Comparison of the Choice Effect and the Distance Effect in a Number-Comparison Task by fMRI

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Abstract

Behavioral and neurophysiological studies of numerical comparisons have shown a “distance effect,” whereby smaller numerical distances between two digits are associated with longer response times and higher activity in the parietal region. In this experiment, we introduced a two-choice condition (between the smaller/lower or the larger/higher of two digits) and examined its effect on brain activity by fMRI. We observed longer response times and greater activity with the choice of smaller numbers (“choice effect”) in several brain regions including the right temporo-parietal region, (pre)cuneus, superior temporal sulcus, precentral gyrus, superior frontal gyrus, bilateral insula, and anterior cingulate cortex. These regions correspond to areas that have been suggested to play a role in attentional shift and response conflict. However, brain activity associated with the distance effect disappeared even though the behavioral distance effect remained. Despite the absence of the distance effect on brain activity, several areas changed activity in relation to response time, including regions that were reported to change activity in both a distance effect and a reaction-time-related manner. The result suggested that the level of task load may change the activity of regions that are responsible for magnitude detection.

Introduction

When human subjects compare the values of two numbers in number-comparison tasks, the relationship between response time (RT) and numerical distance (the difference between the two numbers) is inverse, irrespective of the number of words, Arabic numerals, or number of objects constituting each number. In other words, recognition of a small distance (SD) between two numbers (and quantities) requires more time than does recognition of a large distance (LD). This phenomenon is referred to as the distance effect [1,2].

Consistent with psychological findings, several neuroimaging studies have revealed that activity changes in the parietal cortex are significantly modulated by the magnitude of the numerical distance [3,4,5,6,7,8,9,10], with greater activation during the processing of SD than of LD. Clinical studies of patients with lesions of the parietal lobes have also demonstrated the importance of the parietal cortex in numerical manipulation [11,12,13,14,15,16]. Results from studies using tasks involving choosing the larger number have shown that repetitive transcranial magnetic stimuli (rTMS) delivered to the left parietal scalp site induced longer RTs only in SD condition but not in LD condition suggesting that the parietal cortex is involved in comparisons of magnitudes [17].

In the same number comparison task, the effect of choice has been described in relation to the magnitude of numbers. Well-documented effect was called spatial numerical association of response codes (SNARC) effect [18]. In a binary response setting, it has been found that relatively small numbers are reacted to faster with the left hand than with the right hand. This SNARC effect is thought to originate from the fact that the mental number line is oriented from left to right (in the case of left-right reading cultures), so that there is congruity between small numbers and left-side responses and between large numbers and right-side responses.

However, unlike the distance effect, the effect of choosing between a larger and smaller object has not been extensively studied from a neurophysiological perspective. Dehaene [2] showed that RTs were significantly longer when choosing smaller than when choosing larger numbers. His result was supported by Horaguchi et al. [19] who used near-infra red spectrometry (NIRS) as a neuroimaging technique for identifying the brain regions responsible for the choice effects associated with a number-comparison task involving Arabic numerals. They detected a difference between the two choice conditions (the smaller digit choice: SC vs. the larger digit choice: LC) and showed that the activity in the right temporo-parietal region was higher under the SC condition. However, they could not detect a difference between the two distance conditions (SD vs. LD). Due to the limitation of NIRS measurements, they could not identify neuronal processes that were occurring during the task.

A number of studies, including those using unit recording in monkey brains [20,21,22] and fMRI in humans [3,4,8,10,23,24,25], clearly show that the inferior parietal region is involved in numerical processing. The involvement of this region is
also shown in other quantitative information processing such as physical sizes or luminance comparison [6,10,26,27,28]. In monkey parietal cortex, Sawamura et al. [22] reported that the number selective cells and those that responded to task-related cues that had no numerical component were found within the same area.

In addition to the processing of numerical quantity of multiple modalities, the interaction of multiple functions of IPS have also been suggested such as, reaction time [29], time and space perception [30,31], and attention [32,33,34,35]. Gobel et al. [29] argued that the activation of the IPS during magnitude comparison may be related to response-selection rather than number-specific processing, and these 2 functions might be interacting in the IPS [29].

Based on our previous NIRS results [19] we hypothesized that it might be possible to observe the interaction between numerical processing and other functions if we use the same modality (Arabic numbers) but change the decision process. By adding two-choice conditions (to choose either the larger one or the smaller one, instead of choosing merely the larger one) would change neuronal activity associated with the distance effect. It might give us a clue whether the higher levels of activity observed in the parietal region during the number comparison task are solely attributable to numerical processing or represent more general activities, such as attention [36] or reaction time [29].

Methods

Subjects

Thirteen healthy volunteers participated in the fMRI study (nine males, four females; average age: 21.7; all right handed). The study protocol was approved by the institutional (AIST and University of Tsukuba) ethics committees and conformed to the ethical standards contained in the 1964 Declaration of Helsinki. All subjects provided informed consent prior to their participation in the study.

