

Cognition and Neurosciences

Neural correlates of variable working memory load across adult age and skill: Dissociative patterns within the fronto-parietal networkLARS NYBERG,^{1,2,3} ERIKA DAHLIN,^{1,2,3} ANNA STIGSDOTTER NEELY⁴ and LARS BÄCKMAN⁵¹*Integrative Medical Biology (Physiology section), Umeå University, Umeå*²*Radiation Sciences (Diagnostic Radiology), Umeå University, Umeå*³*Umeå Center for Functional Brain Imaging (UFBI), Umeå*⁴*Department of Psychology, Umeå University, Umeå*⁵*Aging Research Center, Karolinska Institutet, Stockholm*

Nyberg, L., Dahlin, E., Stigsdotter Neely, A. & Bäckman, L. (2009). Neural correlates of variable working memory load across adult age and skill: Dissociative patterns within the fronto-parietal network. *Scandinavian Journal of Psychology*, 50, 41–46.

We examined neural changes related to variations in working memory load by using an *n*-back task with three levels and functional magnetic resonance imaging. Younger adults were divided into high- and low-performing groups (Young-High; Young-Low) and compared with older adults. Relative to Young-High, capacity-constraints in working memory were apparent between load 1–2 for the elderly and between load 2–3 for Young-Low. Capacity-constraints in neural activity followed this pattern by showing a monotonically increasing response in parietal cortex and thalamus for Young-High, whereas activity leveled off at 1-back for the elderly and at 2-back for Young-Low. The response in dorsal frontal cortex followed a similar pattern with the addition that the magnitude of activation differed within capacity limitations (Old > Young at 1-back; Young-Low > Young-High at 2-back). These findings indicate that an important determinant of WM capacity is the ability to keep the frontal cortex adequately engaged in relation to current task demands.

Key words: fMRI, working memory load, capacity-constraints.

Lars Nyberg, Department of Integrative Medical Biology, Umeå University, SE-90187, Sweden. E-mail: lars.nyberg@physiol.umu.se

Working memory (WM) has been defined as a system of limited capacity that is crucial for the temporary storage and manipulation of information (Baddeley, 2000). The neural basis for capacity limitations in WM has attracted much interest. Functional neuroimaging findings from studies with children (Klingberg, Forsberg & Westerberg, 2002), younger adults (Braver, Cohen, Nystrom, Jonides, Smith & Noll, 1997; Callicott, Mattay, Bertolino *et al.*, 1999; Linden, Bittner, Muckli *et al.*, 2003), older adults (Mattay, Fera, Tessitore *et al.*, 2006), and schizophrenic patients (Jansma, Ramsey, van der Wee & Kahn, 2004), as well as individual-difference (Osaka *et al.*, 2003, 2004; Vogel, McCollough & Machizawa, 2005) and training (Olesen, Westerberg & Klingberg, 2004) research relate capacity limits in WM to multiple brain loci, notably in fronto-parietal areas.

In several studies, WM capacity has been examined by manipulating load in some version of the running span or *n*-back task (Cohen, Perlstein, Braver *et al.*, 1997). The basic idea is to determine how brain activity is changing as a function of parametric manipulations of *n* (e.g., 1, 2, or 3 back). The two major mapping functions reflect (i) capacity-unconstrained responses (Fig. 1a), where brain activity increases linearly as a function of increasing load, and (ii) capacity-constrained responses (Fig. 1b), where brain activity increases up to a certain level and then decreases (typically an increase from 1-back to 2-back and no increase (similar or decreasing level) from 2-back to 3-back).

An unresolved issue concerns the exact mapping between WM load and regional brain activity. In some early studies, brain activity in dorsolateral prefrontal cortex (DLPFC; Braver *et al.*, 1997) and parietal cortex (Braver *et al.*, 1997; Cohen *et al.*, 1997) followed a capacity-unconstrained (monotonically increasing) response across load. However, in a subsequent study (Callicott *et al.*, 1999), activity in DLPFC as well as parietal cortex followed a capacity-constrained response, with brain activity decreasing from 2- to 3-back. In still another study (Linden *et al.*, 2003), there was a capacity-unconstrained response in DLPFC, whereas activity in various parietal and posterior frontal (e.g. SMA) regions followed a capacity-constrained function. To further complicate matters, a recent study reported that the mapping function between load and brain activity differs between younger and older adults (Mattay *et al.*, 2006). Specifically, in dorsal frontal cortex older adults showed greater activation than younger adults at low WM load. At higher load the pattern was reversed due to a monotonic decreasing trend for older adults along with an opposite tendency for younger adults (Fig. 1c).

