The Neuronal Correlate of Bidirectional Synesthesia: A Combined Event-related Potential and Functional Magnetic Resonance Imaging Study

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Abstract

■ The neuronal correlate of a rare explicit bidirectional synesthesia was investigated with numerical and physical size comparison tasks using both functional magnetic resonance imaging and event-related potentials. Interestingly, although participant I.S. exhibited similar congruity effects for both tasks at the behavioral level, subsequent analyses of the imaging data revealed that different brain areas were recruited for each task, and in different time windows. The results support: (1) the genuineness of bidirectional synesthesia at the neuronal level, (2) the possibility that discrepancy in the neuronal correlates of synesthesia between previous studies might be task-related, and (3) the possibility that synesthesia might not be a unitary phenomenon. ■

INTRODUCTION

Synesthesia (from the Greek roots syn-‘‘union’’ and aesthesis-‘‘sensation’’) is a phenomenon involving abnormal binding, in which certain stimuli automatically evoke an additional percept. Determining the neuronal basis that subserves such unusual binding may provide unique insights into the way in which sensory systems become organized developmentally, the way in which sensory and nonsensory information processing are integrated, and the origins of conscious sensory experience. However, the underlying mechanisms of synesthesia are still a mystery. In recent years, advanced neuroimaging methods such as functional magnetic resonance imaging (fMRI) have been used to compare the brain activity of synesthetes and nonsynesthetes (Rich et al., 2006; Sperling, Prvulovic, Linden, Singer, & Stirn, 2006; Steven, Hansen, & Blakemore, 2006; Blakemore, Bristow, Bird, Frith, & Ward, 2005; Hubbard, Armanm, Ramachandran, & Boynton, 2005; Weiss, Zilles, & Fink, 2005; Elias, Saucier, Hardie, & Sarty, 2003; Nunn et al., 2002). Most of these studies examined the neuronal correlates of grapheme–color synesthesia, that is, the experience of color (i.e., the concurrent; Grossenbacher & Lovelace, 2001) when perceiving graphemes (i.e., the inducer). These studies yielded mixed results. Some studies support the idea that synesthesia is due to anomalous functioning of occipito-temporal areas such as V4/V8 (Sperling et al., 2006; Hubbard et al., 2005; see also Steven et al., 2006; Nunn et al., 2002; Aleman, Rutten, Sitskoorn, Dautzenberg, & Ramsey, 2001; Weiss, Shah, Toni, Zilles, & Fink, 2001, for similar findings with words as inducers; but see Rich et al., 2006). Others found that synesthetic experience is correlated with abnormal activation of the parietal lobes (Steven et al., 2006; Weiss et al., 2005; Elias et al., 2003).

fMRI is limited in its temporal resolution. Therefore, the observance of activation in the visual or parietal areas cannot be taken as clearcut evidence for the stage of activation in the chain of processing. For example, the activation of parietal areas can stem from semantically related activation (e.g., numerical meaning; Cohen Kadosh, Cohen Kadosh, Kaas, Henik, & Goebel, 2007; Brannon, 2006; Dehaene, Piazza, Pinel, & Cohen, 2003; see also Elias et al., 2003 for a study with a synesthete). However, it could also reflect top–down processes (Lamme & Roelfsema, 2002) that contribute to the consciousness of synesthetic perception. Hence, it is surprising that the number of event-related potential (ERP) studies, which have the potential to add important knowledge regarding the mental chronometry of synesthetic experiences, is negligible (Sagiv, Knight, & Robertson, 2003; Schiltz et al., 1999). Moreover, the two ERP studies that did examine synesthesia yielded contradicting results. Sagiv et al. (2003) showed an early negative modulation of the ERP component between 150 and 200 msec (i.e., N170), whereas Schiltz et al. (1999) found a difference in the P300 component, which reflects cognitive processes at a postperceptual stage.

The conflicting results from fMRI and behavioral studies led some researchers to suggest that synesthetes can be divided into at least two distinct groups: (1) those with perceptually mediated synesthesia expressed in the abnormal activation of visual areas, and (2) those with

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semantically mediated synesthesia expressed in the abnormal activation of the parietal lobes. Some termed the former group projectors and the latter group associators (Dixon, Smilek, & Merikle, 2004); or lower synesthetes and higher synesthetes, respectively (Ramachandran & Hubbard, 2001b).

Aside from the individual differences in the synesthetic group, which might contribute to the discrepancies between the different imaging and neurophysiological studies, a second possibility is that these results are task-specific. Namely, the differences in the results might be attributed to the different tasks that were used (see Hubbard & Ramachandran, 2005 for a similar view).

