognitive task improvement and PFC maturation. Neuroimaging studies have supported these observations. Comparisons of neural activity differences in children and adults indicate frontal activation differences between these two groups (Bunge et al., 2002). Imaging methods specifically designed to measure white matter integrity (i.e., diffusion tensor imaging) have shown reduced PFC connectivity (i.e., increases in "radial diffusivities") in younger children (ages 7–13), compared to adults (ages 18–31). Importantly, increased frontal connectivity (i.e., restrictions in radial diffusivities) predicted faster RTs among children. These results suggest the hypothesis that one important factor determining developmental improvements in cognitive performance is processing efficiency associated with axonal maturation of PFC.

Similar to results from developmental literature, cognitive aging researchers have observed systematic correlations (Cerella, 1991) between the RTs of older adults and those of younger adults (see also Hale et al., 1987; Kail and Salthouse, 1994) across different kinds of tasks. These observations suggest that a global processing speed factor mediates age-related performance differences. Salthouse (1996a) has documented pervasive influences of cognitive slowing on information processing tasks. Across studies, median correlations on the order of 0.45 between processing speed and higher-order cognitive tasks have been observed. Significant attenuations of age-related performance differences when simple processing speed (as measured by DSST; e.g., Salthouse, 1992) was statistically controlled have also been observed. Such systematic relationships have led to the hypothesis that slowing of the component operations that comprise higher cognitive tasks accounts for age-related performance differences (see e.g., Fisk et al., 1992 for a different perspective).

Similar to child development research, neurocognitive aging research implicates PFC as the neural substrate for age-related efficiency changes. In animals and humans, brain aging is characterized by atrophy of neocortical gyri, widening sulci, and ventricular dilation (e.g., Raz, 2000). Anatomical studies suggest that PFC may be more vulnerable to deleterious age effects compared to other regions (e.g., Kemper, 2002; Raz et al., 1997, 2000; Haug and Eggers, 1991) possibly due specifically to white matter changes (Peters, 2002; Peters and Sethares, 2004; Madden et al., 2004; Ross et al., 2005). These structural changes appear to correspond with age-related changes in cognitive function (West, 1996) and performance changes that accompany age-related disease (Medina et al., 2006; Sawamoto et al., 2002; Small et al., 2000). Functional neuroimaging evidence also implicates PFC in age-related cognitive decline (Rypma et al., 1999; Rypma and D'Esposito, 2000; Reuter-Lorenz et al., 2000; Cabeza, 2002; Stebbins et al., 2002; Rypma et al., 2005). In one study, for instance, Rypma and colleagues (2001) observed relatively greater age-related differences in PFC during WM task performance than in other brain regions. Together, these results implicate a primary role for PFC white matter changes in processing efficiency increases in development and decline in aging.

Efficiency explanations have been proposed to account for performance changes that accompany brain-related disease. Evidence to support such explanations comes from studies showing relationships between performance on complex cognitive tasks and simple processing speed tasks (Brebion et al., 1998; 2000). Brebion and colleagues (1998), for instance, demonstrated significant attenuation of working memory performance differences between patients and controls when processing speed, as measured by the DSST, was statistically controlled. Replication of these results under both deep and shallow encoding conditions (Brebion et al., 2000) and under conditions of varying encoding time (Hartman et al., 2003) lends support to the idea of efficiency-related deficits in schizophrenia.

Neuroimaging studies implicate PFC in schizophrenic pathophysiology. One study, for instance (Callicott et al., 2000), compared PFC activity of high-functioning schizophrenics and controls during performance of a continuous performance task (CPT) in which, on each trial, 4-item arrays of digits appeared and subjects were required to match them with those seen a prespecified number of trials earlier, requiring subjects to continually monitor and update their memory for the digit arrays. The important result was that, with increasing task difficulty, schizophrenics showed performance decreases relative to controls but PFC activation increases relative to controls. Importantly, this pattern of results was limited to dorsal regions of PFC.

Neuroimaging studies in healthy adults also support efficiency explanations of individual differences by showing reduced activation in faster than in slower individuals on complex spatial and working memory tasks (e.g., Haier et al., 1988, 1992; Kosslyn et al., 1996; Larson et al., 1995; Rypma and D'Esposito, 1999; Rypma et al., 2002; Rypma et al., 2005). In one study for instance, Haier et al. (1992) had 8 subjects perform a spatial reasoning task, Raven Progressive Matrices. Next, they recorded subjects' glucose metabolic rate (GMR; measured by PET) during performance of a complex visual manipulation task ("tetris") both before and after extensive practice. In addition to observing GMR reduction after learning, they observed that the extent of GMR reduction was correlated with subjects' scores on the Raven Progressive Matrices. Similarly, Kosslyn et al. (1996) have observed neural activity reductions for faster, compared to slower subjects on a mental imagery task. Consistent with these results, Rypma and D'Esposito (1999) observed a significant correlation between subjects' memory search rate and PFC activity.

These results suggest a specific model of neural efficiency in which the integrity of structural connections between brain regions is reflected in PET and fMRI activation. Specifically, they suggest that more direct connections between task-critical brain regions may correspond to decreases in task-related neural activity and improvements in performance (cf. Vernon, 1988; Cerella, 1991; Rypma and D'Esposito, 1999, 2000). Reductions in processing speed and corresponding activation increases in multiple sclerosis, a condition known to compromise white matter integrity, in addition to other clinical conditions provide support for this "neural efficiency" hypothesis (Chiarvalloti et al., 2003; Lange et al., 2005; Vernon, 1987).