A capacity-constrained response in parietal cortex (Callicott *et al.*, 1999; Linden *et al.*, 2003) is consistent with findings that parietal regions constitute a key neural locus of capacity limitations in WM (Todd & Marois, 2004). Activity in specific frontal regions may reflect compensatory responses (Persson, Nyberg, Lind *et al.*, 2006), with relative over-activation when WM load

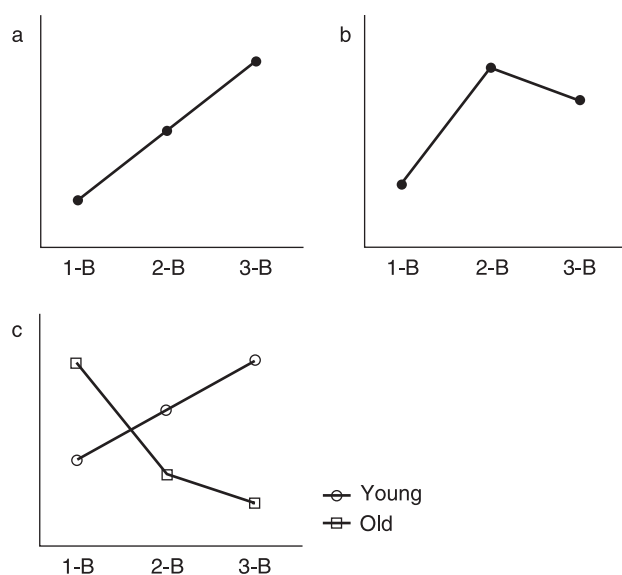


Fig. 1. Manipulations of n in n -back working memory tasks have revealed both capacity-unconstrained responses (a) and capacity-constrained responses (b) in brain-activity changes. The mapping function between load and brain activity typically differs between younger and older adults (c), with older adults showing greater activation than younger at low load with a reversed pattern at higher load.

is still within but approaching capacity limitations, and a leveling off or drop in activity levels as capacity limitations are exceeded (Mattay *et al.*, 2006).

In the present functional magnetic resonance imaging (fMRI) study, we included a n -back task with three levels of load (1-2-3) and compared three groups of participants that differed with regard to levels of performance at higher levels of load when capacity was heavily taxed: (1) a high-capacity young group (Young-High), (2) a young group with lower capacity (Young-Low), and (3) a group of older adults that had the lowest capacity (Old). On the basis of the hypothesized relation between fronto-parietal activity and WM capacity constraints outlined above, activity in the parietal cortex was predicted to follow a capacity-unconstrained response in the Young-High group and show signs of constraints between 1- and 2-back for Old and between 2- and 3-back for Young-Low. A similar pattern was predicted for posterior parts of frontal cortex with the additional expectation that the magnitude of activation would differ within capacity limitations such that Old > Young at 1-back and Young-Low > Young-High at 2-back.

METHODS

Participants

Young participants were recruited through e-mail to students at Umeå University, Sweden, and older participants were recruited through newspaper advertisements in a local daily newspaper. All participants reported being in good physical and mental health, not colour blind, and right handed. A median-split based on 3-back performance divided the sample of younger adults into Young-High ($N = 11$) and Young-Low ($N =$

Table 1. Subject characteristics ($M \pm SD$)

	Young-High	Young-Low	Old
Female/Male	6/5	4/7	9/2
Age	23.64 (2.91)	23.55 (2.12)	68.82 (1.47)
Years of education	13.36 (1.40)	13.46 (1.06)	14.96 (2.43)
Depression ^a	3.45 (3.24)	4.36 (3.23)	3.91 (2.34)
Verbal ability ^b	22.27 (3.58)	21.91 (2.63)	24.91 (3.65)
Mental status ^c	29.09 (0.70)	29.09 (1.04)	28.91 (0.70)

^a Beck Depression Inventory (BDI; Beck & Steer, 1996).

^b SRB1 (Dureman & Sälde, 1959), maximum score = 30.

^c Mini-Mental State Examination (Folstein *et al.*, 1975).