Synesthesia and Directionality

Another issue under debate is the question of directionality. Previously, it was commonly held that synesthesia was unidirectional, that is, only the inducer (e.g., digit) triggered the concurrent (e.g., color) (Beeli, Esslen, & Jancke, 2005; Martino & Marks, 2001; Ramachandran & Hubbard, 2001b; Mills, Boteler, & Oliver, 1999). Recently, however, we and others have shown that the inducer might sometimes also be triggered by the concurrent, and thus that synesthesia might be bidirectional in some synesthetes (Cohen Kadosh, Tzelgov, & Henik, in press; Johnson, Jepma, & de Jong, 2007; Cohen Kadosh & Henik, 2006c; Cohen Kadosh, Sagiv, et al., 2005; Knoch, Gianotti, Mohr, & Brugger, 2005). Some of the studies showed that the bidirectionality occurs at a more implicit level (Johnson et al., 2007; Cohen Kadosh, Sagiv, et al., 2005; Knoch et al., 2005), when the synesthetes could not report on such a bidirectional experience. Another case showed that it can also occur at an explicit level (Cohen Kadosh, Tzelgov, et al., in press; Cohen Kadosh & Henik, 2006c). For example, when I.S., a digit–color synesthete, compared the height of two lines (i.e., line comparison task), the line colors modulated his performance. That is, in the *congruent* condition, a longer line was presented in a color that was induced by a larger digit (e.g., 6), and a shorter line was presented in a color induced by a smaller digit (e.g., 5). In the *incongruent* condition, a longer line appeared in a color that was induced by a smaller digit and a shorter line appeared in a color that was induced by a larger digit (Cohen Kadosh & Henik, 2006c). I.S. spontaneously reported that the colors of the lines evoked the perception of the corresponding digits, thus showing an explicit experience of bidirectionality.

Currently, bidirectionality in synesthesia has been shown only by using behavioral methods. It is important to show that bidirectionality also takes place at the neuronal level. We recruited I.S. as a participant in the current study because his reaction times (RTs) showed a large and stable effect [in order of hundreds of milliseconds (Cohen Kadosh & Henik, 2006c), rather than tens of milliseconds in the case of implicit bidirectionality (Johnson et al., 2007; Cohen Kadosh, Sagiv, et al., 2005)], which we hoped would lead to a less noisy, more prominent, and noticeable effect in the current neuroimaging experiments.

In contrast to all previous imaging studies that investigated the neuronal correlate of synesthesia, the current study used both fMRI and ERP in order to examine both spatial and temporal aspects of processing. Two comparison tasks were used: (1) a triangle comparison and (2) a numerical comparison. In the triangle comparison, the task was similar to the line comparison task that we mentioned above (Cohen Kadosh & Henik, 2006c), aside from the fact that in the current task the participant had to compare the height of the triangles rather than line length, while ignoring the colors of the triangles. The numerical comparison was similar to a previous study that showed a slower RT as a function of synesthetic congruity (hereafter, congruity). Namely, RTs were faster for (synesthetic) congruent conditions (digits in their corresponding colors) than for (synesthetic) incongruent conditions (each digit in the color corresponding to that of the other digit) (Cohen Kadosh & Henik, 2006a).

On the brain level, the rationale for comparing incongruent versus congruent conditions is that, in the incongruent condition, synesthetes will try to inhibit the irrelevant dimension which interferes with their performance. For example, in the size congruity paradigm, which is similar to the paradigm that we used here, non-synesthetes need to process two digits for their physical size while ignoring their numerical value (e.g., 2 4). It has been shown that the intraparietal sulcus is more activated in the incongruent condition than in the congruent condition due to the need to inhibit the processing of the irrelevant numerical magnitude, independent of response selection (e.g., Cohen Kadosh, Cohen Kadosh, Linden, et al., 2007; Cohen Kadosh, Cohen Kadosh, Schuhmann, et al., 2007; Kaufmann et al., 2005; Pinel, Piazza, Le Bihan, & Dehaene, 2004). Similarly, in the current study, the incongruent condition should yield greater activation than the congruent condition due to the need to inhibit the synesthetic experience when it interferes with task performance.

We chose numerical and physical size comparisons because previous findings showed that both comparative tasks are similarly processed at both the behavioral and the brain levels (Cohen Kadosh, Cohen Kadosh, Linden, et al., 2007; Cohen Kadosh, Cohen Kadosh, Schuhmann, et al., 2007; Cohen Kadosh, Henik, et al., 2005; Kaufmann et al., 2005; Pinel et al., 2004; Fias, Lammertyn, Reynvoet, Dupont, & Orban, 2003).