Not all neuroimaging results have been consistent with this view. Some studies have shown between-subject performance differences in which greater task-dependent activation was observed in higher than in lower performing individuals (e.g., Newman et al., 2003; Larson et al., 1995; Gray et al., 2003). In one study for instance, Gray and his colleagues performed a study similar to Haier et al.'s (1992; see above) in which, prior to fMRI scanning, subjects performed the Raven Progressive Matrices task. During scanning, subjects performed a complex CPT working memory task in which subjects viewed single letters that appeared sequentially. They were required to respond each time they observed the re-appearance of a letter that had also occurred 3 trials earlier. The difficulty of the task was varied by the occasional occurrence of "lure" trials in which a letter repeated either 2, 4 or 5 trials previously. Unlike the Haier et al. (1992) results described above, they observed greater CPT-related neural activity in subjects with higher, compared to those with lower accuracy in Raven performance in a number of different brain regions.

Divergent patterns of activation–performance relations across neuroimaging studies may occur for a number of reasons. In the studies reviewed above, different tasks were employed in the different studies. One possibility suggested by the discrepant results in the Gray et al. (2003) and Haier et al. (1992) studies, for instance, is that the nature of activation–performance relations may be task-dependent. It may be that the CPT task used by Gray et al. (2003) and the tetris task used by Haier et al. (1992) emphasize different cognitive mechanisms. Other studies using relatively complex tasks have also shown divergent results (e.g., Tower-of-London; Newman et al., 2003; Sternberg-type delayed-response; Rypma et al., 1999; backward digit-span; Larson et al., 1995). The complex tasks used in prior studies are useful for delineating the cerebral topography of the networks that mediate performance on these tasks. Their complexity, however, makes it difficult to isolate the source of empirical ambiguities between studies because of the complex simultaneous interplay of processes, abilities, and strategies that individuals use to perform these tasks. Raven performance, for instance, appears to depend on at least 4 constituent processes (Babcock, 1994).

In this study, we sought to investigate the nature of activation–performance relations in a single task that requires a relatively limited set of cognitive mechanisms and minimizes the role that particular abilities and strategies might play in the results. The DSST task may reasonably be said to be such a task as it is considered to measure a unitary construct, processing speed (e.g., Salthouse, 1992, 1996a; Wechsler, 1981). First, correlations between DSST and full-scale WAIS scores are high (ranging from .51 to .74) and are not known to vary with age (Wechsler, 1981). Second, relations between processing speed and performance do not appear to depend on other abilities such as motor speed (e.g., Erber, 1981; Salthouse, 1992) or working memory (e.g., Erber et al., 1981; Fry and Hale, 1996; Jensen, 1998; Salthouse, 1991). Third, it has been identified as a central construct accounting for major proportions of variance in higher-level cognitive tasks including both working memory (e.g., Kyllonen and Christal, 1990) and Raven performance (e.g., Ackerman et al., 2002; Babcock, 1994).

In addition to the possibility that differing activation–performance relations are *task-dependent*, another possibility (suggested by these and other discrepant results) is that the nature of activation performance relations may be *region-dependent*. For instance, while Gray et al. (2003) observed significant positive correlations between CPT-related activity and Raven performance in dorsal and ventral PFC, Haier et al. (1992) observed the greatest correlations between Tetris-related activity and Raven performance in superior PFC regions. Such region specificity in activation–performance relations has even been observed within individual studies (e.g., Kosslyn et al., 1996). These results suggest the hypothesis that individual differences in activation–performance relations may differ across different brain regions. One aim of the present study was to test this hypothesis in a limited set of regions whose activation is known to vary between individuals. Another possibility is that neural efficiency and BOLD activity are not related in any simple way. Accordingly, we tested the idea that those brain regions showing *less* activity (e.g., Haier et al., 1988; Neubauer et al., 2004) with better performance may be functionally related to those regions showing *more* activity with better performance (e.g., Gray et al., 2003; Newman et al., 2003) using connectivity analyses. Other possible factors that could influence variance in results between studies include different imaging modalities (with varying spatial resolutions), different experimental designs (e.g., event-related or block designs), the different populations available at different sites, and different neuroimaging analysis methods that have been employed across studies.

In this study, we sought to test the extent to which individual differences in processing speed are related to neural activity. Our strategy was to relate neural efficiency and processing speed as directly as possible by observing fMRI activation while individuals performed a relatively simple task with known processing speed sensitivity, the DSST, in a specific frontoparietal network where performance-related variation in neural activity has been observed across a broad range of tasks (Newman et al., 2003; Larson et al., 1995; Rypma and D'Esposito, 1999; Maccotta and Buckner, 2004; Poldrack et al., 1998; Corbetta et al., 1995; Smith and Jonides, 1999). Thus, we sought to observe performance-related variation in neural activity using one analysis method with high spatial resolution in a common set of brain regions within one group, performing a single task with known sensitivity to individual differences in processing speed, the DSST.

The DSST may be considered to be a reasonable measure of processing efficiency. It is simple enough to involve only a few elementary cognitive operations yet complex enough to involve more than just sensorimotor functions. Additionally, it has been validated in correlational studies with other speeded-processing tasks, high-level cognitive and intelligence tests (Brebion et al., 2000; Salthouse, 1996a,b; Salthouse, 1992; Wechsler, 1981). Finally, among processing speed measures, it is most adaptable to MRI–environmental constraints.