11) group. The Old group ($N = 11$) was selected such that all participants performed below the level of all individuals in the Young-High group in 3-back. Participant characteristics are presented in Table 1. The study was approved by the ethics committee of Umeå University. All participants were informed about the purpose of the investigation and their right to terminate participation at any point in time, and gave written informed consent to participate.

Procedure and task

Participants received instructions on the n -back task before entering the scanner. During scanning, they viewed stimuli on a screen via a mirror mounted on a head coil. Stimuli were presented in white on a black background using the E-prime 1.1 software (Psychology Software Tools, PA, USA), which also recorded behavioral performance. The n -back task consisted of 27 lists; nine 1-back lists, nine 2-back lists and nine 3-back lists in random order (Callicott *et al.*, 1999). The lists consisted of 10 items (digits between 1–9) and each item was presented for 1.5 s with a cross presented for 0.5 s between each item. A baseline cross was presented for 20.0 s after every 9th list. Subjects indicated whether or not each item in the list matched an item that occurred one, two, or three items back. To respond, participants used their right hand (index finger = “Yes”; middle finger = “No”). The number of correct yes-responses was used as the dependent measure due to higher load differentiation between correct yes-responses compared to correct no-responses (Table 2; Verhaeghen & Basak, 2005). As there were four possible correct yes-responses per list, the maximum score was 36. In the calculation of reaction times only correct responses were included, and in the calculation of load cost and SD only correct yes-responses were included.

fMRI data acquisition

Images were acquired using a 1.5 T Philips Intera scanner (Philips Medical Systems, Netherlands). Functional T2*-weighted images were obtained with a single-shot gradient echo EPI sequence used for blood oxygen level dependent imaging. The sequence had the following parameters: repetition time: 3,000 ms (33 slices acquired), echo time: 50 ms, flip angle: 90°, field of view: 22 × 22 cm, 64 × 64 matrix and 4.4 mm slice thickness. Five dummy scans were performed prior to the image acquisition to eliminate signals arising from progressive saturation. After acquisition, the images were transferred to a PC and converted to Analyze format.

Statistical analyses

Functional images were analyzed with Statistical Parametric Mapping Software (SPM2, <http://www.fil.ion.ucl.ac.uk/spm>; Wellcome Department of Imaging Neuroscience, London, UK) implemented in Matlab 7.1 (Mathworks Inc., MA, USA). All images were corrected for slice

Table 2. *n*-back performance (*M* ± *SD*)

	Young-High	Young-Low	Old
Correct Yes 1-back	34.73 (1.90)	33.09 (2.21)	29.82 (3.87)
Correct Yes 2-back	33.45 (2.62)	31.27 (3.20)	26.36 (3.78)
Correct Yes 3-back	28.82 (4.64)	24.36 (1.86)	21.91 (3.62)
Correct No 1-back	51.55 (3.33)	52.09 (1.45)	47.55 (8.87)
Correct No 2-back	52.18 (4.09)	51.73 (2.28)	47.09 (8.24)
Correct No 3-back	51.36 (4.95)	50.55 (3.70)	45.82 (9.46)
FA 1-back	0.64 (1.03)	1.36 (1.21)	4.27 (8.75)
FA 2-back	0.64 (1.21)	1.82 (2.18)	4.64 (7.35)
FA 3-back	0.91 (1.14)	3.09 (3.65)	5.64 (8.86)
RT 1-back (ms)	682.00 (45.13)	665.53 (70.64)	899.91 (119.31)
RT 2-back (ms)	745.64 (104.05)	745.69 (99.48)	936.94 (114.56)
RT 3-back (ms)	795.05 (106.16)	818.75 (92.27)	936.17 (125.63)
Load cost 1-back – 2-back (%)	3.69	5.50	11.60
Load cost 2-back – 3-back (%)	13.84	22.10	16.88
Load cost 1-back – 3-back (%)	17.02	26.38	26.53
<i>SD</i> 1-back – 2-back	0.57	0.67	0.90
<i>SD</i> 2-back – 3-back	1.28	2.73	1.20

timing, realigned and unwarped, normalized to standard anatomical space defined by the MNI atlas (SPM2), and smoothed using an isotropic 8.0 mm FWHM Gaussian filter kernel. Statistical analyses were performed on a voxel-by-voxel basis by modeling the active and baseline conditions convolved with the hemodynamic response function. Applying the general linear model to the data resulted in least-square estimates for each participant. The individual contrast images were then used for random-effects group analyses.