Stimuli

Pairs of numerical numbers (black) with visual angles of 1.47°×0.73° (height×width) were presented as stimuli; the margins from the center to the inside and outside of each digit were 1.27° and 2.00°, respectively. The stimuli were presented on a screen in the fMRI experiment. A red fixation point (diameter approximately 0.57° visual angle) was displayed at the center of the monitor throughout the experiment to eliminate eye movement and related brain activity. The instructions for the choice required in each task were presented in Japanese on the screen before the beginning of each session. The pairs of digits were divided into two categories of numerical distance: small distance (SD) and large distance (LD). The SD pairs included distance sizes (D) 1, 2, and 3 (total of 18 pairs). D = 1 pairs included 1–2, 2–1, 3–4, 4–3, 6–7, 7–6, 8–9, and 9–8; D = 2 pairs included 1–3, 3–1, 4–6, 6–4, 7–9, and 9–7; and D = 3 pairs included 1–4, 4–1, 6–9, and 9–6. LD included distance sizes 5, 6, and 7 (total of 18 pairs). D = 5 pairs included 1–6, 6–1, 2–7, 7–2, 3–8, 8–3, 4–9, and 9–4; D = 6 pairs included 1–7, 7–1, 2–8, 8–2, 5–9, and 9–3; and D = 7 pairs included 1–8, 8–1, 2–9, and 9–2. Extreme values such as 1 or 9 were displayed with equal frequency in both distance pairs, and the middle number (5) was never displayed. Each pair was displayed only once within a block.

Task Design

Participants were instructed to compare two digits, which were displayed on a screen and viewed through a prism mirror within a MRI scanner, and to choose either the larger or the smaller digit. The task program was controlled by E-prime (Psychology Software Tools, Inc., Pittsburgh, PA, USA). We used a block design, and the task sequence is shown in Figure 1.

One session contained four blocks, each of which consisted of one combination of the two distance conditions (18 LD or 18 SD pairs)×2 choice conditions (LC or SC). Each pair appeared only once per block, and the order of blocks was randomized. Blocks

![Figure 1. Task sequence of fMRI sessions.](https://example.com/figure1.png)

**Figure 1. Task sequence of fMRI sessions.** The session for each task included an instruction period, a resting period (in which only a fixation point was displayed), and a task period. Subjects were instructed to stare at a fixation point throughout the session and to select the correct digit as quickly as possible after a pair of digits was displayed. Instructions about which digit to select (larger/smaller) were visually presented before the beginning of each block (fMRI task).

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were separated by the presentation of a 58-sec fixation point. At the beginning of each session, the fixation point was presented for 10 sec. Task switching of choice was introduced between blocks, and the order of choice was randomized across subjects. One block was composed of a 2-sec initial presentation of the instructions (“Choose the larger/smaller digit”), a 2-sec fixation point, repeated (18 times) presentations of pairs of digits (2 sec), and the fixation point again (1 sec) (in total, 4 sec + 3 sec × 18 = 58 sec). Stimulus presentation was set to 2 sec, as response times sometimes exceeded 1 sec but never exceeded 2-sec in preliminary studies. After the presentation of each pair of digits, subjects were asked to respond as quickly as possible by using their second or third finger to press the one of the two buttons on the response pad (MRI-compatible Joystick, Resonance Technology, Inc., Los Angeles, CA, USA) that corresponded to the side on which the correct digit appeared. The stimulus disappeared after 2 sec even when participants did not respond. Each subject received two sessions: in one, the right hand was used, and in the other, the left hand was used to cancel out any effect of which hand was used. The order of hands was counterbalanced across subjects.

Figure 2. Average response times of 4 conditions. Error bars indicate standard errors of mean. The result of two-way ANOVA showed significant main effects of distance and choice, but no interaction between the two.

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Behavioral Analysis

RT for each subject under four conditions were statistically analyzed by two-way repeated-measures analysis of variance (ANOVA). The factors used in the ANOVA were distance (SD, LD) and choice (SC, LC).

fMRI Parameters

A time-course series of 242 volumes (per session) was acquired with T2*-weighted, gradient echo, echo planar imaging (EPI) sequences with a 3.0-T MRI system (Signa Horizon; General Electric Medical Systems, Milwaukee, WI) equipped with a standard birdcage head coil. Each volume consisted of 16–18 slices with a slice thickness of 6.0 mm (2.0-mm gap). Parameters for fMRI were set as for Kowatari et al. [37]. The TR was 2000 ms, the TE was 30 ms, and the flip angle was 70°. The digital in-plane resolution was 64 × 64 pixels. The first five volumes were discarded to stabilize magnetization. For anatomical information, high-resolution T2-weighted images of the same slices of EPI scans were acquired with a spin echo sequence, with a 20-cm field of view (256 × 256 matrix, 16–18 slices, TR 5,000 ms, TE 70 ms).

fMRI Analysis

The image data were analyzed using Statistical Parametric Mapping 5 (SPM5; Welcome Department of Imaging Neuroscience, London, UK; http://www.fil.ion.ucl.ac.uk/spm) implemented in MATLAB (MathWorks, Natick, MA). To correct for the head motions of each subject during MRI, the images were realigned to the first EPI volume. All the EPI volumes were then co-registered with high-resolution T2-weighted images of the same slices of EPI scans, and all volumes were spatially normalized to the SPM5 template (Montreal Neurological Institute; MNI) space. Subsequently, all normalized images were smoothed using an isotropic Gaussian kernel (8 mm³ full-width at half-maximum) to increase the signal/noise ratio in the images. A 128-sec temporal high-pass filter was applied to the data to remove low-frequency baseline drift in the BOLD signal.

