J Neurophysiol 107: 1748–1755, 2012.
First published December 28, 2011; doi:10.1152/jn.00082.2011.

Covert attention regulates saccadic reaction time by routing between different visual-oculomotor pathways

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Submitted 31 January 2011; accepted in final form 21 December 2011

Guan S, Liu Y, Xia R, Zhang M. Covert attention regulates saccadic reaction time by routing between different visual-oculomotor pathways. *J Neurophysiol* 107: 1748–1755, 2012. First published December 28, 2011; doi:10.1152/jn.00082.2011.—Covert attention modulates saccadic performance, e.g., the abrupt onset of a task-irrelevant visual stimulus grabs attention as measured by a decrease in saccadic reaction time (SRT). The attentional advantage bestowed by the task-irrelevant stimulus is short-lived: SRT is actually longer ~200 ms after the onset of a stimulus than it is when no stimulus appears, known as inhibition of return. The mechanism by which attention modulates saccadic reaction is not well-understood. Here, we propose two possible mechanisms: by selective routing of the visuomotor signal through different pathways (routing hypothesis) or by general modulation of the speed of visuomotor transformation (shifting hypothesis). To test them, we designed a cue gap paradigm in which a 100-ms gap was introduced between the fixation point disappearance and the target appearance to the conventional cued visual reaction time paradigm. The cue manipulated the location of covert attention, and the gap interval resulted in a bimodal distribution of SRT, with an early mode (express saccade) and a late mode (regular saccade). The routing hypothesis predicts changes in the proportion of express saccades vs. regular saccades, whereas the shifting hypothesis predicts a shift of SRT distribution. The addition of the cue had no effect on mean reaction time of express and regular saccades, but it changed the relative proportion of two modes. These results demonstrate that the covert attention modification of the mean SRT is largely attributed to selective routing between visuomotor pathways rather than general modulation of the speed of visuomotor transformation.

cue; express saccade; inhibition of return; gap

REACTION TIME SERVES AS A simple but efficient method for studying the process of sensorimotor transformation. When humans and nonhuman primates perform a practiced visually guided saccadic task, saccadic reaction times (SRT or saccadic latency) follow a skewed normal distribution (Carpenter and Williams 1995). Changing either the characteristics of the external visual stimulus or the internal brain state can alter SRT (Boch et al. 1984; Schiller et al. 2004; Weber et al. 1992). For example, when a blank interval (gap) is introduced between fixation point offset and saccadic target onset, SRT distribution becomes a bimodal profile: some saccades, called "express saccades", have a short latency (~100 ms in humans and ~80 ms in monkeys), whereas others, called "regular saccades," have a longer latency (~150 ms in humans and ~140 ms in monkeys; Fischer and Boch 1983; Fischer and Ramsperger 1984). This bimodality has been generally agreed to arise from the coexistence of two saccadic pathways, although it is controversial which exact neural circuits mediate express and regular saccades (Isa and Hall 2009; Schiller and Tehovnik 2001). The dispute was mainly caused by the conflicting observation about whether visual information could be conveyed from superficial layers to deeper layers within the superior colliculus (SC; Behan and Appell 1992; Edwards 1980; Isa and Hall 2009; May 2006; Mays and Sparks 1980; Schiller et al. 1974; Sprague 1975). One assumption was that a posterior circuit including SC and lateral intraparietal cortex (LIP) mediated express saccades, and an anterior circuit including frontal eye field (FEF) mediated regular saccades (Schiller and Tehovnik 2001). Alternatively, a shorter pathway, starting from retina and visual cortex to superficial layers of SC and then to deeper layers of SC, was proposed to mediate express saccade (Isa 2002; Isa and Hall 2009). Regardless of the dispute, the two modes of SRT reflect the involvement of two distinct pathways and thus can be used as a psychophysical probe to access the process of visuomotor transformation.

Inhibition of return (IOR) exemplifies the influence of covert attention on visuomotor transformation. In the classic cued visual reaction time task (Posner 1980), subjects are instructed to make a saccade to a target that appears soon after the brief appearance of a task-irrelevant cue, regardless of the location of the cue. Nevertheless, the task-irrelevant cue markedly affects the mean SRT: comparing saccades to the cued with uncued locations, SRT is shorter soon after the onset of the task-irrelevant cue but becomes longer ~200 ms later (Klein 2000; Posner and Cohen 1984). This phenomenon of lengthening the SRT when the cue-target onset asynchrony (CTOA) is long is called IOR. The phenomenon of IOR has been attributed to various mechanisms such as the limited duration of attention at one specific location (Posner et al. 1985), perceptual impairment (Gibson and Egeth 1994), and activation of oculomotor intention (Rafal et al. 1989). In the present study, the behavioral task is modified from the conventional IOR paradigm in which the covert attention was induced by the sudden onset of a salient visual stimulus (cue) without making a saccade to it.