To identify regions with a load-sensitive pattern of activation, we used a conjunction approach asserting that all contrasts involved were individually significant at the predefined threshold (Nichols, Brett, Andersson, Wagner & Poline, 2005). The conjunction analysis included [3-Back – 1-Back] and [1-Back – rest] and was thresholded at $p < 0.005$ uncorrected (cluster size > 10 voxels). All 22 young individuals were included. We determined load-sensitive regions for young only in order to establish a form of “baseline patterns” against which age-related changes could be compared. To compare the three groups, ANOVAs with repeated measure on the last factor were computed on data from the local maxima from the regions showing a load-sensitive pattern. Visualization of significant effects on brain templates and histogram plots were done using in-house developed software (*DataZ*).

RESULTS

Behavioral performance

Performance on the *n*-back task is presented in Fig. 2. A 3 (Group: Young-High, Young-Low, Old) × 3 (Load: 1, 2, 3) mixed ANOVA revealed main effects of group ($F_{2,30} = 29.02$, $MS_{\text{error}} = 13.40$, $p < 0.001$), and load ($F_{2,60} = 81.91$, $MS_{\text{error}} = 6.02$, $p < 0.001$), as well as a significant group by load interaction ($F_{4,60} = 3.55$, $MS_{\text{error}} = 6.02$, $p = 0.012$). Follow-up 2 × 2 ANOVAs showed that there was a significant drop in performance for the Old group relative to the Young-High group between 1- and 2-back ($F_{1,20} = 4.47$, $MS_{\text{error}} = 4.57$, $p < 0.05$), whereas the corresponding analysis for the Young-Low versus Young-High groups did not reveal a significant effect ($F_{1,20} = 1.24$, $MS_{\text{error}} = 5.92$, $p = 0.28$). By contrast, a significant difference emerged between the two young groups between 2- and 3-back ($F_{1,20} = 7.25$, $MS_{\text{error}} = 4.29$,

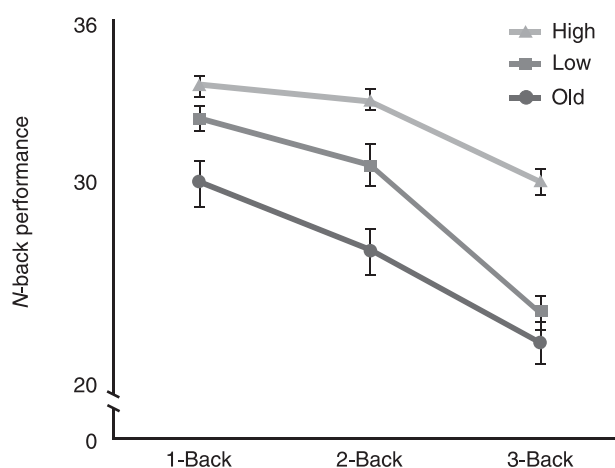


Fig. 2. All groups showed a decrease in number of correct yes-responses as a function of load, but the functions varied. Error-bars represent standard errors around the means.

$p < 0.05$). Further, the drop in performance between 1-back and 2-back for the older adults was close to 1 *SD* (Table 2), but considerably lower for the younger groups. This pattern suggested that capacity was heavily taxed already at 1-back for the elderly. Between 2-back and 3-back the Young-Low showed a much more pronounced drop relative to Young-High. On the basis of these behavioral results and calculated load costs (Table 2), capacity constraints in neural activity were predicted to appear between 1- and 2-back for the Old group and between 2- and 3-back for the Young-Low group.

