Connectivity measures in the Poffenberger paradigm indicate hemispheric asymmetries

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Summary

The Poffenberger paradigm is a well-known measure of interhemispheric transfer delays, calculated on the basis of the crossed vs uncrossed reaction time difference (CUD). However, the proper interpretation of CUD is extensively debated in the literature. In this study we used connectivity measures in an attempt to interpret CUD from the perspective of functional connectivity. Accordingly, we tried to define functional couplings in the Poffenberger paradigm; we used a simple choice version of the paradigm, and included a stimulation only (SO) condition for comparison. As an index of functional coupling we employed partial directed coherence, exploiting bilateral grouping of the electrodes to compute intra- and interhemispheric connection weight ratios (CWRs). Our findings indicated modulations in functional weights in relation to the SO condition, rather than the crossed and uncrossed conditions, such that the response executed by the right hemisphere yielded a decrease in intra-, yet an increase in interhemispheric CWRs, whereas the left hemisphere interactions showed connectivity patterns similar to the SO condition irrespective of the side of movement. Overall, our results suggest modulation of connectivity in the same/similar system, which was found to be optimized, in terms of hemispheric asymmetries, to different tasks.

KEY WORDS: CUD, EEG, functional connectivity, hemispheric asymmetry, PDC, Poffenberger paradigm

Introduction



The Poffenberger paradigm is a traditional measure of interhemispheric transfer time (IHTT), based on ipsi- and contralateral reaction times (RTs) to lateralized visual stimulation. In his experiments, Poffenberger used these RTs to calculate the crossed vs uncrossed time difference (CUD), i.e. "the difference in response times between the 'uncrossed' condition, in which sensory stimuli and motor responses are ipsilateral, and the 'crossed' condition in which sensory stimuli and motor responses are contralateral" (lacoboni and Zaidel, 2000), with the premise that the uncrossed condition is characterized by intrahemispheric interactions, i.e. a left hand (LH) response to a left visual field (LVF) stimulus (LVF+LH) or a right hand (RH) response to a right visual field (RVF) stimulus (RVF+RH), whereas the crossed condition is characterized by interhemispheric interactions (LVF+RH or RVF+LH). A metaanalysis of several studies indicates CUD to be approximately 4 ms (Marzi et al., 1991).

Interpretation of CUD as the synaptic or callosal delay, however, is controversial. In their functional MRI (fMRI) study, lacoboni and Zaidel (2004) suggested that it represents an axonal conduction delay through callosal fibers, proposing that the crossed condition is a process consisting of multiple types of information flowing through the corpus callosum including sensory-motor integration, motor intention, decision making and response preparation, as they showed higher activations in the right superior parietal cortex during crossed vs uncrossed conditions and concluded that CUD might be a correlate of 'motor intention'.

Another view defines CUD as a net result of a balancing of inter- vs intrahemispheric costs, and considers inconsistencies in measured CUDs to be associated with changes in experimental conditions, such as stimulus eccentricity, motor preparation load, type of decision, etc. (for a review, see Braun et al., 2003). Interpretation of CUD as IHTT has also been criticized by Kinsbourne (2003), in whose proposed model for the lateralized stimulation condition, the corpus callosum is defined as a mediator, able to co-activate the unengaged hemisphere, as in preparation for response, and distribute attentional capacity between the hemispheres, in order to achieve atomicity of action in spite of the dual processors. It is also emphasized in his model that the approach was stripped of all variables of interest (i.e. expectancy, conflict in responses, stimulus-response compatibility); as an alternative view he argued that intrahemispheric cortico-cortical connections, by co-activating their intrahemispheric target areas, could possibly play a role in the maintenance of a balance between the two hemispheres.

In another fMRI study, it has been shown that even in the uncrossed condition visual information was processed bilaterally and that both crossed and uncrossed conditions are associated with similar spatial patterns of activated areas (Martuzzi et al., 2006). On the basis of these results, the authors concluded that distinct visuomotor networks may not be involved in the handling of the crossed condition, and interpreted CUD as a modulatory index of the strength of responses for the same brain network, rather than selective activation of brain regions resulting in longer reaction times.

