RAPID REPORT

WHEN CONDITIONED RESPONSES "FIRE BACK": BIDIRECTIONAL CROSS-ACTIVATION CREATES LEARNING OPPORTUNITIES IN SYNESTHESIA

B. MEIER* AND N. ROTHEN

University of Bern, Institute of Psychology, Muesmattstr. 45, 3000 Bern 9, Switzerland

Abstract—In grapheme-color synesthesia, the letter "c" printed in black may be experienced as red, but typically the color red does not trigger the experience of the letter "c." Therefore, at the level of subjective experience, cross-activation is usually unidirectional. However, recent evidence from digit-color synesthesia suggests that at an implicit level bidirectional cross-activation can occur.

Here we demonstrate that this finding is not restricted to this specific type of synesthesia. We introduce a new method that enables the investigation of bidirectionality in other types of synesthesia. We found that a group of grapheme-color synesthetes, but not a control group, showed a startle in response to a color-inducing grapheme after a startle response was conditioned to the specific corresponding color. These results implicate that when the startle response was associated with the real color an association between shock and the grapheme was also established. By this mechanism (i.e. implicit cross-activation) the conditioned response to the real color generalized to the synesthetic color. We suggest that parietal brain areas are responsible for this neural backfiring. © 2007 IBRO. Published by Elsevier Ltd. All rights reserved.

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In synesthesia the sensory input of one modality activates brain areas which are normally not involved in processing the input of that modality (Nunn et al., 2002; Ward and Mattingley, 2006). The result is an additional phenomenological experience, for example, a color experience for a black letter, a taste experience for a word, or a sound experience for a smell. The specific association between triggering stimuli (i.e. inducers) and resultant synesthetic experiences (i.e. concurrents) is constant, acquired early in life and stable across time (Grossenbacher and Lovelace, 2001; Baron-Cohen et al., 1987). Although there is a myriad of possible types of synesthesia, the most studied inducers are linguistic units such as words, letters and numerals, and the most common concurrents are colors (Beeli et al., 2005; Luria, 1968; Cytowic, 1989;

Simner and Ward, 2006; Simner et al., 2006). These types of grapheme-color synesthetes differ systematically according to the locus of their experience and the stage of processing during which synesthesia arises (Dixon et al., 2004; Ramachandran and Hubbard, 2001). For projector or lower synesthetes colors are experienced like real colors on the surface of the physical stimulus and accordingly lower perceptual processes are involved. For associator or higher synesthetes colors are experienced in the "mind's eye" and accordingly higher cognitive processes are involved. In general, the synesthetic experience is triggered automatically, and while synesthetes can voluntarily retrieve the inducers that evoke given concurrents, the process does not appear to be automatic (Mills et al., 1999; Ramachandran and Hubbard, 2001). In addition, encountering a concurrent, for example a specific color, typically does not invoke the experience of its inducer, for example a specific digit (but see Cohen Kadosh and Henik, 2006a for an exception). Therefore synesthesia has been described as a unidirectional phenomenon (Mills et al., 1999; Beeli et al., 2005).

However, recent findings challenge this view. Specifically, in digit-color synesthesia, several studies suggest bidirectionality at an implicit level (Brugger et al., 2004; Cohen Kadosh and Henik, 2006b; Cohen Kadosh et al., 2005; Knoch et al., 2005). Brugger et al. (2004) found faster left-hand responses for colors associated with small numbers and faster right-hand responses for colors associated with large numbers in digit-color synesthetes. Cohen Kadosh et al. (2005) asked digit-color synesthetes to decide which one of two digits was numerically larger. They found a facilitation of performance whenever the synesthetic colors elicited by the digits indicated a larger distance than the relevant numerical values. Knoch et al. (2005) used a modified random generation task in which they asked digit-color synesthetes to generate random sequences of colors. Their results showed a similar pattern of counting bias as it is known from traditional number generation tasks. All these studies show that color information evoked numerical information and therefore they suggest bidirectionality at an implicit level. However, cross-activation in these studies may be rather due to the specific connection between colors and digits on the mental number line than representing a general mechanism in synesthesia. In the present study, we show that implicit cross-activation is not restricted to digit-color synesthesia. We