Method

Subjects

Twelve participants (ages 18–27, 7 M, 5 F) were recruited from the Rutgers University—Newark and University of Pennsylvania campuses. Subjects were excluded if they had any medical, neurological, or psychiatric illness, or if they were taking any type of prescription medication.

Behavioral task

Subjects were brought into the laboratory, signed consent, and given a standard battery of questionnaires (to determine their MRI

compatibility), a paper and pencil version of the DSST task, from the Wechsler Adult Intelligence Scale. Briefly, it consists of a code table that represents pairings of digits and nonsense symbols. Arrayed down the page are rows of vertically paired boxes with nothing in the bottom box and a digit in the top box. The subject's task is to write into the bottom box the symbol that goes with the digit in the top box, according to the code table. Subjects are given 90 s to complete as many digit–symbol pairings as possible. Following completion of the questionnaires, subjects were trained on the computerized DSST task. Subjects were then brought to the neuroimaging suite, given brief practice with the task, and then inserted into the scanner. On each fMRI scanning trial, a code table containing digit–symbol pairs and a single digit–symbol probe appeared simultaneously (Fig. 1) for 4 s. If the probe-pair matched one of those in the table, subjects pressed a right-thumb button; otherwise, they pressed a left-thumb button. There was a total of 500 trials in 10 scanning runs. On half the trials, the probe-pair matched one of the digit–symbol pairs in the code table, on the other half, the probe-pair did not match one of the pairs in the code table. RT was measured as the time from the onset of the stimulus (i.e., code table and probe-pair presentation) to the time that the subject made a response. Subjects were required to respond within the 4 s that the stimuli appeared on the screen. We used an event-related design that allowed us to examine blood-oxygen-level-dependent (BOLD) signal changes separately during each trial event.

MRI technique

Imaging was performed on a 1.5 T SIGNA scanner (GE Medical systems equipped with a fast gradient system for echoplanar imaging. A standard radiofrequency head coil was used with foam padding to comfortably restrict head motion. High-resolution sagittal and axial T1-weighted images were obtained from every subject. A gradient echo, echoplanar sequence (repetition time = 2000 ms, echo time = 50 ms) was used to acquire data sensitive to the blood-oxygen-level-dependent (BOLD) signal. Resolution was 3.75 × 3.75 mm in-plane and 5 mm between planes (thus 21 axial slices were acquired). Twenty seconds of gradient and radiofrequency pulses preceded the actual data acquisition to allow tissue to reach steady state magnetization.

Data analysis

Off-line data processing was performed using Voxbo software on Linux workstations. Data were motion corrected using a slice-wise motion compensation method to remove spatially coherent signal changes using a partial correlation method and by applying a 6-parameter rigid-body, least-squares realignment routine. fMRI signal changes that occurred during trial events were modeled with covariates comprised of time-shifted, BOLD hemodynamic response functions (HRFs) derived from each subject individually (Aguirre et al., 1999).

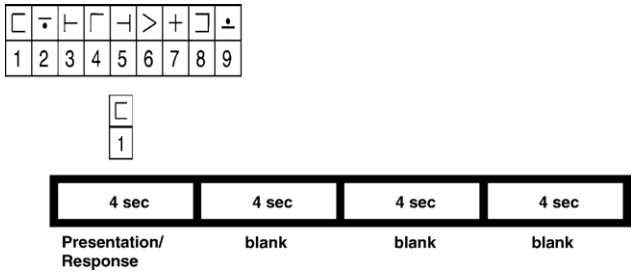

Fig. 1. Trial-sequence of the modified DSST task. On each trial, a novel code table appeared in the middle of the screen while a probe digit–symbol pair appeared below it. These stimuli stayed on the screen for 4 s followed by variable intertrial intervals (0, 4, 8, or 12 s).

fMRI data were analyzed using the general linear model (GLM) modified to account for serially correlated error terms that result from temporal correlations in fMRI data. A time-domain representation of the 1/F power structure of MRI signal and a filter that removes frequencies below 0.025 and above 0.25 was placed in the model to account for low-frequency confounds and artifacts at the Nyquist Frequency. Additionally, trial–effect covariates were included in the model to account for mean signal associated with each trial (Zarahn et al., 1997).

Relationships with each trial event and the ITI were assessed by contrasts yielding t statistics (with ~1195 df) involving the parameter estimates and error terms that corresponded to the covariates that modeled each trial event. t values for the spatially averaged time series were derived from each ROI for each subject. t values and RTs were then z-standardized across the sample to illustrate the distributions of the scores (Hays, 1988).

We sought to test hypotheses of region dependence in performance–activation relationships using a specific set of regions where activation–performance relations have been observed in previous studies. The restriction of our analyses to specific brain regions increased our power to detect significant effects both in GLM and Granger analyses (see below). Data analyses were performed in 8 ROIs where activation was observed in this task across the 2 hemispheres, dorsal PFC (DPFC; Brodmann Area 9; BA 9), posterior PFC (BA 46), ventral PFC (VPFC; BA 44), and parietal cortex (BA 40). ROIs were created by first drawing them on an average representation of subjects' brains normalized to a standardized coordinate frame (Talairach and Tournoux, 1988). Each subject's anatomical and functional data were then normalized into this space. Because some individual variability is preserved in this normalization process, we adjusted each subject's ROIs after normalization to better correspond to the anatomical images of some subjects and thus more accurately demarcate the intended brain regions.

In analyses examining suprathreshold cortical activity, ROI-wise corrected false-positive rates were controlled with Bonferroni correction, yielding thresholds of approximately $t = 3.7$. Granger causality methods were used to study dynamic interactions between cortical regions. Granger causality between two regions can be defined as the extent to which the data from one region at one point in time improve the prediction of another region's data at a later point in time (Goebel et al., 2003).

