

See discussions, stats, and author profiles for this publication at: <https://www.researchgate.net/publication/322798676>

Coordinated neural, behavioral, and phenomenological changes in perceptual plasticity through overtraining of synesthetic associations

Article in *Neuropsychologia* · January 2018

DOI: 10.1016/j.neuropsychologia.2018.01.030

CITATION

1

READS

209

4 authors:



Nicolas Rothen

Universität Bern

52 PUBLICATIONS 728 CITATIONS

[SEE PROFILE](#)



David J Schwartzman

University of Sussex

13 PUBLICATIONS 70 CITATIONS

[SEE PROFILE](#)



Daniel Bor

37 PUBLICATIONS 2,444 CITATIONS

[SEE PROFILE](#)



Anil K Seth

University of Sussex

196 PUBLICATIONS 6,975 CITATIONS

[SEE PROFILE](#)

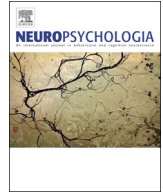
Some of the authors of this publication are also working on these related projects:



Serial Dependence in Visual Variance [View project](#)



Perceptual Uniformity across the Visual Field [View project](#)



Coordinated neural, behavioral, and phenomenological changes in perceptual plasticity through overtraining of synesthetic associations

Nicolas Rothen^{a,b,d,*}, David J. Schwartzman^{a,c}, Daniel Bor^{a,c,e}, Anil K. Seth^{a,c}

^a Sackler Centre for Consciousness Science, University of Sussex, Brighton, UK

^b Department of Psychology, University of Sussex, Brighton, UK

^c Department of Informatics, University of Sussex, Brighton, UK

^d Institute of Psychology, University of Bern and Distance Learning University, Switzerland

^e Department of Psychology, University of Cambridge, UK

ARTICLE INFO

Keywords:

Cortical excitability
Cortical plasticity
Perceptual processing
Electroencephalogram (EEG)
Transcranial magnetic stimulation (TMS)

ABSTRACT

Synesthesia is associated with additional perceptual experiences, which are automatically and consistently triggered by specific inducing stimuli. Synesthesia is also accompanied by more general sensory and cortical changes, including enhanced modality-specific cortical excitability. Extensive cognitive training has been shown to generate synesthesia-like phenomenology but whether these experiences are accompanied by neurophysiological changes characteristic of synesthesia remains unknown. Addressing this question provides a unique opportunity to elucidate the neural basis of perceptual plasticity relevant to conscious experiences. Here we investigate whether extensive training of letter-color associations leads not only to synesthetic experiences, but also to changes in cortical excitability. We confirm that overtraining synesthetic associations results in synesthetic phenomenology. Stroop tasks further reveal synesthesia-like performance following training. Electroencephalography and transcranial magnetic stimulation show, respectively, enhanced visual evoked potentials (in response to untrained patterns) and lower phosphene thresholds, demonstrating specific cortical changes. An active (using letter-symbol training) and a passive control confirmed these results were due to letter-color training and not simply to repeated testing. Summarizing, we demonstrate specific cortical changes, following training-induced acquisition of synesthetic phenomenology that are characteristic of genuine synesthesia. Collectively, our data reveal dramatic plasticity in human visual perception, expressed through a coordinated set of behavioral, neurophysiological, and phenomenological changes.

1. Introduction

Synesthesia is an ontogenetic variant of healthy human development characterized by specific additional experiences in response to normal sensory input. For instance, in grapheme-color synesthesia the letter “A” printed in black (inducer) may elicit a red color experience (concurrent). The concurrent experience is automatically triggered and is not under voluntary control. Although, the specific associations are inter-individually idiosyncratic but intra-individually highly consistent (Ward, 2013), large-scale studies also show reliable consistencies across individuals (e.g., Simner et al., 2005; Witthoft et al., 2015). Furthermore, grapheme-color synesthesia is associated with a specific neural profile (e.g., Brang et al., 2008; Brang et al., 2011; Esterman et al., 2006; Hubbard et al., 2005; Muggleton et al., 2007; Rouw and Scholte, 2007, 2010), which includes increased cortical excitability (Terhune et al., 2011) and increased visual perceptual processing (Barnett et al.,

2008b). The associative nature of synesthesia motivated early attempts to induce synesthesia by means of associative learning (Howells, 1944; Kelly, 1934). However, it was not until very recently that the acquisition of synesthetic phenomenology in response to graphemes using associative training was successful (Bor et al., 2014). This recent finding, together with established neural characteristics of genuine synesthesia, provides a unique opportunity to elucidate the neural basis of perceptual plasticity relevant to conscious experiences. We therefore set out to examine whether training-induced synesthesia-like phenomenology is accompanied by neural changes characteristic of genuine synesthetes.

Genuine grapheme-color synesthesia (henceforth synesthesia if not otherwise specified), is accompanied by enhanced modality-specific cortical excitability. For example, application of transcranial magnetic stimulation (TMS) to primary visual cortex reveals that grapheme-color synesthetes had significantly lower phosphene thresholds in

* Correspondence to: Institute of Psychology, Center for Learning Memory and Cognition, University of Bern, Fabrikstrasse 8, 3012 Bern, Switzerland.
E-mail address: nicolas.rothen@gmail.com (N. Rothen).

comparison to non-synesthetes, whereas there was no group difference when motor thresholds were tested by TMS applied to the motor cortex (Terhune et al., 2011; cf. also, Terhune et al., 2015a, 2015b). Demonstrating enhanced sensory-perceptual processing, electroencephalographic (EEG) measurements showed that grapheme-color synesthetes exhibit an enhanced response for specific visual evoked potential components (VEPs; measured over occipital and parieto-occipital areas), compared to non-synesthetes while they viewed high contrast checkerboard patterns; note that these checkerboard patterns did not themselves elicit synesthetic experiences (Barnett et al., 2008b).

Behaviorally, synesthesia is characterized by the consistency and the automaticity of synesthetic associations. The ‘gold standard’ in diagnosing synesthesia is the test of consistency (Baron-Cohen et al., 1993; Eagleman et al., 2007). Participants are presented with potential synesthetic inducers (e.g., letters and numbers) several times in random order and are required to select the corresponding concurrent experience (e.g., color). An individual-specific measure of consistency can be derived from the average distance in color-space across repeated selections of the same inducer. While synesthetes can rely on their perceptual experiences to perform this task, non-synesthetes have to rely on memory. Thus, synesthetes are far more consistent in this task than non-synesthetes. The automaticity of synesthetic associations is assessed with adapted Stroop-type tasks (Stroop, 1935). Grapheme-color synesthetes are faster at making a decision about a congruently colored letter in comparison to an incongruently colored letter. This would not be the case if the associations had to be triggered voluntarily (e.g., Dixon et al., 2004; Rothen et al., 2013b; Ward et al., 2007).

