# A functional dissociation of conflict processing within anterior cingulate cortex

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**Goal-directed behavior requires cognitive control to regulate neural processing when conflict is encountered. The dorsal anterior cingulate cortex (dACC) has been associated with detecting response conflict during conflict tasks. However, recent findings have indicated not only that two distinct subregions of dACC are involved in conflict processing but also that the conflict occurs at both perceptual and response levels. We clarified a functional dissociation of the caudal dACC (cdACC) and the rostral dACC (rdACC) in responding to different sources of conflict. The cdACC was selectively engaged in perceptual conflict whereas the rdACC was more active in response conflict. Further, the dorsolateral prefrontal cortex (DLPFC) was coactivated not with cdACC but with rdACC. We suggest that cdACC plays an important role in regulative processing of perceptual conflict whereas rdACC is involved in detecting response conflict.**

Goal-directed behavior often requires humans to overcome interference caused by distraction. The Stroop task[1] is one of the most frequently employed paradigms for studying human ability to control cognition in the face of interference. Subjects are asked to name the color of colored words. Response time (RT) is increased in naming the ink color of an incongruent stimulus (e.g., “RED” printed in blue ink) compared to a neutral stimulus (e.g., “XXXX” printed in blue ink). This is referred to as the Stroop interference effect. The conflict monitoring theory suggests that the dorsal anterior cingulate cortex (dACC) plays a role in detecting conflict in tasks such as the Stroop task and the flanker task[2], and the dorsolateral prefrontal cortex (DLPFC) engages in resolving the conflict[3-6]. An important aspect of this theory is that the conflict is caused at the response level.

In recent years, however, increasing numbers of neuroimaging studies have suggested that cortical responses to conflict depend on the source of conflict [7].

Specifically, it has been suggested that rostral dACC (rdACC) recruitment is restricted to the response conflict whereas caudal dACC (cdACC) is involved in pre-response conflict[8-10]. A neuropsychological study of patients with legions in cdACC or rdACC has supported this dissociation[11]. Other neuroimaging studies[12-15] and a recent review[16] found that two distinct regions within rostral and caudal dACC are involved in conflict processing but that the functions of the two subregions were not differentiated. We localized the coordinates of dACC activations reported in the previous studies and identified two distinctive subregions of dACC, which correspond to posterior rostral cingulate zone and anterior rostral cingulate zone[17] (Figure 1).

We assumed that rdACC and cdACC are involved in the conflict tasks and dissociated by the source of conflict: perceptual conflict recruits cdACC whereas response conflict recruits rdACC. We employed a version of the Stroop matching task used in a previous behavioral study[18] that allowed measurement of perceptual conflict and response conflict separately. Experimental tasks were composed of two conditions, a color-response condition (CR) and a word-response condition (WR), in which each condition included incongruent and neutral trials. Thus four types of trials were included; incongruent CR (iCR), neutral CR (nCR), incongruent WR (iWR) and neutral WR (nWR). Response conflict was minimized in iCR as subjects were only required to identify the sample color by selecting the corresponding color from two color cues and thus the interference effect was assumed to be caused by perceptual conflict at the pre-response level. In contrast, response conflict was maximized in iWR in which subjects were to translate the ink color of the colored word stimulus into a verbal representation, inhibiting the prepotent processing. Thus, the interference effect in WR was caused by both perceptual and response conflict.

Behavioral performance on the tasks showed that hit rates of each subject were higher than 96% in all conditions. RT was analyzed using a two-way repeated-measure

ANOVA (Figure 2). The results showed significant main effects of both conflict ($F_{(1,12)}$= 43.222, MSe=.013, p=.000) and response modality ($F_{(1,12)}$= 38.747, MSe=.059, p=.000), as well as a significant interaction effect ($F_{(1,12)}$= 18.086, MSe=.005, p=.001). The interference effect was greater in WR (284 ms) than in CR (125 ms). Since the response cues of iWR induced response conflict but the sample of iWR also included perceptual conflict, we calculated the response interference effect (i.e., 159 ms) by subtracting nWR from iWR in each subject. There was no significant difference between the sizes of the two interference effects ($t_{(12)}$=.933, p=.369) nor a significant correlation between them (r=.285, p=.345). These results do indicate, however, that the Stroop interference effect is caused by both perceptual and response conflicts[18,19].

