

Working Memory Capacity, Indirect Semantic Priming, and Stroop Interference: Pattern of Interindividual Prefrontal Performance Differences in Healthy Volunteers

Markus Kiefer, Michelle Ahlegian, and Manfred Spitzer
University of Ulm

Using neuropsychological models of prefrontal function, the authors investigated the pattern of interindividual prefrontal performance differences in healthy volunteers. Using a correlation and an extreme group approach, they compared verbal and visuospatial working memory capacity with performance on the Stroop interference task as a measure of executive control and on the direct and indirect semantic priming tasks as a measure of semantic access. Subjects with low visuospatial working memory capacity exhibited increased Stroop interference. Subjects with low verbal memory capacity showed increased priming and Stroop interference only. The study shows that prefrontal functioning varies interindividually, forming patterns of performance differences. These findings suggest that working memory, executive control, and semantic retrieval are functionally related to some extent.

Keywords: prefrontal cortex, executive control, working memory, semantic priming, interindividual difference approach

Considerable evidence from neuropsychological and neuroimaging studies has been accumulated showing that prefrontal areas subserve performance in a variety of tasks probing partly heterogeneous cognitive functions (Duncan & Owen, 2000; Fuster, 1996). In this study, we address the issue of interindividual performance differences in prefrontal functioning in healthy subjects. Our research was motivated by the assumption that a pattern of interindividual performance differences in various prefrontal tasks might emerge because they are functionally linked as a result of a common neural substrate in the prefrontal cortex.

It has been well established that prefrontal areas support working memory functions (D'Esposito et al., 1998; Goldman-Rakic, 1995; Smith & Jonides, 1998). According to Baddeley (1986), working memory comprises modality-specific verbal and visuospatial short-term storage subsystems and the central executive system involved in the active manipulation of information. There is evidence that verbal and object working memory depends more strongly on left prefrontal regions, whereas spatial working memory is lateralized to right prefrontal areas (Smith & Jonides, 1999; Smith, Jonides, & Koeppe, 1996). Alternatively, it has been suggested that working memory function can be partitioned according to the processes involved: Short-term storage of information involves ventral prefrontal regions, whereas active manipulation relies on dorsolateral prefrontal areas (Petrides, 1995, 1996). However, evidence regarding the regional specialization of prefrontal cortices in terms of particular working memory subcomponents is heterogeneous, and the question of how working memory should

be partitioned is still a matter of an ongoing controversy (Duncan, 2001; Owen, 2000; Zuroski et al., 2002).

The prefrontal cortex has also been associated with executive control, a cognitive function theoretically closely related to the central executive component of working memory (Braver & Cohen, 2000; Cohen & Servan-Schreiber, 1992; Norman & Shallice, 1986; Posner & DiGirolamo, 1998). Several neuropsychological theories propose an executive control system that organizes cognition and behavior when routines are not available or are ineffective for task performance. The notion of an executive control system (or supervisory attentional system) was originally motivated by the observation that patients with prefrontal lesions frequently exhibit disorganized behavior (Norman & Shallice, 1986). These patients show deficits in executive tasks such as conflict resolution during the Stroop interference task (Perret, 1974; Vendrell et al., 1995) and set shifting during the Wisconsin Card Sorting Test (Drewe, 1974; Milner, 1963). The relevance of prefrontal areas for these aspects of executive control functions has later been confirmed in various neuroimaging studies (Carter, Mintun, & Cohen, 1995; Pardo, Pardo, Janer, & Raichle, 1990; Peterson et al., 2002). Models of prefrontal function therefore propose that prefrontal areas, in particular the dorsolateral prefrontal cortex, support active manipulation of information by using context information (e.g., a task-relevant goal) and interference blocking of competing information (Braver & Cohen, 2000; Cohen & Servan-Schreiber, 1992; Duncan, 2001; Kane & Engle, 2002).

The prefrontal cortex not only contributes to working memory and executive control function but also plays an important role in semantic processing. Prefrontal activation has been observed in a variety of semantic tasks, such as use generation (Petersen, Fox, Posner, Mintun, & Raichle, 1988; Posner, Petersen, Fox, & Raichle, 1988), classification (Demb et al., 1995; Vandenberghe, Price, Wise, Josephs, & Frackowiak, 1996), and semantic priming (Wagner, Desmond, Demb, Glover, & Gabrieli, 1997). Spitzer and colleagues (Kiefer, Weisbrod, Kern, Maier, & Spitzer, 1998;

Markus Kiefer, Michelle Ahlegian, and Manfred Spitzer, Department of Psychiatry, University of Ulm, Ulm, Germany.

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Correspondence concerning this article should be addressed to Markus Kiefer, Department of Psychiatry, University of Ulm, Leimgrubenweg 12, 89075, Ulm, Germany. E-mail: Markus.Kiefer@medizin.uni-ulm.de

Spitzer, 1997; Spitzer, Braun, Hermle, & Maier, 1993; Weisbrod, Maier, Harig, Himmelsbach, & Spitzer, 1998) proposed that left prefrontal areas focus retrieval of semantic information to meaning aspects related to the context (see also the center-surround mechanism suggested by Carr & Dagenbach, 1990). Semantic information itself is thought to be stored in other cortical areas. A similar view is held by Wagner, Paré-Blagoev, Clark, and Poldrack (2001), who suggested that the left prefrontal cortex guides semantic retrieval. However, both views differ from each other in one respect: The latter view is restricted to controlled semantic retrieval processes, whereas the first view also applies to automatic retrieval processes.

The notion of the focusing role of the prefrontal cortex in semantic retrieval has been originally inferred from semantic priming studies in thought-disordered schizophrenic patients. Semantic priming generally refers to the facilitation of a response to a target stimulus that is preceded by a semantically related prime (Neely, 1977). Thought-disordered schizophrenic patients, in whom prefrontal dysfunction was observed in several studies (Berman, Torrey, Daniel, & Weinberger, 1992; Dolan et al., 1995; Weisbrod, Kiefer, Marzinzik, & Spitzer, 2000; but see Vogetley & Falkai, 1999, for deficits in other brain regions), frequently exhibited increased semantic priming for directly (*hen-egg*) and indirectly (*lemon* [sour]–*sweet*) related prime–target word pairs, compared with healthy control subjects (Maher, Manschreck, Redmond, & Beaudette, 1996; Manschreck et al., 1988; Spitzer, Weisker, Maier, Hermle, & Maher, 1994; Weisbrod et al., 1998). Priming is increased particularly at short stimulus onset asynchronies (SOAs) of 200 ms for indirectly related prime–target word pairs, which are associated only via a mediating link (Spitzer, 1993; Spitzer et al., 1993). Control subjects, in contrast, usually showed under this experimental condition little or no indirect priming (Balota & Lorch, 1986; de Groot, 1983; Kiefer et al., 1998; Spitzer et al., 1993).

