Short- and Long-range Neural Synchrony in Grapheme–Color Synesthesia

Gregor Volberg, Anna Karmann, Stefanie Birkner, and Mark W. Greenlee

Abstract

Grapheme–color synesthesia is a perceptual phenomenon where single graphemes (e.g., the letter “E”) induce simultaneous sensations of colors (e.g., the color green) that were not objectively shown. Current models disagree as to whether the color sensations arise from increased short-range connectivity between anatomically adjacent grapheme- and color-processing brain structures or from decreased effectiveness of inhibitory long-range connections feeding back into visual cortex. We addressed this issue by examining neural synchrony obtained from EEG activity, in a sample of grapheme–color synesthetes that were presented with color-inducing versus non-color-inducing graphemes. For color-inducing graphemes, the results showed a decrease in the number of long-range couplings in the theta frequency band (4–7 Hz, 280–540 msec) and a concurrent increase of short-range phase-locking within lower beta band (13–20 Hz, 380–420 msec at occipital electrodes). Because the effects were both found in long-range synchrony and later within the visual processing stream, the results support the idea that reduced inhibition is an important factor for the emergence of synesthetic colors.

INTRODUCTION

Synesthesia is the experience of cross-sensory perception where stimulation of one sensory modality causes sensations in other sensory modalities that were not physically stimulated. A common form is grapheme–color synesthesia, where the viewing of achromatic letters or digits induces an impression of a specific color (Simner et al., 2006). This form of synesthesia is investigated in this study. For example, one of our participants experiences the color red when viewing the otherwise achromatic letter “B,” and another participant sees yellow along with the digit “2.”

One predominant hypothesis on the origin of synesthetic experiences is the local cross-activation model (Ramachandran & Hubbard, 2001). According to this hypothesis, synesthesia is a consequence of increased neural cross-wiring between grapheme-processing visual word form area (VWFA) in anterior parts of occipito-temporal cortex and the posteriorly adjacent color processing region V4. Work on animal models suggests that V4 receives massive connections from temporal cortex in the fetal brain, which are reduced in further brain development because of neural pruning (Kennedy, Batardiere, Dehay, & Barone, 1997). This pruning is assumed to be incomplete in synesthetes so that residual connections remain between VWFA and V4 (Spector & Maurer, 2009). As a consequence, grapheme representations in VWFA entail the activation of color representations in V4 so that the impression of colored graphemes occurs. The local cross-activation model was supported by results of imaging studies as well as MEG and EEG studies. For example, a recent diffusion tensor imaging study revealed more anisotropic diffusion for synesthetes in left parietal, right temporal, and bilateral frontal regions, suggesting increased neural connectivity in these areas (Rouw & Scholte, 2007; cf. Jäncke, Beeli, Eulig, & Häning, 2009). In line with this finding, a recent MEG study revealed that synesthetes, but not controls, showed coactivation of V4 while viewing graphemes and that V4 activation occurred simultaneously with neural activity in form-processing regions (Brang, Hubbard, Coulson, Huang, & Ramachandran, 2010). The coactivation was observed as early as 110 msec after grapheme onset. Consistent with the local cross-activation model, this finding suggests that synesthetic colors arise in early visual processing (see also Brang, Kanai, Ramachandran, & Coulson, 2011; Barnett et al., 2008; Cohen Kadosh & Henik, 2007).

Alternatively, it has been suggested that synesthesia is not an early sensory phenomenon, but rather it emerges in mid- to high-level vision and at later stages of processing. This view is mainly motivated from results of behavioral studies where, as a generic paradigm, color-inducing graphemes (inducers) are presented along with real-colored target stimuli with the task to identify the target’s color (e.g., Mattingley, Rich, Yelland, & Bradshaw, 2001). If the perceived color of an inducer is incongruent to that of the target, then the associated responses interfere and
RTs increase. Using this rationale, Mattingley et al. (2001) found that inducers produced interference only if they were presented sufficiently long to be available for attentional selection and overt report. Likewise, later studies revealed a reduced interference under conditions with high attentional load (Mattingley, Payne, & Rich, 2006) or within the attentional blink, a state with limited allocable attentional resources (Rich & Mattingley, 2010). A possible explanation for these results was provided by the disinhibited feedback model (Grossenbacher & Lovelace, 2001; see also Smilek, Dixon, Cudahy, & Merikle, 2001). According to this view, graphemes are processed up to a level where representations from unisensory cortices converge, presumably in STS. STS provides feedback connections to unisensory cortices, which are inhibited in normal brains. In synesthetes, the inhibition is thought to be incomplete so that feedback can propagate down to visual cortex and activate a non-veridical color representation. Within this architecture, color coactivation does not occur “horizontally” between cross-connected sensory areas, but “vertically” in the visual stream hierarchy after full processing of the grapheme. Because this difference is crucial for our study, we will in the following refer to the opponent views as the horizontal and the vertical approach, respectively.

Evidently, the horizontal and the vertical approach to synesthesia differ with respect to the assumed timing of color coactivation (Brang et al., 2010) as well as to the assumed extent of the neural assemblies involved into inducer processing. According to the horizontal model, synesthetic colors emerge early in the visual processing stream and as a result of sharply confined brain activity within left fusiform gyrus. In contrast, according to the vertical model, the color sensation occurs later in visual processing and requires coordinated activity of broader neural networks. Results from neuroimaging studies suggest an increased structural connectivity in synesthetes’ brain, on a local (Rouw & Scholte, 2007) as well as on a global scale (Hänggi, Wotruba, & Jäncke, 2011). However, whether color sensations in grapheme–color synesthesia are associated with short- or long-range network activity is not yet known. Also, it is unclear how long-range communication would be implemented within ongoing brain activity. These questions were addressed in this study by investigating neural synchronization within EEG oscillations.

Oscillatory brain responses reflect rhythmic changes in neural excitability, with each cycle containing a time window where the sensitivity for synaptic input and spike output is maximal. To allow for efficient communication, time windows of maximal excitability need to be aligned or synchronized. By doing so, distant neurons can be transiently linking into large-scale neural assemblies (Fries, 2005). On the EEG sensor level, long-range synchrony can be indexed as the degree by which phase differences between sensor pairs are constant in repetitive trials (phase-locking value, PLV; Lachaux, Rodriguez, Martinerie, & Varela, 1999). Additionally, we obtained two indices for quantifying changes in local synchrony. The power is the squared amplitude of an oscillation ($\mu^2$). It increases if local neural assemblies fire synchronously and contain evoked (phase-locked to stimulus onset) as well as induced components (not phase-locked to stimulus onset). The intertrial coherence (ITC; also denoted as phase-locking factor; Tallon-Baudry, Bertrand, Delpuech, & Pernier, 1996) is a further measure of local synchrony. It increases if the phase of an oscillation relative to the stimulus onset is constant on repetitive trials and thus captures only evoked components.