For fMRI data, we compared incongruent trials with neutral trials for CR and WR separately (Figure 3a and Supplementary Table 1). The results showed that when subjects performed CR, cdACC activity (peaked at y=16) was greater on iCR than on nCR. In contrast, both cdACC and rdACC (peaked at y=16 and at y=33, respectively) showed greater activity on iWR than on nWR. However, the comparison of iCR with nCR includes only perceptual conflict, whereas the comparison of iWR with nWR includes both perceptual and response conflicts. Thus we analyzed the same data using a two-way ANOVA using factors of the conflict (incongruent vs.neutral) and the response modality (WR vs. CR) in order to measure perceptual conflict and response conflict separately (see Figure 3b and Supplementary Table 2). We found a positive main effect of the conflict in cdACC (peaked at y=5). In contrast, an interaction effect (i.e., [iWR – nWR] – [iCR – nCR]) was significant in rdACC (peaked at y=27). The main effect of response modality (i.e., [WR – CR]) was not significant in any subregion of ACC. We depicted BOLD signal changes of each trial type in the ROIs within both cdACC and rdACC in figure 4. In comparisons of peak activation between iCR and nCR and between iWR and nWR using paired-sample t-tests (two-tailed), the cdACC activation was higher in iCR than in nCR ($t_{(12)}$=2.360, p=.036) and in iWR than in nWR

($t_{(12)}$=3.303, p=.006). In contrast, in the rdACC region, the peak activation was higher in iWR than in nWR ($t_{(12)}$=2.963, p=.012), whereas iCR and nCR were not different ($t_{(12)}$=.442, p=.666).

To test the relationship between neural activity (i.e., the conflict effect) and behavioral responses (i.e., the interference effect), we calculated conflict effects of each subject using the peak value of the BOLD signal changes (i.e., iWR - nWR for the response conflict and iCR - nCR for the perceptual conflict) in both cdACC and rdACC. The results showed that the positive correlation between the interference effect observed in CR and the perceptual conflict effect was significant in cdACC (r=.623, p=.023) but not in rdACC (r=.402, p=.173). In contrast, the interference effect in WR and the response conflict effect showed a significant positive relationship in rdACC (r=.740, p=.004) but not in cdACC (r=.508, p=.076). The estimated response interference effect was highly correlated with rdACC activity (r=.748, p=.003) but not with cdACC activity (r=.424, p=.148).

An additional important finding was observed in DLPFC (see Supplementary Table 1; Brodmann area (BA) 9; Talairach coordinates: 48, 13, 27). The comparison of the incongruent condition with the neutral condition showed enhanced neural activity of DLPFC in WR but not in CR. In other words, DLPFC was coactivated with rdACC but not with cdACC. The coactivation of DLPFC and rdACC was also observed in the two-way ANOVA as the positive interaction effect which reflects response conflict (see Supplementary Table 2; BA 46; -42 19 21). DLPFC activation in the main effect of conflict was mainly caused by iWR since no activation of DLPFC was observed in comparison of iCR with nCR. fMRI results showed a functional dissociation of the conflict processing within dACC, in which response conflict recruits rdACC whereas perceptual conflict involves cdACC in accordance with previous studies[8-10,15]. The coordinates within each subregion of dACC are similar to the mean coordinates of the

previous studies (see Figure 1). Our ROI analyses confirmed this dissociation, in which response conflict results in greater activation in rdACC. In addition, the level of cdACC activation was highly related to the interference effect caused by perceptual conflict but not by response conflict. According to these findings, it is reasonable to expect that error processing is specific only to rdACC. Studies have supported this expectation, finding that cdACC was specific to the conflict but not to error processing, while rdACC showed error-related activation[10,20].

Cortical response to conflict processing has been observed in rdACC[8,9,21,22] while others found it in cdACC[5,6,23]. One possible interpretation of this disagreement is that those studies did not separate response-specific conflict from perceptual conflict and thus the cdACC activation in their studies might represent an accumulated effect of two types of conflict. Another potential interpretation is that the studies employed a predefined ROI within cdACC[24] or that a large region across dACC was activated by both pre-response and response[25].