In the first-level analysis, the fMRI signal obtained from each subject during each session was fitted with a hemodynamic response function to detect significant increases from the rest condition. T-statistic maps were acquired from each subject for the four conditions: LC/LD, LC/SD, SC/LD, and SC/SD. These four t-statistics maps were used in the second-level analysis, for a group comparison using a random-effect model with a two-way ANOVA (distance × choice). The results were reported as p-value

Table 1. ANOVA table of response time analysis.

| Source of variation | Sum of Squares | Degrees of Freedom | Mean Squares | F-value |
|---------------------|----------------|--------------------|--------------|---------|
| Subject(S)          | 347328.0944    | 12                 | 28944.0079   |         |
| Choice(A)           | 4658.1156      | 1                  | 4658.1156    | 25.7    |
| SxA                 | 2175.091       | 12                 | 181.2576     |         |
| Distance(B)         | 72941.5735     | 1                  | 72941.5735   | 46.95   |
| SxB                 | 18641.9924     | 12                 | 1553.4994    |         |
| AxB                 | 293.0249       | 1                  | 293.0249     | 0.39    |
| SxAxB               | 8886.7957      | 12                 | 740.5663     |         |
| Total               | 454924.6881    | 51                 |              |         |

**p < 0.001.

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with uncorrected for multiple comparison (Punc), Punc < 0.001 with an extent threshold of >50 voxels.

To compare the effect size of each condition (LC/LD, LC/SD, SC/LD, and SC/SD), averaged BOLD signal intensity of defined areas was calculated using MarsBaR (http://marsbar.sourceforge.net) for 4 conditions.

Defining Areas that Change Activities in Relation to RT

To elucidate the areas that represent response time on the number-comparison task, we used the average RTs of all subjects under each of four conditions (LC/LD, LC/SD, SC/LD, SC/SD) as the parameter of the contrast vector for second-level analysis. The results were reported as p-value with Family-wise error correction (PFWE), PFWE < 0.05.

Results

Behavioral Results

Figure 2 shows averaged RT in the fMRI task across subjects. The RT (+S.E.M) under the LC/LD condition was 498.7±22.2 ms; under the LD/SC condition, it was 512.9±19.2 ms; under the LC/SD condition, it was 568.9±24.8 ms; and under the SD/SC condition, it was 592.6±30.6 ms. The results of a two-way ANOVA (Table 1) showed significant main effects for distance (F(1,12) = 46.95, p<0.001) and choice (F(1,12) = 25.70, p<0.001), but the interaction between distance and choice was not significant. (F(1,12) = 0.40, p = 0.54). Error rates for each condition was very low (LC/LD: 0.21%; LC/SD: 1.07%; SC/LD: 0.64%; SC/SD: 2.56%) and significant difference was observed in factor of

Table 2. MNI coordinates and statistical details for areas that were activated in each condition.

| Area/s | side | voxel size | T value | Z value | x | y | z |
|--------|------|------------|---------|---------|---|---|---|
| LC/LD  | Inferior occipital gyrus | Left | 329 | 6.26 | 5.33 | -22 | -90 | -12 |
| LC/LD  | Supplemental motor area | Left | 100 | 4.42 | 4.03 | -6 | 6 | 54 |
| LC/LD  | Postcentral gyrus | Left | 205 | 4.39 | 4 | -44 | -32 | 44 |
| LC/LD  | Inferior occipital gyrus | Right | 50 | 4 | 3.7 | 24 | -92 | -8 |
| LC/SD  | Lingual gyrus | Left | 885 | 8.13 | 6.42 | -20 | -90 | -12 |
| LC/SD  | Supplemental motor area | Left/Right | 1186 | 6.65 | 5.57 | -6 | 6 | 56 |
| LC/SD  | Postcentral gyrus/Superior parietal gyrus | Left | 1997 | 5.64 | 4.92 | -46 | -32 | 50 |
| LC/SD  | Vermis | Right | 1979 | 5.12 | 4.55 | 4 | -66 | -18 |
| LC/SD  | Lingual gyrus | Right | 269 | 5.02 | 4.48 | 24 | -90 | -10 |
| LC/SD  | Precentral gyrus/Medial frontal gyrus | Left | 606 | 4.42 | 4.02 | -30 | -14 | 56 |
| LC/SD  | Insula | Left | 435 | 4.39 | 4 | -46 | 0 | 8 |
| LC/SD  | Putamen | Left | 76 | 3.79 | 3.52 | -22 | -4 | 12 |
| SC/LD  | Lingual gyrus | Left | 5643 | 7.96 | 6.32 | -20 | -90 | -12 |
| SC/LD  | Supplemental motor area | Left/Right | 2520 | 7.44 | 6.04 | -6 | 6 | 54 |
| SC/LD  | Postcentral gyrus/Superior parietal gyrus | Left | 3702 | 6.19 | 5.28 | -48 | -32 | 50 |
| SC/LD  | Insula | Left | 2080 | 5.36 | 4.72 | 40 | 6 | 4 |
| SC/LD  | Insula | Right | 842 | 4.67 | 4.22 | 42 | 10 | 2 |
| SC/LD  | Superior temporal gyrus | Right | 65 | 3.73 | 66 | -42 | 24 |
| SC/LD  | Inferior parietal gyrus | Right | 435 | 4.97 | 3.68 | 50 | -40 | 58 |
| SC/LD  | Precentral gyrus | Right | 209 | 3.92 | 3.63 | 36 | -8 | 56 |
| SC/SD  | Lingual gyrus | Left | 2887 | 7.29 | 5.95 | -22 | -90 | -12 |
| SC/SD  | Supplemental motor area | Left | 1563 | 6.91 | 5.73 | -6 | 6 | 54 |
| SC/SD  | Postcentral gyrus/Superior parietal gyrus | Left | 3633 | 6.37 | 5.4 | -48 | -32 | 48 |
| SC/SD  | Precentral gyrus/Medial frontal gyrus | Left | 2206 | 5.2 | 4.61 | -46 | 4 | 30 |
| SC/SD  | Superior parietal gyrus/Inferior parietal gyrus | Right | 2570 | 4.8 | 4.31 | 24 | -68 | 50 |
| SC/SD  | Lingual gyrus | Right | 195 | 4.55 | 4.13 | 22 | -90 | -10 |
| SC/SD  | Caudate/Thalamus | Right | 280 | 4.03 | 3.72 | 14 | -8 | 18 |
| SC/SD  | Thalamus | Left | 103 | 3.85 | 3.58 | -12 | -16 | 6 |
| SC/SD  | Pallidum | Right | 54 | 3.57 | 3.35 | 24 | -2 | 6 |