Early attempts to induce synesthetic phenomenology focused on sound-color synesthesia (Howells, 1944; Kelly, 1934). These historic studies used associative training procedures over several weeks, including a minimum of 2000 stimuli in a subset of participants (Kelly, 1934) or approximately 30,000 stimuli (Howells, 1944). The results were mixed. Only the latter study appeared partly successful in inducing synesthetic phenomenology (Howells, 1944). No (recorded) further attempts were made to induce synesthetic phenomenology until more than half a century later (e.g., Meier and Rothen, 2009; Rothen et al., 2011; Colizoli et al., 2012). These more recent studies focused on grapheme-color synesthesia, which is currently the best studied form of synesthesia (see Rothen and Meier, 2014 for a review). Most involved daily training sessions of a few minutes, over periods lasting from a few days to maximally 4 weeks. Training sessions typically consisted of a single task which was based on explicit or implicit associative learning procedures, during which participants were presented with “congruent” (to-be-learned grapheme-color associations) and “incongruent” stimuli (not-to-be-learned grapheme-color associations). The ratio of congruent to incongruent trials ranged from 1:0 to 1:8, across different studies. While most studies found behavioral evidence that associations became automatic over the course of the training (especially those with fewer incongruent trials), none of them found evidence for synesthetic phenomenology. For instance, after training, participants were faster at making a color decision about a grapheme when it was presented in a congruent, in comparison to an incongruent, color (i.e., synesthetic Stroop effect; Meier and Rothen, 2009), but did not report altered phenomenology (e.g., additional color experiences).

Recently, Bor et al. (2014) demonstrated that it is possible for non-synesthetes to acquire synesthetic color phenomenology in response to letters. In comparison to previous training studies, this study employed an extensive battery of adaptive cognitive training tasks and only reinforced congruent letter color pairings. The daily training lasted approximately 60 min per day for 9 weeks (5 days per week). After five weeks the participants passed the synesthetic consistency test, showed a synesthetic Stroop effect, and – critically – reported synesthetic phenomenology. However, potential neurophysiological changes associated with these effects were not measured in this study.

To examine the neural basis of perceptual plasticity relevant to conscious experience, we investigated the phenomenological

(subjective reports), behavioral (consistency and automaticity) and neural (cortical excitability) consequences of extensive training of synesthetic associations (letter-color associations). In order to control for changes that may arise purely because of extensive training, rather than because of the specific letter-color associations we employed, we also tested an active control group. This active control underwent an alternative training regime that employed analogous letter-symbol pairings, but which did not involve color associations. We also tested a passive control group, which underwent repeated testing but no associative training between the testing sessions.

We hypothesized that for the experimental (letter-color) group, post-training compared to pre-training testing would reveal reports of synesthetic phenomenology, increased grapheme-color consistency, enhanced automaticity for the trained associations (i.e., synesthetic Stroop effect), and enhanced cortical excitability (i.e., reduced phosphene thresholds to TMS and enhanced VEPs to checkerboard patterns). By contrast, these changes were not expected for the passive control group. For the active control group, who were trained on letter-symbol associations, we expected to find enhanced automaticity for the trained associations, but crucially no changes in color-related perceptual phenomenology and thus no changes in cortical excitability.

2. Materials and methods

Participants were only allowed to take part in the study if they did not report any instances of synesthesia during a recruitment interview and remained naïve as to the purpose of the study throughout the experiment. Experiments 1 and 3 consisted of a training paradigm, and a testing battery repeated before and after training; Experiment 2 consisted of repeated testing only. The testing battery consisted of TMS- and EEG-based tests for visual cortical excitability (Figs. 1A and 2A-B) and behavioral tests for consistency of letter-color associations (Fig. 3A) and automaticity of letter-color (Exp. 1 and 2) or letter-symbol (Exp. 3) associations (Fig. 4A). The testing session after the training further included a semi-structured interview for assessing perceptual phenomenology during exposure to individual letters of the alphabet. The battery was conducted before and after a five week training period (Exp. 1 and 3) or a five week training-free interval (Exp. 2). The training was conducted 5 days per week for 5 weeks, with each training session lasting approximately 60 min per session. The training was conducted to consolidate 13 specific letter-color associations (Exp. 1; cf. Bor et al., 2014) or to consolidate 13 specific letter-symbol associations (Exp. 3). Experiments 1, 2, 3 were designed and conducted consecutively. Therefore, pre- and post-training analyses were conducted separately for each experiment prior to a collective analysis encompassing all experiments. Experiments were undertaken with the understanding and written consent of each participant.

2.1. Sample size determination

We conducted a-priori power analyses for the neurophysiological parts of the study (i.e., TMS and EEG), because these were the novel and central aspects of present study. A-priori power was estimated based on the effect sizes of Terhune et al. (2011) for the TMS part and Barnett et al. (2008a) for the EEG part, corresponding to a power of 99% with $N = 6$ for the TMS part and a power of 95% with $N = 18$ in the predicted direction for the EEG part. The final N was further based on practical aspects: the study had to be conducted during term-time while the participating students were present on campus. Another crucial factor was how many participants could be tested in the relevant labs (especially EEG and TMS lab) during pre- and post-testing in order that the whole study would still fit into one term at the University of Sussex. Moreover, the number of students who were willing to participate and who fulfilled the inclusion criteria (i.e., no synesthetic experiences prior to the study) was another factor.