Another important finding was also found in DLPFC (BA 9/46), which was coactivated with dACC only when response conflict occurred. This supports previous studies in which DLPFC plays an important role in cognitive control by resolving prepotent responses[5,21]. Even though the interference effect was observed and the perceptual conflict activated cdACC, no activation was observed in DLPFC when no response conflict occurred. These results suggest that DLPFC is involved in resolving only response conflict. However, previous studies reported coactivation of DLPFC, in which they found cdACC activation to pre-response conflict such as semantic conflict[8] and target detection[10]. One possible interpretation of this disagreement is that the task conditions of those studies might have required additional top-down processing from DLPFC such as a change of response selection strategy[26].

Taken together, we suggest that distinct subregions of dACC are involved in conflict processing: cdACC is engaged in perceptual conflict and rdACC is involved in response conflict. DLPFC seems specifically recruited only for response conflict, which indicates that only response conflict requires top-down cognitive control processing in order to override prepotent responses. These results support the conflict monitoring theory[3], but it might be possible to add a perceptual conflict module to the current conflict monitoring theory as a mediator. However, it is unclear how the brain resolves the perceptual conflict that occurred in the present study. One plausible suggestion is that cdACC plays a role in regulative processing at a perceptual level even if no response conflict occurs[27]. This regulative model would present more general account in the conflict monitoring system.

## METHODS SUMMARY

Thirteen neurologically healthy right-handed volunteers (ages 19 - 32; five females) without color blindness participated in this study. We used a variation of the Stroop color-word task in which a sample and a set of two alternative cues were presented in a screen. All words in the samples and response cues were presented in Korean. Experimental conditions were composed of four types of conditions; iCR, nCR, iWR and nWR. The iCR and nCR included two colored rectangles as response cues whereas in iWR and nWR the response cues were two color names in words. The task required subjects to match the color of the sample with a corresponding response cue. All experimental stimuli and null events continued for 2 sec and inter-stimulus-intervals averaging 2.9-second followed. All trial types were replicated 48 times in randomized order.

Images were acquired with a 3-T MRI system (Oxford magnet, Varian console magnet built by ISOL, fMRI center at KAIST in Daejeon, Korea). T2*-weighted gradient echo planner images (EPI) with 20 interleaved slices were acquired for the functional images (TR=2sec, TE=35ms, FA=85°, matrix=64X64, in-plane resolution=3.44mm, thickness=5mm) which were composed of 2 runs (294 volumes per run). T1-weighted images were also obtained.

SPM5 was used for image preprocessing and statistical analyses. Temporal and spatial disparities between slices were corrected and then the images were normalized to a standard MNI-305 T1-weighted image and accordingly resampled by isotropic 3mm voxels. The images were then spatially smoothed with an 8mm FWHM Gaussian kernel. Each condition was included in constructing a general linear model using a canonical hemodynamic response function. Contrast images were constructed by comparison of experimental events with null events. The contrast images were

submitted to group-level random-effects analyses (thresholded at $p<.05$ corrected using the false discovery rate[28]). Paired-sample t-tests and a two-way ANOVA were used.