In this study, we aimed to address the meaning of CUD from the perspective of functional connectivity, since the above-mentioned studies all tackled the problem from the perspective of functional activation. Yet, functional activation and functional coupling represent different views of the same phenomena. In order to address the debate over the interpretation of CUD, we used connectivity measures, attempting to define functional couplings in the Poffenberger paradigm, our aim being to define possible connectivity differences between the crossed and uncrossed conditions. We used partial directed coherence (PDC) to derive connectivity measures in frequency domains, and calculated intra- and interhemispheric connection weight ratios (CWRs) by means of location-based grouping within the left and right cerebral hemispheres. We hypothesized that if the axonal delay interpretation is correct, our results should show higher interhemispheric CWRs for the crossed condition: otherwise, we should observe modulations in interactions not only for the crossed condition but for all task combinations.

Methods

Subjects

Nine right-handed subjects (2 females, 7 males, aged 30–50 years, mean±SD 35±7.2 years) participated in the study after providing their written consent. The subjects had normal or corrected vision and no history of any neurological or psychiatric disorder. This study was approved by Hacettepe University Medicinal, Surgical, and Pharmacological Research Ethics Board, and complied with the Code of Ethics of the World Medical Association (B30.2.HAC.0.20.05.04/2241) (Declaration of Helsinki).

Experimental paradigm

We used the simple choice (Go-NoGo task) version of the Poffenberger paradigm. The subjects sat comfortably with their arms in a relaxed position, in a very dimly lit, electrically shielded room covered with a black material. Lateralized visual stimulation was performed using a black apparatus with two bilaterally positioned 0.5 mm diameter white LEDs and a central white circle with the same diameter to serve as the central fixation point. The two LEDs were placed 7 cm from the central fixation point and at a 1 cm center-to-center vertical distance from each other. The distance between the subjects and the stimulation plane was 57 cm (Fig. 1). ON-OFF LED periods, and the related triggers sent to the EEG recording system, were controlled via a custom-designed microcontroller (PIC 16F84, Microchip, Chandler, AZ) circuit. The ON state of a LED was set to last 25 ms, and provision was made for 3-4 s inter-stimulus intervals.

The subjects were instructed to fixate on the central fixation point during the experimental sessions. The experiments started with the stimulation only ('No Response') condition, in which the sessions of LVF and RVF trials were randomized for the single subject. A wrist extension constituted a response. One LED ON was defined as the instruction to move (Go), two LEDs ON was defined as the instruction not to move (NoGo). In each session, Go/NoGo tasks were randomized with 50% probability. The uncrossed and crossed conditions were acquired in separate sessions and their sequence was randomized across the subjects (Table I).

EEG recording

EEG, horizontal electro-oculogram (HEOG) and EMG activity associated with wrist extension were recorded during the experiments using a Synamps Amplifier (Neuroscan Inc., Herndon, VA), at 5 ksps sampling rate with filters set to DC-1 kHz frequency range. All channels were referenced to the left ear, and the FT7 and FT8 electrodes on the EEG cap were excluded to obtain additional channels needed for differential EMG, which was recorded at the wrist extensor muscles of both arms (Fig. 2). EMG electrodes were placed as recommended by Davis (1959) to detect wrist extensions.

Continuous EEG data were filtered using a second order Butterworth filter to include only 0.1–70 Hz range and re-referenced to the linked ears, after which epochs covering 200 ms pre- and 800 ms post-stimulus time in-



Figure 1 - Experimental setup.

The distance between the stimulation apparatus and the subject was 57 cm. Two LEDs were placed 7 cm from the central fixation point and were separated by a vertical distance of 1 cm. ON-OFF periods of LEDs, and related triggers sent to the EEG recording system were controlled by a microcontroller (PIC 16F84) circuit designed by us. One LED ON was defined as the instruction to move (Go), two LEDs ON was defined as the instruction not to move (No-Go). The LED/LEDs was/were ON for 25 ms with 3-4s interstimulus intervals. This figure shows LVF condition; for RVF conditions LEDs on the right were used.

Table I - Sequence of sessions.

1	Stimulation only (No response)	LVF RVF
2a	Uncrossed conditions	LVF-LH RVF-RH
2b	Crossed conditions	LVF-RH RVF-LH

Abbreviations: LVF=left visual field stimulus; RVF=right visual field stimulus; LH=left hand response; RH=right hand response. In each session, Go/NoGo tasks were randomized with 50% probability. Subjects started with the 'No Response' condition and the LVF and RVF sessions were randomized across the subjects. The sequence of four crossed-uncrossed conditions was randomized across the subjects.

tervals were extracted for each event. Epochs were manually checked for eye movement and blink artifacts, and contaminated ones were excluded from further analysis. In order to ensure peripheral stimulation during trials, HEOG recordings were also examined in detail for any saccades towards stimuli. Similarly, EMG recordings were examined to exclude epochs influenced by subject errors in the Go and NoGo tasks (i.e. no wrist extension in Go, or wrist extension in NoGo).