Because increased direct and indirect priming in schizophrenic patients was observed at short SOAs, at which strategic priming processes are less effectively used (Neely, 1977, 1991), we assume that schizophrenic patients exhibit exaggerated automatic priming processes (Spitzer et al., 1993). We propose that the prefrontal cortex focuses automatic spreading activation in semantic networks so that it reaches only closely related nodes (e.g., *lemon-sour*), a suggestion that has been confirmed in an event-related potential study on indirect priming (Kiefer et al., 1998). Because of dysfunctional prefrontal information processing in schizophrenic patients, spreading activation during semantic access is stronger and far-reaching, resulting in increased direct and indirect priming effects. In addition to this semantic deficit, schizophrenic patients are also impaired in working memory and executive tasks (Frith, 1992; Kiefer, Apel, & Weisbrod, 2002; Spitzer, 1993). These findings in schizophrenic patients suggest that prefrontal dysfunction may likewise affect performance in various cognitive tasks, possibly because of a common or overlapping neural substrate in prefrontal areas.

As mentioned previously, there is considerable agreement that the prefrontal cortex is involved in various cognitive functions, including working memory, executive control, and semantic processing (Carpenter, Just, & Reichle, 2000; Duncan, 2001; Duncan & Owen, 2000). It is also well established that interindividual differences in working memory capacity cannot only be found in

comparisons between patient and healthy control groups but can also be observed within the healthy population (for reviews, see Just, Carpenter, & Keller, 1996; Kane & Engle, 2003). These interindividual differences in working memory capacity have been related to differences in prefrontal functionality (Conway, Kane, & Engle, 2003; Kane & Engle, 2002; King & Kutas, 1995). Typically, working memory capacity is measured with memory span tasks (e.g., Reading Span, Operation Span) that require both the maintenance and manipulation of memory items. When performance differences between low- and high-span subjects have been compared in other tasks (Just & Carpenter, 1992; Just et al., 1996; Kane & Engle, 2002), low-capacity subjects showed poorer performance in complex sentence comprehension (Just & Carpenter, 1992; King & Kutas, 1995), demonstrated more interference in the Stroop task (Kane, Bleckley, Conway, & Engle, 2001), and reacted slower and less accurately in an antisaccade task (Kane et al., 2001) compared with high-capacity subjects. In all these studies, the effects of interindividual differences in working memory capacity were assessed in tasks that impose strong demands on active manipulation of information and response conflict resolution. Hence, all these tasks require executive processes (for a discussion, see Conway et al., 2003; Kane & Engle, 2002). To our knowledge, it has not been investigated yet whether high- and low-capacity subjects also differ in a priming task that shares the involvement of prefrontal areas but does not evoke executive or working memory processes. Priming differences between low- and high-capacity subjects would suggest that different prefrontal functions, even if they do not involve executive processes, are not entirely independent of each other but are functionally related to some extent. Interindividual differences in indirect priming have already been observed in a previous study; healthy subjects with elevated scores on a scale measuring schizophrenic language disturbances showed increased indirect priming (Moritz et al., 1999). However, because working memory tests were not administered in that study, the relation between priming and working memory capacity could not be determined.

In the present work, we tested the hypothesis that working memory, executive function, and focus of semantic priming are functionally related in a behavioral study using a correlation and an extreme group approach. Our research is based on the assumption that working memory, executive control, and focusing of semantic retrieval share a common neural substrate in the prefrontal cortex and are, therefore, functionally linked. We hypothesized that interindividual performance differences in various prefrontal tasks form a specific pattern. In a sample of 63 healthy volunteers, we assessed verbal and spatial working memory capacities with memory span tests, which required only maintenance of information (Digit Span Forward, Block Span Forward) or both maintenance and active manipulation of information (Digit Span Backward, Block Span Backward). Furthermore, subjects performed a Stroop interference task to probe for executive control and the direct and indirect semantic priming task to test for the focus of spreading activation during semantic access. We assumed that direct and indirect semantic priming does not require executive processes. In a first analysis, we assessed the correlation pattern across these prefrontal tasks. In a second analysis, we formed extreme groups according to subjects' working memory capacity (high- vs. low-capacity subjects), and we compared performance of these subject groups in the two other prefrontal tasks. Working

memory capacity was taken as an index for prefrontal functioning because working memory span has been intensively studied, and working memory span tasks have been found to reliably activate the prefrontal cortex in neuroimaging studies (Bor, Duncan, & Owen, 2001; Owen, 2000; Owen et al., 1998). If prefrontal functions are related to some extent, specific interindividual differences in prefrontal task performance should emerge. Given what is known about the contribution of the prefrontal cortex to these cognitive functions, we predicted that low working memory capacity should be associated with increased Stroop interference and increased direct and indirect priming.

Method

Subjects

Entire sample. The entire sample consisted of 63 native German speakers with normal or corrected-to-normal vision and without any signs of neurologic or psychiatric disorders. Subjects were debriefed with a standardized short anamnestic interview regarding neurologic and psychiatric symptoms or previous treatment and were tested for intact color vision with the Ishihara color tables (Velhagen & Broschmann, 1997). In addition, they were given a standardized questionnaire asking for psychotic symptoms (Stüllwold, 1991) to exclude subjects with unrecognized psychosis. All subjects signed a written informed consent before participating in the study.

Extreme groups of working memory capacity. Extreme groups were formed post hoc according to subjects' individual verbal and visuospatial working memory capacity. The Digit Span Forward and Backward tasks from the Hamburg-Wechsler Intelligenztest für Erwachsene—Revision (Tewes, 1994) were used to test verbal working memory storage as well as both storage and manipulation. The tasks require subjects to orally repeat digit sequences read by the experimenter in the same order (forward) or in the reversed order (backward). The set size at which subjects recalled all two available sequences correctly was taken as their digit span. Visuospatial working memory was tested with the Corsi Block Tapping Test (Corsi, 1995). Subjects had to tap on blocks spatially arranged on a board either in the same order or in the reversed order as previously presented by the experimenter. The set size at which subjects repeated all three available sequences correctly was taken as their block span.

Separately for each of the four working memory tests (Digit Span Forward and Backward, Block Span Forward and Backward), extreme groups were formed: The best performing third of subjects were included in the high-capacity subject group, and the last third in the low-capacity subject group. Demographic data of the extreme groups are shown in Table 1.

For each working memory test, high- and low-capacity subject groups were compared with *t* tests for differences in age and in years of formal education. In both Verbal Digit Span tests (Forward, all *ps* > .09; Backward, all *ps* > .20) and in the Block Span Backward test (all *ps* > .14), groups were comparable in these variables and did not differ from each other significantly. In the Block Span Forward test, however, significant group differences in age, $t(40) = 2.36, p < .05$, and years of education, $t(40) = -2.61, p < .05$, were observed: Low scorers were older and less educated than high-capacity subjects. To ensure that possible group differences in the other prefrontal tests were not mediated by variables other than working memory capacity, we conducted analyses of covariance with age and years of education as covariates.

Separately for each memory test, we assessed gender distributions across high- and low-capacity subject groups using chi-square tests. Distribution of female and male subjects did not differ significantly between groups for both Digit Span tests ($\chi^2 < 1, p > .55$) and for the Block Span Backward test, $\chi^2(1, 42) = 2.35, p > .12$. For the Block Span Forward test, significant distributional differences were obtained, $\chi^2(1, 42) = 7.36, p < .01$, with relatively more male subjects in the high-capacity subject group and more female subjects in the low-capacity subject group. To address the issue of whether there are gender-related differences in Stroop interference and indirect priming effects, which could mediate differences between working memory extreme groups, we formed an age- and education-matched sample of 23 male and female subjects, respectively. Because female and male subject groups did not differ significantly from each other in these tasks (all *Fs* < 1.45), we can exclude the possibility that a different distribution of female and male subjects might have biased the results.