To study the mechanisms underlying the modulation of reaction times by covert attention, we took advantages of both gap effect and IOR by introducing a gap interval to the cueing paradigm (cue gap paradigm; Fig. 1; Abrams and Dobkin 1994), expecting that the cue could induce covert attention and the gap could elicit the bimodal distribution of SRT. This enabled us to test two different hypotheses about how a task-irrelevant cue can affect SRT: *1*) changing the route of visuomotor signal transmission between the express and regular saccadic pathways, leading to changes in the proportion of express vs. regular saccades (Fig. 2*A*, *top*); and *2*) changing processing speed, resulting in a shift of the mean SRT for

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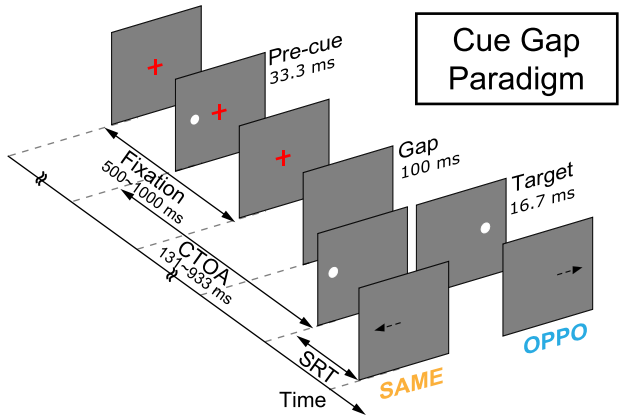

Fig. 1. Schematic diagram illustrates the cue gap paradigm. The duration of each frame is indicated beside the frames. The subjects were instructed to keep fixation at the red cross (in the center of screen) despite the sudden onset of a task-irrelevant cue (either left or right) and then make a saccade to the target stimulus (either left or right) as soon as possible. Cueing condition differs in the interval between the onset of the cue and the target stimulus (CTOA) and also differs in the spatial relationship between the cue and the target, either on the same side (SAME trial) or opposite sides (OPPO trial). Different trials were mixed randomly in a session, and the SAME trials and OPPO trials occurred with equal probability. SRT, saccadic reaction time.

either one or both modes of saccades (Fig. 2*A*, *bottom*) but no change in the proportion of express and regular saccades. Here, we measured the effect of a task-irrelevant cue on gap saccades in normal human subjects. We found that the cue modulated the relative proportion of two modes rather than shifted the reaction time of either mode. These findings support the routing hypothesis.

METHODS

Subjects. Thirteen 22-to-35-yr-old healthy human subjects were initially trained in a gap paradigm for several days. All subjects showed the expected training effect on developing express saccades, but the profiles of SRT distribution varied among subjects. Not all subjects showed a clear bimodal distribution of saccadic latencies in the gap paradigm. Because our statistical model required a clear bimodal distribution of SRTs in the gap paradigm, we chose for further study only the six subjects who showed a clear bimodality of their SRT distribution. One of them (GS) was an author, whereas the others (YJ, GJ, LZ, ZL, and ZZ) were naïve to the purpose of this study. The results did not show a difference between the author and naïve subjects. Experiments were conducted under a protocol approved by Institute of Neuroscience, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences.

Apparatus. Visual stimuli were presented on a 21-in. monitor (Sony Multiscan G520) controlled by a computer running MATLAB (The MathWorks) with Psychtoolbox (PTB-3; Brainard and Pelli). The vertical refresh rate was 120 Hz, and the spatial resolution of the monitor was set at 1024 × 768 pixels. Seated in a light-isolated room, the subject viewed the monitor from a distance of 80 cm using a chin and forehead rest to stabilize head position. Luminance was measured with a photometer (LS-110; Konica Minolta). We measured eye position at a sample rate of 1 kHz using a video-oculography eye tracker (EyeLink 1000 Desktop; SR Research), which was controlled by MATLAB software. All data analysis was done with MATLAB version 2007b.

Data collecting procedure. The total testing time for each subject per day was <60 min. Experiments were divided into sessions, each of which lasted for <13 min, followed by an intersession interval of ~10 min. At the beginning of each session, we orally instructed the subject about the paradigm and calibrated the eye tracker by monitoring the position of the right eye. We began to collect data when the subjects' correct percentage reached 90% (eye movement initiated within 500 ms after target onset and ended within a 3 × 2° window centered at target location and without breaking fixation) and the two modes of the SRT distribution had to become well-separated. It usually took subjects several days to reach this criterion, but this time differed from subject to subject.