Participants were presented with inducers or non-inducers and were asked to identify the color of a subsequently presented congruent or incongruent target. According to the horizontal approach, synesthetic colors emerge early in the visual processing stream and within locally confined brain structures. If this assumption is correct, then we expect to see an early increase of local oscillatory power or ITC for inducers compared with non-inducers. In contrast, the vertical approach proposes large-scale communication between visual cortex and higher-level structures of visual perception. If this idea is correct, then one should see an increased number of couplings (PLV) for inducers compared with non-inducers. Furthermore, one would expect to see this effect on relatively late stages of processing.

METHODS

Participants

Participants were recruited by an appeal in a local radio station. Possible candidates were invited to finish a Web-based standardized test battery for the assessment of grapheme–color synesthesia (Eagleman, Kagan, Nelson, Sagaram, & Sarma, 2007). It uses a color consistency test where participants are presented with a full set of graphemes and are asked to indicate their corresponding color experience on a RGB color palette (red/green/blue, 256 by 256 by 256 color values, scaled to lie between 0 and 1). Each grapheme is presented three times. A color variation score $v_j$ is computed for each grapheme $j$ by summing up the absolute differences in color values R, G, and B for all paired comparisons of the first, second, and third grapheme presentation. The total color variation score $V$ is then obtained by taking the average of color variation scores $v_j$ belonging to color-inducing graphemes, as reported by the subject. Low variations (high consistency) of color judgments are indicative for true synesthesia.

On the basis of the results of the test battery, 10 candidates were selected as participants for the actual experiment. Two of them were excluded after an initial EEG analysis because of pronounced electrode artifacts. One further participant was excluded because behavioral data indicated that she did not fulfill the task as instructed. Thus, seven participants (six women and one man, 20–54 years, mean age = 39 years) remained in
the sample. Their color variation scores $V$ are given in Table 1 (last column). The mean $V$ score was 0.69, with a standard deviation of 0.16. All participants had a normal or corrected-to-normal vision and were right-handed by self-report. Possible neurological or psychiatric disorders were excluded.

### Stimuli and Procedure

Participants were seated in an electrically and acoustically shielded chamber in front of a monitor with externally located power supply. A chin rest was used to prevent head movements during EEG acquisition and to ensure that the viewing distance remained constant at 38 cm. Stimuli were presented on a 17-in. flat screen monitor with a resolution of 1280 by 1024 pixels and a vertical refresh rate of 60 Hz. The stimulus presentation and response registration were done with the Psychophysics Toolbox (Brainard, 1997) running on Matlab 7.5 (Mathworks, Inc.) and a Dell Optiplex 745 PC.

A secondary aim of this experiment, not addressed in the present work, was to investigate the role of spatial attention for the emergence of synesthetic colors. Therefore, we used a Posner-like spatial cueing paradigm, which involves left- or right-hemifield presentations of a target stimulus (Posner & Driver, 1992). The target was a colored rectangle that occurred shortly after the presentation of a grapheme. To avoid that the grapheme onset elicits endogenous shifts of attention toward the target location, which could counteract the voluntary shift of attention induced by the spatial cue, the grapheme was shown bilaterally in the left and right hemifield.

A typical trial sequence is depicted in Figure 1. The stimuli were presented on a uniformly gray background (luminance = 4.3 cd/m²), and a white fixation cross was seen in the screen center throughout the experiment. Trials started with the presentation of two squares (size 3.5° by 3.5° of visual angle) positioned 7.5° left and right of the fixation mark, respectively. To prevent color aftereffects that might alter the synesthetic color impression, the squares were filled with randomly colored dots. After 2000 msec, an arrowhead appeared at the left or at the right side of the fixation mark indicating the position of the target. After 2000 msec, two graphemes centered within frames of random dots were shown at the previous square locations. The graphemes were capitals written in 30 pt Helvetica font type (1.4° of visual angle). They were always identical, were always drawn in objectively white color, and could either be inducers or non-inducers. For each subject, exactly one inducer and one noninducer grapheme was defined. The color-inducing grapheme was selected as the grapheme with the minimum

### Table 1. Color-inducing and Non-color-inducing Graphemes as Used in the Present Study for All Seven Participants

<table>
<thead>
<tr>
<th>Participant</th>
<th>Inducer and CIE Coordinates ($X$, $Y$, $Z$)</th>
<th>Noninducer</th>
<th>$V$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>B (0.45, 0.29, 0.12)</td>
<td>#</td>
<td>0.73</td>
</tr>
<tr>
<td>2</td>
<td>7 (0.58, 0.52, 0.20)</td>
<td>9</td>
<td>0.65</td>
</tr>
<tr>
<td>3</td>
<td>2 (0.72, 0.86, 0.13)</td>
<td>0</td>
<td>0.93</td>
</tr>
<tr>
<td>4</td>
<td>4 (0.39, 0.23, 0.06)</td>
<td>#</td>
<td>0.62</td>
</tr>
<tr>
<td>5</td>
<td>E (0.50, 0.77, 0.27)</td>
<td>#</td>
<td>0.86</td>
</tr>
<tr>
<td>6</td>
<td>3 (0.50, 0.30, 0.12)</td>
<td>2</td>
<td>0.57</td>
</tr>
<tr>
<td>7</td>
<td>E (0.43, 0.27, 0.11)</td>
<td>P</td>
<td>0.49</td>
</tr>
</tbody>
</table>

The inducer color was estimated by a color consistency test (Eagleman et al., 2007) and transformed into CIE 1931 color space. Noninducers were selected based on the subjects’ report of not seeing a concurrent color with that specific grapheme. Participants 1, 4, and 5 reported seeing synesthetic colors for all graphemes so that a hash was used as noninducer. The fourth column shows the color variation score $V$, see text for details.

Figure 1. Schematic depiction of a typical trial sequence. The task was to identify the color of a target frame surrounding a color-inducing or a non-color-inducing grapheme.
color variation score as obtained during the participant’s recruitment. The noninducing grapheme was selected based on the participant’s verbal report of not experiencing any concurrent color (see Table 1). After 150 msec, the frame and the grapheme on the nontarget side disappeared and the frame on the target side took a predefined color. This could either be white or matched to the photism associated with the inducer. Thus, the frame color could either be congruent or incongruent to the color impress produced by the grapheme (its photism or objective color). For example, an inducer with a blue photism could either match (blue photism/blue frame) or mismatch (blue/white) the color of the target square so that the associated responses were either congruent or incongruent. Analogously, the objective color of the noninducer, which was always white, could either match (white/white) or mismatched (white/blue) the target frame color, activating either congruent or incongruent responses.

The task was to identify the color of the frame as fast and as accurate as possible. Participants responded with the key and the index finger of the right hand using the left and right button of a standard PC mouse. Each button was the correct response option in 50% of trials. The mapping of response buttons to colors (matching synesthetic color or white) was balanced across participants. The trial sequence proceeded after the key press or after a timeout of 2000 msec was reached. The next trial started with a random delay drawn from a normal distribution with mean of 1500 msec and standard deviation of 300 msec.