Materials and Procedure

Stroop interference task. Subjects were presented with a computer version of the Stroop interference task, which was used in an earlier study (Hepp, Maier, Hermle, & Spitzer, 1996). Stimuli were either color names (German words for *red*, *yellow*, *blue*, *green*, and *brown*) or a string consisting of Xs (XXXX). All stimuli were presented in five different colors (red, yellow, blue, green, and brown) in the center of a computer screen. In the congruent condition, presentation color and the color name matched (40 trials); in the incongruent condition, presentation color and the color name did not match (40 trials). The neutral condition consisted of the string of Xs in different colors (40 trials). The subjects' task was to name as quickly and as accurately as possible the presentation color of the stimuli. Voice onset of the naming response was measured with a voice-activated relay (voice key) connected to the computer. Each trial started with the presentation of a fixation cross for 700 ms, which was replaced by the colored stimuli. Stimuli remained on the screen until the subject's response. The experimenter initiated the next trial by a mouse click. Trial order was initially pseudorandomized—with the restriction that the same presentation color

Table 1
Demographic Data of High and Low Working Memory Capacity Groups (*n* = 21)

Demographic variable	Digit Span				Block Span			
	Forward		Backward		Forward		Backward	
	High	Low	High	Low	High	Low	High	Low
Gender								
Women	13	13	11	13	6	15	10	15
Men	8	8	10	8	15	6	11	6
Age (years)	44.90 (10.4)	38.76 (12.0)	36.76 (13.1)	41.57 (10.6)	33.38 (12.9)	42.14 (11.1)	38.95 (11.7)	43.95 (9.6)
Education (years)	9.95 (1.82)	10.48 (1.91)	10.76 (2.07)	10.29 (1.73)	11.71 (1.79)	10.24 (1.86)	10.76 (2.04)	9.95 (1.56)
Working memory span	6.61 (0.86)	4.38 (0.74)	5.90 (0.99)	3.04 (0.58)	6.09 (0.30)	4.33 (0.73)	5.71 (0.71)	3.90 (0.30)

Note. Standard deviations are in parentheses.

and color name were not immediately repeated—and thereafter kept constant for all subjects. At the beginning of the session, 21 training trials were run. The experimenter recorded the correctness of the naming responses as well as possible disturbances of voice-onset measurement (erroneously activated voice key through breathing, coughing, etc.).

Direct and indirect priming tasks. Stimuli and procedure were adopted from an earlier study (Spitzer et al., 1993) and are therefore only briefly described. Word pairs (primes and targets) were sequentially presented in the center of a computer screen. Primes were always German words. The critical pairs consisted of targets involving real German words (108 pairs), and the other 108 pairs were distractors with legally spelled pseudowords as targets. Semantic relatedness between prime and target of the critical pairs was varied by including 36 nonrelated pairs (*leaf-car*), 36 indirectly related pairs (*lemon-sweet*), and 36 directly related pairs (*hen-egg*). Subjects' task was to read the first word silently and then to decide as quickly and accurately as possible whether the second string of letters was a real German word (lexical decision). Subjects indicated their decisions with a keypress on the computer keyboard. They responded with the dominant hand using the index finger for "yes" responses and the middle finger for "no" responses.

Each trial was initiated by the experimenter by a mouse click. Trials started with a fixation point for 700 ms, followed by presentation of the prime for 200 ms. In one condition, the target was immediately presented, thereafter resulting in an SOA of 200 ms. In the other condition, the target was displayed after an interstimulus interval of 500 ms, yielding an SOA of 700 ms. SOA was varied to distinguish between automatic and controlled priming processes. The target was displayed until the subject had responded. The entire stimulus set was split into two subsets of 108 pairs each, A and B, which included half of the word pairs of the three semantic relation conditions (18 pairs each) as well as half of the word-pseudoword distractor pairs (54 pairs). Stimulus Subsets A and B were assigned to the two SOA conditions in a counterbalanced fashion across subjects. Trials of the two SOA conditions were blocked, and all subjects started with the SOA = 200-ms condition followed by the SOA = 700-ms condition. Within each block, trial order was initially randomized and thereafter kept constant. At the beginning of the experiment, subjects performed 24 training trials, and an additional 5 practice trials were run immediately before each block.

Results

Correlation Analysis

The pattern of interindividual prefrontal task performance differences was assessed in a correlation analysis for the entire sample of 63 subjects. Verbal (digit span forward and backward, respectively) and visuospatial working memory capacity (block span forward and backward, respectively), direct and indirect priming measures calculated separately for the short and long SOAs (reaction time [RT] difference between nonrelated and related conditions), as well as Stroop interference measures (RT difference between incongruent and congruent conditions) were entered as variables, and pairwise Pearson product-moment correlations were calculated. We note that because of small variations in the working memory span tasks (range of four memorized items in the Block Span tasks and range of six items in the Digit Span tasks), correlations cannot be very high. Intercorrelations between span tasks were significant, ranging from .38 to .58 (all $ps < .01$). Results for the correlations between span tasks on the one hand and Stroop interference and priming on the other hand are shown in Table 2.¹ Except for the Digit Span Forward task, significant negative correlations with Stroop interference were found for all span tasks. For the Digit Span Forward task, the correlation

Table 2

Results From the Correlation Analysis Between Working Memory Span Tests and Between Stroop Interference and Priming

Working memory measure	Stroop interference	Priming			
		SOA = 200 ms		SOA = 700 ms	
		Direct	Indirect	Direct	Indirect
Digit Span Forward					
<i>r</i>	-.19	-.05	-.17	-.30	-.12
<i>p</i>	.144	.712	.191	.017	.332
Digit Span Backward					
<i>r</i>	-.35	.08	-.18	-.39	-.23
<i>p</i>	.005	.530	.158	.002	.067
Block Span Forward					
<i>r</i>	-.38	.04	-.09	.14	.06
<i>p</i>	.002	.748	.501	.266	.641
Block Span Backward					
<i>r</i>	-.31	.01	-.13	.05	.03
<i>p</i>	.013	.921	.317	.675	.845

Note. Shown are Pearson product-moment correlation coefficients and *p* values of significance tests. Significant correlations and *p* values are highlighted in bold. SOA = stimulus onset asynchrony.

reached only trend level, although the result pattern was the same as that for the other tasks: High working memory capacity was associated with decreased Stroop interference.

Direct and indirect priming measures correlated significantly with the verbal working memory task but not with the visuospatial working memory task. Direct semantic priming at the long SOA showed negative correlations with Digit Span Forward and Backward tasks. The correlation between indirect priming and Digit Span Backward reached only trend level at the short and long SOAs. The correlation pattern was identical for all priming measures: High verbal working memory capacity was associated with decreased priming. Direct and indirect priming were intercorrelated at the short ($r = .67, p < .01$) and at the long ($r = .51, p < .01$) SOAs. Priming measures between SOA levels were not correlated for either indirect ($r = .02, p > .88$) or direct ($r = -.05, p > .70$) priming. Stroop interference and direct priming at the long SOA exhibited a positive correlation that reached trend level ($r = .23, p = .07$); subjects prone to strong Stroop interference showed increased priming.