Brain activity

In keeping with previous observations, the analysis of the fMRI data revealed a distributed set of brain regions where brain activity increased as a function of load (Fig. 3, Table 3). Fronto-parietal

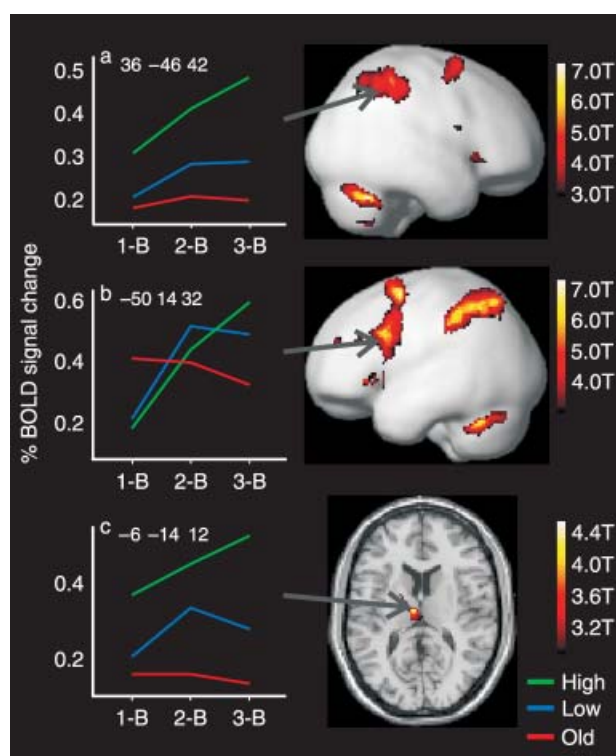


Fig. 3. A conjunction analysis ([3-back – 1-back] AND [1-back – rest]) identified regions with a load-sensitive activation pattern in fronto-parietal and sub-cortical areas. For the Young-High group, brain activity increased as a function of load, indicating capacity unconstrained responses. In a right inferior parietal region (a) a capacity constrained response was seen for the Old group between 1- and 2-back and for the Young-Low group between 2- and 3-back. A left frontal area (b) revealed a response pattern where the Old group showed greater activation at the lowest load level compared to both younger groups, although they exhibited activity decreases with increasing load. A capacity constraint response was seen for the Young-Low group between 2- and 3-back. In thalamus (c) a capacity constrained response was again seen between 1- to 2-back for the Old group and between 2- and 3-back for the Young-Low group.

regions were part of this activation pattern. The brain regions where load dependent group differences in activation were found are further analyzed below.

Several of the parietal regions showed a capacity-unconstrained response for the Young-High group, along with signs of constraints for the Young-Low and Old groups. A significant group difference was found for a right inferior parietal region (Fig. 3a), where a 3 (Group: Young-High, Young-Low, Old) \times 3 (Load: 1, 2, 3) mixed ANOVA revealed a significant interaction ($F_{4,60} = 2.95$, $MS_{\text{error}} = 0.006$, $p < 0.05$). Subsequent analyses showed that the capacity constraint was apparent already between load 1 and 2 for the Old group [2 (Group: Old, Young) \times 2 (Load: 1, 2) ANOVA $F_{1,31} = 3.28$, $MS_{\text{error}} = 0.004$, $p = 0.08$; 2 (Group: Old, Young-High) \times 2 (Load: 1, 2) ANOVA $F_{1,20} = 3.88$, $MS_{\text{error}} = 0.004$, $p = 0.06$], and between load 2 and 3 for both the Old and the Young-Low group [2 (Group: Old and Young-Low, Young-High) \times 2 (Load: 2, 3) ANOVA $F_{1,31} = 5.07$, $MS_{\text{error}} = 0.004$, $p < 0.05$].

Table 3. Brain areas showing general activity increases as a function of load

Region of activation	Peak-coordinates
L Frontal lobe	-50 14 32 -6 14 50 -6 8 64 -26 2 60 -54 12 18 -30 14 28 -32 26 -2
R Frontal lobe	24 8 66 26 -2 54
L Parietal lobe	-32 -56 48 -24 -68 56 -46 -42 48 -42 -52 52 -42 -36 38
R Parietal lobe	44 -42 54 40 -52 52 52 -34 50 30 -60 54 36 -46 42
Cerebellum	0 -72 -20
L Cerebellum	-38 -58 -32 -32 -66 -28 -38 -74 -30
R Cerebellum	8 -78 -22 34 -58 -32 40 -66 -30
L Thalamus	-6 -14 12
R Caudate	18 8 14

Of the frontal regions, the predicted pattern was observed in a left precentral region (Fig. 3b). At this site, the Young-High showed a capacity-unconstrained response whereas the Old group showed a decrease in activity with increasing load. Critically, in keeping with prior findings (Mattay *et al.*, 2006), at the lowest load level the Old group showed significantly greater activation than both young groups [$t(31) = -2.10$, $p < 0.05$]. For Young-Low, a capacity constraint was evident as a significant group by load interaction for loads 2 and 3 [2 (Group: Young-Low, Young-High) \times 2 (Load: 2, 3) ANOVA $F_{1,20} = 6.30$, $MS_{\text{error}} = 0.01$, $p < 0.05$]. As can be seen from Fig. 3b, indicative of a compensatory response, the Young-Low showed greater frontal activation at Load 2 but this difference failed to reach significance ($t(20) = 0.60$, $p > 0.10$).