Figure 2 - EEG electrode placement scheme. Red circles indicate electrodes used in the PDC calculations.

Connectivity analyses

We used PDC to derive frequency-domain connectivity measures. PDC, as a measure of frequency-domain representation of Granger causality (Granger, 1969), is computed by decomposing multivariate partial coherences derived from multivariate autoregressive (MVAR) models (Baccalá and Sameshima, 2001) (Equation 3). Each row of the PDC matrix represents incoming information, and each column is a measure of outgoing information. Since zero time-lagged coefficients are not included in the MVAR model, PDC is assumed to be robust against the volume conduction effect, which propagates without any time delay (Schlögl and Supp, 2006).

$$\begin{bmatrix} x_1(k) \\ \vdots \\ x_M(k) \end{bmatrix} = \sum_{r=1}^{p} A_r \begin{bmatrix} x_1(k-r) \\ \vdots \\ x_M(k-r) \end{bmatrix} + \begin{bmatrix} w_1(k) \\ \vdots \\ w_M(k) \end{bmatrix}$$
(1)

$$A(f) = l - \sum_{r=1}^{p} A_r e^{-2i\pi f r}$$
 (2)

$$|\pi_{ij}(f)| = \frac{|\bar{n}_{ij}(f)|}{\left|\sum_{k=1}^{N} |\bar{A}_{k,j}(f)|^2}$$
(3)

x_i : time series to be modeled (i= 1,2,.... M)

Ar : MVAR model

- p : model order
- $\bar{A}(f)$: Fourier transform of MVAR model A_r
- $\pi_{ij}(f)$: PDC from j to i in the frequency f

In order to reduce the number of parameters to be estimated, before deriving the MVAR coefficients, the individual EEG epochs were down-sampled to 250 sps and the number of electrodes to be modeled was reduced to 22 (Fig. 2; electrodes marked with red circles). The model order was defined as 4 using the Akaike information criterion (Akaike, 1974). MVAR coefficients were calculated using the Levinson-Wiggins-Robinson algorithm implemented in the MATLAB TSA toolbox (Schlögl, 1996-2016). In order to handle problems related to estimation of the MVAR model for event-related potential (ERP) signals, we implemented the methods proposed by Ding et al. (2000).

We calculated mean PDC values for the alpha (8–12 Hz), beta (13–29 Hz) and gamma (30–40 Hz) frequency bands. Since there exist no robust analytical or non-parametric surrogate statistics for the application of PDC over multi-segmented data (i.e. for comparison of experimental tasks and conditions), instead of testing statistical significance for each matrix element we tested the overall results for the PDC matrix, and then issued CWRs as solutions.

In order to obtain intra- and interhemispheric CWRs, we grouped the electrodes according to their location on the left or right cerebral hemisphere. On the basis of this grouping, we chose source and sink elements from the columns and rows, respectively, of the PDC matrix; this step was followed by summation of the selected elements and division of the result by the sum of all the matrix elements. For example, in order to obtain a right interhemispheric CWR, the columns referring to right hemispheric electrodes were chosen as source elements, and the rows representing left hemispheric electrodes were chosen as sink elements (Fig. 3). Since the number of midline electrodes (n=6) is smaller than the number of electrodes on the left and right hemispheres (n=8), midline-related CWR values were excluded from further statistical analysis (Fig. 2).

As the final step, CWRs were calculated separately for all tasks, conditions and frequency bands, and the results were submitted to mixed design repeated ANOVA to test, among conditions and frequency bands, for statistically significant differences between tasks. For this purpose, visual field (LVF, RVF) and response type (no response, uncrossed, crossed) were used as withinsubject factors and connection type (left intra-/interhemispheric, right intra-/interhemispheric) and frequency band (alpha, beta, gamma) as between-subjects factors. Analyses were conducted for the Go and NoGo tasks separately.

Results

Go task

For the Go task, Mauchly's test indicated that the assumption of sphericity had been violated for response type ($\chi^2(2)=20.42$, p<.001) and visual field x response type interaction ($\chi^2(2)=10.44$, p<.005), therefore degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity ($\epsilon=0.84$ and $\epsilon=0.91$, respectively). Only the LVF-uncrossed condition did not satisfy Levene's test of equality of error variance (p<.043) among six levels of repeated measures

groups. No further correction was made since the other variables satisfied the test of equality of error variance of dependent variables across groups.