To summarize the most relevant results of the correlation analysis, both verbal and visuospatial working memory capacity and Stroop interference were negatively correlated. High working memory capacity was associated with decreased Stroop interference. In contrast, priming measures showed substantial correlations only for tasks of verbal working memory capacity. Both measures also exhibited a negative relation: Subjects with high verbal working memory capacity showed decreased priming. The

¹ We also conducted a multiple regression analysis with memory span tasks as predictors and priming measures and Stroop interference as dependent variables. Because of intercorrelations between variables, we obtained significant beta weights only for direct priming at the long SOA for the following predictors: Digit Span Forward = $-.26$, Digit Span Backward = $-.42$, and Block Span Backward = $.35$.

correlation between direct priming and Stroop interference reached trend level; high Stroop interference was associated with increased priming.

Extreme Group Analysis

The pattern of interindividual prefrontal performance differences was further assessed in an extreme group analysis. Separate analyses of variance (ANOVAs) were performed for the different working memory extreme groups (digit span forward and backward, block span forward and backward). Because interactions between congruency or priming on the one hand and working memory capacity on the other hand are of theoretical interest, main effects are not reported in detail for each analysis. This avoids redundancy in the description of the results for the different working memory test extreme groups.

Stroop interference task. Error rate (ER) in the Stroop interference task was analyzed with repeated measures ANOVAs with congruency (congruent, incongruent, neutral) as within-subject factors and working memory capacity (high vs. low) as between-subjects factors (see Figure 1). Fisher's least significant difference (LSD) post hoc tests were used to compare mean differences

between conditions. Significant main effects of congruency were obtained for all working memory extreme groups (all $F_s > 27$, all $p_s < .01$). ER was significantly higher in the incongruent (range = 2.8%–4.9%) condition compared with the congruent (range = 0%–0.2%) and the neutral (0%–0.2%) conditions. The latter two conditions did not differ from each other. Thus, an interference effect on ER was found in all working memory extreme groups. There was a tendency toward higher ER in subjects with low verbal working memory capacity (digit span forward and backward), particularly in the incongruent condition, but the interaction between congruency and working memory capacity did not reach significance ($p < .11$).

RT analysis was based on mean naming latency of correct responses per condition. Responses longer than twice the individual mean (0.49% of the entire data set) and trials with voice key problems (2.5% of the entire data set) were excluded from analysis. Repeated measures ANOVAs were performed on the RT data, with congruency as the within-subject factor and working memory capacity as the between-subjects factor. Significant effects were further assessed with Fisher's LSD post hoc tests. Congruency affected naming latencies in all working memory extreme groups,

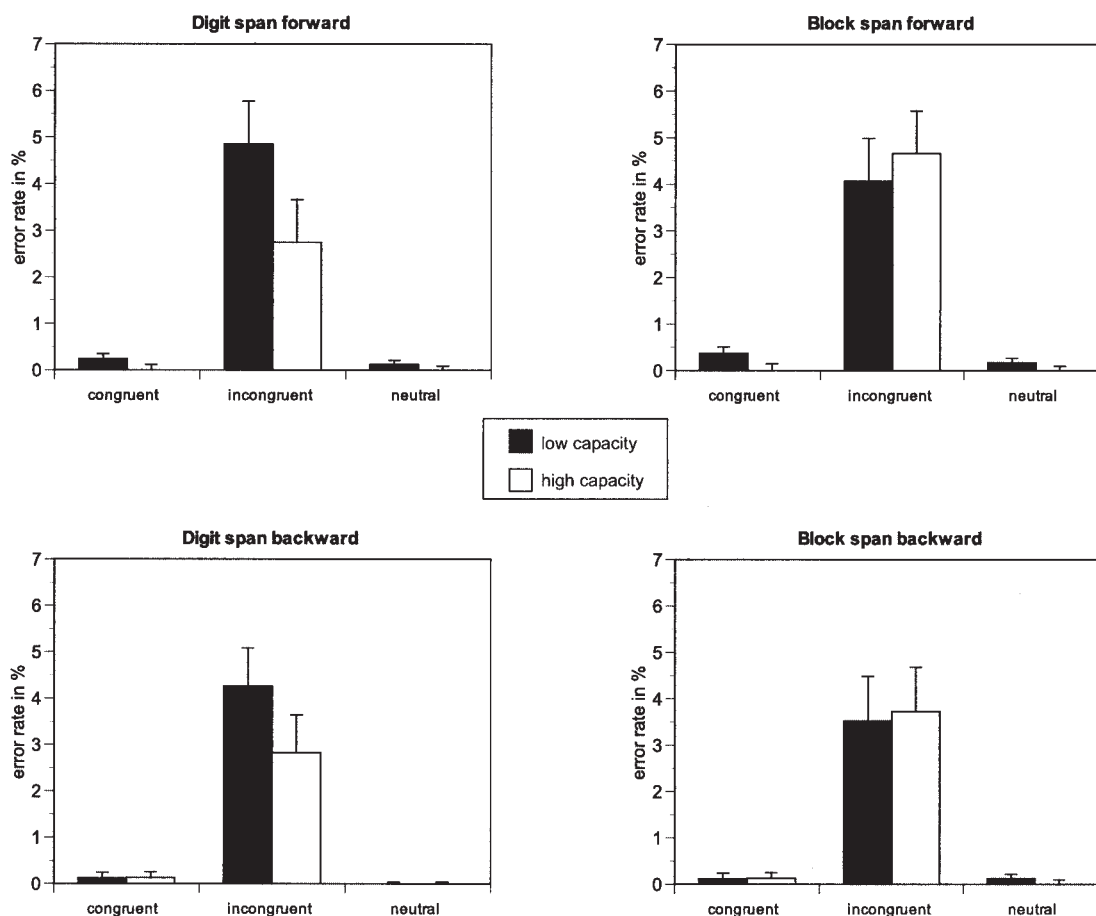


Figure 1. Stroop interference task: Error rate for color naming as a function of congruency and working memory capacity. There were nonsignificant tendencies toward group differences in the digit span extreme groups. Error bars represent the standard error of the mean.

as indicated by main effects (all $F_s > 184$, all $p_s < .01$). Reactions in congruent trials were fastest, followed by neutral trials. Reactions in incongruent trials were the slowest. In post hoc tests, the incongruent condition was significantly different from the congruent and neutral conditions for all working memory extreme memory groups (all $p_s < .01$). However, mean differences between congruent and neutral conditions reached significance in the digit span backward extreme groups ($p < .05$) and reached trend level in all other groups ($p < .07$). Thus, comparable to the ER data, interference effects on naming latency (greater RT for the incongruent than for the neutral condition) were observed for all working memory groups. Facilitation effects (faster RT for the congruent than for the neutral condition) were less reliable across groups.