LC: Choose larger, SC: Choose smaller, LD: Large distance, SD: Small distance. Punc were all <0.001.
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distance ($F(1,12) = 11.14, p<0.01$) but no significant difference was observed in choice ($F(1,12) = 3.6, p=0.08$), or the interaction ($F(1,12) = 1.35, p=0.26$) by ANOVA (distance×choice).

Distance Effect and Choice Effect in fMRI

Table 2 summarizes activated regions under each condition; these are also shown in Figure 3a. The brain activities under the four conditions (two choice conditions: LC or SC×two distance conditions: LD or SD) showed significant differences, with less activity occurring under the LC than under the SC condition. In the contrast between the two choice categories (SC/LD+SD vs. LC/LD+SD), the left insula, right superior temporal sulcus (STS) extending to the right insula, right temporo–parietal junction (TPJ), right anterior cingulate gyrus (ACC), right pre/posterior cuneus, right fronto–parietal regions (precentral gyrus: PreCG, medial frontal gyrus: MFG and superior frontal gyrus: SFG) demonstrated greater changes in the BOLD signal under the SC condition than under the LC condition ($p<0.001$, uncorrected; Figure 3b and Table 3).

On the other hand, no brain region showed a main effect for distance (SD/LC+SC vs. LD/LC+SC) or for the choice–distance interaction ($p>0.001$, uncorrected).

We quantified the BOLD signal change from the rest among these four conditions in the regions listed above (Figure 4). The result showed two major tendencies. One type of reaction was seen in the Insula and ACC, which showed signal increase in both LC and SC conditions with higher increase in SC. The other type was the decrease of the BOLD signal below the resting state in LC condition, with the increased signal above the rest in SC condition. The latter areas included SFG, TPJ, PreCG/MFG, pre/posterior cuneus and STG.

Regions that Changed Activity in Relation to RT

As Pinel et al. [8] and Gobel et al. [29] pointed out, activation associated with numerical-distance judgment cannot be separated from neuronal processes associated with reaction time change. Pinel et al. [8] showed that activation in bilateral IPS and precuneus correlated with the RT in number comparison task. Also in Gobel et al. [29], they compared reaction time and brain activity between the number comparison task and the vertical line detection task and demonstrated that IPS activation varied only with RT changes irrespective of the experimental task. Therefore, we examined areas that changed activity in relation to RT by elucidating areas that changed activity in proportion to the measured RT for each condition (SC/SD>SC/LD>LC/SD>LC/LD: the higher the activity was, the slower the reaction time was). These areas include right IPS, bilateral supplemental motor area, left postcentral sulcus/inferior parietal gyrus, bilateral lingual gyrus, and right cerebellum.