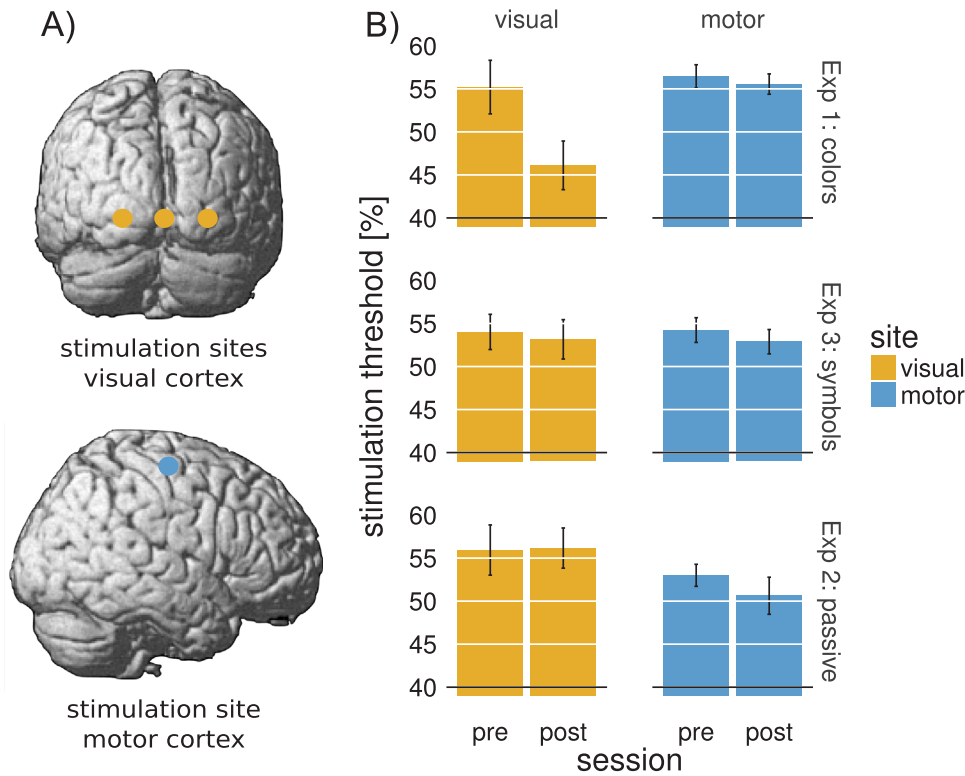


Fig. 1. A) TMS stimulation sites of the visual and motor cortex, respectively. B) Average stimulation thresholds as a function of test session (pre- and post-training) and stimulation site (visual cortex vs. motor cortex). For the experimental group (top, colors), the figure shows a reduced phosphene threshold after the training. The motor threshold was not affected. For the active (middle, symbols) or passive (bottom) control group, training did not affect either threshold. Error bars represent standard errors. Individual thresholds can be found in [Supplemental material](#) (Figure Ind1).

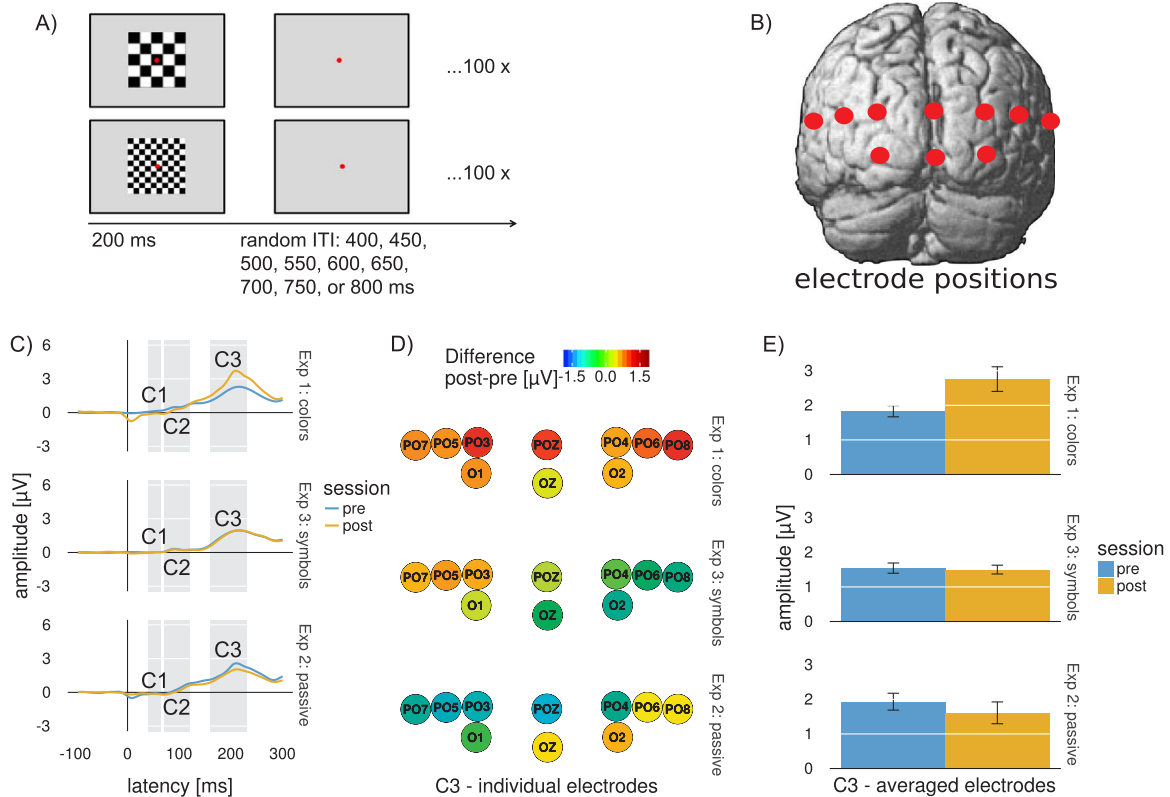


Fig. 2. A) Illustrative trials of the low (top) and high frequency (bottom) checkerboard onset task. B) Positions of the analyzed EEG electrodes for the checkerboard onset task. C) Average VEPs as a function of test session (pre- and post-training). The grey-shaded bars indicate the time windows / components (i.e., C1, C2, C3) of interest. For the experimental group (top, colors), C3 is enhanced after the training. This was not the case for the active control (middle, symbols) and the passive control group (bottom). D) Difference between post- and pre-training VEPs for C3 amplitude as a function of electrode. The VEP differences are most pronounced for the experimental group (top, colors) in comparison to the active (middle, symbols) and passive control group (bottom). E) Data representing averaged C3 VEP amplitude as a function of testing session (pre- and post-training). The top panel highlights the increase in VEP amplitude of the experimental group in contrast to both other groups (active - middle and passive - bottom). Error bars represent standard errors. Individual VEP amplitudes can be found in [Supplemental material](#) (Figure Ind2).