Participants performed 10 blocks of 40 trials in a fully randomized order. Within each block, half of the trials contained inducers and half contained noninducers. Furthermore, half of the trials were congruent and half were incongruent. That is, in half of the trials, the response associated with the color of the target frame was the same as the response associated with the (actual or induced) color of the distractor. In the other half, the responses to the target and distractor color were conflicting. The original task also included a manipulation of cue validity where, in 20% of trials, an invalid cue pointed to the hemifield opposite to the subsequent target location. This factor was not relevant for the purpose of this study so that invalid trials were discarded.

As in Smilek et al. (2001), congruency was included as a factor into the analysis of the behavioral data. For the EEG, a separate analysis of congruent and incongruent stimuli was not suitable because the objective color of the grapheme and the surrounding frame were not balanced within these conditions. Continuing the above example, a congruent inducer stimulus contained a white grapheme and a blue frame, whereas a congruent noninducer stimulus contained a white grapheme and a white frame. Likewise, an incongruent inducer stimulus was made of a white grapheme and a white frame, whereas an incongruent noninducer stimulus was made of a white grapheme and a blue frame. To reveal inducer and noninducer conditions with the objective stimulus colors balanced, congruent and incongruent stimuli were collapsed for the EEG analysis. Thus, 80 trials per condition (inducer vs. noninducer, congruent vs. incongruent) were available for the behavioral data analysis, whereas 160 trials (inducer vs. noninducer) were available for the analysis of the EEG data.

**EEG Recording**

The EEG was recorded from 62 electrodes mounted in an elastic cap (BrainCap-MR64, EasyCap, Herrsching-Breitbrunn, Germany) and referenced to FCz during recording. The positioning and labeling of electrodes were made according to the extended international 10–20 system (Oostenveld & Praamstra, 2001). Impedances were kept below 20 kΩ. The EEG was amplified between 0.1 and 100 Hz and sampled at a rate of 500 Hz (BrainAmp MR plus, Brain Products, Gilching, Germany). After recording, the data were arithmetically re-referenced to an average reference value.

**Data Analysis**

**Behavioral Data**

Error rates as well as RTs were subjected to a 2 by 2 repeated-measure ANOVA with the factors congruency (congruent, incongruent) and grapheme type (inducer, noninducer). To control for outliers in RTs, the fastest and the slowest 5% of responses per condition were eliminated. Such trimmed means are more robust estimates of a central tendency of a distribution, that is, they are less sensitive to nonnormality than untrimmed mean values (Keselman, Algina, Lix, Wilcox, & Deering, 2008; Wilcox, 2005). Trials with incorrect responses were also excluded. Statistics were done with the free R language for statistical computing (R Development Core Team, 2008).

**EEG Data**

**Preprocessing.** The continuous data was segmented into epochs of −2350 to 2650 msec relative to the grapheme onset and baseline-corrected by subtracting the mean over the whole interval. Epochs containing electrode or movement artifacts were removed as well as trials with incorrect behavioral responses. The data were then subjected to an infomax independent components analysis as implemented in the EEGLab toolbox (Delorme & Makeig, 2004) for MATLAB environment (The Mathworks, Inc.). Artifactual components were identified by visual inspection of the component topographies and power spectra. Main sources of artifacts were eye blinks, eye movements, and tonic muscle activity. Components identified as artifactual were removed, and the remaining components were back-projected into
EEG signal space. Epochs were again inspected and rejected if they contained residual artifacts. The rejection rates were between 2.5% and 21.3% per participant (mean 11.7%). That is, 252–312 trials per participants (mean = 283) were available for the analysis. The EEG analysis focused on differences between inducer and noninducer conditions. Congruent and incongruent trials were collapsed to that end (see “Stimuli and procedure”).

EEG postprocessing was accomplished with custom MATLAB code and the Fieldtrip toolbox for MATLAB developed at the F.C. Donders Centre, Nijmegen, Netherlands (www.ru.nl/fcdonders/fieldtrip/).

**Power, ITC, and PLV calculation.** Time–frequency decomposition was done using a single taper (Hanning) windowed Fourier transform. Data were filtered every 10 msec from 4 to 60 Hz in frequency steps of 1 Hz. To obtain a suitable time and frequency resolution, the filter window length was adopted to contain seven cycles of the respective center frequency. Thus, the filter length and the frequency resolution decreased linearly with increasing center frequency, from 7 sec and 0.14 Hz at 1 Hz center frequency to 0.17 sec and 5.88 Hz at 60 Hz center frequency. To examine event-related power changes, the percentage power increase or decrease relative to a baseline period was computed as \( 100 \times \left( \frac{|A(t,f) - A_{b}(f)|}{A_{b}(f)} \right) \) for each trial \( t \) and frequency \( f \). This quantity is obtained for each trial \( t \) and at frequency \( f \), and \( A_{b}(f) \) is the mean amplitude over the baseline interval. The baseline for frequencies \(<21 \text{ Hz}\) was from \(-600\) to \(-100 \text{ msec}\) relative to grapheme onset. For higher frequencies, the baseline was from \(-300\) to \(0 \text{ msec}\).

ITC and PLV were computed with the same filter and baseline settings as described above. The phase information is retained in the corresponding Fourier spectra of the frequency decomposition. It can be illustrated as a vector within unity circle that represents the phase angle \(\phi\) of an oscillation at a given time point \( t \) and at frequency \( f \), \(\phi(t,f)\). This quantity is obtained for each trial \( n \) within one condition and then averaged by taking the circular mean. The length of the resultant vector is ITC. It indicates the phase consistency for a given \((t,f)\) over successive trials, reaching a values of 1 if the phase is constant in repeated trials and 0 if it is random.

In a similar manner, PLV quantifies the consistency of phase differences \(\theta(t,f)\) between signals obtained at two different sensors (Lachaux et al., 1999). It is computed as \(\Phi(t,f) = \Phi_1(t,f) - \Phi_2(t,f)\) for each trial \( n \) that belongs to one condition and then averaged over trials by taking the circular mean. The length of the resultant vector is PLV. A value of 1 indicates constant phase differences, and a value of 0 indicates that they are random. The PLV between two sites can be artificially high because of volume conduction where the sensors pick up activity of the same neural source. To reduce the impact of volume conduction, sensor data were transformed to current source density before PLV calculation using the CSD toolbox for MATLAB (Kayser, 2009). Furthermore, PLV is larger for smaller trial counts so it is often advised to use an equal number of trials per condition for PLV statistics. Because of the overall large number of trials (>100 for each inducer and noninducer), such adjustment of trial count was not necessary in our case (see Vinck, Oostenveld, van Wingerden, Battaglia, & Pennartz, 2011, for a discussion).

**Source analysis.** Sources of local oscillatory brain activity (power or ITC) were reconstructed for significant time and frequency ranges. The head models for source analysis were based upon individual head shapes obtained from structural magnetic resonance imaging with a 3-T MR head scanner (Siemens Allegra, Erlangen, Germany).