The only significant main effect was connection type $(F(3,96)=100.36, p<.001, \eta_p^2=.76)$, which indicated existence of asymmetries in intra-/interhemispheric connections of the left and right cerebral hemispheres (Fig. 4a). The right interhemispheric CWR was the highest CWR among all conditions (p<.001). Connection type showed an interaction with response type $(F(5.03,160.89)=2.52, p<.031, \eta_p^2=.07)$ and also with visual field x response type $(F(5.44,173.91)=2.56, p<.025, \eta_p^2=.07)$. These interactions suggested the existence of significant differences in connection type in relation to response type.

Post-hoc tests with Bonferroni correction demonstrated that RVF stimulation (compared with LVF stimulation) was associated with a higher right intrahemispheric CWR in the no response condition (Fig. 5a) (p<.029) and a lower left intrahemispheric CWR in the crossed condition (p<.001) (Fig. 5c). When response types were compared, no significant differences were found between the crossed and uncrossed conditions in relation to connection type. Modulation of intrahemispheric connections in relation to change in condition was observed only in LVF stimulations, such that the no response condition was associated with a lower right interhemispheric CWR (p<.023) and higher right intrahemispheric CWR (p<.042) compared with the uncrossed condition (Fig. 6a). The crossed condition also gave lower right intrahemispheric CWR values compared with the no response condition (p<.006). For LVF stimulations, the introduction of a task yielded a decrease in interhemispheric CWR values and an increase in intrahemispheric CWR values in the right hemisphere. In RVF stimulations, we observed no significant differences in relation to response type (Fig. 6b).

NoGo Task

For the NoGo task, Mauchly's test indicated that the assumption of sphericity was satisfied for response type ($\chi^2(2)$ =4.86, p<.088) and visual field x response type interaction ($\chi^2(2)$ =1.39, p<.500). The LVF-crossed and RVF-no response conditions did not satisfy Levene's test of equality of error variance (p<.001 and p<.002)

among six levels of repeated measures variables. No further correction was done since the other variables satisfied the test of equality of error variance of dependent variables across groups.

The only significant main effect was connection type (F(3,96)=58.31, p<.001, $\eta_p^2=.65$), which indicated the existence of asymmetries in intra-/interhemispheric connections of the left and right cerebral hemispheres (Fig. 4b). As in the Go task, the right interhemispheric CWR was the highest CWR among all conditions and tasks. The connection type showed an interaction with visual field (F(3,96)=4.98, p<.003, $\eta_p^2=.14$) and also with visual field x response type interaction (F(6,192)=4.84, p<.006, $\eta_p^2=.13$). These interactions suggested the existence of significant differences in connection type in relation to visual field.

Post-hoc tests with Bonferroni correction demonstrated, in the no response condition, that LVF stimulation compared with RVF stimulation yielded lower left intrahemispheric (p<.002), higher left interhemispheric (p<.004), and lower right interhemispheric (p<.001) CWRs compared with RVF stimulation (Fig. 5a). In the uncrossed condition, LVF stimulation, compared with RVF stimulation, yielded a lower right intrahemispheric CWR (p<.025) (Fig. 5b). When response types were compared, there was no significant difference between crossed and uncrossed conditions in relation to connection type. LVF stimulations in the no response condition yielded lower left intrahemispheric (p<.049) and right interhemispheric (p<.006) and higher right intrahemispheric (p<.019) and left interhemispheric (p<.032) CWRs compared with the uncrossed condition (Fig. 6a). RVF stimulations, on the other hand, yielded higher left intrahemispheric CWR values (p<.017) in the no response condition compared with the crossed condition (Fig. 6b).

Go vs NoGo

In order to compare Go and NoGo tasks, all experimental conditions were submitted to one-way ANOVA with type of task as the independent variable for all connection types separately. Under RVF stimulation conditions, the NoGo task, in comparison with the Go task, was found to yield higher left intrahemispheric CWRs in the no response condition (F(1,52)=4.25, p<.044, $\eta_p^2=.07$),



Figure 3 - Method for calculating intra- and interhemispheric connection weight ratios.

higher right intrahemispheric CWRs in the uncrossed condition (*F*(1,52)=5.35, p<.025, η_p^2 =.09) and higher left interhemispheric CWRs in the crossed condition (*F*(1,52)=5.57, p<.022, η_p^2 =.10) (Fig. 7).