The design of this study allowed us to examine several questions: (1) Combining neuroimaging data from fMRI and ERP measurements in the same synesthete would enable us to examine the timing and the anatomical distribution of the synesthetic experience. This would provide us with the opportunity to examine whether the activation in perceptual areas occurs in an earlier time window (e.g., N170; Sagiv et al., 2003), and whether the activation in areas that are associated with high-cognitive functions (e.g., parietal lobes) occurs together with the modulation of postperceptual components such as the P300 (e.g., Schiltz et al., 1999). (2) The use of two tasks would allow us to study the effects of task on the brain mechanisms involved in the synesthetic experience. Previous researchers argued for the existence of a nonunitary mechanism *between* synesthetes (Dixon & Smilek, 2005; Hubbard et al., 2005; Dixon et al., 2004). In contrast, the current study was designed to examine the question of whether synesthesia is unitary *within* an individual synesthete. If synesthesia is a unitary phenomenon, then the source of the interference should stem from the same brain area, and in the same time window. However, if the synesthetic experience is due to multiple mechanisms, we would expect to find several brain areas involved and with different timing, depending on task requirements. (3) Our methodological approach should make it possible to examine, for the first time, the neuronal correlates of bidirectionality (by using the triangle comparison task). In this case, we would expect to find activation in number-related areas in the absence of numerical presentation.

In light of the previous fMRI findings, we focused on activation in both occipito-temporal areas, as well as the parietal lobes (Sperling et al., 2006; Hubbard et al., 2005; Weiss et al., 2001, 2005; Elias et al., 2003; Nunn et al., 2002; Aleman et al., 2001). We also looked at the N170 and P300 that were reported in earlier ERP studies (Sagiv et al., 2003; Schiltz et al., 1999).

METHODS

Participants

I.S. is a 27-year-old right-handed male student, who experiences colors that are projected on stimuli such as digits, alphabetical letters, and days of the week. He has not experienced any other type of synesthesia. We documented his strong bidirectional synesthesia in previous works (Cohen Kadosh, Tzelgov, et al., in press; Cohen Kadosh & Henik, 2006c). Six naive controls (matched for age, sex, handedness, and education) were also tested.

All participants had no history of neurological or psychiatric disorders and all gave informed consent to participate in the study. Each participant underwent electroencephalography (EEG) and fMRI measurements in two separate sessions. The EEG measurements were always followed by the fMRI measurements. The study was approved by the local ethics committee. Due to failure in collecting the data from the EEG for one participant and excessive head movement during the fMRI measurement from two other participants, these control participants were omitted from the analysis of these measurements.

Stimuli

The experiment comprised two experimental tasks: a triangle comparison and a numerical comparison. Stimuli consisted of either two stimuli (two triangles or two digits) that appeared at the center of a computer screen. The center-to-center distance between the two stimuli subtended a horizontal visual angle of 5.2°.

In the triangle comparison task, stimuli consisted of two triangles with 1.5° (small triangle) or 2.2° (large triangle) of the visual angle. The participants had to compare the physical sizes of triangles. In the congruent condition, the larger triangle appeared in a color that (for I.S.) was induced by a larger digit (e.g., 8), and the smaller triangle appeared in a color induced by a smaller digit (e.g., 7). In the incongruent condition, the larger triangle appeared in a color that was induced by a smaller digit and the smaller triangle appeared in a color that was induced by a larger digit.

In the numerical comparison task, stimuli consisted of two digits that subtended 1.85° of the visual angle. The participants were asked to compare the numerical values of digits. For the congruent condition, each of the two digits appeared in the colors that corresponded to these digits for I.S. For the incongruent condition, each digit appeared in the color that corresponded to the other digit in the pair (Figure 1). We used the same colors for each task, and for each condition. For example, the colors used for the incongruent condition in the triangle comparison were the same colors that were used for the incongruent condition in the numerical comparison.

In order to avoid task switching, numerical and triangle comparisons were performed in separate blocks. Congruent and incongruent conditions were presented randomly in both comparison tasks.

Procedure

Participants were asked to decide which of the two stimuli in a given display was physically (triangle comparison condition) or numerically (numerical comparison condition) larger. The instructions emphasized both accuracy and speed. Participants were asked to attend only to the relevant dimension (either triangle size or numerical magnitude), and to ignore the colors. They indicated their choices by pressing one of two horizontal keys corresponding to the side of the display with the selected member of the pair. Participants were asked to keep their eyes fixed at the fixation cross at the center of the screen throughout the experiment and to avoid eye movements and blinks. In the ERP experiment, the times between the onsets of two consecutive stimuli were 3200 to 3400 msec, with an average of 3300 msec, and stimulus presentation time was 1500 msec. In the fMRI experiment, the times between the onsets of two consecutive stimuli were 4000 and 8000 msec, with an average of 6000 msec, and stimulus presentation time was 1000 msec.