Granger analyses were performed by first extracting time series from each region-of-interest. Each time series was fit using a full vector autoregressive model. Briefly, in a vector autoregressive process, the time series data sets assume that the current time point is functionally related to its N previous time points. For this study, a 5th order vector autoregressive process was used for each of the eight ROIs[1]. Five time points (10 s) were sequentially

[1] We determined an optimal autoregressive order based on prior estimates of onset-delay and phase-delay variances (Lee et al., 1995; Boynton et al., 1996; Saad et al., 2003).

omitted, and its effect in predicting the output was calculated. Submodel fits were then carried out for each time series data set compared with the other time series data sets. Time point omission from one regional time series permitted characterization of its influence on other subsequent time points in other regional time series. The significance level for each of them was tabulated for within group analysis.

The Granger analysis we performed used F statistics to test whether lagged information on a time series (variable) ***y*** provided any statistically significant information about another time series (variable) ***x*** in the presence of lagged ***x***. If not, then "***y*** did not cause ***x***." The vector autoregression model we used assumed an autoregressive lag length p and estimated the following unrestricted equation by ordinary least squares (OLS):

$$x(t) = c_1 + \sum_{i=1}^{p} a(i)x(t-i) + \sum_{i=1}^{p} b(i)y(t-i) + u(t) \quad (1)$$

where *x(t)* and *y(t)* are the two time series being evaluated for causality, t is the current time point, *a(i)* and *b(i)* are the linear prediction variables for x and y, c_1 is the time series mean, u is the error of the fit, and p is the lag length.

The F statistic tested the null hypothesis (Ho: $b(1)=b(2)=b(3)=\ldots b(p)=0$) using the following simplification of Eq. (1):

$$x(t) = c_1 + \sum_{i=1}^{p} g(i)x(t-i) + e(t) \quad (2)$$

where *x(t)* is the time series being evaluated for causality, t is the current time point, *g(i)* is the linear prediction variable for x, e is the error in fit, and p is the lag length.

If the F test

$$F_{y,x} = \frac{\left(\sum_{i=1}^{T} e(i) - \sum_{i=1}^{T} u(i)\right)^2 \Big/ p}{\left(\sum_{i=1}^{T} u(i)\right)^2 \Big/ (T-2p-1)} \quad (3)$$

(where T is the total number of time points, p is the lag length) was greater than tabular significance values, then the null hypothesis (***y*** does not cause ***x***) was rejected, and the alternative "***y*** causes ***x***" is accepted.

This procedure was performed on the data from all regions, and their influences on all other regions were computed. Each time series data set was modeled, and the submodel was compared against the other time series data sets. Submodel fits and directional causality were then tabulated for each of the time series data sets. This process was repeated until all the possible combinations were obtained. Model diagnostic tests and resulting significance levels were estimated from the submodel fit matrix (Goebel et al., 2003). Directed influences between the different regions were calculated for two different significance levels (.05 and .10). Influences were considered significant for $ps<.05$. They were considered trends when $0.05>p<0.10$.

Causality matrices between the different regions were obtained from slower and faster subjects (separated by median DSST performance) and grouped together to form slower and faster groups. Element-wise differences between the faster and slower groups were calculated to find interregional differences between slower and faster subjects. The differences obtained were then mapped onto a schematic axial representation of the brain corresponding to $z=+28$ in the atlas of Talairach and Tournoux (1988).

Results

Behavioral performance

Behavioral analyses indicated uniformly high accuracy with minimal interindividual variability ($M=97.0\%$, SD=0.01). RTs were fast with more interindividual variability (1331.5 ms, SD=177.4) than was observed in accuracy. Slower and less accurate performers had lower DSST scores than faster and more accurate performers ($p=0.02$).

Imaging data

fMRI analyses indicated activation in a network of PFC and parietal regions across subjects. There was considerable interindividual variation in the location and spatial extent of these BOLD changes. Strong relationships between regional cortical involvement and response speed were also observed. Fig. 2 shows regional activation in the fastest subject (A) and in the slowest subject (B). In PFC, BOLD effects in Subject B showed a greater spatial extent than in subject A while the opposite effect appeared in parietal cortex.

Regression analyses of individuals' z-standardized mean RT and regional BOLD signal change, as measured by spatially

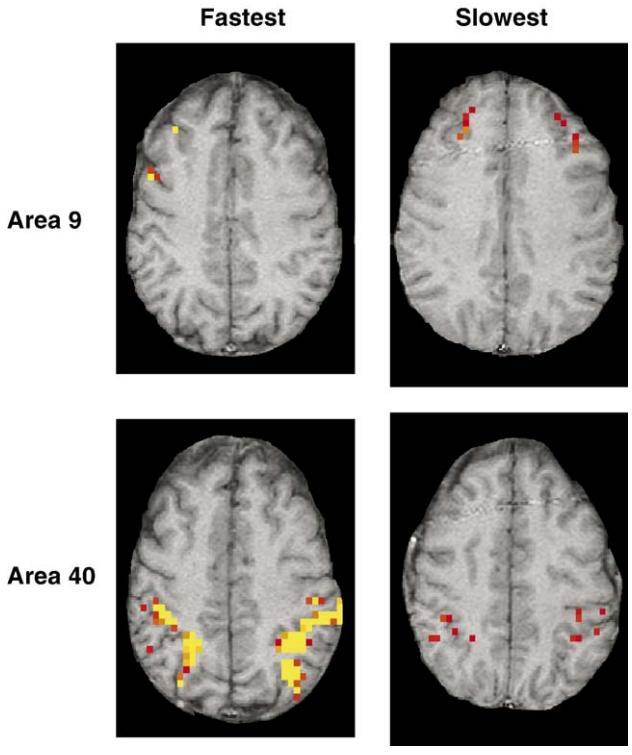

Fig. 2. Cortical activity in the fastest and slowest individuals in an ROI showing less activity for the fastest than for the slowest individual (BA 9, DPFC) and in an ROI showing more activity for the fastest than for the slowest individual (BA 40, parietal cortex), indicating region-specific brain–behavior relationships.