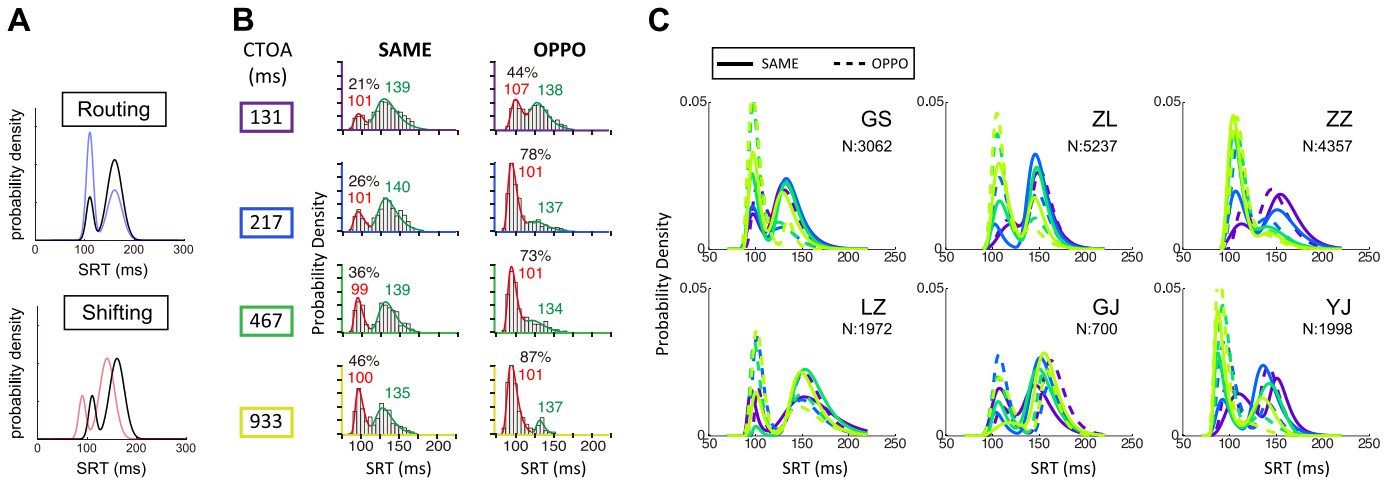

Fig. 2. Cue induces changes in relative proportion of express vs. regular saccades. *A*: predications of the 2 hypotheses. Routing hypothesis expects the change in the relative proportion of express saccades vs. regular saccades, reflecting 1 peak to grow larger and the other to become smaller (see the comparison between the blue and the gray curves, *top*). Shifting hypothesis expects the change in the reaction times for each mode of saccade, leading to the shift of the peaks (see the comparison between the red and the gray curves, *bottom*). *B*: SRT distributions for an example subject. Eight histograms (with bin width of 5 ms) represent the SRTs obtained in different cueing conditions of the cue gap paradigm. *Left* and *right* columns: trials under the SAME and OPPO condition, respectively. Rows: trials under different CTOA conditions. Each curve represents the maximum likelihood estimates with bimodal generalized extreme value distributions of the SRTs, with red and green curves depicting the express saccades and the regular saccades. The fitted parameters P (proportion of express saccade in percent), $Mean_1$ (mean SRT of express saccade), and $Mean_2$ (mean SRT of regular saccade) are shown in black, red, and green, respectively. *C*: SRT distributions for all subjects. Each panel superimposes 1 subject's SRT distributions obtained in all cueing conditions. Data in different CTOA conditions are indicated by colors: from smallest to largest CTOA, the SRT distributions are represented in purple, blue, green, and yellow curves, respectively. Data from SAME and OPPO trials are denoted by solid and the dashed lines, respectively. *N* denotes the total trial number. The proportions of express saccade are markedly modulated by the cue.

Visual stimuli and eye position detection. Screen background was uniformly illuminated at 4.6 cd/m^2. The fixation point was a red orthogonal cross (0.3° in length). The cue and the saccadic target were round white dots with a blurred edge (0.7° in diameter, 29.2 cd/m^2). Gaze position was recorded from 200 ms before the fixation spot disappeared to the end of trial. A trial would be aborted if the subject broke fixation, that is, the recorded eye position fell out of an invisible $3 \times 3°$ square window centered at the fixation point during fixation period.

Gap paradigm. This is a training paradigm. In each trial, the fixation point appeared at the center of screen from the beginning of the trial and lasted for a variable period of 500, 750, or 1,000 ms; 100 ms after the fixation disappeared, the saccadic target appeared randomly at 7° to the left or right of the fixation point for 16.7 ms. The subject was instructed to gaze at the fixation cross until the saccadic target appeared and to make a saccade to the target as rapidly as possible.

Cue gap paradigm. This served as the main task for the present study, as illustrated in Fig. 1. It differs from the gap paradigm by the addition of a cue for a brief period (33.3 ms) that appeared randomly during the fixation period at 6.3° to the left or right of the fixation point. After a 100-ms gap interval, the saccade target appeared with the same duration and location as in the gap paradigm. The cue and the target could appear either on the same side ("SAME" trial) or the opposite side ("OPPO" trial), and CTOA varied from trial to trial within a session (ranging from 131 to 933 ms with logarithmically chosen steps). Subjects were instructed to make a saccade to the saccadic target as rapidly as possible but not to react to the cue.

Manual paradigm. This task was designed as a control for testing whether the temporal characteristic of IOR in our experiments shared similar features with the classic IOR, as measured by the manual reaction time (MRT). This task differs from the cue gap paradigm by the presence of the center fixation point throughout the whole trial. The subject was instructed to gaze at the fixation point throughout the trial and to press a key with the right hand once he/she detected the onset of the target.

Analysis of SRT. We defined the saccadic initiation time as when the eye velocity exceeded 30°/s and lasted for >5 ms. The SRT is defined as the time interval between saccade target onset and saccade initiation. Saccades satisfying the following criteria were analyzed: *1*) the eye position did not vary >1° in the 100 ms immediately before the saccade. This ensured proper fixation before saccade. *2*) Saccade duration was between 10 and 50 ms. *3*) Saccade occurred ≥70 ms after the target onset. *4*) Saccadic end point fell within $3 \times 2°$ window centered around the saccadic target. To rule out outliers and make accurate fitting, we further filtered out a few trials for which SRT probability density was lower than ~0.0028 in the SRT distribution of each subject's pooled data. Mean SRT was calculated as the arithmetic mean of the SRTs.

