

Hemispheric integration is critical for intact error processing

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ABSTRACT

We provide for the first time direct clinical evidence for the critical role of hemispheric integration in intact error processing. We tested three patients with partial callosal disconnection. Two anterior patients could not correct their errors in a unilateral version of a visuomotor learning task for which they previously exhibited callosal disconnection, whereas, they corrected most of their errors in two visual matching tasks (comparing abstract shapes or faces) that they could transfer between the hemispheres. An opposite pattern emerged in a posterior patient. He could not correct his errors in unilateral versions of the same visual matching tasks, for which he previously exhibited callosal disconnection. However, he corrected most of his errors in the visuomotor learning task he was able to transfer between the hemispheres.

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1. Introduction

Humans are able to detect their errors in the absence of external feedback (Rabbitt, 1966). This allows for incredibly rapid and remarkably efficient error correction. The known timeline of the corrective response starts in parallel (Rodríguez-Fornells, Kurzbuch, & Münte, 2002) with the electrophysiological marker of error detection, the error-related negativity (ERN, Falkenstein, Hohnsbein, & Hoormann, 1990; Gehring, Goss, Coles, Meyer, & Donchin, 1993), and when instructed to do so, participants correct nearly all their errors (Fiehler, Ullsperger, & von Cramon, 2004). Neurocognitive models of error correction hold that error correction is subserved by an error processor that is sensitive to conflict (conflict model, Carter et al., 1998; Yeung, Botvinick, & Cohen, 2004) or to mismatch between the incorrect and the correct responses (comparator model, Gehring et al., 1993; Falkenstein, Hohnsbein, Hoormann, & Blanke, 1991; Coles, Scheffers, & Holroyd, 2001). The cortical neural substrates of the error processor are assumed to involve the medial pre-frontal cortex (MPFC, especially the anterior cingulate, (ACC), Carter et al., 1998), and the lateral prefrontal cortex (LPFC, Gehring & Knight, 2000).

With respect to a differential or synergetic involvement of the two hemispheres, neuroscientific accounts of error processing are silent. This is not surprising considering that the left and the right ACC are very close to each other and that the spatial resolution of EEG is rather poor. Moreover, while imaging techniques have finer spatial resolution than EEG, its full resolution potential is rarely used, preventing discernment of left from right in the MPFC (Lutcke & Frahm, 2008). Nevertheless, there are several lines of evidence that suggest either hemispheric specialization or hemispheric cooperation in error/conflict processing.

1.1. Evidence for lateralization of the error process

With respect to hemispheric specialization, Rubia et al., 2001, reported left hemisphere specialization while Garavan, Ross, and Stein (1999) and Taylor et al. (2006), reported right hemisphere specialization for conflict monitoring. Lutcke and Frahm (2008), used high resolution fMRI to show right ACC activation during conflict monitoring whereas, the dorsal anterior cingulate (dACC) and the left rostral anterior cingulate (rACC) were activated solely for error related process (note however, that in this study responses were limited to the right hand. Different patterns may occur for bimanual or left hand reactions). Using diffusion tensor imaging (DTI), Westlye, Walhovd, Bjørnerud, Due-Tønnessen, and Fjell (2009) showed that the fractional anisotropy (FA) in the left posterior cingulate correlated with ERN amplitude. Hochman, Eviatar,

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Breznitz, Shaul, & Nevat (2009a), using half visual field presentation (HVFP), also reported left hemisphere superiority for the ERN (however, responses were limited to the right hand). The lateralization of the ERN to the left gain some support from a study by Swick and Turken (2002), who describe a patient with a lesion to the left dorsal ACC region. This patient exhibited reduction of both the ERN and corrective behavior.

A series of behavioral studies using HVFP by Zaidel and his colleagues, showed different laterality patterns for different post error compensatory behaviors. Error feedback presented to the right hemisphere (RH) caused a decrease in error rate (Iacoboni, Rayman, & Zaidel, 1997; Kaplan & Zaidel, 2001) while the same feedback presented to the left hemisphere (LH), increased latency on post error trials (Kaplan & Zaidel, 2001). The diversity of the laterality patterns observed for different error related indices, raises the possibility that the error process is a complex routine where several mechanisms, each allocated to a different hemisphere are orchestrated, shifting back and forth between the hemispheres.

1.1.1. Evidence for hemispheric integration in error processing

Hemispheric integration in error processing is suggested by a series of electrophysiological studies of patients with lateral frontal lesions on either side. These studies consistently report a reduction of the ERN (Gehring & Knight, 2000; Hogan, Vargha-Khadem, Saunders, Kirkham, & Baldeweg, 2006; Ullsperger & von Cramon, 2006; Ullsperger, von Cramon, & Muller, 2002; Swick & Turken, 2002), suggesting that a single frontal lobe is insufficient for error processing (Gehring & Knight, 2000). Moreover, in a study by Kaplan and Zaidel (2002, unpublished doctoral dissertation) two patients with complete commissurotomy were unable to correct their choice errors in a flanker task, suggesting that hemispheric integration is critical for error processing. Hochman and Eviatar (2004, 2006) also demonstrated a pattern suggesting hemispheric integration in error correction in a number of behavioral studies with healthy participants. These studies used HVFP to show dissociations between the hemisphere producing the initial, erroneous response and the hemisphere that corrects the errors.

1.1.2. Hypothesis

We describe three case studies of patients with partial callosal disconnection. Two patients had an anterior lesion, and one patient had a posterior lesion. The corpus callosum (CC) is the largest fiber collection connecting between the cerebral hemispheres (see, Zaidel & Iacoboni, 2002 for a review). Callosal fibers are heterogeneous in their microstructural organization (LaMantia and Rakic, 1990; Schulte, Sullivan, Muller-Oehring, Adalsteinsson, & Pfefferbaum, 2005), and task specific (Funnell, Corballis, & Gazzaniga, 2000; Reuter-lorenz & Baynes, 1992). Thus, a patient with a partial CC lesion may not be able to transfer certain types of information, depending on the location of the lesion. Assuming that computations utilized by the error process rely on the same type of information used for task performance (Coles et al., 2001; Resulaj, Kiani, & Wolport, 2009), these patients can serve as a model of unilateral error-processing, against which, an account of bilateral error processing will be tested.

An account of bilateral error processing requires that error processing related information will be transferred between the hemispheres. Consequently, for tasks that the disconnected brain cannot transfer, error correction will be disrupted regardless of the side performing the task, and critically, this should be true even when no hemispheric transfer is required for task performance per se (i.e., the task can be performed by either hemisphere, all task relevant information is presented to one side, and the response is produced with the contralateral hand). Alternatively, if the error process is lateralized to one, specialized hemisphere, lack of communication between the hemispheres should not affect corrective

behavior, provided that the specialized hemisphere is given all relevant task information and the task is performed by the contralateral hand. Finally, if each hemisphere has the ability to process its own errors, the lack of transfer between sides should not affect contralateral corrective responses regardless of which side performs the task at hand.