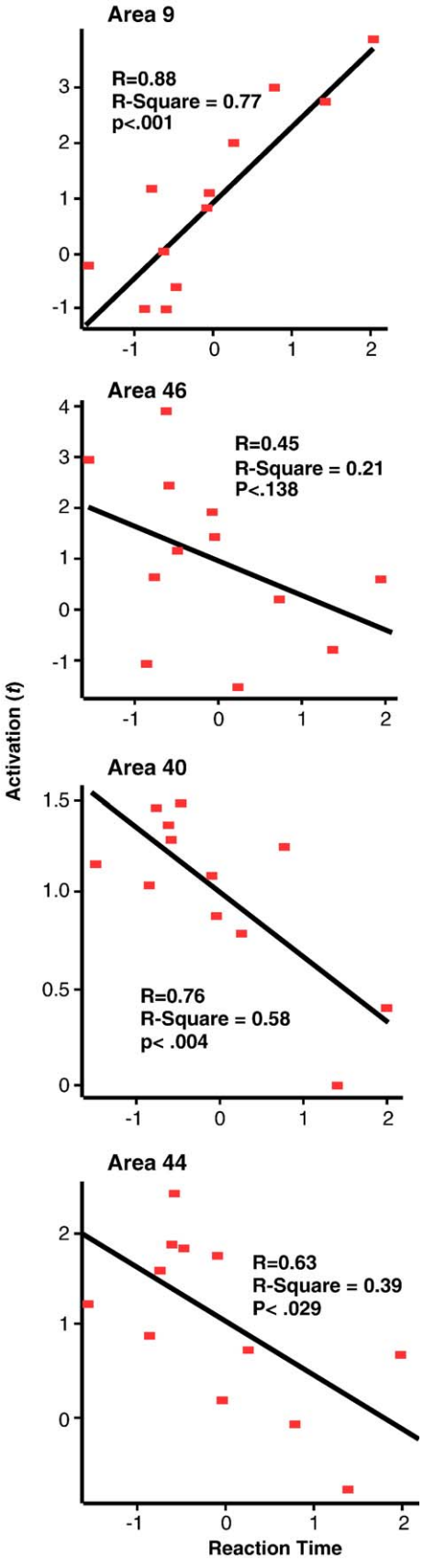

Fig. 3. Results of regression analyses between ROI-wise cortical activity and RT. Scatterplots show regional mean t values for each individual plotted against their standardized RTs.

Table 1
Results from permutation of RT and parameter estimates (β)

Region	Slope	RMS residual	p
BA 9	0.62	0.0002	0.02
BA 46	−0.45	0.001	0.15
BA 44	−0.68	0.001	0.02
BA 40	−0.70	0.001	0.005

averaged t statistics (Fig. 3), characterized activation–performance relationships in different brain regions. DPFC (BA 9) showed a significant positive correlation (slope=0.88, r^2=.77, p<.01), consistent with neural efficiency explanations of performance speed. Posterior PFC regions (i.e., BA 46) showed no such relationship. Significant negative correlations were observed in ventral PFC (VPFC, BA 44; slope=−0.76, r^2=0.39, p<0.03) and parietal regions (BA 40; slope=−0.76, r^2=0.58, p<0.004).

We sought to further ascertain the source of these relationships using analyses that were (1) independent of error in fMRI signal measurement and (2) were robust to the power limitations of a relatively low N design. Thus, we used parameter estimates (that measure task-related signal variation independent of error; e.g., Rypma and D'Esposito, 2000) in combination with a non-parametric resampling method (Rypma et al., in press) to assess relationships between fMRI signal and individual subjects' RTs.

Table 1 shows the slope of the regression of parameter estimates (βs) on individual subjects' RTs in standard units with respect to the sample used to fit the line. To assess the statistical significance of these relationships, we applied distribution-free permutation tests. These results were consistent with those based on t in two important ways. Qualitatively, BA 9 was positively correlated with RT, and BAs 46, 44, and 40 were negatively correlated with RT. Quantitatively, relatively strong associations (i.e., larger slope and r^2 values) between fMRI activity and RT were observed in BAs 9 and 40, relatively weaker associations (i.e., smaller slope and r^2 values) were observed in BAs 46 and 44. Indeed, the regression of β on RT was nonsignificant in BA 46, similar to the t-based analysis.

These results indicated that the relative speed of individuals' performance varied with the activity of specific brain regions. As can be seen in Fig. 3, the nature of these activation–performance relationships varied across brain regions. RT increases were related to increased DPFC involvement, but decreased VPFC and parietal involvement. Using Granger causality analyses (Goebel et al., 2003), we directly tested the hypothesis that, among slower individuals, prefrontal (possibly executive) systems guide posterior systems. Granger causality was used to evaluate causal influences between brain regions by measuring the extent to which activation changes in one region affected (i.e., reliably preceded) those in other regions at later points in time. Thus, it permitted characterization of the strength and direction of influence between discrete brain regions (Goebel et al., 2003).