The actual measurements were preceded by a short training session of 24 trials. The triangle comparison task was presented first in order to avoid any influence from the digits in the numerical comparison task on the triangle comparison task (which was use to examine the bidirectionality in I.S.). Each condition appeared 96 times (in the ERP experiment) or 48 times (in the fMRI experiment). The presentation of the experiments and the collection of the behavioral data were controlled by a personal computer using E-Prime (Psychology Software Tools, Pittsburgh, USA).

Design

The manipulated variable was congruity (incongruent or congruent). We measured RT and accuracy as a function of this manipulation.

EEG Recording and Analysis

Electroencephalographic data were acquired using a 128-Ag/AgCI electrode Geodesic Sensor Net (Electrical Geodesics, Oregon, USA) with 16-bit digitizing at 250 Hz. During recording, all channels were referenced to the Cz electrode. Throughout measurements impedances were kept below 40 kΩ. EEG data preprocessing and analysis were performed using the Netstation platform 4.1 (Electrical Geodesics).

The EEG data analysis included only trials with correct responses. For the ERP analysis, raw data were digitally low-pass-filtered at 15 Hz (passband gain: −0.1 dB; stopband gain −40.0 dB; rolloff: 2.0 Hz) and segmented into epochs from 200 msec prestimulus presentation until 800 msec after stimulus onset. Segments with activity exceeding ±70 μV in any channel were excluded from further analysis. Not more than 25% of trials were discarded due to artifacts (Picton et al., 2000). Bad channels were replaced using spherical splines. Data were averaged and re-referenced to an average electrode. The averages were then baseline corrected, with the 200-msec prestimulus period serving as baseline. Further statistical analysis focused on the N170 and the P300 components. The N170 was defined as the largest negative deflection within a predefined time window (160–200 msec poststimulus onset). Mean area amplitudes were calculated on individual averages at the Oz electrode (analogous to electrode no. 76 in the EGI system). The P300 was defined as the largest positive deflection within a predefined time window (352–452 msec poststimulus onset). Mean area amplitudes were calculated on individual averages at the Pz electrode (analogous to electrode no. 68 in the EGI system).

fMRI Scanning and Analysis

Whole-brain fMRI data were acquired with a 1.5-T Philips Intera scanner using a gradient-echo, echo-planar imaging sequence (18 axial slices; repetition time/echo time = 2000/60 msec; flip angle = 90°, field of view = 210 × 210 mm, voxel size: 3.28 × 3.28 × 5 mm). Stimuli were presented on a 7.5-in. LCD monitor (IFIS-SA, MRI Devices, Waukesha, WI, USA). Each run comprised the acquisition of 320 volumes. Stimulus presentation was synchronized with the fMRI sequence at the beginning of each trial. Each scanning session included the acquisition of a high-resolution T1-weighted three-dimensional volume (voxel dimensions = 1 × 1 × 1 mm) for coregistration and anatomical localization of functional data. Data were preprocessed and analyzed using the BrainVoyager QX 1.4 software package (BrainInnovation, Maastricht, The Netherlands). The first four volumes of each run were discarded to allow for T1 equilibration. 3-D motion correction and Talairach transformation (Talairach & Tournoux, 1988) were performed for the remaining set of functional data of each participant. The 3-D functional dataset was resampled to a voxel size of 3 × 3 × 3 mm, followed by further preprocessing, including linear trend removal, temporal high-pass filtering (high pass: 0.00647 Hz), and autocorrelation removal. The predictor time courses were convolved with a gamma distribution to account for the shape and delay of the hemodynamic response. Error trials were modeled separately. Because the screen properties and the lighting in the scanner room were different from those for the ERP experiment, we matched again the exact colors to digits for I.S. prior to the experiment. However, although this did not affect the performance of I.S., some of the control participants complained that one of the pairs sometimes confused them as the digits differed in their luminance compared to the background. Indeed, when we looked at each pair separately, we found a trend toward interference for this pair. This result is in line with previous results that showed luminance level affects comparative judgment (Cohen Kadosh & Henik, 2006b). Hence, we excluded this pair from the behavioral analyses. However, the inclusion or exclusion of this pair did not affect the functional data. In addition, when the same procedure was applied to I.S., it did not affect his behavioral or his functional data.