2. Method

2.1. Participants

2.1.1. Anterior patients

Patient 1 (P1): the middle and posterior genu (GII, GIII, see, Aboitiz, Scheibel, Fisher, & Zaidel, 1992) and the anterior body (BI) had been removed (a 3 cm cut, see Fig. 1). P1 was a 20-yr-old right handed male, with twelve years of education, who underwent a surgical intervention in order to remove a septum pellucidum astrocytoma-giant cell a year and a half before the experimental session. Excision of the tumor was by a transcallosal approach. Since the surgical intervention, the patient reports feeling very well and is not medicated. The most recent MRI, about 9 month prior to the experiment, showed no signs of a tumor. There was no radiological or behavioral evidence of extracallosal damage.

Patient 2 (P2): The anterior body (BI) had been removed (a 1.5 cm cut, see Fig. 1). P2 was a 41-yr-old right handed female, with twelve years of education, who underwent a surgical intervention one week before the experimental session in order to remove a colloid cyst from the Foramen of Monro. Excision of the tumor was by a transcallosal approach. The MRI showed complete removal of the tumor without hydrocephalus. There was no radiological or behavioral evidence of extracallosal damage.

2.1.2. Posterior patient

Patient 3 (P3): The posterior part of the isthmus and the anterior part of the splenium had been removed (S1, a 3 cm cut, see Fig. 1). P3 was a 49-yr-old right handed male, with 16 years of education, who underwent a surgical intervention in order to remove a pinealoma pinealoblastoma three and a half years before the experimental session. The tumor was partially removed by a transcallosal approach. The patient suffers from light dysphasia, and hemiparesis of the left side.

The control groups consisted of ten right handed normal individuals. Five with a mean age of 31, SD, 4.27, twelve years of education (YC, young controls) were used as controls for P1, and P2, and five, with a mean age of 55, SD, 2.58, 15 years of education (OC, older controls), were used as controls for P3.

2.2. Experimental design

Patients and matching controls performed three series of tests (neuropsychological evaluation, hemispheric disconnection evaluation, and corrective behavior evaluation). Each participant completed all series within eight weeks, performing no more than two tasks a day. The order of presentation of the tasks was constant for all participants.

Neuropsychological evaluation: The general neuropsychological status of the patients and their controls was assessed using the following clinical tests: a short-term memory test (the digit span subset of the Wechsler Adult Intelligence Scale-Revised), a Semantic Verbal Fluency (SVF) test, and a short 12-problem version (set I) of the Raven's Progressive Matrices (RPM, Raven, 1960, 1976; Burke, 1997).

Disconnection evaluation: Patients and their matching controls performed a series of evaluations of callosal functions, in order to reveal different disconnection signs within the patients group, according to the locus of the callosal lesion. Patients with lesion to the anterior CC have been reported in the past to show intact visuomotor learning in each hemisphere/hand (unilateral learning), but inability to transfer visuomotor information between hemispheres/hands (bilateral learning) (de Guise et al., 1999). Patients with lesion to the posterior CC are perfectly capable of processing visual information within each hemisphere (unilateral processing); however, they show various deficits in the transfer of visual information (bilateral processing) depending to the extent of the lesion, its exact localization and the individual arrangement of the callosal fibers (Zaidel & Iacoboni, 2003; Aboitiz et al., 1992). Thus, we tested our patients for disconnection symptoms using tasks in which visuomotor or visual data from either hemisphere (unilateral condition) or from both hemispheres (bilateral condition) had to be accumulated in order to complete the task at hand. Inability to complete the task in the bilateral condition suggests that the lesioned part of the CC was responsible for the specific transfer of information required for task performance.

2.2.1. Matching and naming of visual stimuli

Participants had to make a same-different judgments to simultaneously presented stimuli, either both to the same visual field (VF, unilateral condition), or one in each VF (bilateral condition) intermixed within a block. Response hand was alternated between blocks. The left visual field (LVF) left-hand and the right visual field (RVF) right-hand conditions are the "pure hemisphere" conditions, where the RH performed the task in the former case and the LH in the latter.

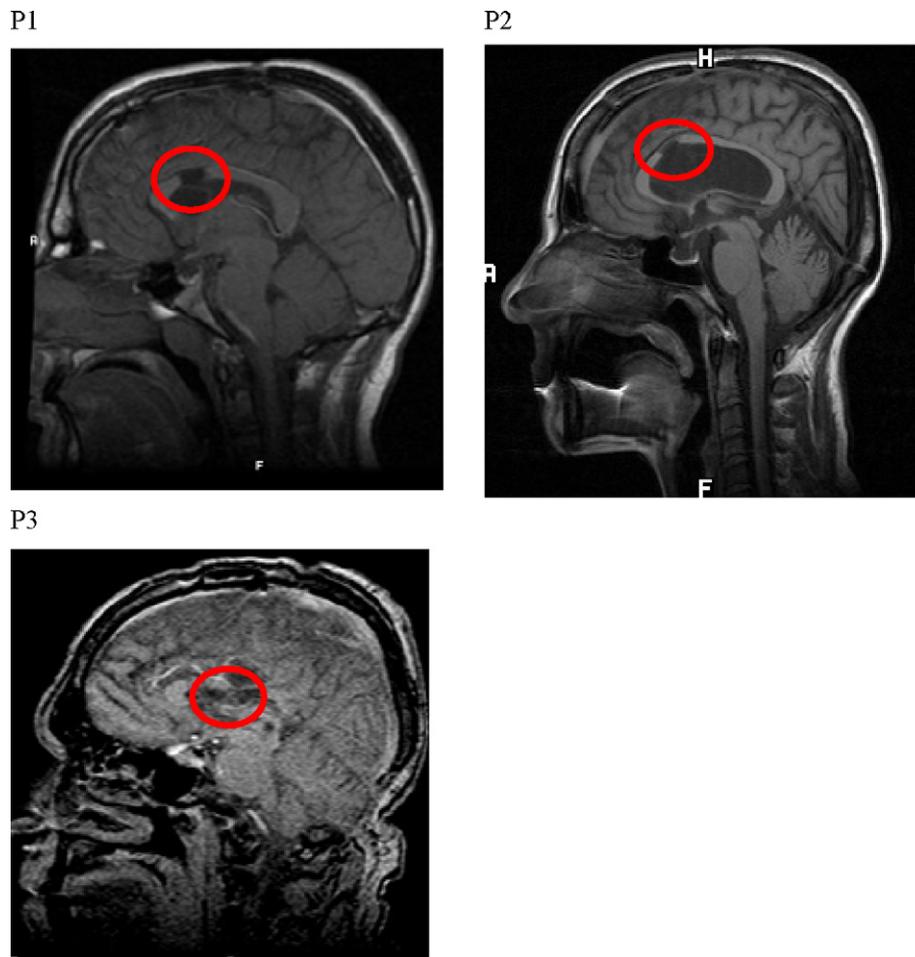


Fig. 1. Magnetic resonance images, midsagittal view, showing the sectioned CC of the patients included in this study. P1, patient 1; P2, patient 2; P3, patient 3.