Fig. 4 shows the results of the Granger causality analyses superimposed on axial slice (z=+28) illustrations taken from a standard atlas. Influences were aggregated for faster (4 males, 2

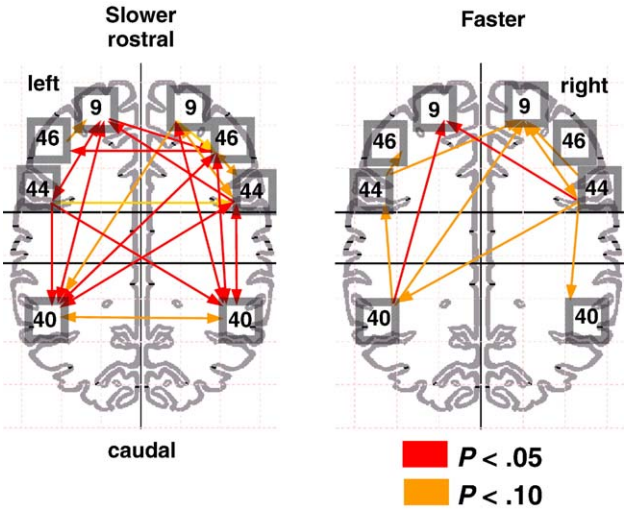

Fig. 4. Results of Granger causality analyses between prefrontal (BAs 9, 46, and 44) and parietal (BA 40) regions superimposed on an axial slice ($z=+28$) illustration taken from a standard atlas. Influences were calculated separately for faster and slower individuals (grouped by median split; arrows indicate significant influences; red=$p<0.05$; yellow=$p<0.10$).

females; *M* age=23) and slower (3 males, 3 females; *M* age=23) groups, as indicated by DSST performance. Arrows in Fig. 4 indicate significant influences (red=$p<0.05$; yellow=$p<0.10$). For illustration of individual differences in Granger relations between brain regions, Fig. 5 shows representative segments of BA 9 and BA 40 time series for the fastest and slowest subjects. The black arrows in this figure illustrate points where BA 9 excursions precede BA 40 excursions.

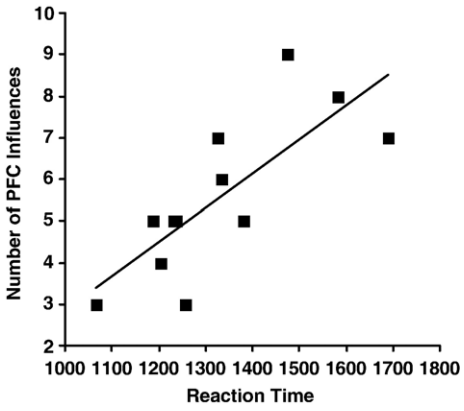

Fig. 6. Scatterplot of connectivity–performance relationships. Scatterplot of the number of BA 9 influences (those extending from BA 9 to other regions identified by the Granger analysis) plotted against individual subjects' RTs (slope=0.77; $r^2=0.60$; $p<0.003$).

The results of this analysis indicated three differences between faster and slower performers. First, there were *quantitative* differences between these groups. Specifically, there were more significant interregional influences for slower than faster performers. This difference was significant according to a Mann–Whitney test ($p=.02$). Second, there were *qualitative* differences between the two groups. Specifically, there were more directed frontal-to-parietal influences than vice versa in slower as compared to faster performers. To test this observation, we regressed individual subjects' RTs upon the number of BA 9 influences, i.e., the number of projections from BA 9 to other ROIs. Consistent with this observation, slower subjects showed more influences extending from BA 9 to other regions than faster subjects (Fig.

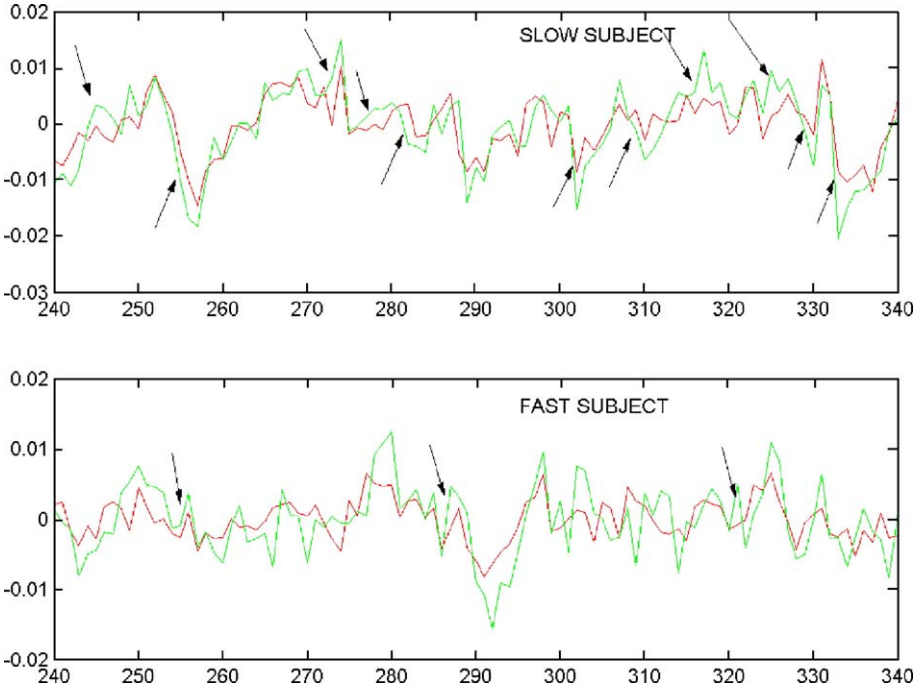

Fig. 5. An example of BA 9 (green line) and BA 40 (red line) time series from the slowest and fastest subjects. Arrows indicate when BA 9 excursions precede BA 40 excursions.