High-resolution sagittal T1-weighted images were acquired using a magnetization prepared rapid gradient-echo sequence (repetition time = \( 2250 \text{ msec}\); echo time = \( 2.6 \text{ msec}\); \( 1 \text{ mm isotropic voxel size}\) to obtain a \(3\)-D structural scan. This sequence is optimized to differentiate between white and gray matter. Realistic four-layer boundary element head models were then constructed for tissues brain, cerebrospinal fluid, skull, and skin. Their relative conductivity was set to 1, 3, 1/30, and 1, respectively. Two participants refused to go into the MR scanner. For them, a generic head model was constructed based on the Montreal Neurological Institute (www.mni.mcgill.ca) template brain distributed with the SPM8 toolbox for MATLAB (www.fil.ion.ucl.ac.uk/spm).

The forward model for source reconstruction was computed using the OpenMEEG plugin for fieldtrip software, on a \(5\)-mm grid of source positions covering the whole-brain compartment (Gramfort, Papadopoulo, Olivi, & Clerc, 2010; Kybic et al., 2005). For the inverse solution, the dynamic imaging of coherent sources (DICS) beamforming approach was used (Gross et al., 2001). It localized the sources of oscillatory brain activity within a given grid of source positions. The resulting volumetric source data were projected onto the inflated standard brain provided with Caret software (brainmap.wustl.edu/caret.html; Van Essen et al., 2001).

**Statistical analysis of EEG data.** Oscillatory brain activity was investigated for five frequency ranges, assessed according to standard EEG frequency band definitions (Kendall, Schwartz, & Jessell, 2000): \(\gamma(5–7 \text{ Hz})\), \(\alpha(8–12 \text{ Hz})\), lower \(\beta(\beta_1, 13–20 \text{ Hz})\), upper \(\beta(\beta_2, 21–30 \text{ Hz})\), and \(\gamma(31–45 \text{ Hz})\). Inferential statistics for the EEG data were generally done on the sensor level, not on source reconstructions.

The statistics were performed in a two-stage strategy. For power or ITC as dependent variable, inducer and noninducer trials were contrasted by paired \( t \) tests at all 63 electrodes simultaneously. This was done in steps of 10 msec from 0 to 600 msec. The number of significant electrodes at each time point was registered, separately for positive and negative differences and with a two-tailed \(\alpha\) of 0.05. To adjust for multiple comparisons, a second analysis stage was administered. At each time point of the
baseline interval, 1000 \( t \) tests were performed on random permutations of the data. The number of significant electrodes was recorded after each run and fed into a permutation distribution, separately for positive and negative effects. Results of the first stage analysis were only accepted if the number of significant electrodes exceeded the 0.975 quantile of the respective permutation distribution for positive or negative effects. With this procedure a correction for multiple comparisons with a two-sided \( \alpha \) of 0.05 was achieved (cf. Maris, Schoffelen, & Fries, 2007).

A similar strategy was also to PLV data, but with less data points because of the high computational demands. PLV was tested for all possible 1953 channel combinations. One-sample \( t \) tests were conducted on the baseline-corrected data, separately for trials with inducers and noninducers and in steps of 20 msec. The number of significant electrodes was recorded, where \( \alpha \) was set to 0.005 (two-tailed). This strategy reduces noise in the first stage of the permutation procedure and has been successfully applied in earlier studies (e.g., Hanslmayr et al., 2007). In the second analysis stage, 500 random permutations of the data were drawn at six equally spaced sample points within the baseline interval. The number of significant electrodes in the inducer and in the noninducer condition was registered, and the difference between both results was fed into a permutation distribution. Differences in the number of significant electrodes as revealed in the first stage analysis were considered significant only if they exceeded the 0.975 quantile or were below the 0.025 quantile of the permutation distribution. As for the power and ITC analysis, a two-tailed \( \alpha \) level of 0.05 was achieved in this way.

**RESULTS**

**Behavioral Data**

The behavioral results are depicted in Figure 2. By trend, responses were faster for congruent (479 msec, \( SD = \)) compared with incongruent (500 msec, \( SD = 102 \) msec) trials, \( F(1, 6) = 5.28, p < .061 \). Further effects were not observed. Notably, the interaction between congruency and grapheme type was far from significance, for RTs as well as for error rates (both \( F < 1 \)).

Because participants saw only a limited number of stimuli (one inducer and one noninducer grapheme and rectangles with the associated colors), adaptation or habituation might have been occurred. Both habituation and adaptation result in a decreased sensitivity for the adapted sensory event and thus produce an increase in RTs (Wassermann & Miller, 1997). Contrarily, the present data showed the opposite effect of a near-linear RT decrease from Block 1 to Block 10, \( r = -0.92, p < .001 \), as can be expected because of learning. Thus, habituation or adaptation did not occur.

**Power**

The results of the power analysis are summarized in Table 2 (left). The first column gives the critical number of electrodes that need to be exceeded to obtain a significant effect at \( \alpha = 0.05 \), two-tailed and corrected for multiple comparisons. The second column gives the maximum number of electrodes with a significant positive (inducer > noninducer) or negative (noninducer > inducer) difference at a given time bin. The third and the fourth columns give the corresponding \( p \) value and, if

| \( \theta \) | \( i > n \) | 10 | 2 | .59 | – | 8 | 4 | .28 | – | 1 | n > i | 10 | 1 | .93 | – | 8 | 1 | .88 | – | 1 | \( \alpha \) | n > i | 11 | 0 | 1 | – | 8 | 3 | .44 | – | 1 | \( \beta_1 \) | n > i | 9 | 2 | .64 | – | 6 | 9 | .01 | 380–420 | 1 | \( \beta_2 \) | n > i | 9 | 6 | .13 | – | 7 | 4 | .26 | – | 1 | \( \gamma \) | n > i | 8 | 9 | .04 | 590 | 6 | 6 | .08 | 590 | 1 |

Critical values of the permutation distribution (Crit \( n \)) as well as the maximum number of significant electrodes (Max \( n \)) for a given time bin are shown for each frequency band, separately for trials with inducers (\( i > n \), inducer > noninducer) and negative (\( n > i \), noninducer > inducer) differences. Time ranges are given in milliseconds. For sake of completeness, significant (\( p < .05 \), bold typeface) as well as marginal significance (\( p < .1 \), normal typeface) time ranges are reported. See text for details on the statistical analysis.
significant, the time range where the effect was observed. To avoid a selective data presentation that might bias the interpretation of the results toward the vertical approach, we also report marginal significant results for measures of local synchrony (power and ITC, \( p < .1 \)). Effects that reached conventional significance levels (\( p < .05 \)) are marked in bold typeface.

Head topographies for marginal significant or significant results are given in Figure 3, plotted on a timeline from \(-400 \) to \(600 \) msec relative to the grapheme onset. They show the electrodes included into a given effect, where the color indicates the corresponding \( p \) value as obtained by permutation tests. The data revealed two marginally significant differences showing more power in the noninducer compared with the inducer condition. They occurred in the \( \alpha \) (360–410 msec) and in the higher \( \beta \) (600 msec) band and included frontocentral and central electrodes, respectively (Figure 3A). Only in the \( \gamma \) band, there was a significant result. It occurred 590 msec after stimulus presentation and showed a larger power increase for inducers compared with noninducers that at frontal and right parietotemporal sites (Figure 3B).