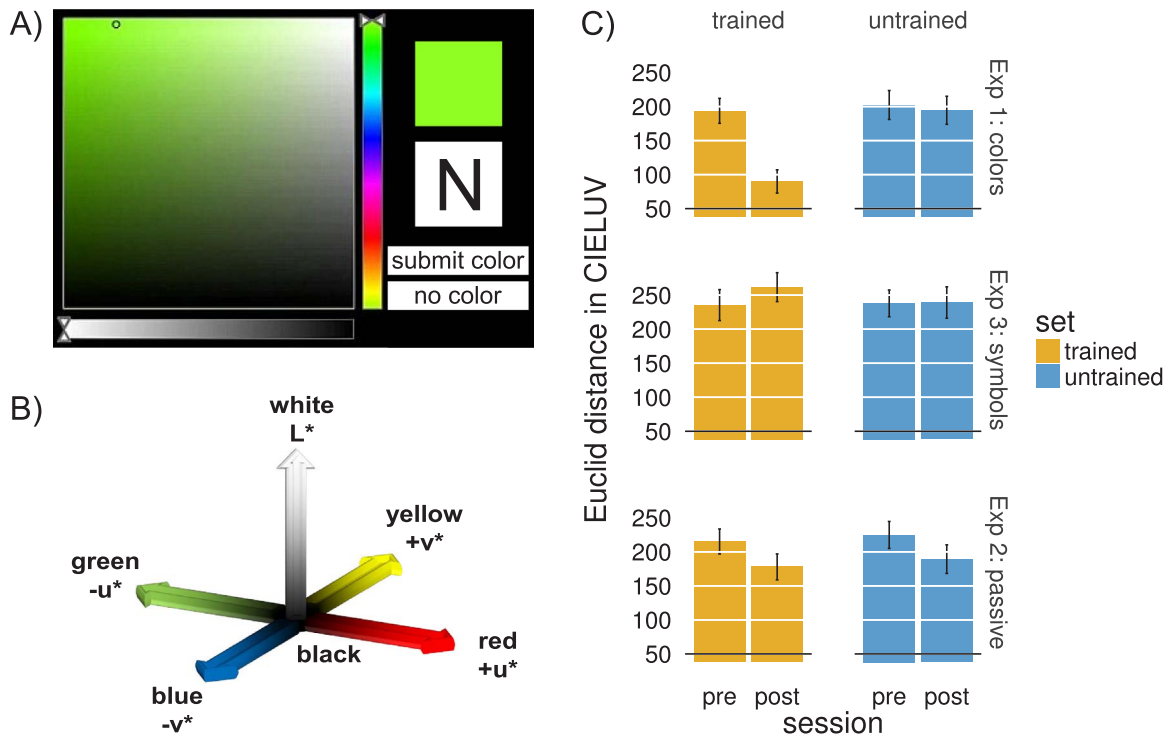


Fig. 3. A) Illustrative trial of the consistency test in which a color has to be picked for each letter of the alphabet (and each number from 0 to 9) three times in randomized order. B) Depiction of the CIELUV color space which was used to calculate Euclidian distances between the colors picked for the different instances of a given letter or number. C) Average consistency as a function of test session (pre- and post-training) and letter set (trained vs. untrained); lower values indicate smaller distances in color space and hence higher consistency. For the experimental group (top, colors), the figure shows a substantial increase in the consistency of color associations for the trained letters after training. This was not the case for the active control group (middle, symbols) or for the passive control group (bottom). Error bars represent standard errors. Individual performance can be found in [Supplemental material](#) (Figure Ind3).

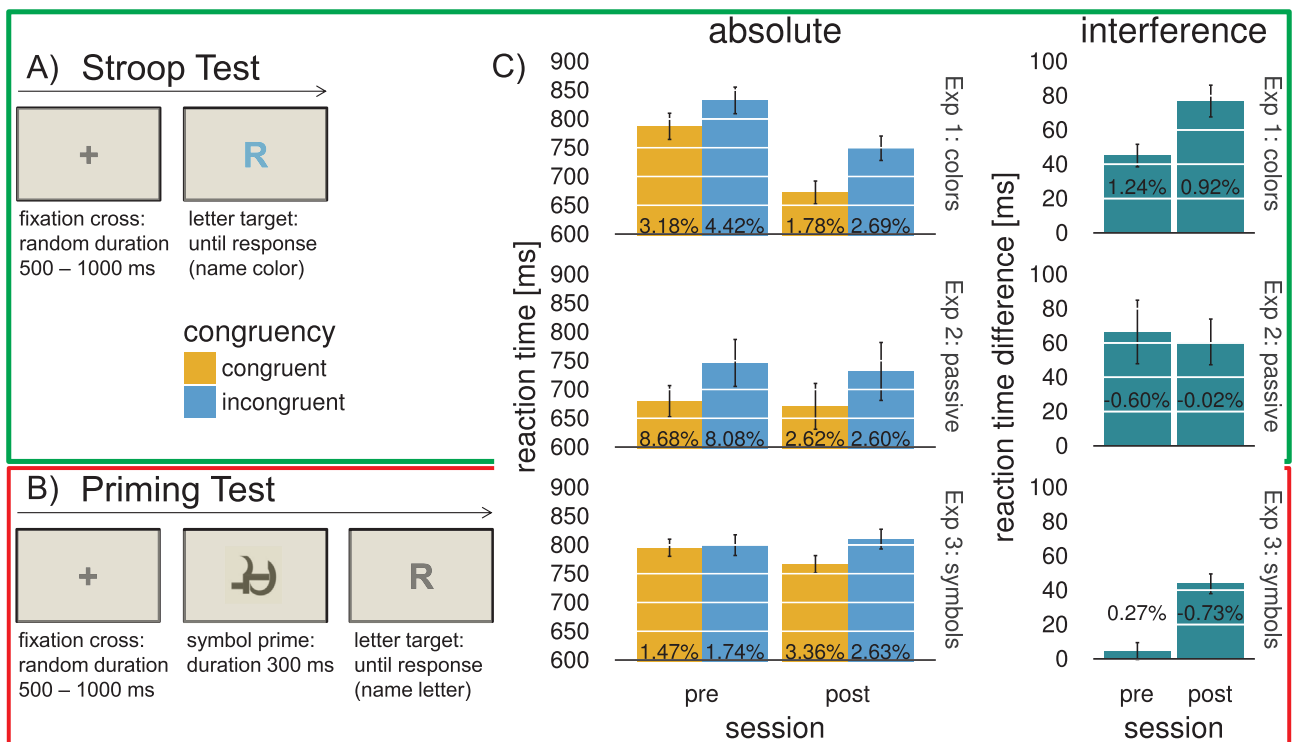


Fig. 4. A) Illustrative trial of the Stroop test (Exp. 1 and 3) and B) the priming test (Exp. 2). C) Average synesthetic Stroop / priming effect as a function of test session (pre- and post-training) and congruency (congruent vs. incongruent). For the experimental group (top, colors), the figure shows larger synesthetic Stroop interference (i.e., incongruent minus congruent) following training. For the passive control group (middle), Stroop interference was not affected by test repetition. For the active control group (bottom, symbols), the interference effect had a similar magnitude as for the experimental group. Error bars represent standard errors. Error rates are indicated in percent for each condition and in terms of Stroop / priming interference (i.e., congruent minus incongruent). Individual performance can be found in [Supplemental material](#) (Figure Ind4).