Table 3. MNI coordinates and statistical details for areas that activate in contrast [SC – LC].

| Area                          | side | voxel size | T value | Z value | x    | y    | z    |
|-------------------------------|------|------------|---------|---------|------|------|------|
| Superior temporal sulcus      | right| 371        | 5.06    | 4.5     | 46   | −2   | −18  |
| Superior frontal gyrus        | right| 75         | 4.31    | 3.95    | 24   | 6    | 66   |
| Temporo-parietal junction     | right| 280        | 4.29    | 3.93    | 66   | −22  | 12   |
| (pre)cuneus                   | right| 161        | 4.17    | 3.84    | 16   | −64  | 34   |
| Insula                        | left | 358        | 4.05    | 3.74    | −38  | 12   | 2    |
| Precentral gyrus/Medial frontal gyrus | right | 196   | 4.02    | 3.72    | 54   | 2    | 20   |
| Anterior cingulate gyrus      | right| 109        | 3.87    | 3.59    | 8    | 8    | 40   |
These regions did not overlap those that showed higher activity in SC than in LC (Figure 5, Table 4).

Discussion
Differential Effects of Distance and Choice in Brain Activity

Our behavioral data confirmed the presence of both the distance effect (longer RTs under the SD compared with the LD condition), and the choice effect (choosing the smaller digit caused a slower RT under both the LD and SD conditions). Behaviorally, RT was longer with SC than with LC, and the fMRI results indicated the choice effect such that the slower the RT was (SC), the higher the BOLD signal change became. However, in contrast to the choice effect, no brain region showed a main effect for distance (SD vs. LD). As no distance effect was observed in brain activity, it is unlikely that brain activity may reflect error rates, because significant difference of error rates was observed only between LD and SD, but not between LC and SC.

These results contradict other imaging studies that have shown activity differences between SD and LD, with higher activity in SD [4,5,6,7,8,10,37]. These other studies showed that the bilateral posterior intra-parietal sulcus (IPS), right precuneus, and right MFG showed higher activity under the SD than under the LD condition. As we used the same combination of 2 digits as other experiments that showed clear BOLD signal change associated with distance effect [4,5,6,7], the absence of distant effect in brain activity was not due to the lower sensitivity of stimuli that we used. Therefore the major difference between ours and other experiments was that their tasks were performed under the instruction “to choose the larger number” and did not use the two-choice condition as we did. In our experiment subjects had to switch choices between blocks, the task load was heavier as the task required constant attention to which choice was required.

Figure 4. Average BOLD signal change from the rest in areas indicated in Figure 3b. Error bar indicates S.E.M. LC: the larger digit choice; SC: the smaller digit choice; LD: large-distance; SD: small-distance. doi:10.1371/journal.pone.0021716.g004

Figure 5. RT-related BOLD signal change. (A) Parametric contrast of regions activated in proportion to the measured RT of each condition (SC/SD > SC/LD > LC/SD > LC/LD) (p<0.05, FWE corrected). The hair line indicates intra-parietal sulcus (IPS). (B) BOLD signal intensity at MNI coordinate (−26, −58, 50). doi:10.1371/journal.pone.0021716.g005
It seems to be our natural tendency that larger numbers are more salient than smaller ones as shown by Merkley [38], when comparing 2 digits, subjects tend to fixate their gaze more often on larger numbers than on smaller numbers. Therefore, in small choice, subjects need to oppose the natural tendency of choosing larger one, and to do so, more number of neuron are to be recruited and takes longer to decide resulting in longer response time.

In SNARC effect, which is a choice-related phenomenon, the mental number line is oriented from left to right (in the case of left-right reading cultures), so that there is congruity between small numbers and left-side responses and between large numbers and right-side responses [18]. However, in our experiment, we designed the task to cancel the SNARC effect; subjects had to respond by right or left hand first and then performed the same task by switching hand. In addition, the combination of the same 2 digits was shown twice with side reversed (e.g. 3-7 and 7-3). Therefore, the choice effect that we observed may be independent from SNARC effect.

Relation to Attentional Networks

In the contrast between the two choice categories (SC(LD+SD) vs. LC(LD+SD)), the left insula, right STS extending to the right insula, right ACC, right TPJ, right frontal regions (PreCG/MFG and SFG) (pre)cuneus, demonstrated greater changes in the BOLD signal under the SC condition than under the LC condition. Among these areas, TPJ, MFG, IPS and (pre)cuneus were described as a part of attentional network in the review by Corbetta et al. [36] and by Behrmann et al. [39]. They described two types of attentional biasing signals; dorsal network or goal-directed (top-down) and ventral network or stimulus-driven (bottom-up). The former is mediated by right MFG/right PreCG, IPS and precuneus [40,41,42,43], and the latter is mediated by the right MFG/PreCG and right TPJ, which is activated independently of the sensory modality and has been implicated in serving a multisensory attentional function [44]. Right hemispheric dominance in attentional function has also been documented [32].

BOLD signal changes in areas that showed higher activation with SC than with LC were shown in Figure 4. Two types of responses were observed; one is associated with the increase of BOLD signal in both SC and LC conditions but with higher activity in SC. The other type showed the decrease of signal intensity from the rest condition in LC but the increase in SC condition. The latter group included right TPJ, right SFG, right PreCG, right STS, and right (pre)cuneus.

It has been suggested that the TPJ coordinates voluntary and stimulus-driven attentional control settings to determine which stimuli effectively compete for attention [45]. In our natural tendency, the larger digit in a pair seems to carry the target-defining feature (i.e., to be more salient); therefore, subjects may have to re-orient their attention each time in the task of choosing the smaller digit. TPJ activation under the SC condition may possibly reflect such an operation.