**ITC**

The results for the ITC analysis are summarized in Table 2 (right). The corresponding head topographies are plotted in Figure 4A and B.

There were generally no effects in the \( \theta \), \( \alpha \), or \( \beta_2 \) band. Two marginal significant results occurred in the lower \( \beta \) band (460–470 msec, noninducer > inducer) and in the \( \gamma \) band (590 msec, inducer > noninducer). They covered central and frontal electrodes, respectively (Figure 4A, B). A short-lasting significant effect was observed in the \( \gamma \) band, 360 msec after stimulus onset, \( p < .05 \) by permutation test. It showed an increased ITC for noninducers compared with inducers at central electrodes (Figure 4A).

The most prominent effect was observed in the \( \beta_1 \) frequency range (Figure 4B). Figure 4C shows the difference time–frequency representation (inducer minus noninducer) at representative electrode Oz. As one can see, inducers compared with noninducers produced an enlarged ITC between 15 and 19 Hz, sharply within the \( \beta_1 \) frequency range. Figure 4D shows the time course of \( \beta_1 \) ITC for inducers and noninducers. Noninducer ITC had a peak 110 msec after stimulus presentation and then rapidly decreased to baseline levels. By contrast, inducer ITC further increased to a second peak at 300 msec and remained larger than noninducer ITC up to 500 msec.

To identify brain regions with increased \( \beta_1 \) activity in the inducer condition, a DICS source reconstruction was performed between 200 and 495 msec, with a center frequency of 17 Hz (Figure 4E). Foci were found in left and right middle occipital gyrus (BA 19), extending to inferior occipital gyrus (BA 18) in the right hemisphere. Moreover, there was increased activity in left fusiform gyrus (BA 20).

**PLV**

The results of the PLV analysis are summarized in Table 3. Momentary effects occurred in the \( \beta_1 \) band at 220 msec, in the \( \beta_2 \) band at 360 msec and at 580 msec, and in the \( \gamma \) band at 360 msec (all \( ps < .05 \)). Note that the most
prominent differences (with \( p < .001 \)) occurred in \( \alpha \) and \( \theta \) frequencies.

The \( \alpha \) PLV effect is depicted in Figure 5A–C. Figure 5A shows the number of significant couplings for inducers and noninducers. There was an early increase in the number of couplings for both conditions. However, this increase occurred earlier for inducers where the maximum number of couplings (\( n = 19 \)) was reached after 120 msec. The corresponding peak for noninducers comprised a similar number of couplings (\( n = 22 \)) but occurred 80 msec later. Because of the latency shift, there was a positive difference (inducer > noninducer) from 100 to 120 msec and a negative difference (noninducer > inducer) at 200 and from 260 to 280 msec (all \( p < .05 \)) after stimulus onset. Figure 5B shows the significant couplings at peak difference, 120 msec after grapheme onset. Couplings in the inducer condition were mainly between left parietal and right central/right frontal sites. This can also be seen in Figure 5C showing, separately for inducers and noninducers, the number of couplings that each electrode receives at three time points around the maximum effect. The major difference is an increased number of couplings for inducers at left parietal sites around 120 msec. The effect had a focus at electrode P7 (three couplings) and extended to centro-parietal (CP5, C5, C3) as well as parieto-occipital (PO7) electrodes.

The second prominent PLV effect was observed in the \( \theta \) band (Figure 5D–F). For both inducer and noninducer conditions, there was an increase of the number of couplings peaking 200 msec after stimulus onset. The maximum number of couplings was \( n = 90 \) and \( n = 97 \) for inducers and noninducers, respectively. After reaching the peak, the number of couplings in the inducer condition decreased to near-baseline levels at 420 msec (\( n = 16 \)). Conversely, for noninducers, the number of
couplings remained well above baseline \((n = 31)\). The difference was significant 280–320 msec and again 360–540 msec after stimulus onset \((p < .01\) at all time bins, see Figure 5D). Figure 5 (E and F) shows that the difference was mainly because of couplings between left and right central as well as between frontal and occipital/parietal sites. The electrodes that received the most couplings in the non-inducer condition were CP2 \((n = 10)\) and CP1 \((n = 9)\), followed by FP2 and AF4 (both \(n = 7\)).

### DISCUSSION OF MAIN EXPERIMENT

In this experiment, we investigated long- and short-range neural synchrony in grapheme–color synesthetes during grapheme processing. Participants were presented with inducers or noninducers and were required to identify the color of a subsequently shown target that was either congruent or incongruent to the perceived color of the grapheme. We examined EEG phase synchrony between channels (PLV) as a measure of long-range synchrony and intertrial phase consistency (ITC) as well as power changes as measures of short-range synchrony. If synesthesia arises because of increased horizontal cross-wiring, then differences between inducers and noninducers should be restricted to early and local increases of neural synchrony. Accordingly, a later and broader pattern of neural synchrony would argue in favor of the idea that synesthetic color sensations rely on vertical long-range communication.

Overall, the results strongly support the vertical approach. There were only a few differences between inducers and noninducers in short-range synchrony. The most prominent one occurred in lower \(\beta\) ITC, with more ITC for inducers compared with noninducers. However, this difference occurred not before 200 msec and was

<table>
<thead>
<tr>
<th></th>
<th>Crit n</th>
<th>Max n</th>
<th>(p)</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\theta)</td>
<td>i &gt; n</td>
<td>10</td>
<td>9</td>
<td>.08</td>
</tr>
<tr>
<td></td>
<td>n &gt; i</td>
<td>9</td>
<td>29</td>
<td>.001</td>
</tr>
<tr>
<td>(\alpha)</td>
<td>i &gt; n</td>
<td>9</td>
<td>16</td>
<td>.001</td>
</tr>
<tr>
<td></td>
<td>n &gt; i</td>
<td>9</td>
<td>13</td>
<td>.05</td>
</tr>
<tr>
<td>(\beta_1)</td>
<td>i &gt; n</td>
<td>9</td>
<td>8</td>
<td>.12</td>
</tr>
<tr>
<td></td>
<td>n &gt; i</td>
<td>9</td>
<td>10</td>
<td>.04</td>
</tr>
<tr>
<td>(\beta_2)</td>
<td>i &gt; n</td>
<td>9</td>
<td>12</td>
<td>.02</td>
</tr>
<tr>
<td></td>
<td>n &gt; i</td>
<td>9</td>
<td>9</td>
<td>.08</td>
</tr>
<tr>
<td>(\gamma)</td>
<td>i &gt; n</td>
<td>9</td>
<td>10</td>
<td>.03</td>
</tr>
<tr>
<td></td>
<td>n &gt; i</td>
<td>8</td>
<td>2</td>
<td>.73</td>
</tr>
</tbody>
</table>

See Table 2 for details.