Most important, magnitude of the congruency effects varied as a function of the subjects' verbal and visuospatial working memory capacity (see Figure 2 and Table 3). Congruency interacted with working memory capacity for both the digit span backward (verbal working memory), $F(2, 80) = 3.386$, $p < .05$, and the block span forward (visuospatial working memory), $F(2, 80) = 7.636$, $p < .01$, extreme groups. In the block span backward group, only a tendency toward this interaction was obtained, but as can be seen from Figure 2, the result pattern is comparable, $F(2,$

80) = 2.201, $p < .11$. Because block span extreme groups differed in age and years of education, we performed an analysis of covariance with these variables as covariates (see *Subjects* in the Method section), which confirmed the observed Working Memory Capacity \times Congruency interaction, $F(2, 76) = 4.548$, $p < .05$. A significant main effect of age, $F(1, 38) = 6.323$, $p < .05$, indicated generally slower reactions with increasing age, but there were no significant interactions of the covariates with congruency (all $F_s < 1.300$, all $p_s > .27$). Thus, it can be ruled out that the observed group differences in the congruency effect were mediated by the age and education variables.

The interactions between working memory capacity and congruency were mainly due to slower responses to incongruent trials in low- compared with high-capacity subjects, indicating a greater interference effect in the low-capacity group (see Table 3). Asterisks indicate significant between-groups differences in Figure 2. Post hoc tests showed that for the Digit Span Backward test, low-capacity subjects responded significantly slower than did high-capacity subjects in the neutral ($p < .05$) and incongruent conditions ($p < .01$). Mean RT differences between subject groups were greater in the incongruent (70 ms) than in the neutral (30 ms) condition. In the congruent condition, groups did not differ

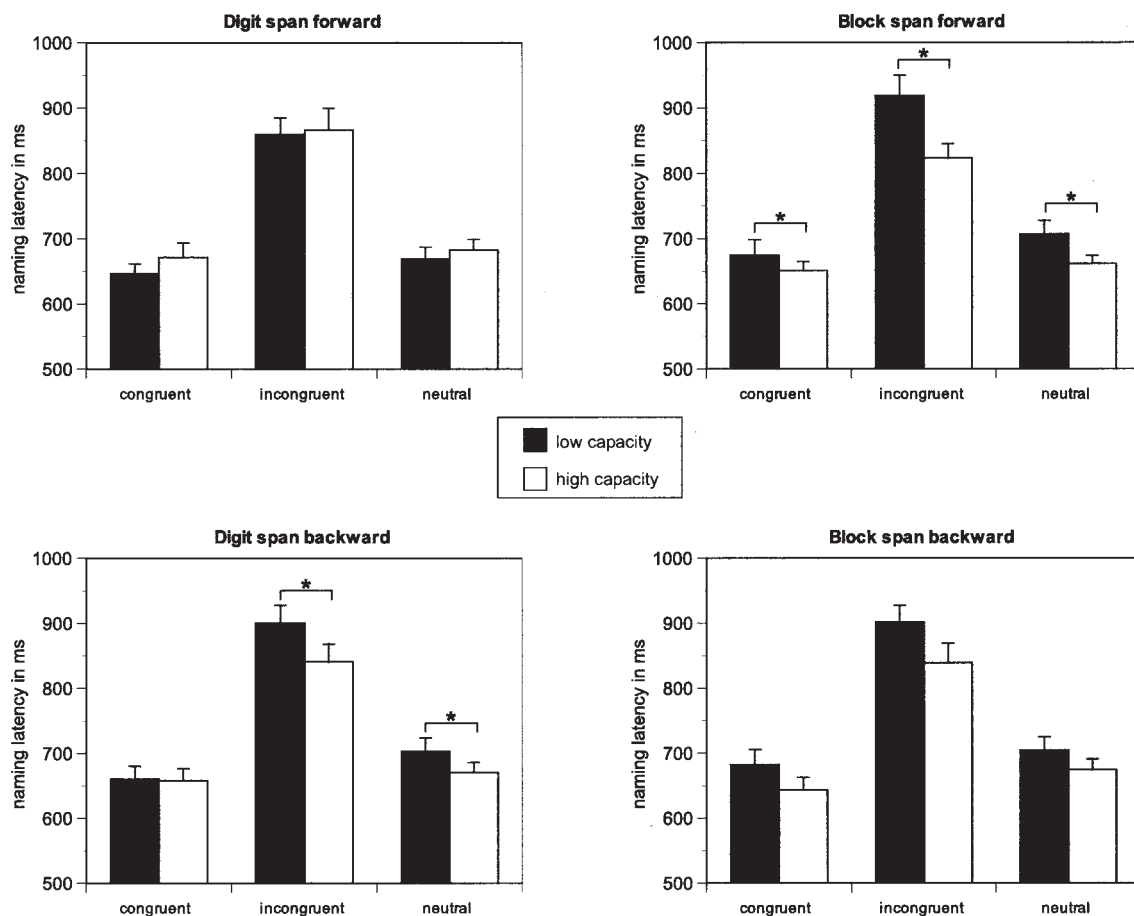


Figure 2. Stroop interference task: Color naming latency as a function of congruency and working memory capacity. Asterisks indicate significant ($p < .05$) group differences. Error bars represent the standard error of the mean.

Table 3

Results From the Extreme Group Analysis: Mean Performance for the Stroop Interference Task (Incongruent – Congruent) and for the Direct and Indirect Priming Tasks (Directly or Indirectly Related – Nonrelated) as a Function of Working Memory Capacity

Working memory group	Stroop interference (ms)	Priming (ms)			
		SOA = 200 ms		SOA = 700 ms	
		Direct	Indirect	Direct	Indirect
Digit Span Forward					
Low	213	61	46	66	42
High	195	65	24	39	19
Digit Span Backward					
Low	240	39	41	75	40
High	183	64	20	38	11
Block Span Forward					
Low	251	51	38	67	36
High	165	56	27	41	27
Block Span Backward					
Low	228	62	43	47	22
High	187	57	31	50	26

Note. Significant interactions between working memory measures and performance measures in Stroop and priming tasks are highlighted in bold. SOA = stimulus onset asynchrony.

from each other significantly. Within-group comparisons revealed that in both groups, reactions were significantly faster to the congruent and neutral conditions compared with the incongruent condition (all p s < .01). However, in the low-capacity group only, RT in the congruent condition was significantly faster than in the neutral condition (p < .05). A similar result pattern emerged for the block span forward extreme groups. Low-capacity subjects exhibited significantly slower reactions in all three congruency conditions, but between-groups RT differences were smallest in the congruent condition (45 ms; p < .05), followed by the neutral condition (71 ms; p < .01), and were greatest in the incongruent condition (132 ms; p < .01). Comparable to the results for the Digit Span test, within-group comparisons showed that in both groups, reactions were significantly faster to the congruent and neutral conditions compared with the incongruent condition (all p s < .01). In the low-capacity group only, congruent trials were associated with significantly faster reactions than were neutral trials (p < .05).

To summarize the findings from the Stroop task, subjects with low working memory capacity (verbal or visuospatial) showed greater interference effects for the incongruent condition than did subjects with high working memory capacity, because responses in the incongruent condition were significantly slower. As low-capacity subjects compared with high-capacity subjects also exhibited slower responses in the neutral condition, a facilitation effect for the congruent condition was obtained.