Analysis of bimodal distribution. To analyze the bimodal distribution of SRT in detail, we needed to obtain accurately the proportion of express vs. regular saccade and the mean reaction times of both modes of saccades. To prevent the possible bias caused by arbitrarily separating two modes, we used the maximum likelihood estimation approach to quantify these parameters: we approximated the bimodal distribution with a function containing undetermined parameters and then fit it with the experimental SRT data to maximize its likelihood so as to get the best estimate of each parameter. We used the generalized extreme value distribution [$GEV_{(\mu,\sigma,\xi)}$] to approximate each mode because the distributions for both modes are skewed. The advantage of the GEV distribution over the Gaussian and log-Gaussian distributions is that GEV allows flexible manipulations of skewness so that it fits the skewed reaction time distribution better. In addition, we used the parameter P to measure the fraction (proportion) of the first (express saccade) mode. Therefore, the probability density function (f_{bm}) of the bimodal SRT distribution is described by the following formula:

$$f_{bm}(x;P,\mu_1,\sigma_1,\xi_1,\mu_2,\sigma_2,\xi_2) = P \cdot f_{GEV}(x;\mu_1,\sigma_1,\xi_1) + (1-P) \cdot f_{GEV}(x;\mu_2,\sigma_2,\xi_2)$$

where the GEV distribution is:

$$f_{GEV}(x;\mu,\sigma,\xi) = \frac{1}{\sigma} t(x)^{\xi+1} e^{-t(x)}$$

where t is:

$$\begin{cases} t(x) = \left(1 + \xi\dfrac{x-\mu}{\sigma}\right)^{-1/\xi}, & \text{if } \xi \neq 0 \\ t(x) = e^{-(x-\mu)/\sigma}, & \text{if } \xi = 0. \end{cases}$$

In the GEV distribution, μ, σ, and ξ represent location, scale, and skewness of the curve, respectively. The mean of this distribution was determined by:

$$\text{mean}_{GEV(\mu,\sigma,\xi)} = \mu + \sigma\frac{\Gamma(1-\xi)-1}{\xi}, \text{ if } \xi \neq 0, \xi<1$$

where Γ is the gamma-function.

In the bimodal SRT distribution function, the probability density varies with x, which represents SRT, and the subscripts 1 and 2 mark the parameters for the first and second modes. The proportion of express saccade was quantified by P, and the mean reaction time of the express and regular saccades by $\text{mean}_{GEV(\mu1,\sigma1,\xi1)}$ and $\text{mean}_{GEV(\mu2,\sigma2,\xi2)}$, respectively.

We analyzed data from each subject separately. We applied the maximum likelihood estimate under each experimental condition. To test the validity of this fitting procedure, we applied the 1-sample Kolmogorov-Smirnov test with $P > 0.03$ indicating good fitting. Only 1 out of 48 data sets across 6 subjects failed to show the lack of fit.

MRT. We also filtered out all MRT for which probability density was lower than ~0.0003. We calculated the mean MRT as the arithmetic mean value for each experimental condition.

Analysis of factors that contribute to mean SRT change. From the bimodal GEV distribution, the mean SRT could be calculated by the following equation:

$\text{Mean}_{SRT} = P \times \text{Mean}_1 + (1 - P) \times \text{Mean}_2$.

Therefore, mean reaction time is only determined by three parameters: P, Mean_1, and Mean_2. P represents the proportion of express saccades, and Mean_1 and Mean_2 are the mean reaction times of the express and regular saccades, respectively.

To investigate which parameter contributes to the change of the mean SRT observed in different cueing conditions, we calculated the predicted Mean_{SRT} caused by changing each parameter independently. The more a parameter contributes to Mean_{SRT} change, the better it predicts the real value of Mean_{SRT}. Here, we use subject GS's data as an example to illustrate the steps of our analysis. *1*) We pooled all of GS's trials from the cue gap paradigm, fitted the distribution of SRT using the bimodal distribution function, and calculated the values of P_{all}, Mean_{1all}, and Mean_{2all}, respectively. *2*) We started to assess the contribution of each parameter to mean SRT. In a given condition, with fitting, we got the values of P_{cur}, Mean_{1cur}, and Mean_{2cur} under this current condition. *3*) We used one parameter calculated from the current condition and used the other two parameters from the whole data set to calculate a predicted mean SRT, and thus we could get three predicted values, which were predicted by the changes of the proportion of express saccades, the mean reaction times of the express saccades, and the mean reaction times of the regular saccades:

$\text{Mean}_{SRT(P)} = P_{cur} \times \text{Mean}_{1all} + (1 - P_{cur}) \times \text{Mean}_{2all}$, predicted by P;

$\text{Mean}_{SRT(\text{Mean}_1)} = P_{all} \times \text{Mean}_{1cur} + (1 - P_{all}) \times \text{Mean}_{2all}$, predicted by Mean_1;

$\text{Mean}_{SRT(\text{Mean}_2)} = P_{all} \times \text{Mean}_{1all} + (1 - P_{all}) \times \text{Mean}_{2cur}$, predicted by Mean_2.

4) We then calculated the $\text{Mean}_{SRT(P)}$, $\text{Mean}_{SRT(\text{Mean}_1)}$, and $\text{Mean}_{SRT(\text{Mean}_2)}$ under all conditions for subject GS. By comparing

the real values of the SRT with the three predicted values, we could delineate which parameter had the greatest effect on the mean SRT to test the routing and shifting hypotheses.