2.2.2. Stimuli and apparatus

Colors: Two tasks were administered: first, a same-different matching task of pairs of primary colors from the following set: red, green, blue, yellow; second, a same different matching task of pairs of shades of the same primary colors. **Letters:** A same different matching task according to a name criterion of letters from the set A, B, D, F, E, G, H, I, J, L, M, N, Q, R, T, Y, and their lower case counterparts. All participants could read English. **Numbers:** Same-different matching task with numbers from 1 to 9. **Nonsense Shapes:** Matching nonsense shapes from the set of Vanderplas and Garvin (1959). **Faces:** Two tasks were administered: First, Matching faces with head on views; second, Matching faces with head on views to 45 degree profile views. The stimuli consisted of photos of five distinct faces.

2.2.3. Procedure

Each type of stimuli was presented to the participants in a different experimental session. Each experimental session included 10 blocks of 100 trials. In each block, the stimuli were equally and pseudo randomly divided between visual fields and between same-different presentations. On half the trials both stimuli appeared in the same visual field and in the other half stimuli were presented to different visual fields. When stimuli were presented to different visual fields, on half of the trials the stimuli were presented at the same horizontal level and on half of the trials they were presented at different horizontal levels. Each block began with a presentation of a 5×5 mm fixation cross surrounded by four empty 2×2 cm squares. These remained on screen until the end of the block. Two squares were positioned above fixation, one to its left and one to its right, and two were positioned below fixation one to its left and one to its right. For each square, the side closest to fixation horizontally was 1.5 cm from its center, and the side closest to fixation vertically was 0.5 cm from the center of fixation. Participants were instructed to respond by pressing the S key for same judgment and the D key for different judgment. Each stimulus appeared for 100 ms inside one of the squares. The next stimulus appeared 1 s following the response. Participants were encouraged to correct their errors.

2.2.4. Visuomotor learning

2.2.4.1. Stimuli and apparatus. The task, originally introduced by Nissen and Bullemer (1987), was adapted from de Guise et al. (1999), who were the first to show that acallosal and callosotomized patients could learn a visuomotor skill within each

hand but could not transfer learning between hands. The stimuli were asterisks 0.35 cm in diameter. Each asterisk could appear at one of four horizontal locations, on a 25 cm high computer screen at 14.5 cm below the top and 7 cm above the bottom of the screen viewed at a distance of 57 cm (at that distance 1 degree of visual angle equals 1 cm on the computer screen). The stimulus locations were separated from each other by 2 cm horizontally. Participants were asked to respond by pressing one of four, horizontally leveled, keys on the top row of the computer keyboard (the numbers 5, 6, 7, 8), which was positioned in front of the monitor such that the four keys were aligned with the four stimulus locations. The keys corresponded to the asterisks from left to right in such a manner that key 5 corresponded to the leftmost asterisk, key 6 to the asterisk on its right and so on. Reaction times and the proportion of correct responses, errors, and correction responses, were recorded. Each asterisk appeared for 100 ms. The next asterisk appeared 500 ms following the response.

2.2.5. Procedure

Participants had to rest their forefinger and middle finger on keys 5 and 6 and their ring finger and little finger on keys 7 and 8 during the first two blocks (right-hand, half session). In the following two blocks the hands were switched. Participants were encouraged to respond as fast and as accurate as possible. The experiment was comprised of four blocks. Each block consisted of four repeated (sequential) sub-blocks and one random sub-block. For the repeated sub-blocks, the location of the stimuli followed a constant sequence of 10 positions. Designating the four possible locations from left to right as A, B, C and D, the sequence was B-A-B-D-C-A-C-B-D-C. Each sequence comprised 10 trials and each sub-block of trials was composed of 10 continuous repetitions of this 10-trial sequence so that each sub-block appeared as a continuous series of 100 trials. The end of one 10-trial sequence and the beginning of the next one was not indicated to the participants. For the random sub-blocks, the locations of the stimuli followed a random sequence. This sub-block also consisted of 100 trials. The random sub-blocks were introduced to ascertain the presence of learning by comparing reaction times between random and repeated sequences. All together, twenty sub-blocks (four blocks) were administered. Sub-blocks 5, 10, 15 and 20 were designated as random sub-blocks while the remaining sub-blocks (1–4, 6–9, 11–14 and 16–19) constituted the learning blocks. Participants were encouraged to correct their errors.

Table 1
Neuropsychological evaluation. Numbers in brackets represent the standard deviations for the control groups.

	P1	P2	P3	YC	OC
Task					
Digit span forward	6.2	5.9	6.2	6.2 (1.3)	6 (0.7)
Digit span backward	4.4	4.2	4.3	4.8 (.84)	4.6 (.65)
Verbal fluency	22	18.3	17.1	20.4 (4.8)	20.8 (3.54)
Raven's matrices	9.2	7.4	6.7	7 (3.1)	7.2 (2.66)

Corrective behavior evaluation: We examined patients' and controls' corrective behavior under conditions where no accumulation of data from both hemispheres is required to complete the task at hand. Hence, a failure to self-correct cannot be attributed to inability to perform the task at hand.

Matching and naming of visual stimuli: In the visual matching tasks used to assess callosal disconnection, the "pure hemisphere" conditions required no hemispheric transfer. Thus, the disconnection tests already included a condition suitable for the examination of corrective behavior. However, the visual disconnection tests did not yield enough errors in the "pure hemisphere" condition. Hence, we ran them again, presenting stimuli either to the left or to the right visual field, but never to both, and used a flanker manipulation to induce errors. We expected deficits in error processing only for tasks for which there was disconnection.

2.2.6. Procedure

The experimental stimuli and procedure were the same as described above for the visual disconnection tests, with the following exception: On each trial two pairs of stimuli were presented one immediately following the other, at the same location and participants were instructed to respond to the second pair only. To induce errors, pairs could be identical (congruent trials) or different (incongruent trials). In each block, pairs of stimuli were equally and pseudo-randomly divided between visual fields and between same-different presentations. There were no bilateral presentations in this paradigm: On half the trials pairs of stimuli appeared in the left visual field and in the other half they appeared in the right visual field. Thus, all stimuli were presented to a single hemisphere, and interhemispheric integration of stimulus information was not necessary for the response. Response hand was altered between blocks. Thus, on contralateral response trials (responses are made with the hand contralateral to the receiving hemisphere), no hemispheric integration was required for both stimulus and response processing. Each pair of stimuli appeared for 100 ms. The next trial began 500 ms following the response. Error correction was encouraged.

2.2.7. Visuomotor learning

In the visuomotor task, learning of a sequence of movements using one hand does not require inter-hemispheric transfer, making the same task used to evaluate callosal disconnection suitable to evaluate corrective behavior within each hand (hemisphere). The error rate within each hand in the disconnection test was high enough to allow for statistical analysis. Thus, we did not run the test again for the examination of corrective behavior. Rather, we used the error correction data collected from each hand, during the disconnection test.

3. Results

3.1. Neuropsychological evaluations

We compared patients' performance with their matching controls using a modified *t*-test introduced by Crawford and Howell (1998). This test allows for a comparison of individual scores against a norm derived from a small sample of control participants. Patients means were compared with the means of their age-matched control groups. As can be seen in Table 1, patients showed normal performance. There were no significant differences between patients and their matching controls (all *t*'s < 1 and *p*'s > .2).