6; note that some points overlap). The standardized regression coefficient was significant (slope = 0.77; $r^2 = 0.60$; $p < 0.003$). Third, we observed more reciprocal connections between BA 9 and other regions for slower than for faster performers. Thus, we tested the possibility that, between subjects, an increase in the number of regions upon which BA 9 exerted influence corresponded with an increase in the number of regions influencing BA 9 in return. We calculated for each subject a "reciprocity index" by multiplying the number of BA 9 influences on other regions by the number of influences on BA 9. Each value was scaled by the mean number of influences to equate for between-subject differences. This calculation would yield maximal values as the number of BA 9 influences approaches the number of influences on BA 9. Deviations away from this reciprocity would yield smaller values. A Mann–Whitney test indicated greater BA 9 reciprocity index values for the slower group (median = 1.5) than for the faster group (median = 0.56; $p = 0.008$). This effect was observed across both hemispheres; tests of these values separately for each hemisphere were not significant.

Discussion

In this study, we tested the hypothesis that individual differences in cortical function (as measured by fMRI signal changes) are associated with individual variability in processing speed (as measured by differences in individuals' DSST performance). The present results supported this hypothesis; we observed considerable variability both in individuals' DSST performance and in their neural activity in a frontoparietal network that has been associated with working memory (e.g., Curtis and D'Esposito, 2003; D'Esposito et al., 2000) and reasoning (e.g., Prabhakaran et al., 1997, 2001; Haier et al., 1988) and whose activation is known to vary with differences in performance (e.g., Maccotta and Buckner, 2004; Nobre et al., 2003; Poldrack et al., 1998). Regression analyses of RT and BOLD signal change indicated that the principal source of variability in individuals' activation was processing speed. Granger causality relationships between brain regions suggested that there were overall more interregional directed influences in slower subjects than in faster subjects, suggesting that efficient interregional communication provides the neural basis of processing speed. Moreover, there were more directed influences from dorsal PFC to other regions for slower than for faster subjects. Thus, these data suggested that the extent and direction of influences between brain regions underlie cognitive efficiency and individual differences in performance.

Performance-related decreases in neural activity

Our results suggested that different brain regions showed different relationships to RT. DPFC regions showed increases in neural activity with increases in RT. This pattern of results is consistent with earlier results using delayed-response working memory paradigms (Rypma and D'Esposito, 1999, 2000; Rypma et al., 2002; Rypma et al., 2005). That set of studies indicated that variability in fMRI data was significantly controlled by individual subjects' performance. Rypma and D'Esposito (1999), for instance, had subjects perform a delayed-response task during fMRI scanning. Subjects were required to encode either 2 or 6 letters, maintain them over a delay, and then retrieve the encoded letters in order to determine whether or not a single letter was or was not part of the encoded memory set. The important result was that, during the retrieval period, large increases in intersubject variability were observed. When we attempted to account for this variability by regressing individual subjects' PFC activity against their RT slopes, systematic increases in PFC activity were observed with increases in RT slope. This result occurred only in DPFC and was significant only in the retrieval period. Subsequent studies have replicated and extended these results (e.g., Gevins and Smith, 2000; Rypma et al., 2002; Grady et al., 2003; 2005; Persson et al., 2004). Rypma and his colleagues speculated that this variability may be related to individual differences in subjects' processing speed. The present results support and extend those results by suggesting that processing speed differences between individuals may not be due to functional differences in one specific region, but rather the nature of the connectivity between task-relevant brain regions.

Performance-related increases in neural activity

Whereas DPFC activity decreased with increased processing speed, activity in parietal and VPFC regions increased with increased processing speed. Such performance-related activation increases replicate results from other laboratories (e.g., Gray et al., 2003; Newman et al., 2003). This region-dependent pattern of qualitative activation–performance differences suggests two possibilities. One possibility is that there is no uniform relationship between cognitive and neural efficiency. It may be that task-critical brain regions are organized in a modular fashion and perform fundamental operations relatively independently. The second possibility, suggested by results of the Granger causality analyses, is that neural efficiency may be related to both increases and decreases in regional activity. Whereas earlier results (e.g., Rypma and D'Esposito, 1999; Rypma et al., 2002) suggested that significant activation–performance variability is limited to dorsal regions of PFC, results from our Granger analyses suggest that these relationships are (1) more extensive and (2) regionally variable in their direction.

The region-dependent nature of these activation–performance relationships suggests that they may be a function of the amount of interaction between brain regions that an individual requires for optimal task performance. Results from the present study showing more significant interregional influences for slower as compared to faster subjects support this hypothesis. Fast DSST performance occurs when parietal cortex and VPFC support visual search processes with minimal executive DPFC control. Slower performance occurs when greater DPFC involvement is required to guide or "drive" other task-relevant brain regions to optimize performance. Results from the present study showing more DPFC influences upon other brain regions for slower as compared to faster subjects support this hypothesis. Our results suggest that these influences are reciprocal. The reciprocity index results indicated that the more that DPFC influenced other regions, the more these regions interacted with DPFC in return. Thus, it may be that slower performance is mediated, not only by increased executive control requirements, but also by increased executive monitoring requirements. Indeed, monitoring functions have been associated with PFC in neurophysiology, neuroimaging, and neuropsychology studies (e.g., Muller and Knight, in press; Rajah and McIntosh, 2006; Petrides, 1995). Together, the present results support the idea that relatively slower adults may require more prefrontal executive control for optimal performance than faster adults. Faster adults may depend less on controlled processing.