In addition to these fronto-parietal sites, a group by load interaction was observed in the left thalamus (Fig. 3c). This region showed a similar pattern as the parietal region, with a capacity-unconstrained response for Young-High and a constraint at a lower load (1-back) for Old [2 (Group: Young, Old) \times 2 (Load: 1, 2) ANOVA $F_{1,31} = 4.12$, $MS_{\text{error}} = 0.01$, $p < 0.05$] and at a higher load (2-back) for Young-Low [2 (Group: Young-Low, Young-High) \times 2 (Load: 2, 3) ANOVA $F_{1,20} = 7.20$, $MS_{\text{error}} = 0.006$, $p < 0.05$].

DISCUSSION

The present findings support and extend previous reports on how brain activity in frontal and parietal regions during WM performance is influenced by load and individual-differences in capacity. The behavioral results confirmed that the load manipulation was effective in inducing capacity constraints, but the magnitude of decline, and hence the WM load at which the capacity was heavily taxed, differed across groups. Specifically, in comparison to the Young-High group, the Old group showed signs of decline already between 1- and 2-back and the Young-Low group showed a significant performance drop between 2- and 3-back.

The fMRI analyses revealed a neural correlate of the group by capacity constraint in WM within inferior parietal cortex. That is, whereas inferior parietal activity continued to increase as a function of how much information had to be retained in WM for the Young-High group, activity leveled off as a function of capacity for the Old (at 1-Back) and Young-Low (at 2-Back) groups. This finding is in agreement with previous proposals that the parietal cortex is a key neural locus of capacity limitations in WM (Todd & Marois, 2004). In addition, in keeping with some previous observations (Callicott *et al.*, 1999), the results suggested a capacity-constrained response also in the thalamus.

The activation pattern in a dorsal frontal region also adhered to a capacity-constrained response function. However, there was a critical difference in activation magnitude between the frontal response pattern and that seen in parietal cortex and thalamus. Specifically, in the parietal cortex and thalamus, the magnitude of activity corresponded to the behavioral data at all three load levels (Young-High > Young-Low > Old), with a magnification of group differences in magnitude as a function of load. By contrast, in the frontal region, the magnitude of activation differed within capacity limitations such that Old > Young at 1-back and Young-Low > Young-High at 2-back. This observation is consistent with recent findings by Mattay and colleagues (2006). They suggested that greater frontal activity may reflect dynamic reallocation of resources to maintain task performance, possibly in response to suboptimal dopaminergic signaling (Backman, Nyberg, Lindenberger, Li & Farde, 2006).

A recent study found that fronto-striatal activity was significantly related to working-memory capacity and influenced load-dependent activity in parietal cortex (McNab & Klingberg, 2008). That finding was based on an individual-difference analysis of younger adults, indicating that a similar control mechanism could account for the current differences within the group of young subjects. Indeed, the frontal region where a load effect was observed in the present study was in close proximity to the middle frontal activity reported by McNab and Klingberg (2008). Moreover, we observed a general load-effect in the caudate nucleus, and a *post-hoc* analysis revealed a load effect for younger but not older adults in this region (Fig. 4). Thus, the differences between the young groups could be explained in terms of variability in the effectiveness of fronto-striatal control over encoding and/or updating (O'Reilly, 2006) in working memory, and additional changes in the old group could reflect age-related changes in