RESULTS

Changes in the proportion of express vs. regular saccades. To study how the cue modifies the bimodal distribution of SRTs, we analyzed the SRT distribution from 6 subjects in cue gap paradigm for all of the different CTOA durations. As is shown in Fig. 2*B*, 1 subject's SRT data are displayed in 4 × 2 histograms as an example, which contains both SAME and OPPO trials (2 columns) and 4 different CTOA durations (4 rows). Each SRT histogram was fitted with a bimodal GEV distribution function (see METHODS), and then we examined the proportion of express saccade (P, marked with percentage in black in Fig. 2*B*) and the mean reaction time of the express and regular saccades ($Mean_1$ and $Mean_2$, marked in red and green, respectively, in Fig. 2*B*). We also performed a 1-sample Kolmogorov-Smirnov test for each bimodal GEV fit to test its validity. We defined a good fit as having a P value >0.03 (see METHODS).

We found that: *1*) the proportion of the express saccades changed progressively with increasing CTOA for both SAME and OPPO conditions. *2*) When CTOA was large (in lower 3 rows), the proportion of express saccade was smaller in the SAME condition than that in the OPPO condition, suggesting that at longer intervals the cue inhibited the generation of express saccades to its position but had less effect on the generation of express saccade to other positions. *3*) The mean reaction times for both types of saccades ($Mean_1$ and $Mean_2$) remained relatively unchanged despite cueing conditions. These results clearly indicate that a task-irrelevant cue markedly affects the relative proportion of express vs. regular saccades while leaving the mean reaction time of each type of saccade largely unchanged.

Because of the variation among subjects, we analyzed each subject's SRT distributions separately and displayed the data in Fig. 2*C*. For each subject, the curves of SRT distributions from all eight cueing conditions were superimposed: data from different CTOA conditions were indicated with different colors; SAME and OPPO conditions were denoted with solid and dashed lines, respectively. Note that the relative areas of the two peaks change markedly with different cuing conditions in all subjects, indicating the variation of the proportion of express saccades vs. regular saccades. However, the positions of the peaks are less consistent among subjects. Although the positions of the first peaks remain unaltered in all subjects, the second peaks remain almost unaltered in subjects GS, LZ, ZL, and ZZ and shift a little bit in subjects YJ and GJ. Intuitively, the raw data in Fig. 2 suggest that the cue modulates the proportion of the two modes of saccade and thus support the routing hypothesis.

Consistence between proportion change and mean SRT change. We have observed the phenomenon that the cue modulated the proportion of express saccade. Is there any correlation between the changes in proportion of express saccades with the changes in the mean SRT under cue modulation? In other words, does the change in proportion of express saccades in our study reflect IOR effect as that in mean SRT? To answer these questions, we plotted the proportion of express saccade in SAME and OPPO trials as a function of CTOA, as is displayed in Fig. 3. Data from all subjects show the common feature: when the CTOA is larger than ~200 ms, the proportions of express saccades in the SAME trials (dark yellow triangles linked with dashed curve) become markedly lower than that in OPPO trials (dark blue triangles linked with dashed curve), which indicates the inhibition of generating express saccade to the cued location. This feature resembles the IOR phenomenon measured with mean SRT in previous studies. To assess visually the correlation between the proportions of express saccades and mean SRT, we plotted the mean SRT in the same figure for direct comparison. For all subjects, when the CTOA is larger than ~200 ms, the mean SRTs in the SAME trials (light yellow circles linked with solid curve) become markedly longer than that in OPPO trials (light blue circles linked with solid curve), which signifies typical IOR. The proportion of express saccade and the mean SRT show similar dependence on CTOA: the higher the proportion of express saccade, the shorter the mean SRT. Such consistency

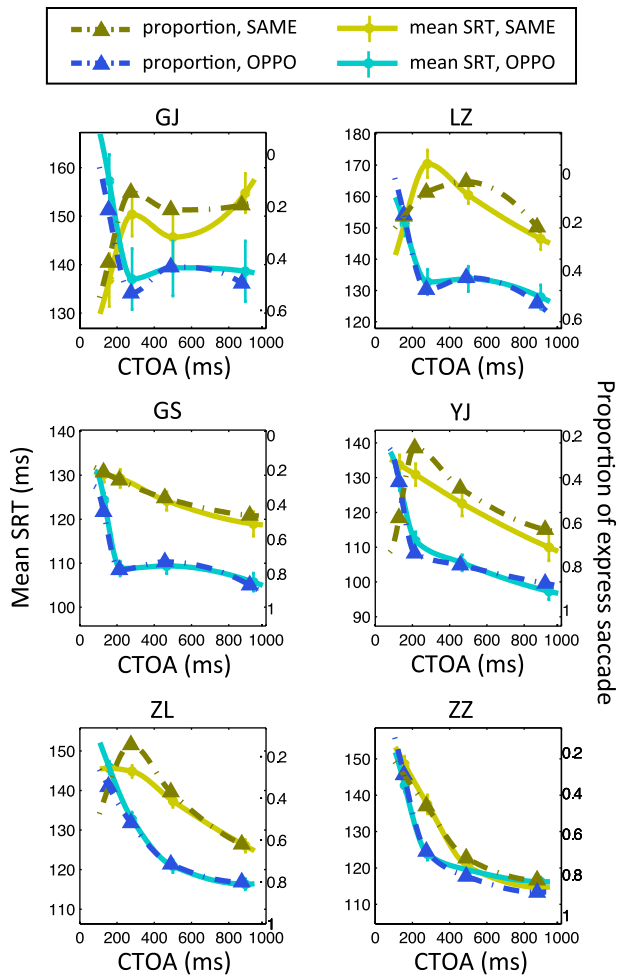

Fig. 3. Correlation between mean SRT and proportion of express saccade. Results from each subject are presented separately in each panel. Data points with error bars (±2 SE) connected by solid curves represent mean SRTs, for which values could be read from the *left* axis; triangles connected with dashed lines represent the proportion of the express saccade, for which values could be read from the *right* axis. Data from SAME and OPPO trials are marked by yellow and blue colors, respectively. The proportion and the mean SRT showed similar dependence on CTOA.

suggests that the cue-evoked covert attention modulates SRT through regulating the proportion of express saccade.