2.2. Participants

The experimental group (Exp. 1) consisted of 22 non-synesthetes. Three participants did not complete the training according to the instructions (reflecting low motivation) and were excluded. Another participant was an outlier in terms of age and was also excluded. Only 3 of the 18 remaining participants (15 women, $M_{\text{age}} = 23$, $SD = 3.08$) were psychology students. All participants had normal or corrected to normal visual acuity and normal color vision (see [Supplemental methods](#)).

For the passive control group (Exp. 2), we tested a total of 14 non-synesthetes. One participant terminated the experiment early during the first session. Another three participants did not attend the second session. Only 2 of the 10 remaining participants (7 women, $M_{\text{age}} = 21$, $SD = 3.51$) were psychology students. All participants had normal or corrected to normal visual acuity and normal color vision. None of the participants in Exp. 2 had participated in Exp. 1.

The active control group (Exp. 3) consisted of a total of 18 non-synesthetes. One participant was excluded as they did not turn up for training. None of the remaining 17 participants (14 women, $M_{\text{age}} = 23$, $SD = 5.07$) were psychology students. All participants had normal or corrected to normal visual acuity and normal color vision. None of the participants in Exp. 3 had participated in Exp. 1 or 2.

2.3. TMS

We followed the protocol of a previous study ([Terhune et al., 2011](#)). Single pulse TMS was applied to left, midline, and right primary visual and right motor cortices while participants wore a blindfold ([Fig. 1A](#)). For each of the visual cortex sites and participants, the lowest intensity that elicited phosphenes in five or more out of ten trials was recorded as the phosphene threshold. A similar method was used to find the motor threshold, which was defined as the lowest intensity for which a movement could be detected in the first dorsal interosseus muscle of the left hand in five or more of ten trials. Thresholds over the primary visual cortices were averaged prior to analysis. Participants entered the analysis only when both thresholds (i.e., motor and phosphene) were obtained for both pre- and post-training assessments: $N = 9$ (Exp. 1), $N = 8$ (Exp. 2), and $N = 17$ (Exp. 3). The pattern of the results was identical when all available data points were included (i.e., also incomplete cases; see [Supplemental Results Fig. S3](#)).

2.4. EEG

EEG was continuously recorded during a monocular (i.e., dominant eye) passive viewing task. EEG data were epoched from -100 to 300 ms after stimulus onset, EEG signals that exceeded $\pm 75 \mu\text{V}$ were excluded ([Odom et al., 2010](#)). Similar to [Barnett et al. \(2008a\)](#), VEPs were measured from parieto-occipital (PO7, PO5, PO3, POz, PO4, PO6, PO8) and occipital (O1, Oz, O2) electrodes to the onset of high and low spatial frequency checkerboard patterns ([Fig. 2A and B](#); see also [Supplemental methods](#)).

2.5. Behavioral tests

The behavioral tests (except for the priming task of the active control, Exp. 3) were adopted from our previous study ([Bor et al., 2014](#)) and were conducted before and after training. We administered the internet-based standardized grapheme-color consistency test (www.synesthete.org; [Eagleman et al., 2007](#)). Each participant was presented with the graphemes A–Z and 0–9 three times in randomized order (108 trials). The task was to select a color that best fit with each grapheme and to use their first instinct, and to always choose a color for each grapheme ([Fig. 3A](#)). We also administered a synesthetic Stroop task (Exp. 1 and 2) consisting of 130 trials. For half of the trials, one of the 13 trained letters was presented in a color congruent with the

trained association, and for the other half the color was incongruent ([Fig. 4A](#)). The order of stimulus presentation was randomized. Participants were instructed to state the screen-color of the presented letter as quickly as possible into a microphone (see [Supplemental methods Table S1](#)). The Stroop task was adapted into a priming task for the active control group (Exp. 3). The task was identical with the only exception that participants were not presented with colored letters but with prime-target pairs (symbol-letter) that were either congruent or incongruent with the trained associations ([Fig. 4B](#); see also [Supplemental methods Table S2](#)). Participants were instructed to verbally name the presented letter as quickly as possible into a microphone.

2.6. Phenomenological interview

The phenomenological interview was conducted following completion of all behavioral tests in the post-training session. The post-training interview was the first instance that participants were asked about their color experiences (Exp. 1) or symbol experiences (Exp. 3). Participants were first asked to name the color / symbol that had been associated with each letter, then describe the effort required in translating a letter to its associated color / symbol, and vice versa. Participants were then shown a printed A4 page of the 13 trained letters, presented in black ink, and asked “Look at this page that has the 13 letters you have been trained over the last 5 weeks to associate with 13 specific colors / symbols. I want you to describe any associated color / symbol experience you have when looking at these letters.” Participants were then allowed to freely report any associated color / symbol experience. The interview was recorded for later analysis and a summary can be downloaded from [Multimedia Component 1](#).

To minimize demand characteristics potentially driving participants' responses within the phenomenological interview, the term ‘synesthesia’ was not referred to at any time during the study; upon inclusion in the study participants were instead informed that they would be trained on specific letter-color / symbol associations to see if this would improve their short-term memory. Nonetheless, to assess the possible impact of demand characteristics on our results, following completion of the study a debriefing email was sent to all participants informing them of the additional objectives of the study i.e., to investigate if it was possible to train grapheme-color synesthesia in a more general non-synesthetic population. Participants were asked to respond ‘yes’ or ‘no’ to the email to signal their awareness of this additional objective.