---

**Table 3.** Summarizes the Results of the Statistical Analysis of PLV Differences

---

Figure 5. Results of the PLV analysis for the \(\alpha\) (left column, A–C) and \(\theta\) (right column, D–F) frequency range. (A, D) Show the number of significant couplings for inducers and noninducers. Gray bars indicate time bins with significant differences between inducers and noninducers. (B, E) Lines between electrodes mark significant couplings, shown at times of maximum difference between conditions (120 and 520 msec, respectively). (C, F) Head topographies showing the number of couplings for each electrode around the time of peak difference.
significant only after 380 msec. Two further short-lasting effects were seen in the γ band, with increased ITC for noninducers compared with inducers, and increased power for inducers compared with noninducers. As for β ITC, both effects occurred late within the processing stream, 360 and 590 msec after stimulus onset, respectively. Thus, local and early increases of neural synchrony, as predicted by the horizontal approach, were not observed in our data.

At the same time, the data showed two obvious effects in long-range neural synchrony within α and θ frequency bands. Within α, there was an early (100–120 msec) increase in the number of α couplings for inducers compared with noninducers. It mainly included left parietal and occipital electrodes with P7 exhibiting the maximum number of couplings. With respect to θ, we observed a later (<280–560 msec) decrease in the number of couplings for inducers compared with noninducers. The effect involved central (CP1, CP2) as well as frontal (AF4, FP2) electrodes. Thus, taken together, inducer processing was associated with a larger early α network and a smaller later θ network. Because such modulations of long-range synchrony are predicted from the vertical hypothesis, our results are more in line with this approach.

Four possible objections to our results need to be addressed before we can proceed with the general discussion. A first problem might arise from the use of bilateral grapheme displays. It has been reported that synesthetic color impressions are less vivid (Brang & Ramachandran, 2009) or even diminish (Ramachandran & Hubbard, 2001) if the inducers are presented at far eccentricities. One might therefore question whether in our experiment the induction of synesthetic colors worked as intended. The behavioral data show that this was the case. We obtained a marginally significant effect of congruency and grapheme type. This shows that inducers produced interference similar to that seen for noninducers, and thus, we assume that inducers produced a sensation of color. It should also be noted that Ramachandran and Hubbard (2001) found a vanished color impression only for eccentricities >11°, whereas our inducers were presented at 7.5° eccentricities. This result is therefore not at odds with the Ramachandran and Hubbard (2001) study.

A second critical point arises from the fact that our correction for multiple comparisons was based on the number of significant electrodes. This strategy might favor the detection of later occurring “cognitive” effects with broader topographic distributions, at the expense of earlier occurring and more focused “perceptual” effects. Consequently, it might be inappropriate to test the predictions of the horizontal approach. To rule out this argument, we performed a control analysis where time points and topographic ROIs were identified by means of a “microstate” analysis of global field power (see Michel et al., 2004). For each frequency band, mean power or ITC differences between inducers and noninducers were examined at the local maxima of global field power. The only indication for an early difference occurred in parieto-occipital γ ITC 100 msec after stimulus onset, where the results showed an ITC decrease for inducers compared with noninducers, t(6) = −2.62, uncorrected p < .05. This difference is in the opposite direction from that predicted by the horizontal approach. At the same time, we reproduced our finding of a later (600 msec) parieto-occipital β ITC increase for inducers compared with noninducers, t(6) = 2.63, uncorrected p < .05. Thus, the results were largely in line with those obtained with the permutation approach. We are therefore confident that the analysis strategy was valid.

Third, it might be problematic that three of the synesthetes saw a hash mark (“#”) as their noninducing character. Unlike letters and digits, which have a familiar meaning and a semantic representation, presumably the hash mark does not. Thus, the EEG results might have arisen from this difference alone, as opposed to any difference in experienced color between inducer and noninducer conditions. To rule out this possibility, a control analysis was performed for all significant findings obtained in the main analysis where the character that was used as a noninducer, hash versus nonhash symbol, served as a between-subject variable. Power and ITC differences between inducers and noninducers were averaged across significant channels to that end, at the time point where the grand mean difference obtained in the main analysis was maximal (see Table 2 and Figures 3–4). To examine PLV differences, the permutation procedure described in the main analysis was performed separately for hash and nonhash groups, and the number of significant electrode pairings in the inducer and the noninducer condition was compared by means of χ² tests, at the time point where the original PLV effect was maximal (see Figure 5). The results showed no differences between hash and nonhash groups with respect to power, ITC, or PLV differences. Power differences were small and insignificant throughout [α, 600 msec: t(5) = 0.79, p > .4; β, 260 msec: t(5) = −0.31, p > .7; γ, 590 msec: t(5) = −0.4, p > .7], as were ITC differences [β₁, 410 msec: t(5) = −0.77, p > .4; β₂, 470 msec: t(5) = 0.06, p > .9; γ, 360 msec: t(5) = −1.51, p > .19; γ, 590 msec: t(5) = −0.03, p > .5]. Similarly, the number of significant electrode pairings in the inducer and noninducer condition did not differ between the hash and nonhash groups [8, 300 msec: χ²(1) = 2.55, p > .1; 6, 520 msec: χ²(1) = 0.90, p > .3; α, 120 msec: χ²(1) = 0.07, p > .7; α, 220 msec: χ²(1) = 0.07, p > .7; α, 260 msec: χ²(1) = 0.55, p > .4; β₁, 220 msec: χ²(1) = 0.002, p > .9; β₂, 360 msec: χ²(1) = 0.002, p > .9; β₂, 580 msec: χ²(1) = 0.18, p > .67; γ, 360 msec: χ²(1) = 0.001, p > .9]. Thus, the differences between inducers and noninducers described in the main analysis did not arise from the use of hash symbols as noninducers in some subjects.

Finally, one might object that the within-subject control condition (i.e., the noninducer condition) was not appropriately balanced across subjects in our design.
Ideally, a grapheme that is an inducing stimulus for one synesthete should serve as a noninducing stimulus for another synesthete. With this factor not being controlled, it remains possible that the observed results for long-range connections and the lack of findings for short-range connections were because of the specific task conditions or stimuli used. To rule out this possibility, we decided to perform a follow-up experiment with a matched sample of nonsynesthetic control subjects that were presented with the same set of inducing and noninducing graphemes as the matching synesthete. If the observed effects in the main study were because of the task or stimuli used, then they should show up for the control subjects in the same manner.

FOLLOW-UP EXPERIMENT: SYNESTHETES VERSUS NONSYNESTHETES

Method

Seven control subjects were recruited that, by self-report, had never experienced synesthetic colors when viewing graphemes. They were matched to the synesthetic subjects with respect to age and gender (6 female, 1 male, 25–54 years, mean age = 38.1 years). All participants were right-handed and had normal or corrected-to-normal sight.