The statistical analysis was based on regions of interest (ROIs) in the parietal and occipito-temporal areas. We defined the ROIs with one comparison task serving as a localizer for the other. Namely, in the case of the numerical comparison task, the presentation of the digits helped us to define the putative number form area in the fusiform gyrus. Similarly, the triangle comparison task was used in order to define the high-order color area in the parietal lobe (Claeys et al., 2004; Zihl, 2000). In addition, we also checked these ROIs for a congruity effect in the task where they were used as a localizer (e.g., congruity effect in the fusiform gyrus under the numerical comparison task). In this case, the comparison of congruent and incongruent was still independent because the ROI was based on the activation of both congruity conditions versus rest.

For example, in the case of a congruity effect in the triangle comparison task, first the number form area was defined for each participant separately, based on activation in the fusiform gyrus in the numerical comparison task. Then, in the triangle comparison task, the beta weight for each congruity condition was extracted for each participant, and I.S.'s modulation of brain activation by congruity was compared to the control group's data by applying the procedure for comparing a single case with a control population (Crawford & Garthwaite, 2002; see below). We also compared the congruity effect in the same ROI under the numerical comparison task in order to examine whether the activation in this area is specific or reflects general activation such as general conflict. The same procedure was applied also for defining the ROI for the numerical comparison task in the parietal lobe. We were focused in the parietal and occipito-temporal areas based on the data from the ERP experiment.

We compared I.S.'s data (behavioral, ERP, and fMRI) with the control group's data by applying the procedure for comparing a single case with a control population (Crawford & Garthwaite, 2002). In brief (see Crawford & Garthwaite, 2002, for detailed description), according to this method, the control group cannot be considered a population due to the modest size. Therefore, the single subject's performance is not converted to a z-score based on the control group's mean and standard deviation, and is not referred to the area under the normal curve which has "thinner tails" in comparison to a t distribution. This, in turn, avoids aggravation of the abnormality of individual's score and increases the chance for a Type I error.

In contrast to the use of z-scores, the current method treats the control sample statistics as statistics rather than as parameters and compares the single subject's score to the control group's score by using a noncentral t distribution. Based on the standard deviation, the mean, and the size of the n of the control group, it is possible to determine whether the subject's score falls outside the 95% confidence limit, and the associated p value. The equation for the modified t test is:

$$t(n_2 - 1) = \frac{X_1 - X_2}{SD_2\sqrt{(n_2+1)/n_2}}$$

Where X_1 is the single subject score, X_2 is the mean score of the control group, SD_2 is the standard deviation of the control group's score, and n_2 is the number of subjects in the control group. The test statistic follows a t distribution with n_2-1 as the degree of freedom. Thus, the statistic takes into account the size of the sample and the smaller the size of the sample, the more conservative the t test.

In addition, Monte Carlo simulations confirmed that by using the current test, one can avoid an inflated Type I error rate and overestimate the abnormality of the patient's score, regardless of the size of the control sample (Crawford & Garthwaite, 2005).

RESULTS

Numerical Comparison Task

Behavioral Data

Only I.S. had significantly longer RTs on incongruent than congruent trials [$t(4) = 10.68, p < .001$, and $t(3) = 6.88, p < .005$, for ERP and fMRI, respectively; Figure 2A; all ps are two-tailed]. There were no differences in the error rate between I.S. and the controls.

ERP Results

Visual inspection of the P300 activity on the scalp found the commonly reported centro-parietal distribution (Linden, 2005; Rugg & Coles, 1996). Statistical analysis focused on the Pz electrode. The control group did not show a difference between congruent and incongruent trials, whereas I.S. did [$t(4) = 5.15, p < .01$; Figure 2B]. We examined whether the P300 effect was specific for the numerical comparison by calculating the P300 congruity effect in the case of triangle comparison. The difference between incongruent and congruent was almost absent (i.e., difference of -0.37 μV between incongruent and congruent) and did not differ between I.S. and the control group ($p = .8$).

fMRI Results

The left intraparietal sulcus ($x = -32, y = -65, z = 35$, 964 voxels; Figure 3C), as well as the left angular gyrus ($x = -30, y = -58, z = 26$, 239 voxels), showed a higher activation for the incongruent condition versus the congruent condition for I.S. However, these differences were not present in the control group [$t(3) > 2.98$, $p < .046$; Figure 2C]. In contrast, under the triangle comparison task, the difference between incongruent and congruent in these areas was negligible (i.e., difference of 0.07 or less between the beta values) and did not differ between I.S. and the control group ($p > .53$).