3.1.1. Disconnection evaluation

Matching and naming of visual stimuli: It can be seen (Fig. 2, upper panel) that in the critical bilateral presentation condition, P3 could not compare abstract shapes and head-on to profile faces across the visual fields. His accuracy did not exceed chance performance ($\alpha = .05$, two-tailed binomial). In contrast, the anterior patients and the control groups performed well above chance (Fig. 2, upper panel). All participants, including P3, performed well above chance in the other visual matching and naming tasks (Fig. 2, upper panel).

3.1.2. Visuomotor learning

Visuomotor task: Mean reaction times and proportion of correct responses (a button press that matches the sequence), were subjected to one-way analysis of variance (ANOVA). For each patient, the analysis treated trials as the random variable (each patient ran 20 blocks of 100 trials. Separate means were computed for each block). For controls we conducted the ANOVA across subjects, such that for each block, we used the mean across subjects. To assess the existence of sequence learning within a hand and the transfer of learning between hands, planned comparisons were computed comparing the RT changes within a hand (sequential sub-blocks 1–4 vs. sequential sub-blocks 6–9 for the first hand, and sequential sub-blocks 11–14 vs. sequential sub-blocks 16–19 for the second hand), and between hands (sub-blocks 6–9 vs. sub-blocks 11–14). These data are presented in Fig. 3.

It can be seen that in all participants, a significant RT reduction was observed between the first and the second blocks (P1, $F_{(1,19)} = 35.38$, $p < .0001$; P2, $F_{(1,19)} = 11.08$, $p < .001$; P3, $F_{(1,19)} = 11.14$, $p < .0001$; young controls (YC), $F_{(1,57)} = 6.49$, $p < .05$; older controls (OC), $F_{(1,57)} = 9.67$, $p < .05$), indicating learning within the first hand (which was always the right hand). Critically, only P3, YC, and OC further showed a significant RT reduction between the second (first hand responses) and the third (second hand

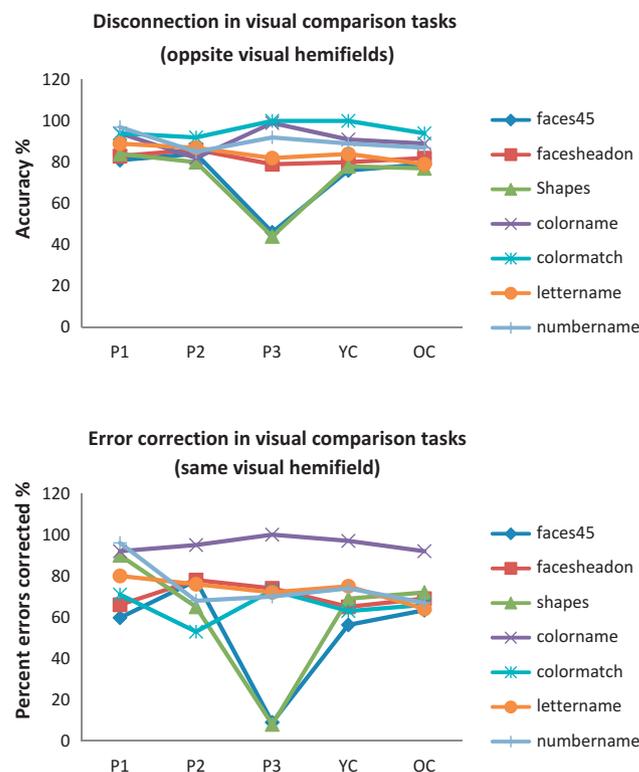


Fig. 2. Disconnection patterns when stimuli to be matched are presented each to a different visual field (upper panel), and self-correction patterns when both stimuli to be matched are presented to the same visual field, thus, no hemispheric transfer is required for task performance (lower panel).

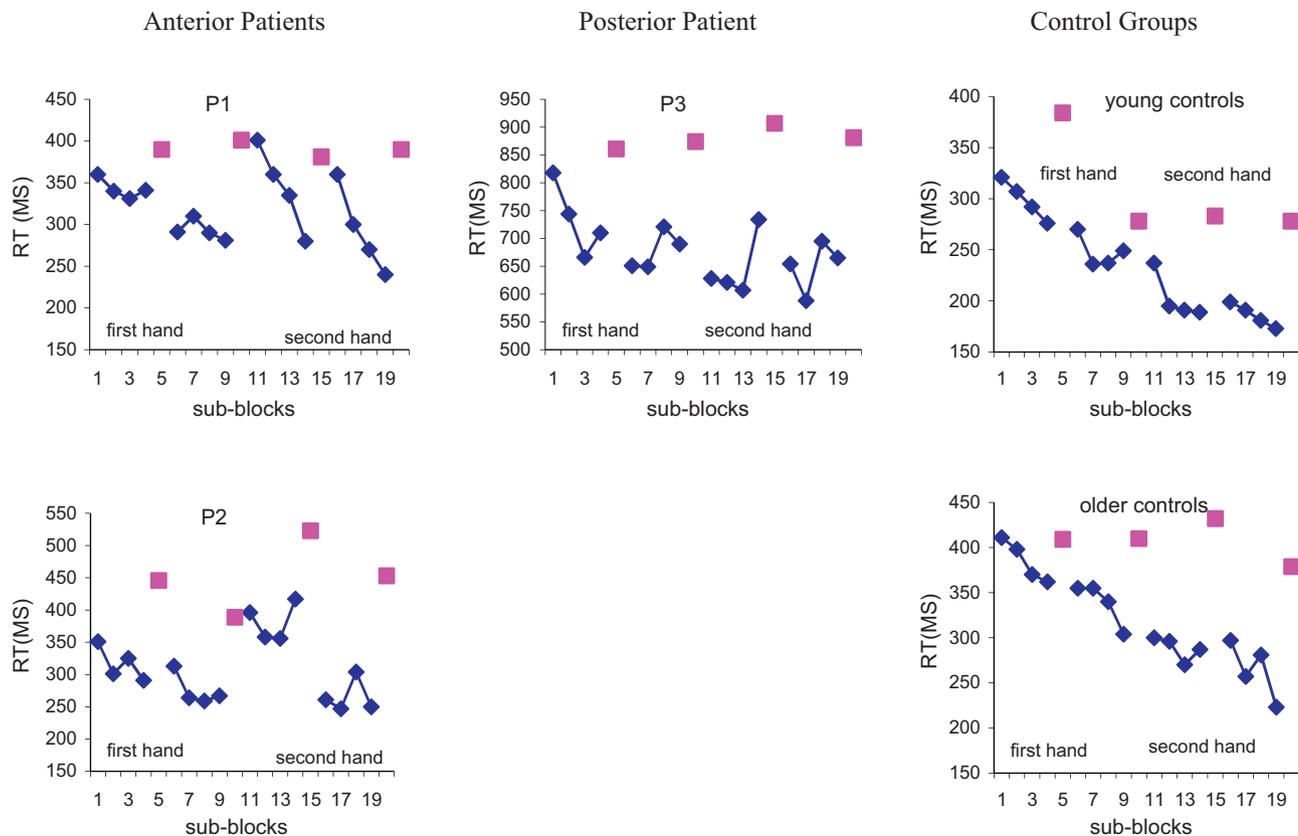


Fig. 3. Unimanual and bimanual learning. Visuomotor skill learning of callosotomized patients and controls expressed as median reaction times for training blocks (each block is comprised of four subblocks). Pink subblocks indicate RT in the random sequences. The first two blocks (1–4, 6–9) were performed with the right hand, and the second two blocks (blocks 11–14, and 16–19) were performed with the left hand. The major finding indicates intact learning within one hand across the first two blocks in the patients with an anterior lesion in the CC, but no learning across hands in these patients (no improvement, and actually a decrement in speed between blocks 2 and 3). The patient with a posterior lesion shows transfer of learning between hands, as did the controls groups.