Direct and indirect priming. ER for the lexical decisions was generally low (less than 3%) and was therefore not further analyzed. RT analysis was based on mean RT of correct lexical decisions on the target words per condition. Responses longer than twice the individual mean were considered outliers and excluded from analysis (0.46% of the data set). Repeated measures

ANOVAs were carried out on the RT data, with semantic relatedness (nonrelated, indirectly related, and directly related words) and SOA (SOA = 200 vs. SOA = 700) as within-subject factors and working memory capacity (high- vs. low-capacity subjects) as between-subjects factors. Fisher's LSD post hoc tests were used to assess mean differences between conditions. As in the previous analysis, separate ANOVAs were performed for the different working memory extreme groups, and main effects of semantic relatedness and SOA and their mutual interactions are not reported in detail for each analysis.

Significant main effects of semantic relatedness were obtained for all working memory extreme groups: all F s(2, 80) > 36, all p s < .01. According to post hoc tests, reactions to directly related target words were significantly faster than those to indirectly related (p < .01) and nonrelated (p < .01) targets. Reactions to indirectly related targets, in turn, were faster than those to nonrelated (p < .01) targets. Thus, as priming (i.e., facilitation of a response) is defined as a positive RT difference between the nonrelated condition and any of the related conditions, we obtained both direct and indirect priming across working memory capacity extreme groups. As expected, direct priming was larger than indirect priming.

Most notably, for the digit span backward extreme group a significant three-way interaction between working memory capacity, semantic relatedness, and SOA was observed, $F(2, 80) = 4.215$, p < .05 (see Figure 3 and Table 3). This interaction was further explored with post hoc tests. At SOA = 200 ms, high-capacity subjects reacted fastest to directly related targets, which differed from indirectly related (p < .01) and nonrelated (p < .01) targets. Mean difference between indirectly related and nonrelated targets was not statistically reliable. Hence, high-capacity subjects exhibited only direct and no indirect priming. For low-capacity subjects, in contrast, mean RTs were significantly shorter for the directly related (p < .01) and indirectly related (p < .05) conditions compared with the nonrelated condition. Mean RTs in the directly related and indirectly related conditions did not differ from each other significantly. Hence, low-capacity subjects demonstrated reliable direct and indirect priming. High-capacity subjects exhibited only direct priming, which tended to be greater than that in low-capacity subjects (p = .14). At SOA = 700 ms, high-capacity subjects showed significantly shorter RTs to directly related targets than to nonrelated targets (p < .01). Mean differences in the indirectly related and nonrelated conditions were not statistically significant. As in the SOA = 200 ms condition, high-capacity subjects showed only direct and no indirect priming. For low-capacity subjects, in contrast, both direct and indirect priming were obtained again. Reactions to directly related targets were significantly faster than those to indirectly related (p < .05) and to nonrelated (p < .01) targets. Reactions to indirectly related targets, in turn, were significantly faster than those to nonrelated (p < .05) targets. As can be seen from Figure 3 and Table 3, both direct and indirect priming were larger in low- than in high-capacity subjects.

To summarize the results from the priming task, subjects with low verbal working memory capacity were susceptible to the effects of direct and indirect priming in both SOA conditions. Subjects with high verbal working memory capacity, in contrast, exhibited only direct but no indirect priming at either SOA. At SOA = 200 ms, indirect priming was greater in low- than in

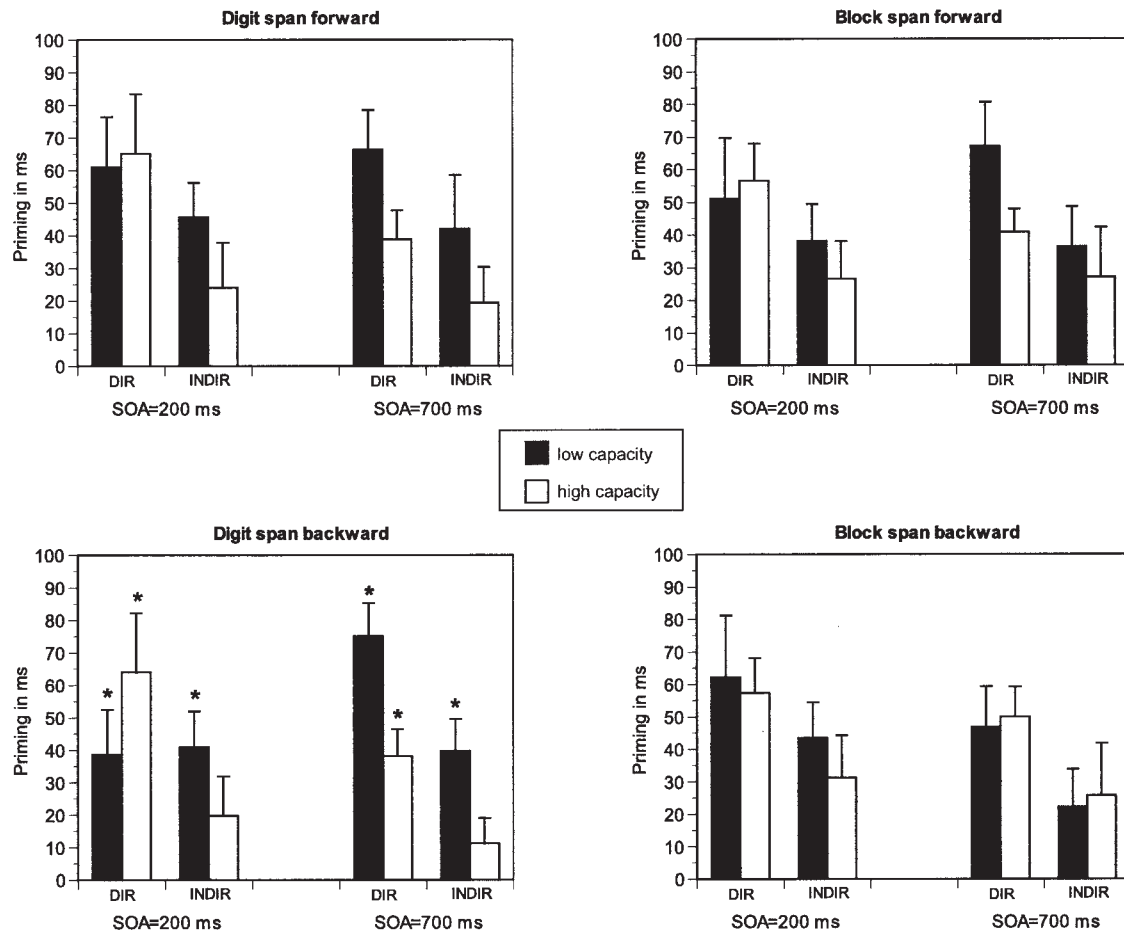


Figure 3. Direct (DIR) and indirect (INDIR) priming task: Reaction time differences between nonrelated and related conditions as a function of stimulus onset asynchrony (SOA) and working memory capacity. Asterisks indicate significant ($p < .05$) priming effects in post hoc tests for the Verbal Working Memory \times Semantic Relatedness interaction. Error bars represent the standard error of the mean.

high-capacity subjects. At SOA = 700 ms, low-capacity subjects showed both more direct and indirect priming than did high-capacity subjects.