Statistical analysis of the origin of mean SRT change. The mean SRT could be affected by three parameters: the proportion of express saccade (P), the mean reaction time of express saccades ($Mean_1$), and the mean reaction time of regular saccades ($Mean_2$). The contributions made by different parameters reflect distinct mechanisms of covert attention modulation: larger contribution of P supports the routing hypothesis, whereas larger contribution of either $Mean_1$ or $Mean_2$ supports the shifting hypothesis. To evaluate the contribution of each parameter, we introduced three predicted mean SRTs corresponding to three parameters, respectively (see METHODS for detailed description). In Fig. 4, we plotted the predicted values against the real values of mean SRT in different cueing conditions and made linear regression on the three groups of predicted values, respectively. If a parameter made a dominant contribution in affecting mean SRT, the predicted values based on it would approximate to the real mean SRTs, and thus they would distribute along the diagonal line with the slope of 1.0. For all subjects in Fig. 4, the mean SRTs predicted by P (red circles) mostly fell along the gray diagonal line, and the fitted slopes (denoted with red numbers) are close to 1.0; conversely, values predicted by $Mean_1$ (blue triangles) and $Mean_2$ (black triangles) do not lie around the diagonal line but around the horizontal lines, for which fitted slopes (denoted with blue and black numbers, respectively) are close to 0.0.

To evaluate further whether the three groups of predicted mean SRTs approximated to the real values, we tested whether the three fitted slopes agreed with 1.0 based on the 97% confidence interval. For P, all but one subject (ZZ) show good agreement, whereas for $Mean_1$ and $Mean_2$, all subjects show significant differences. Therefore, the change of P well predicts the mean SRT change, but the change of $Mean_1$ and $Mean_2$ does not. Moreover, for all subjects, the *F* test with 97% confidence interval demonstrates that the mean SRT variation caused by P is comparable with the actual variation, but variation caused by $Mean_1$ and $Mean_2$ is significantly smaller than the actual variation. Taken together, it is the proportion of the two modes, rather than the reaction times of either express saccade or regular saccade, that dominantly contributes to the mean SRT change. This analysis confirms that the cue-induced covert attention modulates mean SRT by regulating the proportion of express saccades, therefore supporting the routing hypothesis.

The cross-over latency of IOR. The previous cued visual reaction time studies reported that there was typically an early phase of facilitation at the cued location, during which the response to cued position was faster than that to uncued position, and that the time point when the facilitation converted to the inhibition (named cross-over latency) was about 200–300 ms after the cue onset for human subjects (Klein 2000). In our results, the reaction time profiles do not show the early phase of facilitation in all subjects except GJ. Nonetheless, five subjects showed less inhibition at the cued location when the CTOA was <200 ms compared with in larger CTOA conditions (see Fig. 3). We wondered whether the lack of early facilitation in our results was due to the specific manipulations of the cue gap paradigm or because the training shortened the cross-over latencies. Therefore, we tested four of the subjects in the classic manual cued visual reaction time paradigm in which they reported the onset of the target by manually pressing a key. If the earlier cross-over latency were task-specific, the cross-over latency in the manual response task should be different from that in cue gap task; otherwise, the cross-over latency should also be very short. Figure 5*A* shows the comparison of the mean MRT with the mean SRT. For all subjects, the two reaction times showed similar dependence on CTOA, and the cross-over latencies were consistent despite different motor systems being used. Such results indicate that the earlier cross-over latency is not task-specific. We then took a close look at whether the cross-over latencies were affected by training. Figure 5*B* plotted the cross-over latency as a function of the days of data collection in one example subject. Following time, the cross-over latency became shorter. Such a training effect was common in all subjects, which suggested that the early inhibition at the cued location observed in this study might be due to the relatively long period of data collection. Actually, the IOR reported in monkey studies showed that the inhibition phase occurred as early as ~80 ms (Dorris et al. 2002), which could be also caused by the excessive training.