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*Corresponding author. Tel: +41-31-631-40-39; fax: +41-31-631-82-12.
E-mail address: beat.meier@psy.unibe.ch (B. Meier).
Abbreviations: ANOVA, analysis of variance; CS, conditioned stimulus; SCR, skin conductance response; US, unconditioned stimulus.
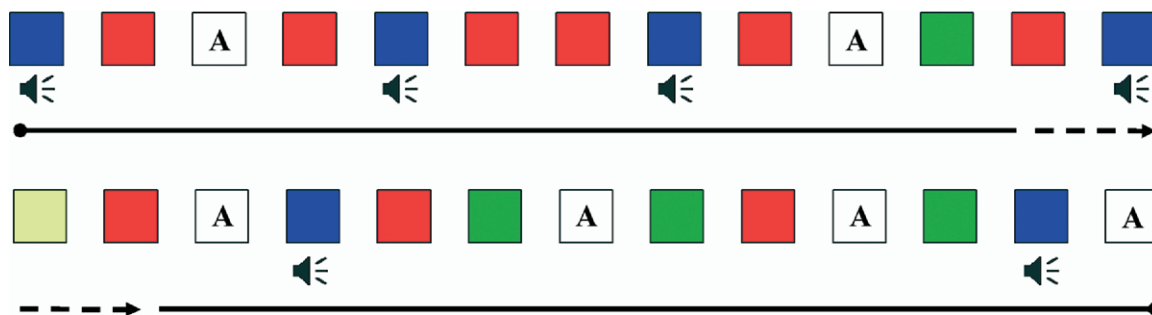
Fig. 1. An example of the procedure (conditioning phase). A startle response (unconditioned response, UR) is conditioned to the blue color (US). Graphemes were selected such that they elicited the color which was coupled with the startling sound during conditioning. For the synesthete in this particular example the letter "A" elicits a blue color experience.

introduce a new method into synesthesia research and demonstrate that implicit cross-activation is a more general mechanism.

We tested a group of 13 grapheme-color synesthetes who were all classified as associators and a matched control group with a modified version of the conditioning procedure introduced by Bechara et al. (1995). Across three phases (habituation, conditioning, and extinction) participants were presented with colored squares. In the conditioning phase one specific color (i.e. red or blue), the conditioned stimulus (CS), was followed immediately by a loud startling sound (a boat horn with 100 dB), which served as unconditioned stimulus (US). For each individual synesthete and his matched control person, the CS-color (i.e. red or blue) was selected such that it corresponded to the synesthete's specific concurrent color experience of the particular grapheme. Throughout the experiment, these graphemes were presented occasionally in black on a white background, but they were never coupled with the US.

For trials followed by a startling sound, we expected that all participants would show a startle reaction for the CS as indicated by an increase in skin conductance response (SCR). For grapheme trials, we expected that synesthetes, but not controls would show a startle response. We hypothesized that this effect would be the result of implicit activation of the grapheme representation during the conditioning trials, which enabled the transfer of the startle response from real colors to synesthetic colors.

EXPERIMENTAL PROCEDURES

Participants

Thirteen synesthetes (7 female and 6 male, M=24.15 years, S.D.=4.14) and 13 controls (7 female and 6 male, M=23.62 years, S.D.=4.11). Controls were matched for age, gender, handedness and education. A test of consistency was conducted in the original test session and in a retest-session 2–3 weeks later (Witthoft and Winawer, 2006). For synesthetes, consistency was $r=.94$ for hue, $r=.85$ for saturation and $r=.58$ for value (brightness). For controls, consistency was $r=.21$ for hue, $r=.26$ for saturation and $r=.24$ for value. All consistency estimates were higher for synesthetes than for controls ($t(24)=7.83$, $P<0.001$ for hue, $t(24)=6.12$, $P<0.001$ for saturation, and $t(24)=2.32$, $P<0.05$ for value).