Triangle Comparison Task

Behavioral Results

For I.S., incongruent trials yielded longer RTs than congruent trials but this was not the case for the controls

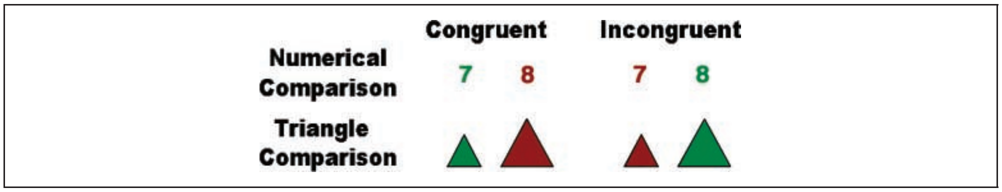

Figure 1. Example of the congruent and the incongruent conditions for both tasks. The participants' task was to compare the digits for their numerical value (numerical comparison task), or the triangles for their physical size (triangle comparison task). In the numerical comparison task, the digits 7 and 8 appeared in the color that I.S. experienced them in the congruent condition. In the incongruent condition, the digit 7 appeared in the color triggered by digit 8, and the digit 8 appeared in the color triggered by digit 7. In the triangle comparison task, the congruent condition consisted of a larger triangle that was colored in a color that was triggered by a large number, and the smaller triangle was in a color that was triggered by a small number. In the incongruent condition the coloring was reversed.

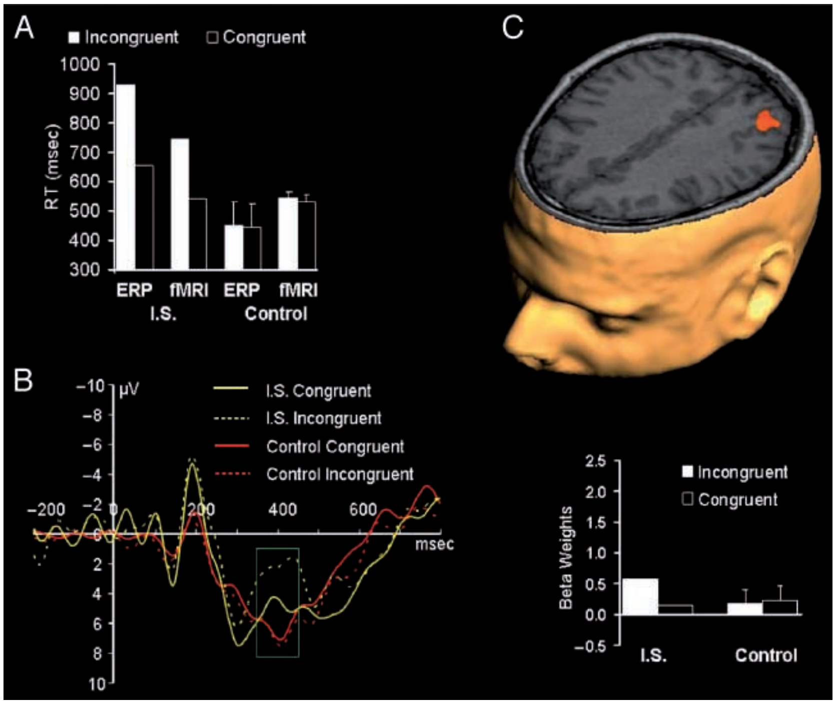

Figure 2. Congruity effect reflected in behavioral (A), ERP (B), and fMRI (C) measurements during the numerical comparison task. Note that the P300 is reduced for the incongruent versus the congruent conditions for I.S., and the intraparietal activation is greater for incongruent condition versus congruent condition. The green frame rectangle indicates the time window under which the congruity effect for I.S. was observed. Error bars depict one standard error of mean (*SEM*).