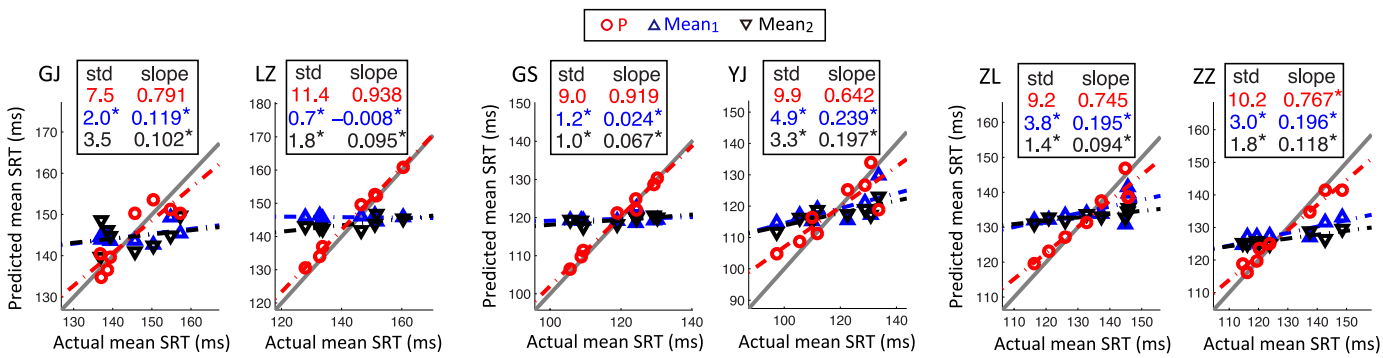

Fig. 4. Contribution of P, $Mean_1$, and $Mean_2$ to the mean SRT. Data from each subject are presented separately in each panel. For each subject, we plotted the predicted mean SRTs against the actual values. The red, blue, and black data points represent the values predicted by the proportion of express saccade (P), the mean reaction time of express saccades ($Mean_1$), and the mean reaction time of regular saccades ($Mean_2$), respectively. The 3 dashed lines indicate the linear regression for the 3 groups of predicted mean SRTs, respectively. Above the data points are the standard deviations (std) of the 3 groups of predicted values as well as the 3 fitted slopes with colors corresponding to the data points. The asterisk beside the std value denotes the significant difference between the predicated values with the actual values based on *F* test (97% confidence), and the asterisk beside the slope values denotes the significant difference from 1.0, both indicating less contribution in the change of mean SRT. Only the changes in P dominantly contribute to the change of the mean SRT.

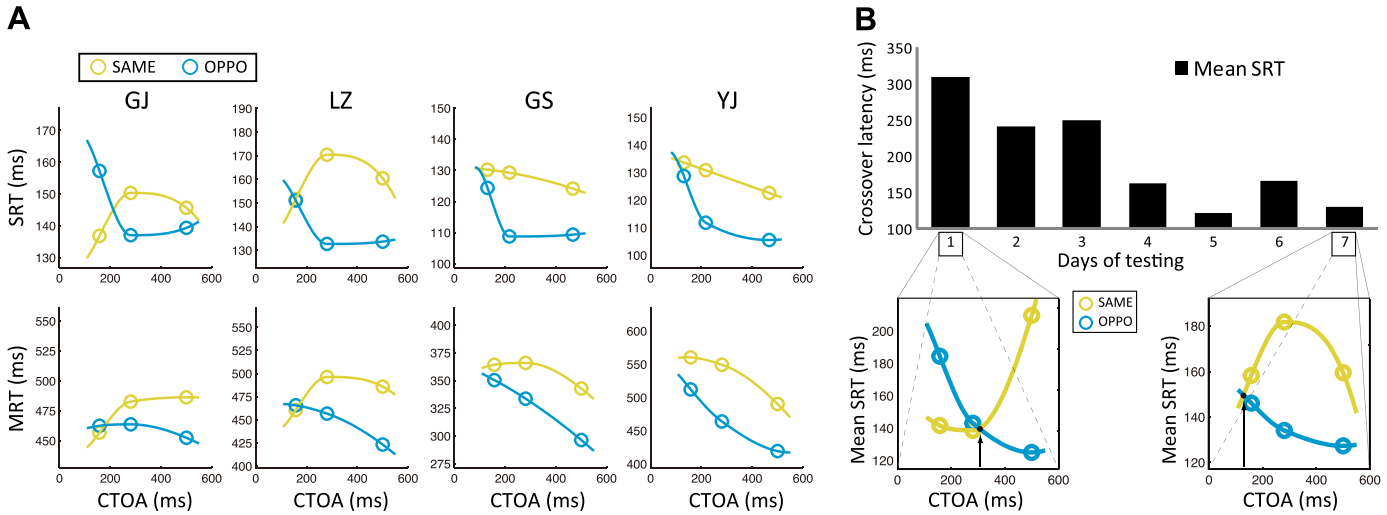

Fig. 5. Cross-over latency of inhibition of return (IOR). *A*: comparison between SRT and the manual response time (MRT) for 4 subjects. For each subject, the *top* represents the data of mean SRT (from the cue gap paradigm) and the *bottom* presents the data of mean MRT (from manual response task) under the SAME (yellow) and OPPO (blue) conditions. SRT and MRT show similar IOR profile and similar cross-over latencies. *B*: subject LZ's data of training effect. The cross-over latency for IOR gradually shortens with the days of testing. Filled bars represent the cross-over latencies calculated from mean SRT curves. The mean SRTs found for different CTOA in the 1st and last day of testing under the SAME (yellow) and OPPO (blue) condition are shown with the cross-over time indicated by the arrow.

DISCUSSION

In this study, we asked how cue-induced covert attention modulates SRT by adding a gap to the conventional cued visual reaction time task and analyzing the SRT distribution. We showed that the cue significantly modulated the relative proportion of express vs. regular saccades rather than the mean reaction times of either mode of saccades. These results suggest that covert attention regulates SRT through selective routing of oculomotor signals between two distinct pathways.

Comparison with previous IOR studies. The most remarkable difference between the present study and conventional cued visual reaction time studies is that we introduced a gap interval to the paradigm. Therefore, the cue gap task combines two phenomena together, IOR and gap effect. This design allowed us to examine the interaction between these two well-known phenomena and to examine the mechanisms of how cue-induced covert attention affects the process of visuomotor transformation. Regardless of the paradigm difference, all of our subjects showed IOR using the mean SRT level as a measure. This is consistent with many reports from previous cued visual reaction time studies (Chica et al. 2006; Klein 2000; Posner 1980; Posner and Cohen 1984; Wang and Klein 2010). This consistency indicates that the cue gap task and the conventional cued visual reaction time task have a similar mechanism of attentional modulation.