The control subjects were presented with the specific set of graphemes that was used for the matching synesthete. The paradigm, the experimental setting, and the parameters for EEG recording and preprocessing were identical to those applied to the synesthetic sample. For comparing EEG results between synesthetes and control subjects, we used the same strategy as for comparing the results of hash and nonhash groups. Power and ITC differences between inducers and noninducers were averaged across significant channels, at the time point where the respective effect was maximal in the primary analysis (see Table 2 and Figures 3–4). The mean differences were subjected to t tests with group (synesthetes, controls) as a between-subject variable. For comparing PLV differences, the number of significant electrode pairings in the inducer and the noninducer condition was obtained separately for the synesthete group and control group and compared by means of $\chi^2$ tests, at the time point where the original PLV effect was maximal (see Figure 5).

Results

Behavioral Data

For the analysis of the behavioral data, error rates as well as RTs were subjected to a 2-by-2 repeated-measures ANOVA with the factors congruency (congruent, incongruent) and grapheme type (inducer, noninducer). The ANOVAs showed no significant results. However, a closer inspection of the data revealed that one participant responded strikingly faster and less accurate than the others, possibly due low commitment or a too liberal response criterion. With this participant excluded, the remaining six participants showed a marginal significant
interaction between the factors congruency and grapheme type \( F(1, 5) = 5.78, p = .06 \). For graphemes that were noninducers for the synesthetic sample, control subjects showed faster responses toward congruent (495 msec) compared with incongruent (524 msec) stimuli. In contrast, for graphemes that were inducers for the synesthetic sample, reactions to incongruent stimuli (500 msec) were faster than those to congruent stimuli (520 msec). There was also a three-way interaction between group (synesthete/control), grapheme type, and congruency. This did not reach significance levels \( F(1, 11) = 2.10, p = .18 \). There were no effects with respect to error rates.

**EEG Data**

The results of the follow-up analysis on power and ITC differences are depicted in Figure 6. It shows difference topographies for mean power (A) and ITC differences (B) in the inducer minus noninducer conditions. Within each panel, the left and right columns show the results for controls and synesthetes, respectively. In all but one comparison the analyses revealed significant differences in synesthetes' brain activity for inducers and noninducers, compared with controls subjects who saw the same set of graphemes. The differences showed up in \( \alpha, \beta_2, \) and \( \gamma \) power \( [\alpha, 600 msec: t(12) = -3.72, p < .01; \beta_2, 360 msec: t(12) = -2.71, p < .05; \gamma, 590 msec: t(12) = 3.24, p < .01], \) as well as in \( \beta_1 \) and \( \gamma \) ITC \( [\beta_1, 410 msec: t(12) = 3.08, p < .01; \beta_1, 470 msec: t(12) = -1.61, p > .1; \gamma, 360 msec: t(12) = -3.37, p < .01; \gamma, 590 msec: t(12) = 3.15, p < .01]. \)

The results of the PLV analysis are depicted in Figure 7. It shows, separately for each time and frequency range under investigation, the number of significant electrode pairings in the inducer and noninducer condition, for synesthetes and for control subjects. Significant differences in the number of electrode pairings were seen in the \( \theta \) and \( \alpha \) frequency range, as well as in the \( \beta_2 \) frequency \( [\theta, 300 msec: \chi^2(1) = 31.83, p < .001; \alpha, 520 msec: \chi^2(1) = 12.52, p < .001; \alpha, 120 msec: \chi^2(1) = 4.75, p < .05; \alpha, 220 msec: \chi^2(1) = 1.21, p > .2; \alpha, 260 msec: \chi^2(1) = 2.12, p > .1; \beta_1, 220 msec: \chi^2(1) = 1.11, p > .7; \beta_2, 360 msec: \chi^2(1) = 7.92, p < .01; \beta_2, 580 msec: \chi^2(1) = 1.53, p > .2; \gamma, 360 msec: \chi^2(1) = 0.001, p > .9]. \) Of special interest are the differences in the \( \alpha \) and \( \theta \) frequency where the strongest effects were observed in the synesthetic sample (first and second row in Figure 7). In the \( \theta \) frequency range, synesthetes showed a decreased number of electrode pairings toward inducers compared with noninducers (300 msec: 74 vs. 90 pairings; 520 msec: 28 vs 58 pairings, respectively). In contrast, control subjects showed the reversed pattern of a decreased number of pairings toward graphemes that served as noninducers for synesthetes (300 msec: 77 vs. 17 electrodes; 520 msec: 39 vs. 22 electrodes). For the \( \alpha \) frequency, synesthetes showed a strongly increased number of electrode pairings in the inducer compared with the noninducer condition (120 msec: 20 vs. 3 electrodes), whereas for controls the number of pairings was similar in both conditions (11 vs. 10 electrodes).

**Discussion of Control Experiment**

To rule out that the pattern of results we obtained in our synesthetic sample were because of the specific task or stimuli used, we recruited a sample of matched controls and compared their brain activity to inducer and noninducer graphemes with those shown by the synesthetes. If the task or the stimuli were the important factor, then the differences we observed in the sample of synesthetes should also show up in a control sample of nonsynesthetes. This was clearly not the case. The power and ITC differences revealed in the synesthetic sample did not occur in the sample of control subjects. Consequently, we found a double dissociation for the variables group (synesthetes, controls) and grapheme type (inducer, noninducer) for all major findings reported in the primary analysis. Remarkably, this includes the significant difference in \( \beta_1 \) ITC (410 msec) where the most pronounced effect occurred in the synesthetic sample. Also the results for
long-range connectivity were different in synesthetes and controls. The major findings in the primary analysis were an early increase in the number of pairings for inducers compared with noninducers in \( \alpha \) frequency and a corresponding decrease at a later time point in the \( \theta \) frequency. This pattern was not observed in the sample of control subjects, the difference between synesthetes and controls being significant in both \( \alpha \) and \( \theta \) frequencies.

Thus, for measures of short-range and long-range connectivity, brain activity in the inducer and noninducer conditions were different for synesthetes compared with controls. This suggests that the results reported in the primary analysis were not because of the graphemes per se or because of the tasks associated with them but were specifically related to the graphemes being color inducers or noncolor inducers for the synesthetes. This notion is also supported by the fact that in most of the follow-up analyses, control subjects did not exhibit any differences between the two grapheme types. Power and ITC differences between inducers and noninducers were significant at three electrodes at most (see Figure 6A and B, left), which is insignificant if corrected for multiple comparisons. As well, the difference in the number of significant electrode pairings for inducer and noninducer graphemes was close to zero (\( \alpha \), 120 and 260 msec) or was at least markedly smaller for controls compared with synesthetes, in eight of nine cases (see Figure 7). We are therefore confident that the results of the primary analysis are valid.

A further remarkable result occurred in the behavioral data. Control subjects responded faster in congruent compared with incongruent conditions if presented with a noninducer but were faster in the incongruent compared with the congruent condition when presented with an inducer grapheme. This is reasonable because graphemes that served as inducers for the synesthetes did not induce colors and corresponding interference effects for the control subjects. For example, whereas for a given synesthete the perceived color “red” induced by an objectively white-colored grapheme is incongruent to a white-colored target frame, the same grapheme and frame colors are congruent for the matching control subject. Therefore, graphemes that served as inducers in the sample of synesthetes produce opposite effects in synesthetes and controls. This observation is in line with our discussion of the primary experiment and further supports the conclusion that our paradigm and stimuli worked as intended.