2.7. Training

The training for both groups (Exp. 1 and Exp. 3) consisted mainly of four different types of tasks in various versions: passive association training (e.g., presentation of letters in their associated color), delayed match to sample (e.g., selection of a color-square associated with a previously presented letter), span-tasks (e.g., remembering the sequence of colors associated with previously presented letters), and N-Back tasks (e.g., detecting if a letter or color matched the stimulus presented “n”-trials back in terms of its specific identity or its associated counterpart). Most of the tasks were adaptive and became more demanding with increasing performance. A detailed description of all training tasks and training performance can be found in the [Supplemental methods / Results](#). For the experimental group (Exp. 1), the training tasks were identical to those in our previous study ([Bor et al., 2014](#)) with the following exceptions: there was no spelling task (see [Supplemental methods / Results Fig. S1 and Tables S1, S3, and S5](#)). The active control group were trained on letter-symbol pairings, with a procedure matching as closely as possible to that of the experimental group (Exp. 1; see [Supplemental methods / Results Fig. S2 and Table S2, S4, and S6](#)). Our motivation for this particular active control design (recognizing that many alternative designs are possible) was to closely match the training and testing demands. In this way, we could test if the

hypothesized phenomenological, behavioral and neurophysiological changes resulting from overtraining synesthetic associations (Exp. 1), could be more parsimoniously explained as being due to extensive associative training (Exp. 3). However, one might argue that this does not rule out the possibility that increased color discrimination ability, which is associated with grapheme-color synesthesia (Banissy et al., 2013; Yaro and Ward, 2007) and which may be achieved in non-synesthetes by training to enhance color categories, is sufficient to induce the neurophysiological profile associated with genuine synesthesia. However, this line of enquiry is an entirely different research question which lies explicitly outside the focus of the present study.

3. Results

3.1. Exp. 1: Training induced synesthetic experiences

After the training, all subjects reported synesthetic phenomenology. Representative statements when asked to freely report their color experiences for achromatic letters include: “I see it in my mind as a replication of the letter but in its color so it's not just a block of color it's the actual letter in the color.”, “The letters are in color.”, “I cannot see the color on the paper but it's in my mind.”, “I see [an] orange ‘o’ floating around.”, “Take ‘y’ as example, when I look at it some yellow thing appears in my mind.”, “I see it (the color) overlaid on the page in the shape of the letter”, “My head is full of that color.”, “Obviously they are black (the letters) but if I look at them and look through, I can see them in the training color.”, “It probably is floating on the surface actually, I would say it is outside.”, “It's kinda basically, I just replace the letter with the colored letter”, “Imagine this paper is invisible and I can see the color, like, on this paper.”. 12/18 participants indicated that the translation from letter to color did not require any effort, 3/18 were undecided and 3/18 said the translation required effort. 10/18 participants used a semantic strategy to memorize the associations, 7/18 did not use a specific strategy and 1/18 used a visual strategy. 14/18 indicated letter to color as the easiest translation direction, with 2/18 indicating color to letter as easier, and 2/18 indicating that both directions were similar. Altogether, these semi-structured interviews provide strong evidence that participants were experiencing synesthesia like phenomenology after training. Critically, 15 out of the 18 participants were completely unaware of the study aims, as confirmed by interview after the study (see Section 2.2 above).

Demonstrating enhanced modality-specific cortical excitability in synesthesia, Terhune and colleagues applied TMS to primary visual cortex and found that grapheme-color synesthetes had lower phosphene thresholds in comparison to non-synesthetes, whereas there was no group difference when motor thresholds were tested by TMS applied to the motor cortex (Terhune et al., 2011). Hence, we hypothesized that if the training-related induction of synesthesia-like experiences was underpinned by enhanced cortical excitability, we should observe a lower phosphene threshold following training, while the motor threshold should remain unaffected. We applied TMS to the primary visual and motor cortices to measure the phosphene and motor thresholds, respectively, both before and after training (Fig. 1A). A two-factorial analysis of variance (ANOVA) consisting of the within subject factors Session (pre-training vs. post-training) and Site (visual vs. motor) revealed a significant main effect of Session [$F(1,8) = 31.97, p < .001, \eta_p^2 = .80$]. Crucially, the interaction was also significant [$F(1,8) = 14.09, p = .006, \eta_p^2 = .64$], due to a significantly reduced phosphene threshold in the post training session [$t(8) = 4.83, p = .001, d = 2.82$]. The motor threshold was not affected by training [$t(8) = 1.40, p = .198, d = .66$]. The main effect of Site did not reach significance [$F(1, 8) = 2.81, p = .132, \eta_p^2 = .26$] (top panel Fig. 1B). This analysis supports our hypothesis of increased cortical excitability due to overtraining of synesthetic associations.

When comparing our findings with previous research demonstrating lower phosphene thresholds in genuine grapheme-color synesthetes in

comparison to non-synesthete controls (Terhune et al., 2011; cf. also, Terhune et al., 2015a, 2015b), it is important to recognize that comparisons of (genuine) synesthetes and controls necessitate a between-subjects design. The successful acquisition of synesthetic experiences (as in the current study), by contrast, allows for within-subject comparisons. That is, the group comparison in studies involving genuine synesthetes and controls corresponds to the pre- / post-training comparison in our current study. Hence, we compared the effect sizes of the relevant interactions which were $\eta_p^2 = .71$ (i.e., Group \times Site) in previous research (Terhune et al., 2011) and $\eta_p^2 = .64$ (i.e., Session \times Site) in the current study. Both effects can be classified as substantial and are broadly comparable in size. Therefore, the magnitude of the training effect on the phosphene threshold is comparable to phosphene threshold differences previously observed between genuine synesthetes and non-synesthetic controls.

Demonstrating increased perceptual sensitivity in grapheme-color synesthetes, a previous EEG study found that grapheme-color synesthetes exhibit enhanced VEP components (measured over occipital and parieto-occipital cortex) than non-synesthetes, in response to high contrast checkerboard patterns, which did not elicit synesthetic experiences (Barnett et al., 2008b). Hence, we hypothesized that the training-related induction of synesthesia-like experiences would result in enhanced visual perceptual processing, as indicated by increases in VEP components after training in response to high contrast checkerboard stimuli. It is important to note that the checkerboard stimuli were not part of any training task and hence they did not trigger the learnt associations. Using EEG before and after training, we measured VEPs (Odom et al., 2010) over occipital and parieto-occipital regions in response to high and low spatial frequency checkerboard patterns (Fig. 2A-B). A two-factorial ANOVA consisting of the within subject factors Session (pre-training vs. post-training) and Frequency (high vs. low) for the VEP component C3 revealed a significant main effect of Session [$F(1,17) = 5.34, p = .034, \eta_p^2 = .24$], due to a larger magnitude positive-going C3 component in the post-training session. The main effect of Frequency and the interaction of Session \times Frequency were not significant [$F_s < 1.49, p_s > .240, \eta_p^2_s < .09$]. The enhanced positive-going C3, after training, supports our hypothesis that overtraining synesthetic associations increases cortical excitability in response to checkerboard patterns, which can be interpreted as reflecting enhanced visual perceptual processing (top panel Fig. 2C-E).