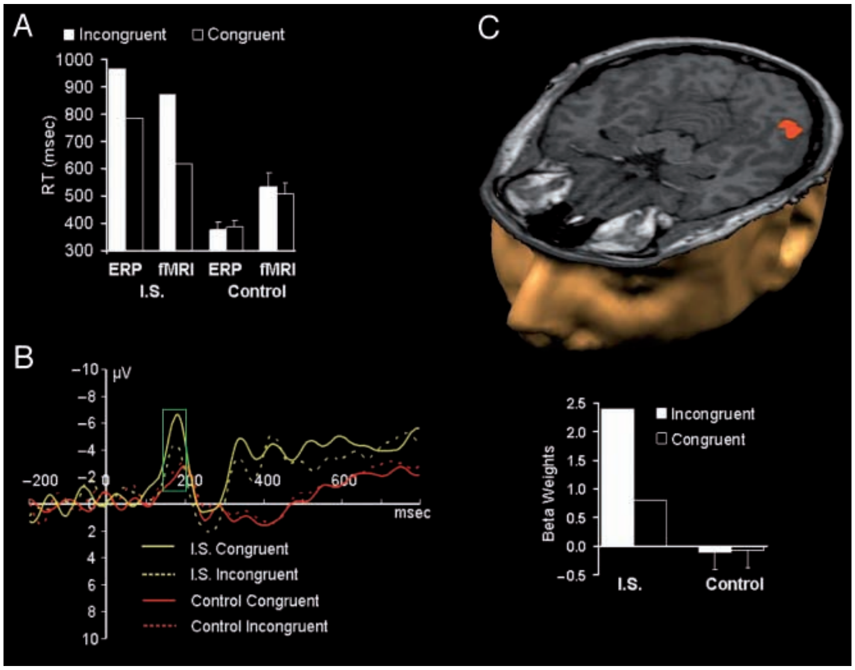

Figure 3. Congruity effect reflected in behavioral (A), ERP (B), and fMRI (C) measurements during the triangle comparison task. Note that the N170 is greater in the incongruent than congruent conditions for I.S., and fusiform activation is greater for the incongruent condition versus the congruent condition. The green frame rectangle indicates the time window under which the congruity effect for I.S. was observed. Error bars depict one *SEM*.

[$t(4) = 40.7$, $p < .001$, and $t(3) = 8.44$, $p < .005$, for ERP and fMRI experiments, respectively]. Again, there were no differences in the error rate between I.S. and the controls (Figure 3A).

ERP Results

Visual inspection of the N170 activity (between 160 and 200 msec after stimulus presentation) on the scalp showed a difference of 2.36 μV between the incongruent and congruent condition for I.S. but not for the controls [$t(4) = 4.7$, $p < .01$; Figure 3B]. Crucially, the N170 effect was not significant under the numerical comparison task; the difference between incongruent and congruent was almost absent (i.e., difference of 0.03 μV between incongruent and congruent) and did not differ between I.S. and the control group ($p = .94$).

fMRI Results

For I.S., the left fusiform gyrus ($x = -41$, $y = -67$, $z = -15$, 262 voxels; Figure 2C) showed a larger activation for the incongruent condition versus the congruent condition, whereas the activation for both conditions was similar for the control group [$t(3) = 25.43$, $p < .001$; Figure 3C]. This effect was specific for the triangle comparison task as indicated by lack of difference between incongruent and congruent between I.S. (i.e., incongruent's beta value minus congruent's beta value = $-.04$) and the control group ($p = .7$).

DISCUSSION

The current study had several aims: (1) to examine the timing and brain areas involved in the synesthetic experience in the same synesthete, (2) to examine how a task modulates brain mechanisms involved in the synesthetic experience, and (3) to reveal the neuronal correlate of bidirectionality.

The Neural Correlates of Synesthesia and the Effects of Task on Synesthetic Brain Activation

Our findings show that the task modulates the area of brain activation and the timing at which it occurs. During the numerical comparison task, the congruity effect modulated activity in the intraparietal sulcus and the angular gyrus in the left parietal lobe, areas that were also found in former research on synesthesia (Weiss et al., 2005; Elias et al., 2003). The ERP results show that the congruity effect modulated the P300 amplitude. The P300 is assumed to reflect stimulus categorization and evaluation (Kok, 2001), and some of its putative generators are located in the parietal lobe (Bledowski et al., 2004, 2006; Linden, 2005). The modulation of the P300 amplitude can therefore be interpreted as an indicator of interference of the irrelevant dimension in the number comparison task. Moreover, our results are in line with the brain localization studies of P300 component (Bledowski et al., 2004, 2006).

In contrast, during the triangle comparison task, the congruity effect modulated activation in the fusiform gyrus, a finding which is in accordance with previous studies that found activation due to synesthetic experience in the occipito-temporal areas (Sperling et al., 2006; Hubbard et al., 2005; Nunn et al., 2002; Aleman et al., 2001; Weiss et al., 2001). In the ERP, the congruity effect modulated the N170, which is assumed to reflect orthographic processing (Bentin, Mouchetant-Rostaing, Giard, Echallier, & Pernier, 1999), and has been found previously in synesthesia (Sagiv et al., 2003). Together, the finding of fusiform gyrus modulation, (representing the activation of the number form area) and the ERP N170 finding (representing orthographic processing) converge to the conclusion that colors activate digits even in the absence of digit presentation.

Altogether, the combined ERP and fMRI measurements, which used two different, though quite similar tasks, show that a task can modulate activation of a brain area, and the time in which such activation occurs. This result might indicate that the differences obtained in the various neuroimaging and neurophysiological studies do not necessarily reflect individual differences among the synesthetic population, but might be only task dependent.