STS in conjunction with IPL, was also suggested as a part of top-down control system [33] This region was also shown higher activation in SC than in LC condition. Similar explanation might be applicable to (pre)cuneus as several authors reported the involvement of (pre)cuneus in attentional system, for attention shift between two stimulus features [46] and at the appearance of unattended stimulus [47].

Inferior parietal lobule is reported as activated region for distance effect [4,5,6,7,8,10,48] but also as a part of attentional network [33,34,35,42,49]. It is plausible that in our experiment, because subjects had to pay attention to the choice as well as the distance, the task load was heavier than in a one-choice experiment. If numerical and attentional operations shared the same neuronal resources in the IPS, an increased demand for attention may have used up resources that would otherwise have been available for numerical processing, leaving fewer neurons to participate in the number-comparison task itself. It is possible that the number of neurons that are required for processing numerical information might be sufficient, but in both LD and SD the BOLD signal change becomes weaker than one-choice task and as a floor effect, the difference in signal intensity between SD and LD become undetectable.

A similar phenomenon has been observed by increasing the task load in experiments that used other tasks. Using a duration-discrimination task, Livesey et al. [50] showed that time-related activity in the right IPS, pre-SMA, and parts of the prefrontal cortex disappeared and reversed in polarity as a function of task difficulty, and they suggested that activity in these regions was related to task demand. Based on the observation that a numerical task impaired a time-estimation task under a dual-task paradigm, Walsh also suggested that processing time and quantity (number) share resources in the parietal cortex [31]. Also, Ballan et al. reported that the distance effect was diminished by visual-noise load [51].

It is possible that the difference between LD and SD in IPS may partly represent RT, as Gobel et al. pointed out [29]. In our experiment too, we observed regions that changed activity in parallel to RT, including IPS, lingual gyrus and precentral gyrus (Figure 5). These RT-related areas did not overlap with regions that showed higher activation in SC than in LC. IPS is always

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**Table 4. MNI coordinates and statistical details for areas that change activity in relation to RT.**

| Area                               | side | voxel size | T value | Z value | p value (FWE) | x     | y     | z     |
|------------------------------------|------|------------|---------|---------|--------------|-------|-------|-------|
| Lingual gyrus                      | Left | 445        | 9.55    | 7.12    | <0.001       | -20   | -90   | -12   |
| Supplemental motor area            | Left/Right | 660     | 8.2     | 6.45    | <0.001       | -6    | 6     | 54    |
| Postcentral sulcus/inferior parietal sulcus | Left  | 549        | 7.21    | 5.91    | <0.001       | -46   | -32   | 48    |
| Lingual gyrus                      | Right | 97         | 6.15    | 5.25    | 0.002        | 24    | -90   | -10   |
| Intra-parietal sulcus              | Left  | 303        | 6.03    | 5.18    | 0.002        | -26   | -58   | 50    |
| Cerebellum                         | Right | 67         | 5.51    | 4.83    | 0.011        | 4     | -68   | -20   |

P-values were all <0.05.

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activated during response selection [32] and is not restricted to number comparison tasks. Therefore, it is possible that IPS neurons are serving for numerical task, response-time related function and attention.

Response Conflict and Attention

Insula and ACC both showed increased activity in both SC and LC but with higher activity in SC (Figure 4). A number of fMRI studies have suggested that one function performed by the ACC involves conflict monitoring or error detection [53,54,55,56]. The role of the insula in this context may also be related to conflict. Several researchers confirmed that conflict processing is reliably associated with activation in the anterior insula as well as in the ACC, prefrontal cortex, and parietal cortex [57]. The SFG has been implicated in the resolution of conflict through the top-down posterior attentional system that contains the TPJ [58,59,60]. Thus, higher activation of ACC and SFG under the SC condition than the LC condition may reflect conflict as well as orienting attention.

smaller number, the SFG may participate in resolving this conflict through the top-down posterior attentional system that contains the TPJ [58,59,60]. Thus, higher activation of ACC and SFG under the SC condition than the LC condition may reflect conflict as well as orienting attention.