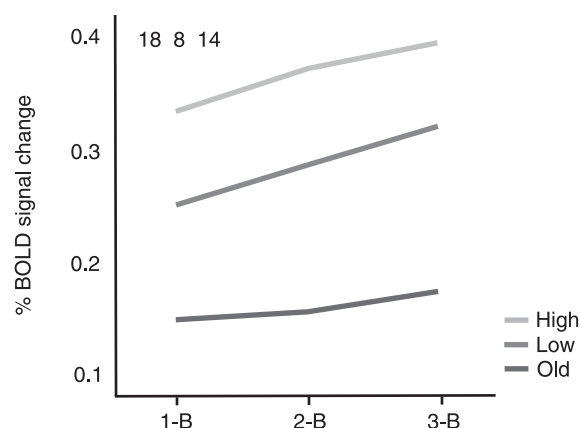


Fig. 4. Capacity constrained activity response in right caudate nucleus ($x, y, z = 18, 8, 14$). There was a significant load effect for younger ($p < 0.01$) but not older ($p > 0.50$) subjects, although the age group by load interaction failed to reach significance ($p > 0.10$).

basal ganglia regions (Buckner, 2004) which would be consistent with our recent findings of age-related striatal changes related to training and transfer following updating training (Dahlin, Stigsdotter Neely, Larsson, Bäckman & Nyberg, 2008).

Taken together, the observed pattern of fronto-parietal cortical and subcortical responses in relation to changes in working memory load is consistent with previous observations (e.g., Sakai, Rowe & Passingham, 2002; Sommer & Wurtz, 2006), and along with the age-related changes it fits the notion that prefrontal cortex precedes the parietal cortex in cognitive control (Brass, Ullsperger, Knoesche, von Cramon & Phillips, 2005). Specifically, an important determinant of WM capacity is the ability to keep the frontal cortex adequately engaged (Goldberg, Berman, Fleming *et al.*, 1998; Mattay *et al.*, 2006), and when capacity is exceeded the frontal response declines. By this view, task-specific training should be expected to lead to reduced frontal activity if the task is within capacity limits already before training, but to increased activity if capacity is constrained prior to training (better able to keep the frontal cortex engaged after training). Recent findings from studies of younger and older adults support this prediction (Dahlin *et al.*, 2008). Future studies should attempt to hold performance constant across age groups in order to clearly separate the influences of performance level and chronological age (Nagel, Preuschhof, Li *et al.*, 2008).

This study was supported by grants from the Swedish Research Council and the Joint Committee for Nordic Research Councils for the Humanities and the Social Sciences (NOS-HS) to Lars Nyberg for a Nordic Center of Excellence in Cognitive Control.

REFERENCES

- Backman, L., Nyberg, L., Lindenberger, U., Li, S.-C. & Farde, L. (2006). The correlative triad among aging, dopamine, and cognition: Current status and future prospects. *Neuroscience & Biobehavioral Reviews*, 30(6), 791–807.