Material and procedure

After electrodes were attached, participants were seated in a comfortable chair, 0.6 m in front of a computer screen. They were asked to relax, to remain silent, and to attend to the slides appearing on the screen. No motor or verbal response was required. Each slide was shown for 2 s, and the interval between two consecutive slides was between 10 and 20 s. The inter-trial interval was determined by the status of the electro-dermal activity. A new slide was not presented if the participant was generating or was in steep recovery limb of an SCR.

SCRs were sampled at 20 Hz with two electrodes, attached to the thenar and hypothenar eminences of the non-dominant hand and they were recorded continuously. For the analysis of the SCRs a data window of 5 s after each stimulus presentation was defined. The event-related SCR was calculated as the difference between the highest amplitude value and the baseline in each data window.

In the habituation phase of the conditioning procedure slides of five different colors (green, blue, yellow, red and white) were randomly presented 12 times for a total of 60 slides. The white slide included a grapheme which was selected for each individual synesthete and her matched control such that it induced either a blue or red concurrent experience for the synesthete. In the conditioning phase, a total of 26 slides were presented in a fixed pseudo-random order: Six slides (which were either blue or red) were followed immediately by a startling sound (US) of 1 s duration. Six grapheme slides which either induced a blue or red color experience in synesthetes and 14 slides which were green, yellow and either red or blue (conversely to the slides followed by the startling sound) were never followed by the startling sound. The specific procedure for the condition with blue CS is depicted in Fig. 1. For the group with red as CS, blue and red slides were used contrariwise. In the extinction phase, the CS (blue or red) and the white slide were presented in an alternating order of two repetitions 12 times each.

RESULTS

The results are presented in Fig. 2. For all statistical analysis alpha level was set at 0.05. First, SCRs for color trials that were followed by the US during the conditioning phase were analyzed. As depicted in the top half, SCRs for the CS increased in the conditioning phase for both, synesthetes and controls. A mixed two-factorial analysis of variance (ANOVA) with Group (synesthete, control) as between-subjects factor and Phase (habituation, conditioning, extinction) as within-subjects factor revealed a significant main effect of Phase ($F(2, 48)=59.8$, $P<0.001$).

No other effect was significant. Tukey post hoc analyses revealed that during conditioning SCRs were significantly higher than during habituation ($P<0.001$) and extinction ($P<0.001$); the latter two conditions did not differ.

Second, SCRs for grapheme trials that were never followed by the US were analyzed. As depicted in the bottom half of Fig. 2, synesthetes, but not controls, showed a startle response for the graphemes printed in black. Again a mixed two-factorial ANOVA was calculated. It revealed a significant Group×Phase interaction ($F(2, 48)=$ 3.30, $P=0.045$). Subsequent t-tests showed that SCRs of the two groups differed in the conditioning phase ($t(24)=2.43$, $P<0.05$), but not during habituation and extinction.

DISCUSSION

The results showed that synesthesia triggers bidirectional representations of inducers and concurrents. While at the level of subjective experience activation of the color was unidirectional, at the level of performance a bidirectional relationship between synesthetic inducers and concurrents existed. As the synesthetic inducer never co-occurred with the US the results demonstrate that indirect activation of the grapheme representation during conditioning is sufficient to establish an association with the startle response which fires back when the grapheme is presented physically.

However, one might argue that our results are compatible with a unidirectional account. Instead of implicit cross-activation of the grapheme representation during conditioning the conditioned startle response may simply generalize to the graphemes that evoke the (synesthetic) colors. However, with this account the mechanism of generalization is not specified. Accordingly, it must be assumed that synesthetic colors are functionally equivalent to real colors. We believe that this assumption may be justified for some kinds of situations and some kinds of synesthesia. Specifically, for projector synesthetes who experience synesthetic colors like real colors a unidirectional account may be adequate. However, the synesthetes tested in the present study were all associators who experience synesthetic colors in their mind's eye. As a consequence the finding of a generalized conditioned reaction in associators requires a different justification how generalization can occur. Implicit cross-activation is a parsimonious and reasonable explanation.