The Neuronal Correlates of Bidirectionality in Synesthesia

We showed here that color in a grapheme–color synesthete activates the number form area in the fusiform gyrus, suggesting that already the experience of color can activate a number-related area. It is important to note that I.S. does not generally experience digits when perceiving color in his daily life. What is the reason for this difference? We suggested previously that engaging participants in a task that requires making numerical judgments might provide an outlet for bidirectionality (Cohen Kadosh, Sagiv, et al., 2005). However, in the triangle comparison task, we did not use a task that involved numerical content. It has been suggested that numbers and physical size are processed by a shared magnitude mechanism (Cohen Kadosh, Henik, et al., 2005; Fias et al., 2003; Schwarz & Heinze, 1998). Therefore, it could be that in a nonnumerical magnitude comparison, task color evokes numbers or more general magnitude perceptions. This suggestion is in line with the cumulative data that numbers are part of a general mechanism for magnitude processing (Walsh, 2003).

What remains to be answered is why synesthetes usually do not experience bidirectionality. We suggest that the synesthetic experience (and possibly the connections) associating colors with digits is masked in daily life, but can be unmasked (Cohen Kadosh & Walsh, 2006) (or disinhibited according to Grossenbacher & Lovelace's, 2001 terminology) under certain conditions. Hence, the differences between I.S. and other synesthetes who do not experience explicit bidirectionality might be due to failure of inhibition or abnormal neuronal connections in I.S.

One neural model of grapheme–color synesthesia suggested that the synesthetic experience occurs because of cross-talk between V4 (which is involved in color processing) and an area in the fusiform gyrus (which is related to graphemic identification) (Ramachandran & Hubbard, 2001a, 2001b, 2003). Another model offered that feedback or reentrant information from the anterior fusiform influences the color experience according to the grapheme's meaning (Dixon, Smilek, Duffy, Zanna, & Merikle, 2006; Smilek, Dixon, Cudahy, & Merikle, 2001). In the case of bidirectionality, color affects activation in an area that is related to digit identification. It is difficult to determine whether this activation is due to cross-talk between V4 and the digit identification area (Ramachandran & Hubbard, 2001a, 2001b, 2003), or whether this activation is modulated by feedback from the anterior fusiform (Dixon et al., 2006; Smilek et al., 2001).

Synesthesia: A Unitary Phenomenon?

Our results challenge the idea that synesthesia is a unitary phenomenon. Rather, it seems more plausible that several brain areas (in parallel or sequential timing) mediate the synesthetic experience. In contrast to other studies that argued for the existence of a nonunitary mechanism that underlie synesthesia between different synesthetes (Dixon & Smilek, 2005; Hubbard et al., 2005; Dixon et al., 2004), the current results show that synesthesia is not unitary even within an individual synesthete. That is, we showed that the synesthetic experience correlated at different time points with different brain areas as a function of task. Note that our conclusion is based on a single subject. However, I.S.'s particular synesthesia was examined using different tasks that were highly similar but still evoked different experiences (i.e., graphemes which evoked colors, and colors which evoked graphemes) and effects. This evidence should be the strongest of its kind to shed light on the question of the unitariness of synesthesia because it did not involve different modalities (e.g., music–color and grapheme–color). Using different modalities (e.g., presenting auditory stimuli vs. visual stimuli) would force one to design different tasks, which in turn would pose alternative explanations for the observed results.

An intriguing question is how the results would look for synesthetes without explicit bidirectional synesthesia in the triangle comparison task. One possibility is that nonexplicit bidirectional synesthetes will show similar performance and brain activation as nonsynesthetes, as their effects will be too variable and small to differ from controls. However, a recent study (Johnson et al., 2007) showed that there are some synesthetes with implicit bidirectionality, whereas others are strictly unidirectional. Hence, another possibility is that participants with implicit bidirectional synesthesia will show smaller brain activation and behavioral effects than I.S., but greater than the control group. Given the brain area (fusiform gyrus) and the timing (160–200 msec after stimulus presentation) of the bidirectional experience in the current study, the reduced activation in the case of the implicit experience of bidirectional synesthesia will be of interest for the field of consciousness (Dehaene, Changeux, Naccache, Sackur, & Sergent, 2006). Indeed, it has been suggested that differentiating the various degrees of synesthesia/awareness (explicit/implicit bidirectional, unidirectional synesthetes, and non synesthetes) could help in studying the mechanisms underlying conscious awareness (Cohen Kadosh & Henik, 2007). However, this issue was out of the scope of the current article and needs to be addressed in future studies.

We believe that future studies should focus on the prevalence and neuronal correlates of bidirectionality in order to provide important information for the study of synesthesia and consciousness.

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