References

1. Moyer RS, Landauer TK (1967) Time required for judgments of numerical inequality. Nature 215: 1319–1320.
2. Dehaene S (1989) The psychophysics of numerical comparison - A reexamination of apparently incompatible data. Perception & Psychophysics 45: 557–566.
3. Cantlon JF, Brannon EM, Carter EJ, Pelphrey KA (2006) Functional imaging of numerical processing in adults and 4-5-old children. Plos Biology 4: 844–854.
4. Chochon F, Cohen L, van de Moortele PF, Dehaene S (1999) Differential contributions of the left and right inferior parietal lobules to number processing. Journal of Cognitive Neuroscience 11: 617–630.
5. Fullbright RR, Manson SC, Skudlarski P, Lacamide CM, Gore JC (2003) Quantity determination and the distance effect with letters, numbers, and shapes: A functional MR imaging study of number processing. American Journal of Neurology 24: 193–200.
6. Kadosh RC, Henik A, Rubinstein O, Mohr H, Dori H, et al. (2005) Are numbers special? The comparison systems of the human brain investigated by fMRI. Neuropsychologia 43: 1238–1249.
7. Kaufmann L, Koppelstaetter F, Delazer M, Siedentopf C, Rhomberg P, et al. (2005) Neural correlates of distance and congruity effects in a numerical Stroop task an event-related fMRI study. Neuroimage 25: 838–890.
8. Pinel P, Dehaene S, Riviere D, LeBihan D (2001) Modulation of parietal activation by semantic distance in a number comparison task. Neuroimage 14: 1013–1026.
9. Pinel P, Le Clec’h G, van de Moortele PF, Naccache L, Le Bihan D, et al. (1999) Event-related fMRI analysis of the cerebral circuit for number comparison. Neuron 10: 1473–1479.
10. Pinel P, Piazza M, Le Bihan D, Dehaene S (2004) Distributed and overlapping cerebral representations of number, size, and luminance during comparative judgments. Neuron 41: 903–907.
11. Dehaene S, Cohen L (1997) Cerebral pathways for calculation: Double dissociation between rote verbal and quantitative knowledge of arithmetic. Cortex 33: 219–250.
12. Dehaene S, Dehaene-Lambertz G, Cohen L (1998) Abstract representations of numbers in the animal and human brain. Trends in Neurosciences 21: 555–561.
13. Delazer M, Benke T (1997) Arithmetical facts without meaning. Cortex 33: 697–710.
14. Grafman J, Passafiume D, Faglioni P, Boller F (1982) Calculation disturbances in adults with focal hemispheric damage. Cortex 18: 37–49.
15. Martory MD, Mayer E, Pajon Af, Amonni JM, Landis T, et al. (2003) Pure global acaulcia following a left subangular lesion. Neurocase 9: 319–328.
16. Mayer E, Martory MD, Pajon Af, Landis T, Delavelle J, et al. (1999) A pure case of Gerstmann syndrome with a subangular lesion. Brain 122: 1107–1120.
17. Andre M, Seron X, Olivier E (2005) Hemispheric lateralization of number comparison. Cognitive Brain Research 25: 283–290.
18. Dehaene S, Bonassi S, Giraud P (1995) The mental representation of parity and number magnitude. Journal of Experimental Psychology-General 122: 371–396.
19. Horaguchi T, Ogata Y, Watanabe N, Yamamoto M (2008) Behavioral and near-infrared spectroscopy study of the effects of distance and choice in a number comparison task. Neurosciences Research 61: 294–301.
20. Nieder A (2005) Counting on neurons: The neurobiology of numerical competence. Nature Reviews Neuroscience 6: 177–190.
21. Nieder A, Miller EK (2004) A parieto-frontal network for visual numerical information in the monkey. Proceedings of the National Academy of Sciences of the United States of America 101: 7457–7462.
22. Saccuman H, Shimizu K, Tanji J (2002) Numerical representation for action in the parietal cortex of the monkey. Nature 413: 918–922.
23. Dehaene S, Spelke E, Pinel P, Stanescu R, Tsivkin S (1999) Sources of mathematical thinking: Behavioral and brain-imaging evidence. Science 284: 970–974.
24. Eger E, Sterzer P, Ross MO, Giraud AL, Kleinschmidt A (2003) A supramodal number representation in human intraparietal cortex. Neuron 37: 719–725.
25. Rickard TC, Romero SG, Basso G, Wharton C, Fitman S, et al. (2000) The calculating brain: an fMRI study. Neuropsychologia 38: 325–335.
26. Piazza M, Pinti P, Le Bihan D, Dehaene S (2007) A magnitude code common to numerosities and number symbols in human intraparietal cortex. Neuron 53: 293–305.
27. Kadosh RC, Kadosh KC, Kaas A, Henik A, Goebl R (2007) Notation-dependent and -independent representations of numbers in the parietal lobes. Neuron 53: 307–314.
28. Kadosh RC, Kadosh KC, Henik A (2008) When brightness counts: The neural correlate of numerical-luminance interference. Cerebral Cortex 18: 337–343.
29. Gobel SM, Johansen-Berg H, Behrens T, Rushworth MFS (2004) Response-selection-related parietal activation during number comparison. Journal of Cognitive Neuroscience 16: 1536–1551.
30. Rao SM, Mayer AR, Harrington DL (2001) The evolution of brain activation during temporal processing. Nature Neuroscience 4: 317–323.
31. Walsh V (2003) A theory of magnitude: common cortical metrics of time, space and quantity. Trends in Cognitive Sciences 7: 483–488.
32. Shulman GL, d’Avossa G, Tansy AP, Corbetta M (2002) Two attentional processes in the parietal lobes. Cerebral Cortex 12: 1124–1131.
33. Spapiro K, Hillstron AP, Husain M (2002) Control of visuotemporal attention by inferior parietal and superior temporal cortex. Current Biology 12: 1320–1325.
34. Corbetta M, Kincade JK, Ollinger JM, McAvoy MP, Shulman GL (2000) Voluntary orienting is dissociated from target detection in human posterior parietal cortex. Nature Neuroscience 3: 292–297.
35. Chambers CD, Payne JM, Stokes MG, Mattingley JB (2004) Fast and slow parietal pathways mediate spatial attention. Nature Neuroscience 7: 217–218.
36. Corbetta M, Patel T, Shulman GL (2000) The reorienting system of the human brain: From environment to theory of mind. Neuron 58: 306–324.
37. Kovatain R, Lee SH, Yamamura H, Nagamori Y, Levy P, et al. (2009) Neural Networks Involved in Artistic Creativity. Human Brain Mapping 30: 1675–1690.
38. Merkley R, Ansari D (2010) Using eye tracking to study numerical cognition: the case of the ratio effect. Experimental Brain Research 206: 455–460.
39. Behrmann M, Geng JJ, Shomstein S (2004) Parietal cortex and attention. Current Opinion in Neurobiology 14: 212–217.
40. Giesbrecht B, Waldorff MG, Song AW, Mangun GR (2003) Neural mechanisms of top-down control during spatial and feature attention. Neuroimage 19: 496–512.