Our results are consistent with previous studies that found implicit activations in color-digit synesthesia (Cohen Kadosh and Henik, 2006a,b; Cohen Kadosh et al., 2005; Knoch et al., 2005). They are also consistent with a recent single case study who found implicit cross-activation across two types of synesthesia within the same individual (Simner and Hubbard, 2006). In addition, the demonstration of conceptual activation of a synesthetic inducer in the present study generalizes previous findings of conceptual induction of synesthesia without a physically present inducer (Dixon et al., 2000; Elias et al., 2003). Our results implicate that it is also possible to trigger the concept of a grapheme by a corresponding real color and to couple this implicitly activated concept with an additional association (i.e. the startle).

On a neural level, the importance of the inferior parietal lobe (in particular the angular gyrus) for mediating the cross-activation between color- and grapheme-representations has been emphasized (Hubbard and Ramachandran, 2005; Ramachandran and Hubbard, 2001). This area is involved in cross-modal processing and multi-sensory integration (Friedman-Hill et al., 1995; Ashbridge et al., 1997) and these types of processes are also required for synesthetic binding. Results from fMRI suggest that the intra-parietal sulcus is also involved in the specific binding of color and grapheme representations (Weiss et al., 2005; see also Nunn et al., 2002). In addition, evidence from TMS suggests that the right parieto-occipital region is necessary for synesthetic binding (Esterman et al., 2006; Muggleton et al., 2007). It is also possible that the effects have emerged due to the involvement of the fusiform gyrus. However, following the model of Ramachandran and Hubbard (2001), cross-activation in the fusiform gyrus would rather be expected in projector or lower synesthetes (cf. Dixon et al., 2006), while cross-activation in higher or associator synesthetes is assumed to occur in the parietal cortex, particularly in the region of the angular gyrus. Although the neural architecture of synesthesia is not yet fully understood, our findings of backfiring of the conditioned startle response upon presentation of the CS-corresponding grapheme suggest that cross-activation is bidirectional on a cognitive and neural level and it is likely
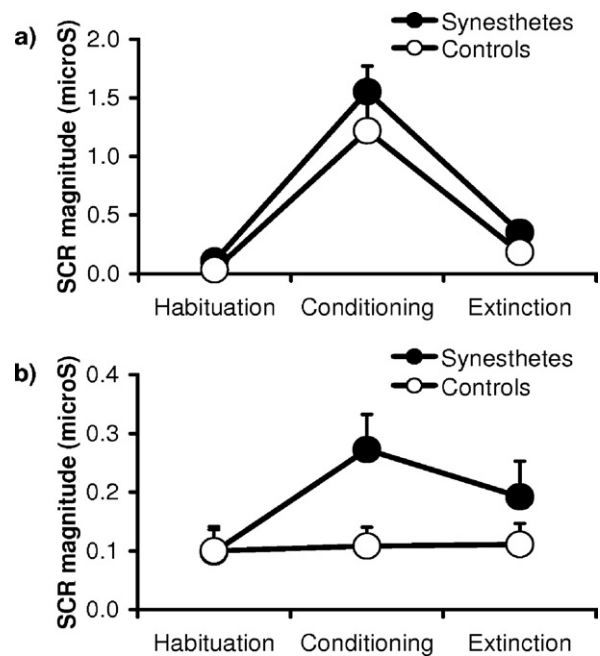

Fig. 2. SCRs of synesthetes and controls. Higher values indicate higher autonomic arousal. Error bars show standard errors. (a) SCRs for colors. These were coupled with a startling sound during conditioning. SCRs did not differ for synesthetes and controls. (b) SCRs for graphemes presented in black against a white background. Synesthetes, but not controls showed an SCR increase.

that this cross-activation is mediated by parietal brain regions.

Aside from furthering our understanding of the underlying mechanisms of synesthesia our study also introduces a new method into the field. This method can be used to investigate different types of synesthesia and we are looking forward to future research that will shed new light on dissociations between conscious experience and unconscious co-activations in synesthesia.

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