Reaction times

Reaction times were measured using EMG channels. The threshold of movement initiation was defined as the mean value of rectified EMG plus 2 times the standard deviation. RTs were submitted to repeated ANOVA with visual field (LVF, RVF) and response type (uncrossed, crossed) as independent variables. Post-hoc tests were



Figure 4 - Asymmetries in intra/interhemispheric CWR of left and right cerebral hemispheres in Go (a) and NoGo (b) tasks. Mean CWR ± 2 standard error of the mean. Right interhemispheric CWR was the highest for all conditions and tasks (p<.001)





Figure 6 - Comparison of effect of response type under LVF (a) and RVF (b) stimulation for Go (left) and NoGo (right) tasks.

Mean CWR ±2 standard error of the mean.



Figure 5 - Comparison of effect of visual fields for No response (a), uncrossed (b) and crossed (c) conditions for the Go (left) and NoGo (right) tasks. Mean CWR ±2 standard error of the mean.



Figure 7 - Comparison of effect of task for No response (a), uncrossed (b) and crossed (c) conditions for LVF (left) and RVF (right) stimulation.

Mean CWR ±2 standard error of the mean.



Figure 8 - Mean reaction times in milliseconds. Error bars indicate ±2 standard error of the mean.

Discussion

In this study, we calculated intra- and interhemispheric CWRs for each hemisphere, and for all conditions and tasks in the Poffenberger paradigm. Our results indicated differences between cerebral hemispheres rather than between crossed and uncrossed conditions, revealing that interhemispheric connections in the right hemisphere had the highest ratio, for all tasks and conditions.

For GO tasks, there was no significant difference in CWRs between crossed and uncrossed conditions triggered by RVF stimulation (Fig. 6b). On the other hand, under LVF stimulation we observed changes in intrahemispheric CWRs for different response types (Fig. 6a). The comparison of LVF and RVF stimulations in the crossed condition indicated higher left intrahemispheric CWRs for RVF, thus meaning a higher weight ratio during crossed condition responses involving the non-dominant hand (nDH) (Fig. 5c). As a second significant result, under LVF stimulation, left intrahemispheric CWR was higher for the uncrossed compared with the crossed and no-response conditions (Fig. 6a); this could mean that, even though both the stimulus interpretation and response initiation were expected to occur in the right hemisphere, the influence of the left hemisphere, as the unstimulated, non-responding hemisphere was greater. The left intrahemispheric CWR increase found during nDH responses might be attributed to the importance of the left hemisphere in motor control. Activationbased approaches indicate involvement of the left hemisphere during nDH movements. Involvement of left motor areas, compared with right motor areas, during ipsilateral movement has previously been shown to be higher, with the left hemisphere having motor templates available for both dominant hand (DH) and nDH movements (Kim et al., 1993, Callaert et al., 2011), which is in accordance with our finding of higher CWR values for the LVF-LH (uncrossed) condition. However, in an EEG study focusing on dynamic modeling of the Poffenberger paradigm by incorporating ERP map segmentation, left motor area involvement was shown only for the

crossed condition of RVF stimulation and not for the LVF-LH condition (Thut et al., 1999). In that study, visual and motor maps were derived, respectively, from stimulus-locked vs response-locked ERPs, leading to the related dynamic changes. Accordingly, in our study we modeled the whole process over a single MVAR model, focusing on functional connectivity rather than regional activation patterns. As far as functional coupling is concerned, it was seen that, contrary to what has been seen with activation-based approaches, the overall involvement of the left hemisphere was more prominent when the stimulus processing and response initiation were localized within the right hemisphere.