Discussion

In the present study, we investigated the pattern of interindividual performance differences in several prefrontal tasks using a correlation and an extreme group approach. In a sample of healthy volunteers, performance in verbal and visuospatial memory span tasks was used as measures of working memory capacity. Working memory performance was compared to performance on direct and indirect priming tasks as an index of semantic retrieval and on the Stroop interference task as an index of executive control. On the basis of the assumption that working memory, executive control, and focusing of semantic retrieval share a common neural substrate in the prefrontal cortex and are functionally linked, we hypothesized that interindividual performance differences in these tasks would form a specific pattern: We predicted that low working memory capacity would be associated with increased direct and indirect priming and increased Stroop interference effects.

Our observation of significant correlations between performance measures on these prefrontal tasks is consistent with the above assumptions. Negative correlations between digit span and block span on the one hand and Stroop interference on the other hand were obtained, and low verbal and visuospatial working memory capacity was associated with increased Stroop interference. Priming measures were negatively correlated with digit span only. Subjects with low verbal working memory capacity showed increased direct and indirect priming. Furthermore, we found a positive correlation between Stroop interference and direct priming at the trend level. This pattern of interindividual prefrontal performance differences was essentially replicated in the extreme group analysis. In subjects with low digit span backward capacity in particular, indirect but also direct priming as well as Stroop interference were found to be increased, compared with subjects with high digit span backward capacity. Subjects with low block span forward capacity exhibited increased Stroop interference only. Our results demonstrate that individuals with low verbal working memory capacity (digit span) exhibit a less focused access to semantic memory and have greater difficulties in resolv-

ing a response conflict compared with high-capacity subjects. Individuals with low visuospatial working memory capacity (block span) experienced the most difficulties in conflict resolution, as demonstrated by their performance in the incongruent condition in the Stroop task. The observed association between working memory capacity and Stroop interference is in line with a previous study, in which higher Stroop interference in subjects with low working memory capacity was also obtained (Kane & Engle, 2003). However, this is the first time that the association between working memory capacity and priming has been observed.

In the extreme group analysis, in contrast to our expectations, direct priming at the short SOA tended to be increased for subjects with high verbal working memory capacity (digit span backward) compared with low capacity subjects. This tendency is puzzling because priming was found to be increased for low-capacity subjects in all other conditions, a result that was consistent with our predictions. We can offer only a tentative explanation for this unexpected finding. Possibly, the shape of the Mexican-hat-like center-surround activation function (Carr & Dagenbach, 1990), which describes the focus of spreading activation in semantic networks, varies in high-capacity subjects depending on the SOA. At a short SOA, activation of the target node (e.g., *thorn*) as well as of directly related nodes (*rose*) may be enhanced, whereas activation of indirectly related nodes (*flower*) is dumped. At a long SOA, however, only activation of the target node is enhanced, whereas activation of both directly and indirectly related nodes is dumped. This post hoc explanation could be tested in a future study by researchers using identity priming in addition to direct and indirect priming (Carr & Dagenbach, 1990) in order to capture the precise shape of the activation function.

We note that the pattern of interindividual differences in our study does not simply reflect a generalized performance deficit in low- compared with high-capacity subjects, such as slower reactions in all task conditions. The opposite is true: Low-capacity subjects reacted comparably slower in the Stroop task, particularly in the incongruent condition, but to a much lesser extent in the neutral condition. Albeit only a nonsignificant tendency, the pattern of results in error rates was comparable. Hence, low-capacity subjects have specific difficulties in overcoming response conflict. In the priming task, in contrast, they reacted comparably faster to indirectly related word pairs resulting in indirect priming effects, whereas in the high-capacity group, indirect priming was not significant. The observed pattern of greater interference and enhanced priming (i.e., facilitation) in the low-capacity groups, therefore, is not trivial and cannot be attributed to unspecific factors such as motor retardation or lack of attention. Hence, the observed interindividual differences in behavioral performance are attributable to a common neural and/or functional level of information processing. Because it is known from neuroimaging studies that all these tasks involve prefrontal areas, we suggest that functionality of a common neural substrate in the prefrontal cortex is a likely candidate for the emergence of the observed performance pattern.

Several explanations regarding the precise neurobiological mechanism underlying this pattern of prefrontal performance differences must be considered. First, prefrontal information processing may depend on the effects of neuromodulators such as the monoamines dopamine and noradrenaline. These neuromodulator systems project diffusely to neurons in prefrontal cortical areas

(Goldman-Rakic, 1987; Robbins, 2000). Through these diffuse projections, activity of these neuromodulator systems is able to exert a global influence on prefrontal functioning (Robbins, 2000). It is possible that interindividual activity of these neuromodulator systems could have mediated the observed pattern of performance differences in working memory, executive control, and semantic retrieval. Both dopamine and noradrenaline are thought to regulate the signal-to-noise ratio of information processing in prefrontal neurons (Braver & Cohen, 2000; Cohen & Servan-Schreiber, 1992; Goldman-Rakic, 1987). It has been suggested that high activity of these neuromodulators in prefrontal neurons is associated with a high signal-to-noise ratio of information processing. Low neuromodulatory activity, in contrast, results in a low signal-to-noise ratio. According to models of dopaminergic action in prefrontal neurons, a low signal-to-noise ratio is associated with decreased working memory performance, increased Stroop interference, and increased semantic priming. The performance pattern predicted by these models corresponds exactly to what we have observed in our data.

Supporting evidence for the neuromodulatory account comes from animal and human pharmacological studies (for an overview, see Robbins, 2000). Dopamine agonists have been demonstrated to improve performance in working memory and executive tasks (Kimberg, D'Esposito, & Farah, 1997; Müller, von Cramon, & Pollmann, 1998), whereas antagonists deteriorate performance (Brozoski, Brown, Rosvold, & Goldman, 1979). Furthermore, administration of L-dopa, a precursor of dopamine, to healthy subjects has been found to *decrease* indirect priming compared with results for a placebo control group, which showed strong indirect priming at the selected long SOA of 700 ms (Kischka et al., 1996). However, the relationship between dopamine availability and performance measures is far from being so simple, as high doses of dopamine agonists are associated with impaired performance (Murphy, Arnsten, Goldman-Rakic, & Roth, 1996).

Second, besides neuromodulation, structural properties of prefrontal neural networks such as local connectivity between neurons or synaptic strength could vary between individuals, resulting in interindividual differences in prefrontal functioning. Because the neural substrates of working memory, executive control, and semantic processing may partially overlap within prefrontal areas (Duncan, 2001) or may be functionally connected (Pantelis et al., 1997), the pattern of prefrontal performance differences across tasks probing different cognitive functions may emerge. Because we investigated a functional relation between performance in several prefrontal tasks at a behavioral level and did not administer pharmacological agents or use neuroimaging techniques, the neurobiological mechanisms that actually underlie observed interindividual task performance differences could not be determined.