responses) blocks (P3, $F_{(1,19)} = 4.58, p < .05$; YC, $F_{(1,19)} = 5.01, p < .05$; OC, $F_{(1,19)} = 11.25, p < .005$), indicating transfer of learning between the hands. By contrast, for both P1 and P2, a significant *increase* in RT was observed between the second, and the third blocks (P1, $F_{(1,19)} = 56.14, p < .0001$; P2, $F_{(1,19)} = 4.78, p < .05$), indicating callosal disconnection. In P3, YC and OC, no learning occurred within the second hand (a comparison of the third and the fourth block, P3, $p > .33$; YC, $p > .39$; OC, $p > .11$), suggesting that these participants had reached maximum performance at the third block. In contrast, in P1 and P2, a significant RT reduction was observed between the third and the fourth blocks ($F_{(1,19)} = 51.0, p < .0001$; $F_{(1,19)} = 5.62, p < .05$, in accordance), suggesting again that these patients had to and could relearn the visuomotor skill when the responding hands were switched.

3.1.3. Corrective behavior evaluation

3.1.3.1. Matching and naming of visual stimuli. In the self-correction version of these tasks, stimuli were always presented to the same visual hemifield (thus not requiring callosal transfer). Here, a response was considered erroneous in case it involved an incorrect button press (error percentage: faces: P1 = 16.7, P2 = 13.5, P3 = 16.5, OC = 23.85, YC = 23.3; shapes: P1 = 14.95, P2 = 15.2, P3 = 14.2, OC = 22.9, YC = 22.95; in the other visual matching tasks individual error rates were never below 8% or over 19%). A response was considered corrective when it was preceded by an incorrect button press. The mean percent of corrective responses of the patients were compared with the means of their age-matched control groups using a modified *t*-test introduced by Crawford and Howell (1998). As seen in the lower panel of Fig. 2, P3 was impaired relative to OC in self-correction on the same tasks for

which he revealed disconnection (faces, $t = -6.790, p = .001$, one-tailed; shapes, $t = -6.386, p = .002$, one-tailed), whereas he did not produce more errors. P1 and P2 neither corrected less, nor produced more errors than YC (all t 's < 1 and p 's $> .2$, one-tailed). No significant differences in error correction and error rates were observed between patients and controls in the other visual matching tasks in which none of the patients revealed disconnection (all t 's < 1 and p 's $> .2$, one-tailed).

3.1.4. Visuomotor learning

As can be seen in panel A of Fig. 4, the error rate for each hand in the version of the task we used to assess hemispheric disconnection, was high enough to allow for statistical analysis of corrective behavior. Thus, for each hand separately, we analyzed the error correction data collected during the disconnection test. As seen in panel A of Fig. 4, no difference in error rate was observed between the anterior patients and YC, neither in the first hand (P1, $t = -1.826, p = .07$, one-tailed; P2, $t = 1.158, p = .2$, one-tailed), nor in the second hand (all t 's < 1 and p 's $> .2$, one-tailed). Critically, as seen in panel B of Fig. 4, both anterior patients showed significantly lower percentage of corrected errors than YC in both hands (first hand, P1, $t = -5.487, p = .003$, one-tailed, P2, $t = -5.549, p = .003$, one-tailed; second hand, P1, $t = -8.843, p = .000$, one-tailed, P2, $t = -6.989, p = .001$, one-tailed). P3 did not produce more errors than OC in the first hand (all t 's < 1 and p 's $> .3$, one-tailed), whereas he produced less errors in the second hand ($t = -2.198, p = .05$, one-tailed). No difference in the proportion of corrections was observed between P3 and OC in both hands (all t 's < 1 and p 's $> .3$, one-tailed).

Flanker effects: The flanker interference effect [(RT on incongruent trials – RT on congruent trials)/congruent RT $\times 100$] is

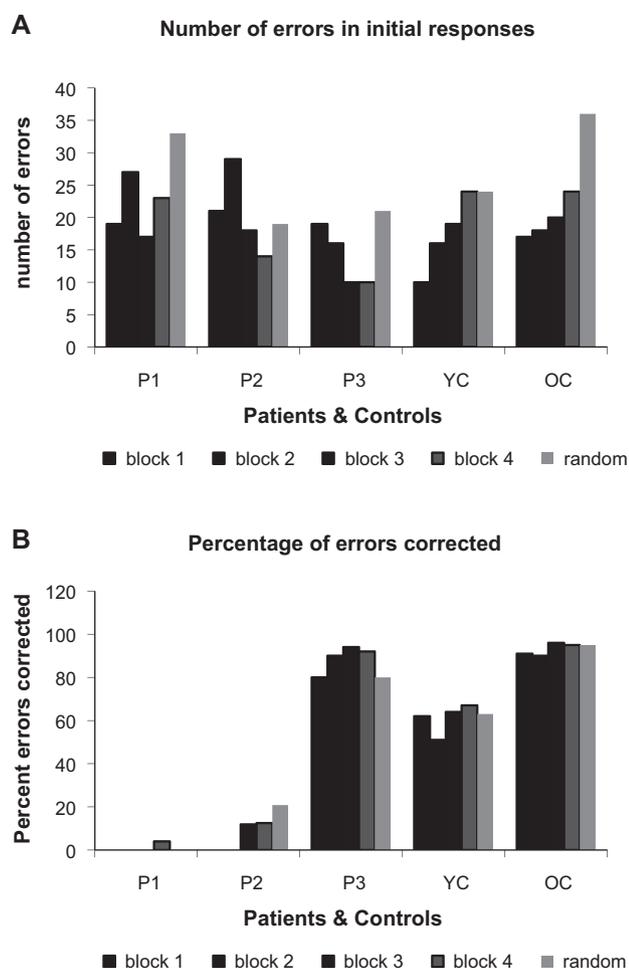


Fig. 4. Panel A: number of errors for a block on initial responses in the visuomotor task (blocks 1–2, first hand; blocks 3–4, second hand). Panel B: Percentage of errors corrected for a block.

considered as an index of pre-response conflict (Swick & Turken, 2002). The difference between P3 and OC was not significant (faces, P3, 13.44%, OC, 15.49%, $t < 1$, $p > .4$; shapes, P3, 9.23%; OC, 12.95%, $t < 1$, $p > .4$), suggesting that the callosal lesion did not affect pre-response conflict monitoring.