These individuals may instead rely upon more automatic processing based in parietal regions and VPFC.

Neural mechanisms of processing efficiency

The present results suggest the existence of a cognitive efficiency mechanism that mediates interindividual performance differences. A similar mechanism may mediate intraindividual performance differences. Neural activity reductions in the presence of performance improvement have been observed in studies that compare neural activity before and after repeated exposure to the same stimuli or task (Haier et al., 1992; Maccotta and Buckner, 2004; Qin et al., 2003; Poldrack et al., 1998). In one study for instance, Poldrack et al. (1998) scanned subjects while they performed a lexical decision task in which, on half the trials, the letter strings appeared mirror-reversed (e.g., Koler, 1968). After the scan, subjects were given extensive training on the task and returned to the scanner where they performed mirror-reading lexical decision again. The important result was that significant performance improvement between scans was accompanied by reductions in fMRI signal.

It may be that such practice-related activation differences reflect intraindividual shifts from relatively effortful to relatively automatic cognitive processes. It is possible that similar mechanisms also mediate interindividual performance differences. The proposal that automatic–effortful processing differences account for between-subject performance differences is not novel (e.g., Hasher and Zacks, 1979). Individual differences in the extent to which cognitive processes are implemented in an "automatic" way (e.g., Shiffrin and Schneider, 1984) may account for the activation–performance relations we observed between individuals in this study (Patterson and Rypma, 2005).

Another possibility suggested by the present results is that practice-related performance gains may be modulated by individual differences in neural connectivity (cf. Haier et al., 1992). Indeed, other studies have shown complex patterns of practice-related activation decreases in some regions, but increases in others (e.g., Petersen et al., 1998; Gevins and Smith, 2000; Lehericy et al., 2005). In one study for instance, Gevins and Smith (2000) required high-ability and low-ability (as measured by WAIS-R performance) subjects to perform an n-back working memory task during EEG recording. Similar to the present results, high-ability subjects showed less prefrontal, and more parietal activity than their low-ability counterparts. This convergence of results is not surprising; full-scale WAIS-R scores and digit–symbol scores are highly correlated (see also Neubauer et al., 2004). The present results suggest that such practice-related increases and decreases in neural activity may reflect connectivity changes between brain regions. Given the extensive training our subjects received prior to scanning, the present results may reflect the end-state of system-wide practice-related changes. Further research examining individual differences in practice-related activation changes, using connectivity analysis methods, could be useful in understanding these complex patterns of results.

The significant modulation of parietal activity by individuals' speed of performance is consistent with the notion that DSST performance depends on visual search mechanisms. Neural activity is known to vary with visual search efficiency. One study, for instance, explicitly manipulated visual search efficiency with systematic variation of feature, conjunction, and "inefficient feature" search (wherein subjects searched for a feature among slightly different distractors) requirements during fMRI scanning. The results from one study indicated modulation of frontoparietal network activity by changes in visual search requirements. Specifically, more activity was observed during conjunction search and "inefficient feature" search than during efficient feature search in the frontoparietal visual search network. Importantly, significant correlations between RT slopes and neural activity were also observed in this study (Nobre et al., 2003).

The present results suggest support for processing efficiency explanations of individual differences in performance. These results are not inconsistent with capacity accounts of brain–behavior relationships that suggest that relative processing-resource availability, indexed by relatively *greater* brain activation, supports faster and more accurate performance. It may be that subjects with relatively higher capacity are those subjects who implement more efficient strategies to perform the DSST relative to those with lower capacity (cf. Larson et al., 1995). We hoped to minimize the role of individual strategy differences through the use of a simple processing speed task. Indeed, systematic investigation of strategy difference accounts of DSST performance differences has yielded null results (Salthouse, 1992). More research is certainly needed to distinguish between effects that result from individual differences in fundamental processing speed differences and those that result from strategic differences employed by different subjects.

Nonetheless, the present results suggest that individual differences in cognitive task performance reflect fundamental differences in prefrontal activity (possibly reflecting differences in the extent of prefrontal control required for optimal performance). The finding in this study that relative increases and decreases in BOLD activity are intimately linked to regional connectivity implicates a central role for axonal structures in interindividual activation differences. It may be that the efficiency of neural interconnections reflects differences in white matter integrity. Anatomical studies have shown individual differences in both white and gray matter that could mediate interactive activation changes between brain regions and subjects' processing speed performance (e.g., Haier et al., 2004, 2005).

The results presented here, region-dependent and interactive activation tied directly to individual subjects' processing speed performance, are consistent with neural efficiency hypotheses (e.g., Vernon, 1983; Haier et al., 1988; 1992; Cerella, 1991; Rypma and D'Esposito, 2000). They are consistent with the hypothesis that individual differences in cognitive task performance reflect fundamental differences in prefrontal activity (possibly reflecting differences in the extent of prefrontal control required for optimal performance), and the efficiency of neural interconnections (possibly reflecting differences in white matter integrity) between brain regions that mediate task performance.

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