These EEG results are fully in line with prior research showing enhanced VEPs in response to high contrast checkerboard patterns in genuine synesthetes in comparison to controls (Barnett et al., 2008b) as well as with behavioral evidence supporting a specific profile of enhanced visual perceptual processing in synesthesia (Banissy et al., 2013, 2009; Yaro and Ward, 2007). We note that the shape of our VEPs differed somewhat from the earlier study with genuine synesthetes (Barnett et al., 2008b), which may be due to small differences in the design of the stimuli and the methods of their presentation. Nevertheless, the effect was remarkably consistent across studies in that only one of the VEP components was enhanced. The original study did not indicate effect sizes and hence, we calculated Cohen's $d = .82$ for that study, which denotes a large effect that is comparable to $d = .79$ of the present study, calculated with the same equation.¹ Moreover, it is important to note that the VEPs between pre- and post-training are largely superimposable except for the affected component (i.e., C3), which further corroborates a specific training-related effect. Altogether, these EEG results, combined with the TMS-based findings of altered phosphene thresholds, show that overtraining of synesthetic associations leads to neurophysiological changes characteristic of genuine synesthesia.

¹ We used the following equation to calculate Cohen's d from the main effect of an F -test: $d = \sqrt{(F((n_t + n_c)/(n_{tn_c} - 1))((n_t + n_c)/(n_t + n_c - 2)))}$ where t = treatment condition (i.e., synesthetes or post-training) and c = comparison condition (i.e., non-synesthetes or pre-training).

In a previously unrelated line of synesthesia research, emerging evidence suggests that many behavioral markers of grapheme-color synesthesia (Dixon et al., 2004; Rothen et al., 2013b; Ward et al., 2007) can be generated through a relatively short period of training of synesthetic associations in non-synesthetic adults (Colzoli et al., 2012; Howells, 1944; Kelly, 1934; Kusnir and Thut, 2012; Meier and Rothen, 2009; Rothen et al., 2011). Hence, to complement the neurophysiological and phenomenological markers of the present training paradigm, we conducted two widely applied behavioral tests - a synesthetic consistency test (Bor et al., 2014; Eagleman et al., 2007; Rothen et al., 2013a) and a synesthetic Stroop test (Bor et al., 2014; Dixon et al., 2004; Meier and Rothen, 2009; Rothen et al., 2011). Both tests were applied before and after training.

The consistency test asks participants to select a color from a continuous color palette for each letter of the alphabet presented sequentially in random order (Fig. 3A). It assesses the consistency with which specific colors are selected by means of measuring distances in three-dimensional color space (Fig. 3B). Smaller values denote higher consistency and are indicative of synesthetic experiences (Eagleman et al., 2007; Rothen et al., 2013a). The results of the consistency test are depicted in the top panel of Fig. 3C. A two-factorial ANOVA consisting of the within subject factors Session (pre-training vs. post-training) and Letters (trained vs. untrained) revealed a significant main effect of Session [$F(1,17) = 16.75, p < .001, \eta_p^2 = .50$], a significant main effect of Set [$F(1,17) = 33.58, p < .001, \eta_p^2 = .66$], and crucially a significant interaction of Session x Set [$F(1,17) = 38.71, p < .001, \eta_p^2 = .69$]. The results show that colors were selected with significantly increased consistency only for the trained letters after training [$t(17) = 5.76, p < .001, d = 1.92$]. This was not the case for untrained letters [$t(17) = .60, p = .555, d = .03$]. Post-training consistency scores were on average below the well-established threshold value of 135, a level indicative of grapheme-color synesthesia (Rothen et al., 2013a), in line with previous studies implementing extensive synesthesia training (Bor et al., 2014) as well as with the TMS and EEG results described above.

The synesthetic Stroop test asks participants to name the veridical color (i.e., the actual color, not the associated color) of a presented grapheme as quickly and accurately as possible (Fig. 4A). The veridical color of the presented grapheme is either congruent or incongruent with its associated color, with equal probability. This test examines whether synesthetic associations are automatically triggered, on the reasoning that automaticity will lead to interference effects and slower response times for incongruent trials. We found a larger difference between incongruent and congruent trials following training (top panel Fig. 4C), indicative of increased interference. A two-factorial ANOVA consisting of the within subject factors of Session (pre-training vs. post-training) and Congruency (congruent vs. incongruent) revealed a significant main effect of Session [$F(1,16) = 30.42, p < .001, \eta_p^2 = .66$], a significant main effect of Congruency [$F(1,16) = 98.66, p < .001, \eta_p^2 = .86$], and crucially a significant Session x Congruency interaction [$F(1,16) = 9.42, p = .007, \eta_p^2 = .37$]. The results show that incongruent colors resulted in greater interference after training [$t(16) = 3.07, p = .007, d = 1.05$]. This indicates that the trained letters automatically triggered their associated colors, in line with previous synesthesia training studies (e.g., Meier and Rothen, 2009) and genuine synesthesia (e.g., Dixon et al., 2004). As with the Consistency results, the results from the Stroop task corroborate the other findings reported in this study.

3.2. Exp. 2: Effects of test repetition

One might wonder whether the results of Exp. 1 (experimental group) could be attributed simply to the repetition of the testing battery, and not to the training paradigm. To address this possibility we conducted Exp. 2, a 'passive control', which demonstrates that mere repetition of testing cannot explain the neural and behavioral changes observed in Exp. 1. We emphasize that the sole purpose of Exp. 2 was to

ascertain, using a smaller sample, that the effects observed in Exp. 1 were not simply due to test repetition, and therefore to make sure we would not waste valuable laboratory resources, prior to testing an active control group.