4. Discussion

A double dissociation emerged between the anterior patients and the posterior patient for both corrective behavior (under conditions that did not require callosal transfer), and callosal disconnection (under conditions that required callosal transfer). The anterior patients could not correct their errors in a visuomotor learning task for which they exhibited callosal disconnection, whereas, they corrected most of their errors in two visual matching tasks (comparing abstract shapes or faces) that they could transfer between the hemispheres. An opposite pattern emerged in the posterior patient. He could not correct his errors in the same visual matching tasks for which he exhibited callosal disconnection. However, he corrected most of his errors in the visuomotor learning task that he was able to transfer between the hemispheres. All patients were able to correct most of their errors in other visual matching tasks that exhibited intact inter-hemispheric transfer. In all the tasks that showed deficits in corrective behavior, patients' accuracy was not worse than that of the controls. Therefore, the failure to self-correct cannot be attributed to difficulties in task performance.

Overall, the results strongly suggest that hemispheric integration is critical for intact, rapid error processing.

In the current study, we used callosal patients as a model of unilateral stimulus–response processing, in order to demonstrate that rapid error processing relies on bilateral stimulus–response computations. The results from the visuomotor task, further suggest that information transfer through task specific channels of the CC serves the error process. The visuomotor task simulated an ecological condition where stimuli are processed bilaterally and the response is produced unimanually. Our results showed that under these conditions, a lesion to anterior CC channels affected both the transfer of visuomotor learning and error processing. Thus, the transfer of visuomotor information through visuomotor task specific CC channels is a prerequisite for the occurrence of rapid error processing in visuomotor tasks. In the visual comparison tasks on the other hand, stimuli were always presented to a single hemisphere. Thus, in these tasks, the lack of error correction only suggests that in the absence of independent stimulus-to-response computations from both hemispheres, error processing would not occur. However, with respect to the involvement of the CC in error processing, then, under ecological conditions where both hemispheres are exposed to and process the stimuli, bilateral computations may occur with no involvement of task specific CC channels. In this case, the critical integration of these computations may take place elsewhere either in the CC or in other inter-hemispheric channels. The nature of the channels that allow for the integration of the results of each intra-hemispheric computation would depend on the characteristics of the transmitted error-processing information. If the transferred information in the visual comparison tasks is comprised of stimulus representations or stimulus–response conjunctions of the type for which disconnection syndrome was demonstrated in those tasks, it is most plausible that task-specific callosal channels also transfer task-specific error information. On the other hand, if the transferred information consists of more abstract error signals, it may be carried by either callosal channels connecting left and right error processing related cortical regions (LPFC, Gehring & Knight, 2000; ACC, Carter et al., 1998; pre-supplementary motor area, Hochman, Eviatar, Breznitz, Shaul, & Nevat, 2009b; Herrmann, Ro'mmler, Ehlis, Heidrich, & Fallgatter, 2004; regions I and II of the CC according to Hofer & Frahm, 2006), or, by inter-hemispheric subcortical channels connecting left and right subcortical structures involved in coding error signals, such as the basal ganglia (Ullsperger & von Cramon, 2006) and the superior culliculus (Krauzlis, Basso, & Wurtz, 1997).

It is probably the case that certain types of error processing can occur within a single hemisphere. Studies of patients with lesions to error processing related regions such as the ACC, BG, and LPFC, often show reduction of the ERN accompanied by relatively intact prevalence of corrective behavior (Hogan et al., 2006; Ullsperger & von Cramon, 2006; Ullsperger et al., 2002; but see, Gehring & Knight, 2000; Swick & Turken, 2002; Modirrousta & Fellows, 2008). It is possible that having ample time to correct, the brain can still orchestrate corrective responses through alternative, perhaps peripheral, slow, error processing mechanisms. In fact, error processing is considered essential for the occurrence of learning (Holroyd, Yeung, Coles, & Cohen, 2005). However, our anterior patients exhibited intact unimanual learning accompanied by reduced rapid error processing. This suggests that our anterior patients had residual ability to process their errors, though perhaps not quick enough to allow for the fast error correction required by the design of the current study.

The advantage of having inter-hemispheric error processing is unclear. According to the conflict account of error processing, the larger the inhibitory connections between the contradicting responses, the larger the conflict and the higher is the probability for error correction (Yeung et al., 2004). The model differenti-

ates between pre-response (occurring on correct trials, prior to response execution) and post-response (occurring on incorrect trials post response execution) conflict. In the current study, P3 and OC did not differ in the magnitude of the flanker effect, suggesting that P3's lesion did not affect his ability to process pre-response conflict. However, once the activation of an incorrect response exceeds threshold (thus, resulting in an error), it might be necessary to recruit more resources in order to suppress its activation. Allocating each computation to a different hemisphere may utilize transcallosal inhibition to increase the weight of the inhibitory connections between the responses, resulting in increased post-response conflict. According to the comparator model (Coles et al., 2001), error processing requires holding a representation of the actual response, to be compared against the representation of the appropriate response. This process could be resource demanding (Gehring & Fencsik, 2001; Hochman & Meiran, 2005), requiring the allocation of each representation (and its associated computation) to a different module/hemisphere. Indeed, in a previous study, we showed that increasing task demands, results in hemispheric division of labor between initial and error processing (Hochman & Eviatar, 2006).

There is, however, another option. As mentioned in the introduction section of this paper, various aspects of the error process seem to dissociate with respect to their laterality patterns. The right hemisphere seems to be specialized for conflict processing (Lutcke & Frahm, 2008; Garavan, Ross, & Stein, 1999; Taylor et al., 2006), whereas the left hemisphere may specialize in error processing per se (Lutcke & Frahm, 2008; Hochman et al., 2009a; Westlye et al., 2009). Most recently, Alexander and Brown (2010) suggested a computational model of mismatch processing in the MPFC (the prediction of response-outcome model, PRO), that involves two interacting modules. One module, *predicts* response outcome, and feeds back to amend or veto a planned action if necessary. The other module alerts for mismatch between the actual and the *predicted* response, and initiates the corrective response. It is possible that the error/response predictor is localized to the right, where conflict and inhibitory control (Aron, Fletcher, Bullmore, Sahakian, & Robbins, 2003) are processed, while the comparator is localized to the left where an error/mismatch is detected. Hemispheric disconnection would prevent both the predictor from refining its predictions through feedback from the comparator, and the comparator from receiving a representation of the predicted response. Moreover, the allocation of error related mechanisms between the hemispheres may go beyond error detection and immediate correction to include error compensation. The right hemisphere seems to be involved in increasing response accuracy (Iacoboni et al., 1997; Kaplan & Zaidel, 2001) while the left hemisphere may control the implementation of a more cautious response strategy by reducing response speed on post error trials (Kaplan & Zaidel, 2001). In sum, it is possible that several mechanisms, each allocated to a different hemisphere are acting in a synchronous manner, constituting the error process.