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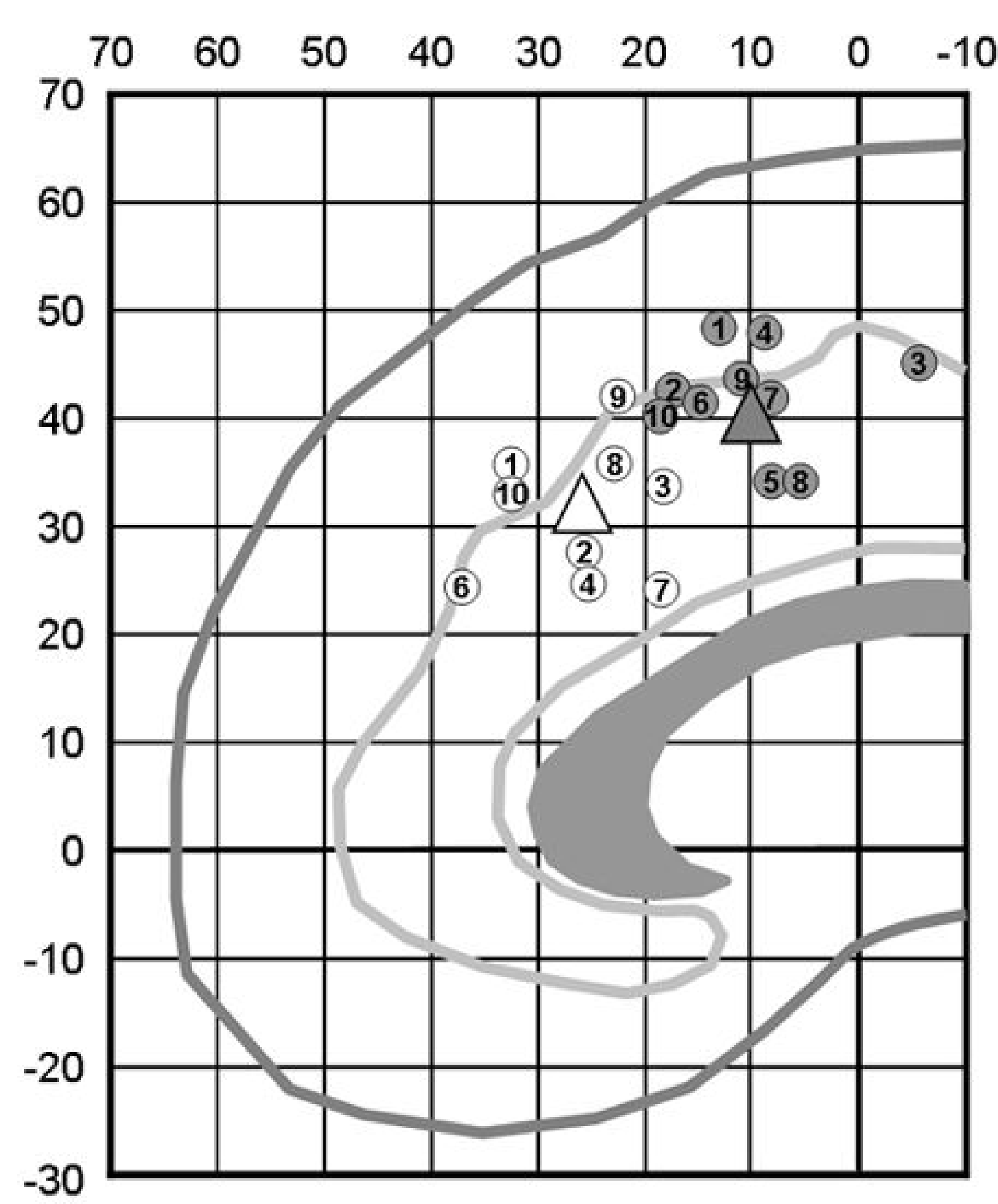
Figure 1. Localization of dACC activations during the Stroop or Stroop-like tasks found in selected studies. The white circles are located within rdACC and the gray circles are located in cdACC. Two triangles indicate the average coordinates of the white circles and of the gray circles. Each location indicates Talairach coordinates[29] showing the highest peak value in each study. The numbers indicate references; 1[9], 2[8], 3[10], 4[15], 5[25], 6[16], 7[12], 8[13], 9[30], 10[14]. Four of these studies (references 1-4) found both cdACC activity sensitive to pre-response conflict and rdACC activity sensitive to response conflict, one study (reference 5) found cdACC activity sensitive to both pre-response conflict and response conflict, and others (references 6-10) found two subregions within dACC sensitive to conflict processing with no functional dissociation. The average coordinates of white circles are x, y, z = 2, 26, 31, and those of gray circles are x, y, z = 1, 10, 42.

Figure 2. Behavioral performance on the Stroop tasks. Each bar represents the mean of RTs in each condition. Error bars indicate the mean ± the standard error of the mean (s.e.m.)

Figure 3. Significant activation within dACC. (A) The conflict effect observed in only cdACC (red) for CR but in both cdACC and rdACC (yellow) for WR. (B) The main effect of conflict (incongruent vs. neutral) showed significant activation in cdACC (red). A positive interaction effect ([iWR - nWR] - [iCR - nCR]) was significant in rdACC (yellow).