Tasks combining gap and cue, similar to our cue gap task, have been used in previous studies to assess the effect of the cue in generation of express saccades as well as the interaction between cue-induced attention and gap effect (Abrams and Dobkin 1994; Schiller et al. 2004). In one study, the cue was always valid in instructing the location and time of saccadic target onset (Schiller et al. 2004). With a fixed CTOA (150 ms), the authors reported that the valid cue increased the percentage of express saccades. Another study tested whether cue-induced attention and the gap effect (which involves the release of attention from the fixation point) modulated SRT using a similar mechanism (Abrams and Dobkin 1994). By showing that gap effect facilitated SRT equally for saccades to cued and uncued targets, the authors argued that the gap (200 ms) effect and cue-induced attention (860-ms CTOA) were mediated by distinct neural mechanisms. We asked a very different question: whether IOR could be not only in the mean SRT, but also in the proportion of express saccades.

Because we were interested in seeing how the percentage of express saccades changed as a function of CTOA, we trained the subjects using a simple gap task until they demonstrated a clear bimodal distribution in SRT and in fact rejected subjects who did not develop a clear bimodal distribution. The previous combined gap and cued-visual attention studies did not adopt intensive training as we did. Although training makes the present study atypical, it mimics both the express saccade experiments and cued visual reaction time experiments in monkeys because behavioral training in monkeys usually takes months. For instance, the cross-over latency of IOR in our study is similar to that in monkey experiments but shorter than that in previous human studies (Dorris et al. 2002; Klein 2000). Since the neuronal mechanisms of IOR and express saccade generation are not clearly understood, it will be interesting to record neuronal responses in the monkeys that perform this cue gap task.

Cue evokes several cognitive functions. The abrupt onset of a task-irrelevant cue might evoke several cognitive activities such as visual attention (Gibson and Egeth 1994; Posner et al. 1985) and intention to make saccade (Rafal et al. 1989). Intertwined cognitive functions have been well-illustrated by single neuron recording in alert monkeys (Bisley and Goldberg 2003; Quian Quiroga et al. 2006; Shadlen and Newsome 2001). The proposed mechanisms of IOR are complicated and controversial. Some IOR studies describe IOR as the inhibition of saccade return (ISR), which could be mediated by local mechanisms (Hooge and Frens 2000), whereas others referred it as inhibition of attention return as suggested by the original studies of IOR (Posner 1980).

Since our cue gap task was modified from the conventional IOR paradigm, we consider the cue-dependent modulation as a form of attention modulation, which is consistent with the classic view of IOR in the original studies.

Neural pathways involved in generating express saccade. Monkeys and humans have two different mechanisms of reflexive visually guided saccades, express and regular saccades. The pathways generating these saccades are, in part, different. Regular saccades are generated by a pathway including the FEF: ablation of the FEF affects the latency of visual and memory-guided saccades (Tehovnik et al. 2000). The SC is clearly important in the generation of express saccades: ablation of the SC eliminates express saccades (Schiller et al. 1987). The activity of buildup neurons in the intermediate layers of the SC closely correlated with the generation of saccades: the higher the buildup activity, the more likely was the generation of express saccades (Dorris et al. 1997). These data suggest that there are two neural pathways for saccades: an anterior one that includes the FEF and a posterior one that requires V1 and the SC. There are two pathways by which V1 could affect the intermediate layers of the colliculus. The first is by a rapid pathway from layer 4B to middle temporal area (MT) to LIP, which results in very short visual latencies of LIP neurons (Bisley et al. 2004). LIP could then relay this information to the SC through the direct projection from LIP to the intermediate layers of the SC. A second pathway goes from layer 5 of V1 to the superficial layers of the SC, which could then relay visual information to the intermediate layers of the colliculus by a pathway within the colliculus (Isa and Hall 2009; Moschovakis et al. 1988). Our results demonstrate that the way in which a task-irrelevant cue first facilitates and then inhibits SRT is by altering the proportion of saccades generated by these two pathways: shorter mean SRT implies a greater proportion of saccades generated by the posterior pathway. Further studies will be required to see whether LIP is necessary for express saccades or whether the direct pathway from V1 to the SC is sufficient.

Because the cross-over latency in the cued MRT task has many of the same characteristics as that in the saccade task, it is possible that the facilitation and subsequent suppression of MRT by a task-irrelevant cue may also arise from a shift in proportion between two different pathways that generate MRT with different latencies. Further study of the reach pathways may well demonstrate an equivalent dual mechanism.

ACKNOWLEDGMENTS

We thank Dr. Si Wu for providing an eye-tracking system for data collection, Dr. Michael E. Goldberg for suggestions on manuscript preparation and English correction, Dr. Muming Poo for help in manuscript preparation, and Dr. Robert Rafal for suggestions and comments.

GRANTS

This study was supported by the Hundred Talents Program, Chinese Academy of Sciences; Pujiang Program, Shanghai Municipal Government; and the State Key Laboratory of Neuroscience, Chinese Academy of Sciences.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

S.G. and Y.L. designed the experiments; S.G., Y.L., and R.X. collected the data; S.G. and R.X. analyzed data and prepared all figures; S.G. and M.Z. wrote and revised the manuscript; M.Z. supervised the experiments.

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