If a decrease in CWR is assumed to be an indication of less involvement/engagement of the corresponding region, it can be concluded, on the basis of our left intrahemispheric CWR results, that responding with the DH to stimulation of the right hemisphere (LVF) is the most optimized condition. If anything, rather than a crossed-uncrossed difference, our results indicate hemispheric lateralization differences, adding to the doubts and discrepancies over interpretation of CUD as an axonal delay. Again for LVF stimulation, we observed a significant decrease in the right intrahemispheric CWR with the introduction of a response, yet no significant difference between crossed (DH) and uncrossed (nDH) conditions, i.e. an increase during subjects' execution of a movement (Fig. 6a). For the right hemisphere, stimulation yielded higher intrahemispheric interactions and if a response was initiated, interhemispheric interactions increased, which was found to be independent of side. both the side of the response and the side of the stimulation. Even though our results lack sufficient topoaraphic detail, we think the eminent right interhemispheric connections may be related to networks involved in attention. During a visuomotor line tracing task, it has previously been shown that an effector-independent network of activation regions (ventral frontoparietal areas) exists in the right hemisphere (Callaert et al., 2011). In that line tracing study, researchers used an experimental design involving stimulation of the central visual field, in a task demanding sustained attention. Considering that our paradigm consisted of a simple choice task, without any need for sustained attention. higher right interhemispheric CWRs independent of effector, task and combination, might be concluded to indicate instantaneous attentional demands, a hypothesis strongly supported by other findings of CUD lengthening in patients with unilateral right parietal lesions (Marzi et al., 2003). The highest CWR values of right intra-/interhemispheric connections can be explained by the conclusion of Heilman and Van Den Abell (1979), who indicated a greater tendency of the right compared to left hemisphere to distribute activation both within and between hemispheres.

For GO tasks, it can be concluded that, when stimulated, the left hemisphere has optimized solutions for the ongoing task and has a similar connectivity pattern irrespective of the side of the movement. On the other hand, stimulation of the right hemisphere yields response-related modulations of interhemispheric connections.

For NoGo tasks the interaction between the side of stimulation and the connection direction was found to be significant. In the stimulation only condition, LVF stimulation was associated with higher left intrahemispheric CWR values compared with the RVF stimulation condition (Fig. 5a). Under LVF stimulation in GO tasks, the uncrossed condition showed higher CWR values compared with every other condition, but for NoGo tasks, there was no significant difference between crossed and uncrossed conditions (Fig. 6). In a magnetoencephalography study with a simple choice paradigm examining response preparation, it was shown that there was contralateral motor activity even for the NoGo stimulus; furthermore, there was bilateral activation even when the stimulus and response were within the same hemisphere (Endo et al., 1999). Kinsbourne (2003) instead argued that the finding of bilateral motor activation/ preparation for no response ('view only') condition was an indication of the existence of an automatic link between input and output with/without explicit or implicit response demands. In the light of these arguments, if our Go and NoGo task results are evaluated together it might be concluded that left intrahemispheric interactions indicate the involvement of the left hemisphere not only in the execution of the movement, but also in decision making or movement planning.

In this study, we used one or two LEDs as the peripheral stimulus and also recorded a stimulation only condition as the control experiment in addition to crossed-uncrossed Go/NoGo tasks. We defined one LED ON as the command to move (Go) and two LEDs ON as the command not to move (NoGo). Comparison of CWRs of the one LED ON and two LEDs ON conditions showed significant inter- and intrahemispheric CWR changes in the left hemisphere. The two LEDs ON condition resulted higher intrahemispheric CWR values during RVF stimulation and higher interhemispheric CWRs during LVF stimulation. We also found that right interhemispheric CWR values were higher during RVF than LVF stimulation. These results were in accordance with the previous conclusion, based on the observation of bilateral motor activation/preparation even during 'view only' (no response) condition, that there exists an obligatory link between input and output even for the no-response condition (Kinsbourne, 2003). However, we observed these differences only in the left hemisphere. In a proposed model for spatial attention based on dissociation between categorical processing, which benefits from a local focus of attention, and coordinate processing, which benefits from a global focus of attention, the left hemisphere was defined advantageous for categorical processing and the right hemisphere for coordinate processing (van der Ham et al., 2014). Our results, showing differential processing of one LED ON and two LEDs ON stimulation might be related to categorical processing in the left hemisphere, and need further investigation.

In conclusion, our results indicate modulations in functional weights in relation to the 'stimulation only' condition, rather than the crossed and uncrossed conditions. Strogatz (2001) indicated that systems with identical structural connectivity can show entirely different behavior if the functional properties of the connections are changed. Even though similar regions were activated during crossed and uncrossed conditions, Kinsbourne (2003) interpreted CUD as a net result of an ensemble of balancing of costs within and between the two hemispheres. In the light of these interpretations of connectivity and CUD, if PDC is assumed to be an efficient tool for representing cortical connectivity patterns, then our results suggest modulation of connectivity in the same/similar system, which was optimized, in terms of hemispheric asymmetries, to different tasks.

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