The allocation of each mechanism to a given hemisphere may be related to hemispheric specialization. For example, the right hemisphere dominance in spatial functions (Corbetta, Miezin, Shulman, & Petersen, 1993; Mesulam, 1999) can be related to its involvement in monitoring functions that become most active under conflict, such as when a mismatch is experienced between motor intention, proprioception and/or visual feedback (Fink et al., 1999; Wenderoth, Debaere, Sunaert, van Hecke, & Swinnen, 2004). On post error trials, the right hemisphere may govern the allocation of spatial attention resources toward target location, resulting in increased accuracy. On the other hand, the left hemisphere specialization for the planning of sequential acts that implicate response selection, preparation and execution (Haaland, Elsinger, Mayer, Durgerian, & Rao, 2004; Schluter, Rushworth, Passingham, & Mills, 1998; Verstynen, Diedrichsen, Albert, Aparicio, & Ivry, 2005), might

relate to its involvement in detecting incorrect selections. On post error trials, the left hemisphere may suspend the completion of the response sequence, resulting in post error slowdown.

Note however, that the lateralization of the error processing functions might be a dynamic process where the control is allocated between sides with respect to hemispheric specialization for the task at hand. For example, Stephan et al. (2003) used an analysis of effective connectivity to demonstrate lateralization of ACC activity during cognitive control that depends on the side occupied with the task at hand. Namely, the right ACC monitored for conflict during a right hemisphere, visuospatial task while the left ACC monitored conflict during a left hemisphere, verbal task. Similarly, the right hemisphere advantage for post error accuracy reported by Kaplan and Zaidel (2001), became progressively less pronounced when error feedback was changed from emotional expression (a process governed by the right hemisphere), to colored squares to words (a left hemisphere process). In contrast, Lutcke and Frahm (2008), used letter stimuli, yet found a right ACC activity during conflict processing. Similarly, Hochman et al. (2009a), reported a left hemisphere advantage for the ERN regardless of hemispheric specialization for the task at hand.

In conclusion, we suggest that error monitoring in choice reaction time tasks relies on two independent computations in the two hemispheres. Disconnection could prevent such division of labor, resulting in loss of error monitoring. In this view, effective error monitoring requires that each hemisphere is able to access the stimuli, that each hemisphere is able to process the task, and that there exists a channel that can transmit the result of these computations. It is for future studies to discern the nature of the error related information that is transferred, the channels through which it is transferred, the exact error related mechanisms that require such transfer and the dynamics of lateralization patterns in error processing.

References

- Aboitiz, F., Scheibel, A. B., Fisher, R. S., & Zaidel, E. (1992). Fiber composition of the human corpus callosum. *Brain Research*, 598, 143–153.
- Alexander, W. H., & Brown, J. W. (2010). Computational model of performance monitoring and cognitive control. *Topics in Cognitive Science*, 1–20.
- Aron, A. R., Fletcher, P. C., Bullmore, E. T., Sahakian, B. J., & Robbins, T. W. (2003). Stop-signal inhibition disrupted by damage to right inferior frontal gyrus in humans. *Nature Neuroscience*, 6, 115–116.
- Burke, E. (1997). In J. D. Bertram (Ed.), *Review of ability and aptitude tests (level A) for use in occupational settings* (pp. 265–271). Leicester: British Psychological Society.
- Carter, C. S., Braver, T. S., Barch, D. M., Botvinick, M. M., Noll, D., & Cohen, J. D. (1998). Anterior cingulate cortex, error detection, and the on-line monitoring of performance. *Science*, 280, 747–749.
- Coles, M. G. H., Scheffers, M. K., & Holroyd, C. B. (2001). Why is there an ERN/Ne on correct trials? Response representations, stimulus-related components, and the theory of error-processing. *Biological Psychology*, 56, 173–189.
- Corbetta, M., Miezin, F. M., Shulman, G. L., & Petersen, S. E. (1993). A PET study of visuospatial attention. *Journal of Neuroscience*, 13, 1202–1226.
- Crawford, J. R., & Howell, D. C. (1998). Comparing an individual's test score against norms derived from small samples. *The Clinical Neuropsychologist*, 12, 482–486.
- de Guise, E., Del Pesce, M., Foschi, N., Quattrini, A., Papo, I., & Lassoche, M. (1999). Callosal and cortical contribution to procedural learning. *Brain*, 122, 1049–1062.
- Falkenstein, M., Hohnsbein, J., & Hoormann, J. B. L. (1990). Effects of errors in choice reaction tasks on the ERP under focused and divided attention. In C. H. M. Brunia, A. W. K. Gaillard, & A. Kok (Eds.), *Psychophysiological brain research* (pp. 192–195). Tilburg, The Netherlands: Tilburg University Press.
- Falkenstein, M., Hohnsbein, J., Hoormann, J., & Blanke, L. (1991). Effects of crossmodal divided attention on late ERP components: II error processing in choice reaction tasks. *Electroencephalography and Clinical Neurophysiology*, 78, 447–455.
- Fiehler, K., Ullsperger, M., & von Cramon, D. Y. (2004). Neural correlates of error detection and error correction: Is there a common neuroanatomical substrate? *European Journal of Neuroscience*, 19, 3081–3087.
- Fink, G. R., Marshall, J. C., Halligan, P. W., Frith, C. D., Driver, J., Frackowiak, R. S., et al. (1999). The neural consequences of conflict between intention and the senses. *Brain*, 122, 497–512.
- Funnell, M. G., Corballis, P. M., & Gazzaniga, M. S. (2000). Insights into the functional specificity of the human corpus callosum. *Brain*, 123, 920–926.