- Baddeley, A. (2000). The episodic buffer: A new component of working memory? *Trends in Cognitive Sciences*, 4(11), 417–423.
- Beck, A. T. & Steer, R. A. (1996). *Beck Depression Inventory Manual, Swedish version*. Stockholm: PsykoFörlaget AB.
- Brass, M., Ullsperger, M., Knoesche, T. R., von Cramon, D. Y. & Phillips, N. A. (2005). Who comes first? The role of the prefrontal and parietal cortex in cognitive control. *Journal of Cognitive Neuroscience*, 17(9), 1367–1375.
- Braver, T. S., Cohen, J. D., Nystrom, L. E., Jonides, J., Smith, E. E. & Noll, D. C. (1997). A parametric study of prefrontal cortex involvement in human working memory. *NeuroImage*, 5(1), 49–62.
- Buckner, R. L. (2004). Memory and executive function in aging and AD: Multiple factors that cause decline and reserve factors that compensate. *Neuron*, 44(1), 195–208.
- Callicott, J. H., Mattay, V. S., Bertolino, A., Finn, K., Coppola, R., Frank, J. A., et al. (1999). Physiological characteristics of capacity constraints in working memory as revealed by functional MRI. *Cerebral Cortex*, 9(1), 20–26.
- Cohen, J. D., Perlstein, W. M., Braver, T. S., Nystrom, L. E., Noll, D. C., Jonides, J., et al. (1997). Temporal dynamics of brain activation during a working memory task. *Nature*, 386(6625), 604–608.
- Dahlin, E., Stigsdotter Neely, A., Larsson, A., Bäckman, L. & Nyberg, L. (2008). Transfer of learning after updating training mediated by the striatum. *Science*, 320(5882), 1510–1512.
- Dureman, I. & Sälde, H. (1959). *Psychometric and experimental-psychological methods for clinical application (In Swedish)*. Uppsala: Almqvist & Wiksell.
- Folstein, M. F., Folstein, S. E. & McHugh, P. R. (1975). “Mini-mental state.” A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, 12(3), 189–198.
- Goldberg, T. E., Berman, K. F., Fleming, K., Ostrem, J., Van Horn, J. D., Esposito, G., et al. (1998). Uncoupling cognitive workload and prefrontal cortical physiology: A PET rCBF study. *NeuroImage*, 7(4), 296–303.
- Jansma, J. M., Ramsey, N. F., van der Wee, N. J. A. & Kahn, R. S. (2004). Working memory capacity in schizophrenia: a parametric fMRI study. *Schizophrenia Research*, 68(2–3), 159–171.
- Klingberg, T., Forssberg, H. & Westerberg, H. (2002). Increased brain activity in frontal and parietal cortex underlies the development of visuospatial working memory capacity during childhood. *Journal of Cognitive Neuroscience*, 14(1), 1–10.
- Linden, D. E. J., Bittner, R. A., Muckli, L., Waltz, J. A., Kriegeskorte, N., Goebel, R., et al. (2003). Cortical capacity constraints for visual working memory: dissociation of fMRI load effects in a fronto-parietal network. *NeuroImage*, 20(3), 1518–1530.
- Mattay, V. S., Fera, F., Tessitore, A., Hariri, A. R., Berman, K. F., Das, S., et al. (2006). Neurophysiological correlates of age-related changes in working memory capacity. *Neuroscience Letters*, 392(1–2), 32–37.
- McNab, F. & Klingberg, T. (2008). Prefrontal cortex and basal ganglia control access to working memory. *Nature Neuroscience*, 11(1), 103–107.
- Nagel, I. E., Preuschhof, C., Li, S.-C., Nyberg, L., Bäckman, L., Lindenberger, U., et al. (2008, April). *Performance level modulates adult age differences in brain activation during spatial working memory task*. Poster presented at the Cognitive Aging Conference, Atlanta, GA.
- Nichols, T., Brett, M., Andersson, J., Wagner, T. & Poline, J.-B. (2005). Valid conjunction inference with the minimum statistic. *NeuroImage*, 25(3), 653–660.
- O’Reilly, R. (2006). Biologically based computational models of high-level cognition. *Science*, 314(5796), 91–94.
- Olesen, P. J., Westerberg, H. & Klingberg, T. (2004). Increased prefrontal and parietal activity post-training of working memory. *Nature Neuroscience*, 7(1), 75–79.
- Osaka, M., Osaka, N., Kondo, H., Morishita, M., Fukuyama, H., Aso, T., et al. (2003). The neural basis of individual differences in working memory capacity: an fMRI study. *NeuroImage*, 18(3), 789–797.
- Osaka, N., Osaka, M., Kondo, H., Morishita, M., Fukuyama, H. & Shibasaki, H. (2004). The neural basis of executive function in working memory: An fMRI study based on individual differences. *NeuroImage*, 21(2), 623–631.
- Persson, J., Nyberg, L., Lind, J., Larsson, A., Nilsson, L.-G., Ingvar, M., et al. (2006). Structure-function correlates of cognitive decline in aging. *Cerebral Cortex*, 16(7), 907–915.
- Sakai, K., Rowe, J. B. & Passingham, R. E. (2002). Active maintenance in prefrontal area 46 creates distractor-resistant memory. *Nature Neuroscience*, 5(5), 479.
- Sommer, M. A. & Wurtz, R. H. (2006). Influence of the thalamus on spatial visual processing in frontal cortex. *Nature*, 444(7117), 374–377.
- Todd, J. J. & Marois, P. (2004). Capacity limit of visual short-term memory in human posterior parietal cortex. *Nature*, 428(6976), 751–754.
- Verhaeghen, P. & Basak, C. (2005). Ageing and switching of the focus of attention in working memory: Results from a modified N-Back task. *Quarterly Journal of Experimental Psychology: Section A*, 58(1), 134–154.
- Vogel, E. K., McCollough, A. W. & Machizawa, M. G. (2005). Neural measures reveal individual differences in controlling access to working memory. *Nature*, 438(7067), 500–503.

Received 7 February 2008, accepted 6 May 2008