41. Liu TS, Slomnick SD, Serences JT, Yanis S (2003) Cortical mechanisms of feature-based attentional control. Cerebral Cortex 13: 1334–1345.

42. Yanis S, Schwarzbach J, Serences JT, Carlson RL, Steimetz MA, et al. (2002) Transient neural activity in human parietal cortex during spatial attention shifts. Nature Neuroscience 5: 995–1002.

43. Yanis S, Serences JT (2003) Cortical mechanisms of space-based and object-based attentional control. Current Opinion in Neurobiology 13: 187–193.

44. Downar J, Crawley AP, Mikulis DJ, Davis KD (2001) The effect of task relevance on the cortical response to changes in visual and auditory stimuli: An event-related fMRI study. Neuroimage 14: 1256–1267.

45. Serences JT, Shomstein S, Leber AB, Golay X, Egeth HE, et al. (2005) Coordination of voluntary and stimulus-driven attentional control in human cortex. Psychol Sci 16: 114–122.

46. Le TH, Pardo JV, Hu XP (1998) T-fMRI study of nonspatial shifting of selective attention: Cerebellar and parietal contributions. Journal of Neurophysiology 79: 1535–1548.

47. Corbetta M, Akbudak E, Conturo TE, Snyder AZ, Ollinger JM, et al. (1998) A common network of functional areas for attention and eye movements. Neuron 21: 761–773.

48. Fias W, Lammertyn J, Reynvoet B, Dupont P, Orban GA (2003) Parietal representation of symbolic and nonsymbolic magnitude. Journal of Cognitive Neuroscience 15: 47–56.

49. Rushworth MFS, Passi T, Sigala PK (2001) Attention systems and the organization of the human parietal cortex. Journal of Neuroscience 21: 5262–5271.

50. Livesey AC, Wall MB, Smith AT (2007) Time perception: manipulation of task difficulty dissociates clock functions from other cognitive demands. Neuropsychologia 45: 321–331.

51. Ballan M, Stackman JR, Henik A, Fuchs A (2010) Spatiotemporal brain dynamics of a two digit number comparison task. Society for Neuroscience 40th annual meeting. San DiegoCA. Society for Neuroscience.

52. Jiang YH, Kamwisher N (2003) Common neural substrates for response selection across modalities and mapping paradigms. Journal of Cognitive Neuroscience 15: 1080–1094.

53. Botvinick M, Nystrom LE, Fissell K, Carter CS, Cohen JD (1999) Conflict monitoring versus selection-for-action in anterior cingulate cortex. Nature 402: 179–181.

54. Braver TS, Barch DM, Gray JR, Mollise DL, Snyder A (2001) Anterior cingulate cortex and response conflict: Effects of frequency, inhibition and errors. Cerebral Cortex 11: 825–836.

55. Garavan H, Ross TJ, Knutman J, Stein EA (2005) A midline dissociation between error-processing and response-conflict monitoring. Neuroimage 20: 1132–1139.

56. Ullsperger M, von Crummen DY (2001) Subprocesses of performance monitoring: A dissociation of error processing and response competition revealed by event-related fMRI and ERPs. Neuroimage 14: 1387–1401.

57. Roberts KL, Hall DA (2008) Examining a supramodal network for conflict processing: A systematic review and novel functional magnetic resonance Imaging data for related visual and auditory stroop tasks. Journal of Cognitive Neuroscience 20: 1063–1078.

58. Corbetta M, Shulman GL (2002) Control of goal-directed and stimulus-driven attention in the brain. Nature Reviews Neuroscience 3: 201–215.

59. Deimon R, Duncan Ji (1995) Neural mechanisms of selective visual attention. Annu Rev Neurosci 18: 193–222.

60. Jones AD, Cho RY, Nystrom LE, Cohen JD, Braver TS (2002) A computational model of anterior cingulate function in speeded response tasks: effects of frequency, sequence, and conflict. Cogn Affect Behav Neurosci 2: 300–317.

61. Cauldon JF, Brannon EM (2005) Semantic congruity affects numerical judgments similarly in monkeys and humans. Proceedings of the National Academy of Sciences of the United States of America 102: 16507–16511.