- Garavan, H., Ross, T. J., & Stein, E. A. (1999). Right hemispheric dominance of inhibitory control: An event-related functional MRI study. *Proceedings of the National Academy of Science, USA*, 96, 8301–8306.
- Gehring, W. J., & Fencsik, D. E. (2001). Functions of the medial frontal cortex in the processing of conflict and errors. *The Journal of Neuroscience*, 108, 624–652.
- Gehring, W. J., & Knight, R. T. (2000). Prefrontal–cingulate interactions in action monitoring. *Nature Neuroscience*, 3, 516–520.
- Gehring, W. J., Goss, B., Coles, M. G. H., Meyer, D. E., & Donchin, E. (1993). A neural system for error detection and compensation. *Psychological Science*, 4, 385–390.
- Haaland, K. Y., Elsinger, C. L., Mayer, A. R., Durgerian, S., & Rao, S. M. (2004). Motor sequence complexity and performing hand produce differential patterns of hemispheric lateralization. *Journal of Cognitive Neuroscience*, 16, 621–636.
- Herrmann, M. J., Roßmüller, J., Ehls, A. C., Heidrich, A., & Fallgatter, A. J. (2004). Source localization (LORETA) of the error-related-negativity (ERN/Ne) and positivity (Pe). *Cognitive Brain Research*, 20, 294–299.
- Hochman, E. Y., & Eviatar, Z. (2004). Does each hemisphere monitor the ongoing process in the contralateral one? *Brain and Cognition*, 55, 314–321.
- Hochman, E. Y., & Eviatar, Z. (2006). Do the hemispheres watch each other? Evidence for a between-hemispheres performance monitoring. *Neuropsychology*, 20, 666–674.
- Hochman, E. Y., & Meiran, N. (2005). Central interferences in error processing. *Memory and Cognition*, 33, 635–643.
- Hochman, E. Y., Eviatar, Z., Breznitz, Z., Shaul, S., & Nevat, M. (2009a). Different laterality patterns of the error-related negativity in corrected and uncorrected errors. *Laterality*, 14, 618–634.
- Hochman, E. Y., Eviatar, Z., Breznitz, Z., Shaul, S., & Nevat, M. (2009b). Source localization of error negativity: Additional source for corrected errors. *Neuroreport*, 20, 1144–1148.
- Hofer, S., & Frahm, J. (2006). Topography of the human corpus callosum revisited – Comprehensive fiber tractography using diffusion tensor magnetic resonance imaging. *NeuroImage*, 32, 989–994.
- Hogan, A. M., Vargha-Khadem, F., Saunders, D. e., Kirkham, F. J., & Baldeweg, T. (2006). Impact of frontal white matter lesions on performance monitoring: ERP evidence for cortical disconnection. *Brain*, 129, 2177–2188.
- Holroyd, C. B., Yeung, N., Coles, M. G. H., & Cohen, J. D. (2005). A mechanism for error detection in speeded response time tasks. *Journal of Experimental Psychology: General*, 134, 163–191.
- Iacoboni, M., Rayman, J., & Zaidel, E. (1997). Does the previous trial affect lateralized lexical decision? *Neuropsychologia*, 35, 81–88.
- Kaplan, J. T., & Zaidel, E. (2001). Error monitoring in the hemispheres: The effect of lateralized feedback on lexical decision. *Cognition*, 82, 157–178.
- Kaplan, J. T., & Zaidel, E. (2002). *The neuropsychology of executive function: Hemispheric contributions to error monitoring and feedback processing*. UCLA Unpublished doctoral dissertation, University of California, Los Angeles, CA.
- Krauzlis, R. J., Basso, M. A., & Wurtz, R. H. (1997). Shared motor error for multiple eye movements. *Science*, 276, 1693–1695.
- LaMantia, A. S., & Rakic, P. (1990). Cytological and quantitative characteristics of four cerebral commissures in the rhesus monkey. *Journal of Comparative Neurology*, 291, 520–537.
- Lutcke, H., & Frahm, J. (2008). Lateralized anterior cingulate function during error processing and conflict monitoring as revealed by high-resolution fMRI. *Cerebral Cortex*, 18, 508–515.
- Mesulam, M. M. (1999). Spatial attention and neglect: Parietal, frontal and cingulate contributions to the mental representation and attentional targeting of salient extrapersonal events. *Philosophical Transactions of the Royal Society of London Series B: Biological Sciences*, 354, 1325–1346.
- Modirrousta, M., & Fellows, L. K. (2008). Dorsal medial prefrontal cortex plays a necessary role in rapid error prediction in humans. *Journal of Neuroscience*, 28, 14000–14005.
- Nissen, M. J., & Bullemer, P. (1987). Attentional requirements of learning: Evidence from performance measures. *Cognitive Psychology*, 19, 1–32.
- Rabbitt, P. M. (1966). Errors and error correction in choice-response tasks. *Journal of Experimental Psychology*, 71(2), 264–272.
- Raven, J. C. (1960). *Guide to standard progressive matrices*. London: HK Lewis.
- Raven, J. C. (1976). *Revised manual for Raven's progressive matrices and vocabulary scale*. Windsor: NFER Nelson.
- Resulaj, A., Kiani, R., & Wolpert, D. M. (2009). Changes of mind in decision-making. *Nature*, 461, 263–267.
- Reuter-lorenz, P. A., & Baynes, K. (1992). Modes of lexical access in the callosotomized brain. *Journal of Cognitive Neuroscience*, 4, 155–164.
- Rodríguez-Fornells, A., Kurzbuch, A. R., & Münte, T. F. (2002). Time course of error detection and correction in humans: Neurophysiological evidence. *Journal of Neuroscience*, 22, 9990–9996.
- Rubia, K., Russell, T., Overmeyer, S., Brammer, M. J., Bullmore, E. T., Sharma, T., et al. (2001). Mapping motor inhibition: Conjunctive brain activations across different versions of go/no-go and stop tasks. *NeuroImage*, 13, 250–261.
- Schluter, N. D., Rushworth, M. F., Passingham, R. E., & Mills, K. R. (1998). Temporary interference in human lateral premotor cortex suggests dominance for the selection of movements. A study using transcranial magnetic stimulation. *Brain*, 121, 785–799.
- Schulte, T., Sullivan, E. V., Muller-Oehring, E. M., Adalsteinsson, E., & Pfefferbaum, A. (2005). Corpus callosal microstructural integrity influences interhemispheric processing: A diffusion tensor imaging study. *Cerebral Cortex*, 15, 1384–1392.
- Stephan, K. E., Marshall, J. C., Friston, K. J., Rowe, J. B., Ritzl, A., Zilles, K., et al. (2003). Lateralized cognitive processes and lateralized task control in the human brain. *Science*, 301, 384–386.
- Swick, D., & Turken, A. U. (2002). Dissociation between conflict detection and error monitoring in the human anterior cingulate cortex. In *Proceedings of the National Academy of Science USA* 99, (pp. 16354–16359).
- Taylor, S. F., Martis, B., Fitzgerald, K. D., Welsh, R. C., Abelson, J. L., Liberzon, I., et al. (2006). Medial frontal cortex activity and loss related responses to errors. *Journal of Neuroscience*, 26, 4063–4070.
- Ullsperger, M., & von Cramon, D. Y. (2006). The role of intact frontostriatal circuits in error processing. *Journal of Cognitive Neuroscience*, 18, 651–664.
- Ullsperger, M., von Cramon, D. Y., & Müller, N. G. (2002). Interactions of focal cortical lesions with error processing: Evidence from event-related brain potentials. *Neuropsychology*, 16, 548–561.
- Vanderplas, J. M., & Garvin, E. A. (1959). The association value of random shapes. *Journal of Experimental Psychology*, 57, 147–154.
- Verstynen, T. D., Diedrichsen, J., Albert, N., Aparicio, P., & Ivry, R. B. (2005). Ipsilateral motor cortex activity during unimanual hand movements relates to task complexity. *Journal of Neurophysiology*, 93, 1209–1222.
- Wenderoth, N., Debaere, F., Sunaert, S., van Hecke, P., & Swinnen, S. P. (2004). Parieto-premotor areas mediate directional interference during bimanual movements. *Cerebral Cortex*, 14, 1153–1163.
- Westlye, L. T., Walhovd, K. B., Bjørnerud, A., Due-Tønnessen, P., & Fjell, A. M. (2009). Error-related negativity is mediated by fractional anisotropy in the posterior cingulate gyrus – A study combining diffusion tensor imaging and electrophysiology in healthy adults cereb. *Cortex*, 19, 293–304.
- Yeung, N., Botvinick, M. M., & Cohen, J. D. (2004). The neural basis of error detection: Conflict monitoring and the error-related negativity. *Psychological Review*, 111, 931–959.
- Zaidel, E., & Iacoboni, M. (2003). *The parallel brain: The cognitive neuroscience of the corpus callosum*. Cambridge, MA: MIT Press.