Figure 4. BOLD signal changes of each trial type with cdACC (the left) and rdACC (the right). Error bars indicate mean ± s.e.m.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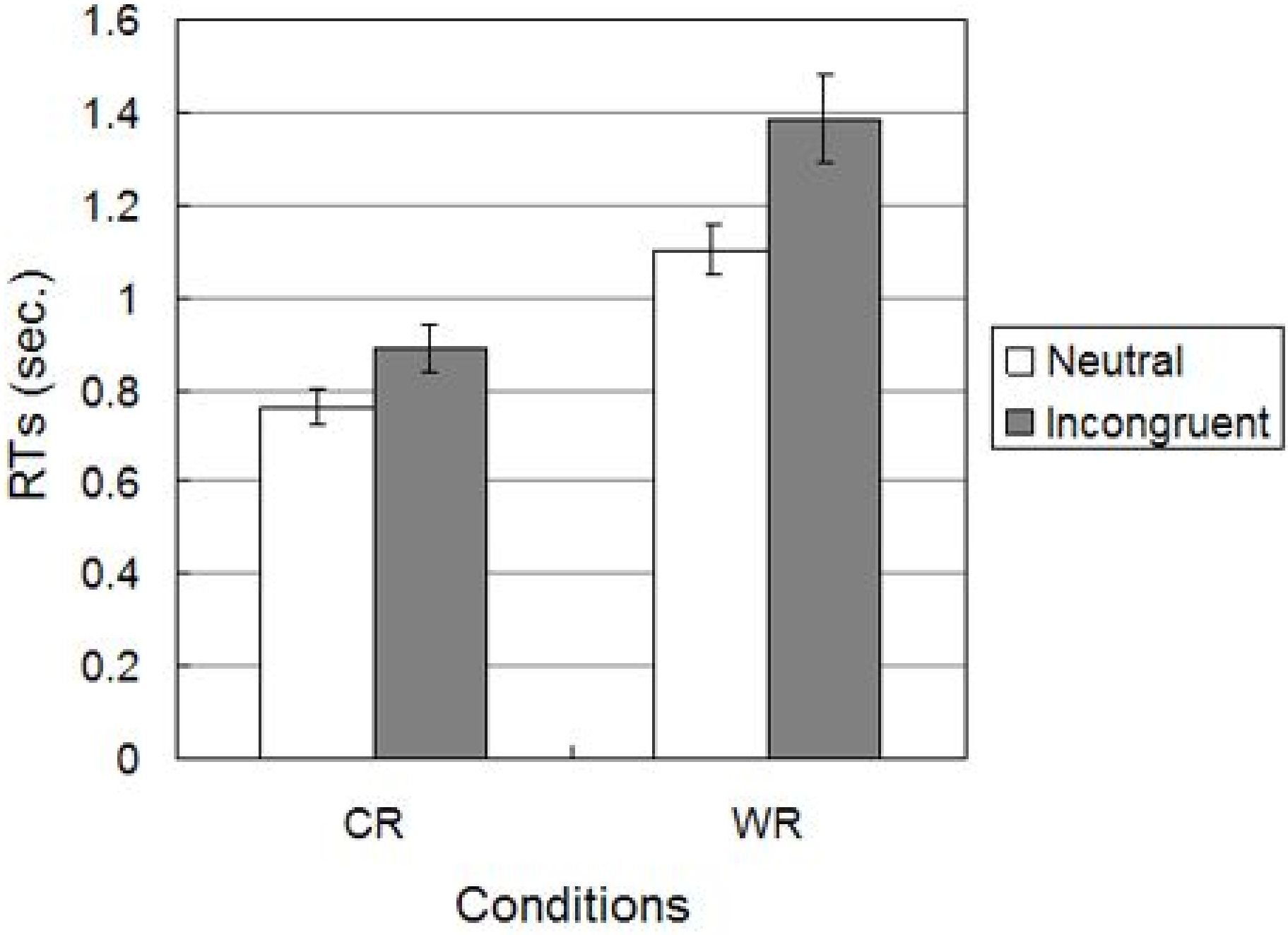