Results from correlation and extreme group analysis showed a comparable but not entirely identical pattern of task performance. For instance, the association between indirect priming measures and Digit Span Backward measures was significant only in the extreme group analysis but not in the correlation analysis. In contrast, a significant association between Digit Span Forward and priming measures was observed only in the correlation analysis. However, if one also considers effects at the trend level, both forms of analyses yield an almost identical pattern of associations. It should be noted that correlation and extreme group analysis have their specific limitations and should be considered complementary.

For instance, the magnitude of correlations strongly depends on the amount of variance in each variable. The small range of working memory span measures—from three to nine (Digit Span) and from two to eight (Block Span)—limits the variability in the data set and therefore constrains the magnitude of correlations for methodical reasons. In contrast, in an extreme group analysis, inverted U-shaped relations between variables cannot be detected, although correlation analysis still can capture the linear part of such relations.

Correlation and extreme group analysis revealed a statistically reliable association only between a subset of measures for task performance. A significant relation between priming measures and working memory was found only for verbal working memory tasks (Digit Span), whereas Stroop interference effects were related to both verbal (Digit Span Backward) and visuospatial working memory capacity (Block Span Forward and Backward) tasks. The relations between particular working memory measures with priming measures and Stroop interference could be due to differential patterns of hemispheric dominance of the tasks. As described in the introduction, verbal working memory and focused access to semantic memory draw predominantly on left prefrontal areas, whereas conflict resolution during Stroop interference involves the prefrontal cortex bilaterally, and visuospatial working memory exhibits a right hemisphere preponderance. However, because the block span forward extreme group shows numerically a similar pattern as the digit span groups, the present data do not support a clear-cut dissociation between verbal and visuospatial working memory domains.

The same argument applies to the findings for the Digit Span Forward measure, which exhibit a similar pattern as for the Digit Span Backward measure, although correlations were smaller and results in the extreme group analysis were not significant. There is evidence from neuroimaging studies that the Digit Span Forward task, which mainly requires maintenance but to a less extent manipulation of information, has been found to recruit the ventrolateral but not the dorsolateral prefrontal cortex (Owen, 2000). Comparable with the present results is the research by Conway, Cowan, Bunting, Theriault, and Minkoff (2002), who observed a link only between general intelligence and the executive control component of working memory, which both recruit the dorsolateral prefrontal cortex (Duncan et al., 2000). They failed to find a link between general intelligence and the maintenance subcomponent. Probably, the magnitude of overlap in the processes and in their neural substrates determines the strength of correlation between two tasks or functions.

The performance pattern of the healthy subjects with low working memory capacity in the present study strongly resembles the pattern found in patients with schizophrenia. In schizophrenia, cognitive deficits have been related to dysfunction of the prefrontal cortex and/or dysfunctional activity of the prefrontal dopamine system. Schizophrenic patients, who are impaired in working memory (e.g., on Digit Span and Delayed Response measures; Kiefer et al., 2002; Park & Holzman, 1992; Spitzer, 1993) and executive functions (e.g., Stroop interference, Wisconsin Card Sorting Test, and Go/NoGo; Goldberg, Weinberger, Berman, Pliskin, & Podd, 1987; Hepp et al., 1996; Weisbrod et al., 2000) show low activity of the prefrontal dopamine system (e.g., Dolan et al., 1995) and hypoactivation in prefrontal areas (e.g., Berman et al., 1992; Weisbrod et al., 2000), although altered activation in the

superior temporal lobe has also been reported (Kubicki et al., 2003). In fact, deficits in working memory and executive tasks have been considered to be the core neuropsychological deficits in schizophrenia (Frith, 1992; Morice & Delahunty, 1996). In addition, patients with schizophrenia also exhibit increased direct and indirect priming (e.g., Spitzer et al., 1993). Although these patients are impaired in neuropsychological tests probing executive control functions, similar to neuropsychological patients with prefrontal lesions (Morice & Delahunty, 1996), the latter have never been investigated with the direct and indirect priming paradigm. Therefore, it remains an open question whether patients with prefrontal lesions would also show increased priming. These parallel findings on cognitive performance in our low working memory capacity subjects on the one hand and in schizophrenic and prefrontal patients on the other hand is remarkable insofar as our subjects did not report any psychiatric or neurologic symptoms. Our results demonstrate that at least some prefrontal performance patterns are not specific for psychiatric and neurologic disorders but can also be observed within a part of the nonclinical population, that is, in subjects with low working memory capacity. This suggests that characteristics of information processing in prefrontal cortical networks vary interindividually, suggesting a continuum of cognitive functioning. In support of this view is research showing a reduction of prefrontal information processing capacity by an additional working memory load in healthy subjects resulting in aphasic-like performance in the comprehension of complex sentences (Miyake, Carpenter, & Just, 1994).

The present findings have important implications for the neuropsychology of prefrontal functions. First, they demonstrate that prefrontal task performance varies interindividually in healthy subjects, forming a specific pattern. Performance in prefrontal tasks is not only functionally related between working memory and executive control, as shown previously (Kane & Engle, 2002, 2003), but also extends to semantic memory retrieval. Several models of prefrontal function propose that working memory capacity and executive control are functionally and neuroanatomically related, if not identical (Braver & Cohen, 2000; Duncan, 2001; Kane & Engle, 2002). It is assumed that the prefrontal cortex supports active manipulation of information by using context information (e.g., a task-relevant goal) and interference blocking of competing information. These processes are typically thought to be applied in working memory and executive tasks, such as the working memory span or the Stroop tasks. It is possible that similar processes are also involved in semantic retrieval in order to focus activation in semantic networks to the target node. Focusing retrieval affords blocking interference from activated, semantically related nodes (see the center-surround mechanism in semantic retrieval suggested by Carr & Dagenbach, 1990), a mechanism quite similar to that proposed to operate in working memory and executive tasks. The assumption of a common mechanism underlying focusing semantic retrieval and executive control is supported by the fact that in the present study, Stroop interference and priming exhibited a positive correlation.

Second, the tasks of the present study not only probe different prefrontal functions (working memory, executive control, and semantic memory retrieval) but also tap into different kinds of processes. Whereas the working memory span and the Stroop interference tasks involve effortful, controlled processing mechanisms (Posner & Snyder, 1975), priming, particularly at

a short SOA of 200 ms, reflects automatic processing mechanisms (Neely, 1991). Hence, our results suggest that the prefrontal cortex is not specifically the neural substrate for controlled processing but also modulates automatic processes. Third, bearing more on methodological issues in neuropsychological studies, the demonstrated pattern of prefrontal performance differences in healthy volunteers requires a careful assessment of subjects serving as healthy controls for patient groups. For instance, if the control group comprises predominantly subjects with low working memory capacity, possible existent deficits in the patient group in the focus of semantic memory access or in conflict resolution could be masked. On the basis of the present results, it may be important to assess working memory capacity in studies of prefrontal functions, even if working memory is not the cognitive function of interest.

In conclusion, our study demonstrates that prefrontal functions vary interindividually in healthy volunteers, forming patterns of performance differences. Subjects with low working memory capacity exhibited increased Stroop interference and increased semantic priming. These findings show that not only working memory and executive function, but also seemingly heterogeneous prefrontal functions such as working memory and semantic retrieval, are functionally related to some extent.

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