**GENERAL DISCUSSION**

Assuming that the paradigm and the analysis strategy of our study are valid, we can now discuss further implications of the results. The data suggest that functional connectivity is different for inducer and noninducer processing. It involves different neural assemblies that are transiently linked together at different stages of processing. To our knowledge, this is the first study where neural synchrony in grapheme color synesthesia has been investigated. Our novel findings thus need to be compared with current knowledge on grapheme-color synesthesia.

The most obvious effect in this study was seen in \( \theta \) PLV, exhibiting a broader network for noninducers compared with inducers 280–560 msec after stimulus onset. In a recent overview, Womelsdorf, Vinck, Leung, and Everling (2010) pointed out that coherent long-range \( \theta \) activity plays an important role for selecting goal-relevant information in choice reaction tasks. By synchronizing \( \theta \) activity between distant brain areas, information can be selected from ongoing neural activity related to, for example, memory retrieval, context processing, or sensory evidence accumulation (Hyman, Zilli, Paley, & Hasselmo, 2010). But \( \theta \) synchronizations also have direct consequences on the targeted brain structures. In situations of high \( \theta \) coherence, inhibitory interneurons were found to transiently suppress the firing of connected pyramid cells (Cardin et al., 2009). That is, long-range \( \theta \) oscillations can modulate the neural output at target regions by increasing local inhibition within that area.

The idea that long-range coupling modulates inhibition fits well with the disinhibited feedback model on synesthesia (Grossenbacher & Lovelace, 2001). According to that approach, synesthetic colors emerge if the visual cortex receives insufficient inhibition during feedback sweeps of neural activation. This lack of inhibition leads to a hyperactivation of visual cortex and ultimately to the activation of an irregular color representation. We propose that this imbalance of inhibition occurs within long-range \( \theta \) networks. Because of idiosyncratic conditions, some graphemes would activate a smaller \( \theta \) network than others within the same person. Because the network has a smaller extent, it administers less inhibition at target locations. This might specifically concern those brain regions relevant for the concurrent sensory color activation. In particular, there might be reduced activity of inhibitory interneurons within color- and grapheme-processing structures. This would lead to spontaneous coactivations of graphemes and color and thus to the impression of a colored grapheme.

Although this proposition is speculative as yet, it is compatible with our second major finding of a \( \beta_1 \) ITC increase for inducers compared with noninducers. The local ITC increase was observed concurrently to the decreased size of long-range \( \theta \) networks and occurred well within the same time interval (~200–500 msec, compare Figures 4A and 5D). It is thus conceivable that the \( \beta_1 \) ITC increase is a consequence of incomplete inhibition arising from smaller \( \theta \) networks. Source reconstructions revealed that the \( \beta_1 \) increase occurred within visual areas, including bilateral middle occipital gyrus and, most importantly, left fusiform gyrus. This structure contains the grapheme processing area VWFA as well as color processing area V4 and has been found to be active
during inducer processing in fMRI (Rouw & Scholte, 2007) as well as MEG studies (Brang et al., 2010). Presumably, neural activity within this brain region leads directly to the emergence of synesthetic colors in perception.

Finally, we consider the finding that inducers compared with noninducers produced a larger α network around 100 msec after stimulus presentation. On first glance, this result seems to contradict the view that synesthesia emerges because of incomplete vertical inhibition. It was argued in this as well as in earlier studies (Brang et al., 2010) that a vertical approach predicts differences between inducers and noninducers only at later stages of processing. However, within our proposition of long-range inhibition through θ synchrony, disinhibition occurs locally, that is, directly within visual cortex and fusiform gyrus. This has implications for the time course of synesthetic color coactivation. It is known that repetitive synchronous stimulation of neurons lead to long-lasting changes in their synaptic efficiency, a process known as long-term potentiation (Cooke & Bliss, 2006). It is conceivable that because of diminished local inhibition the efficiency of neural transmission between neighboring neurons in VWFA and V4 is increased on the long term. This would explain why inducers produced an early difference compared with noninducers. Furthermore, it would explain the results of previous studies where an increased excitability of visual cortex (Barnett et al., 2008) or an early increase of V4 responses (Brang et al., 2010) was found for synesthetes. In either case, decreased local inhibition may increase synaptic efficiency in visual cortex so that it becomes hypersensitive to visual input.

It might be worthwhile to relate our results to the findings from two TMS studies on grapheme–color synesthesia (TMS, Muggleton, Tsakanikos, Walsh, & Ward, 2007; Esterman, Verstynen, Ivy, & Robertson, 2006). Both experiments revealed that stimulation of right posterior parietal cortex disrupted the impression of colored graphemes. The fact that higher visual areas are involved in synesthetic grapheme perception seems to be compatible with our finding of a late long-range synchronization. However, the TMS studies addressed the role of spatial binding in grapheme–color synesthesia, given that color and grapheme features are already available in the visual system. In contrast, the hypotheses investigated here (disinhibited feedback as well as local cross-activation) address the question how the color impression arises. These two lines of research are not too closely related yet, so that it seems premature to integrate their results.

Previous fMRI studies revealed that the brain network connectivity is generally altered in grapheme–color synesthetes compared with nonsynesthete controls. For example, Dovern et al. (2012) compared the resting state fMRI between both groups and found an increased connectivity between primary visual and right frontoparietal brain areas in synesthetes. The fact that the connectivity in synesthetes was increased during resting state suggests that brain networks are fundamentally different in synesthetes and controls, irrespective of the actual perpctual task. It would have been interesting if our data could reveal similar differences between groups, on the fine-grained timescale that can be achieved with EEG. Unfortunately, this study is not well suited for this kind of analysis because the paradigm did not include a resting phase. Task-independent differences between synesthetes and controls could thus not be investigated. The specific contribution of our study is that we identified brain mechanisms related to the irregular perception of color in grapheme–color synesthetes. How these task-induced mechanisms interact with task-independent differences between synesthetes and controls is an interesting topic for future research.

In summary, in this study we found that inducer compared with noninducer processing in synesthetes is associated with a decreased number of long-range θ couplings along with a concurrent increase in β1 ITC within visual cortex. We propose that the θ network exerts local inhibition at target brain regions, which is incomplete in the inducer condition. Accordingly, color representations are coactivated so that the synesthetic impression occurs. We furthermore speculate that because of the locally confined decrease in inhibition the synaptic weights in color and grapheme processing areas might be shaped in a way that the color coactivation becomes increasingly automatic with repetitive stimulus presentations.

Reprint requests should be sent to Dr. Gregor Volberg, Institut für Experimentelle Psychologie, Universität Regensburg, Universitätstr. 31, 93053 Regensburg, Germany, or via e-mail: gregor.volberg@psychologie.uni-regensburg.de.

REFERENCES