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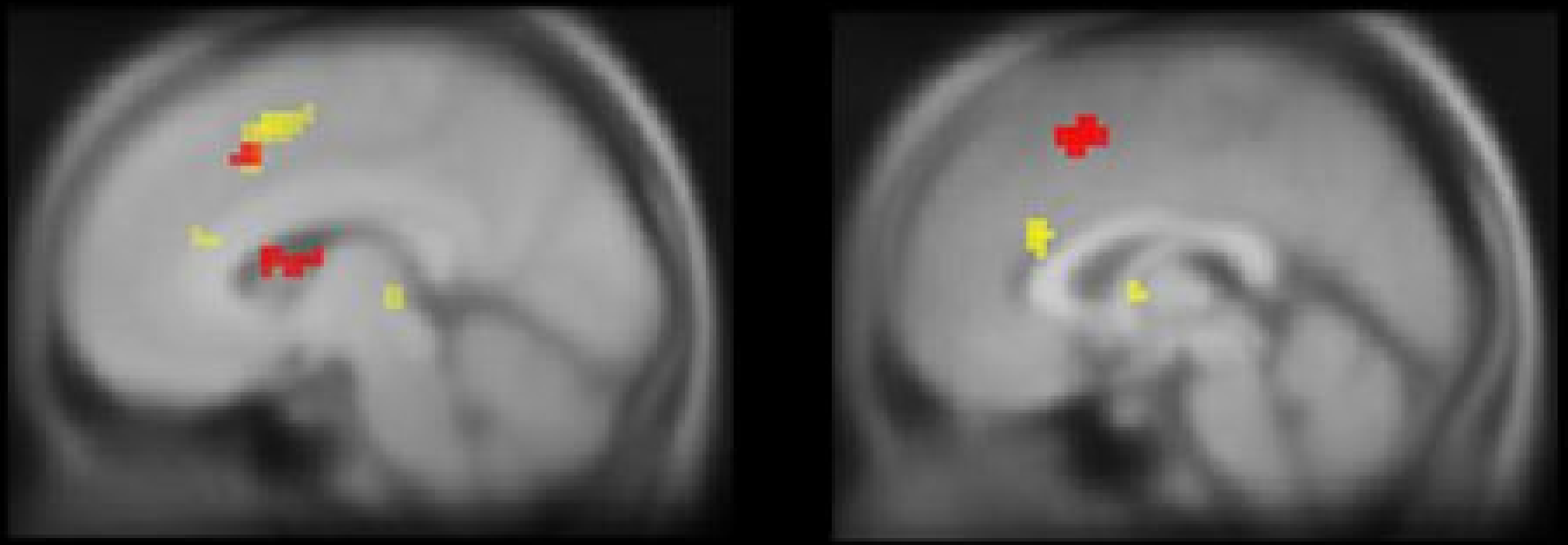
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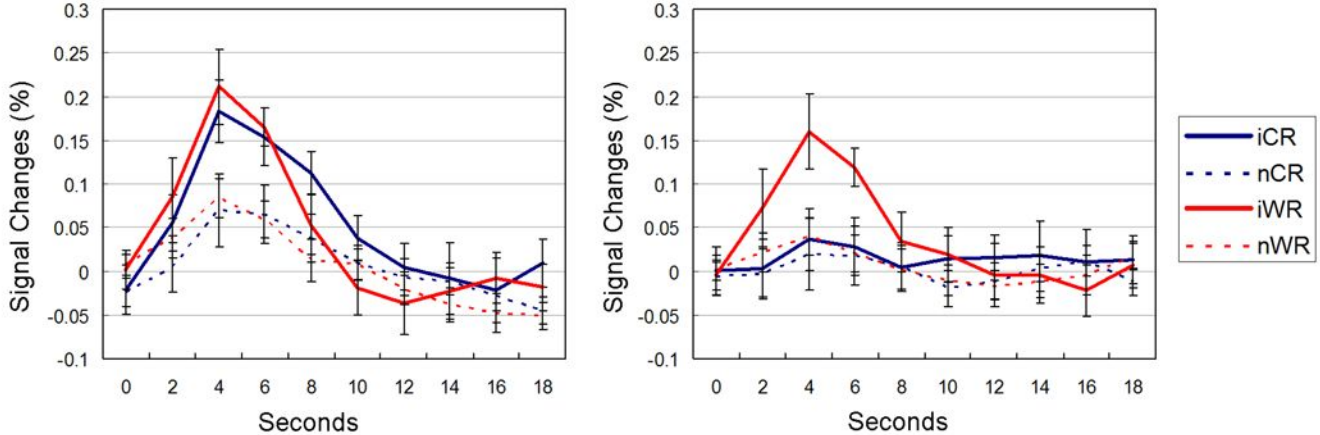
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