The data of the different tests in Exp. 2 were subjected to the same statistical analyses as the corresponding tests of Exp. 1. Repeated testing without training did not lead to any significant changes in either phosphene or motor thresholds; the Session x Site interaction was not significant [$F(1,7) = .97, p = .357, \eta_p^2 = .12$]. Therefore, repeated testing cannot explain the reduced phosphene threshold found in Exp. 1 (bottom panel Fig. 1B). Repeated testing without training did not lead to increased VEPs; neither the main effect of Session nor the Session x Frequency interaction reached significance [$F_s < .78, p_s > .402, \eta_p^2_s < .09$]. Hence, repeated testing cannot explain the increase in VEPs found in Exp. 1 (bottom panel Fig. 2C-E). Furthermore, repeated testing without training did not lead to an increase in consistency for the "trained" letter-set relative to the "untrained" set; the Session x Set interaction was not significant [$F(1,9) = .03, p = .864, \eta_p^2 < .01$]. Thus, repeated testing alone cannot explain the increase in consistency found in Exp. 1 (bottom panel Fig. 3C). Similar to Exp. 1, the passive control group in Exp. 2 exhibited a pre-existing Congruency effect [$F(1,7) = 17.39, p = .004, \eta_p^2 = .71$] in the synesthetic Stroop paradigm, presumably due to the fact that the associations in this study were chosen based on preferences revealed by a large-scale study, involving both synesthetic and normal populations (Simner et al., 2005; cf. also Bor et al., 2014). However, this effect was not affected by test repetition (middle panel Fig. 4C): the Session x Congruency interaction was not significant [$F(1,7) = .30, p = .604, \eta_p^2 = .04$] and Stroop interference did not significantly differ between the pre- and post-training session [$t(7) = .54, p = .604, d = .27$].

3.3. Exp. 3: Training induced automatic symbolic associations

Which of the changes observed in Exp. 1 are due to the specific letter-color training regime we employed, and which might be attributed to general effects of extensive and adaptive cognitive training? In an 'active control' (Exp. 3), participants were trained to associate abstract symbols - rather than colors - to the same thirteen letters used in Exp. 1, again over the course of five weeks. We hypothesized that training in this active control would lead to changes in relevant behavioral measures (e.g., Stroop-like effects), but *not* to additional synesthesia-like phenomenology or neural changes as observed in Exp. 1, on the reasoning that the neural changes accompany the altered phenomenology. Indeed, despite having equivalent training procedures and duration, Exp. 3 did not lead to similar phenomenological experiences or neural changes as in Exp. 1, while similar behavioral effects were observed. These data provide further evidence that the altered phenomenology in Exp. 1 is associated with the neural changes observed in that experiment, since automaticity of associations by itself does not lead to such altered phenomenology.

In sharp contrast to Exp. 1, only 3/17 subjects reported perceptual phenomenology of symbols in response to letters. Representative statements for perceptual phenomenology include: "I see the symbol on the surface wherever the letter is. If I see the letter, I see the main characteristics of the symbol relating to the letter", "I look at the letter and I automatically see the symbol, definitely a visual experience, its right here, it's not in my mind's eye. I imagine the symbol close to the paper". Representative statements for associative phenomenology, reported to some extent by 8/17 participants, include: "I don't see it physically, but it's kind of interchangeable, I am not 100% concentrating on the physical form of the symbol, the two are now interchangeable, I just see the meaning. Similar to knowing a word, you don't have to read each letter", "I imagine the symbol close to the paper. Weaker than imagery for a strong association.", "Letters to symbols, similar to reading Mandarin, a kind of external imagination". 6/17 participants reported no additional experience at all. In terms of

strategy used, 9/17 participants indicated that the translation from letter to symbol did not require any effort and 8/17 said the translation would require effort. All participants used a semantic strategy to memorize the associations. As in Exp. 1, no participants were aware of the aims of the study, as confirmed by post-study interview.

The data of the different tests in Exp. 3 were subjected to the same statistical analyses as the corresponding tests of Exp. 1. Training letter-symbol associations did not lead to any changes in either phosphene or motor thresholds; the Session x Site interaction was not significant [$F(1,16) = .29, p = .598, \eta_p^2 = .02$]. Therefore, the acquisition of letter-symbol associations cannot explain the reduced phosphene threshold found in Exp. 1 (middle panel Fig. 1B). Training letter-symbol associations did not lead to increased VEPs; neither the main effect of Session nor the Session x Frequency interaction reached significance [$F_s < .57, p_s > .463, \eta_p^2_s < .05$]. Hence, the acquisition of letter-symbol associations cannot explain the increase in VEPs found in Exp. 1 (middle panel Fig. 2C-E). Furthermore, training letter-symbol associations did not lead to an increase in (color) consistency for the trained letter-set; although the Session x Set interaction was significant [$F(1,15) = 7.86, p = .013, \eta_p^2 = .34$] subsequent *t*-tests comparing pre- and post-training session separately for trained and untrained letters did not confirm the reliability of the interaction [$t_s < 1.56, p_s > .141, d_s < .56$] and the pattern of the results went in fact in the opposite direction (decrease in consistency). Thus, the acquisition of letter-symbol associations cannot explain the increase in consistency found in Exp. 1 (middle panel Fig. 3C).

To measure the automaticity of the associations between symbols and letters, the Stroop test was modified into a priming test (Fig. 4B). That is, a target letter was preceded by a short presentation of a symbol that was either associated with the target letter during the training (congruent condition) or associated with another letter (incongruent letter). In line with previous research (Dixon et al., 2004; Meier and Rothen, 2009) and our expectations, congruent prime-target pairings showed faster responses than incongruent prime-target pairings after but not before the training (Fig. 4 C, bottom row). The increase of the interference effect was in fact of similar magnitude as for the experimental group (Exp. 1, Fig. 4C, top). The observations were confirmed by a significant Session x Congruency interaction [$F(1,16) = 35.56, p < .001, \eta_p^2 = .69$] and by direct comparison of the interference effect before and after training [$t(16) = 5.96, p < .001, d = 2.05$].

3.4. Collective analysis across experiments

Additional analyses across Exp. 1, 2, and 3 adding the factor *Group* (experimental, active, passive) to the original experimental design conservatively demonstrate the reliability of the reported effects. Analyzing the noninvasive brain stimulation data revealed a triple interaction Group x Session x Site [$F(2,31) = 9.75, p = .001, \eta_p^2 = .39$] due to the lower post-training phosphene threshold in the experimental group (Exp. 1), but not in the passive (Exp. 2) or active (Exp. 3) control groups. Analyzing neurophysiological measures in response to high- and low-frequency checkerboard patterns with a four-factorial design consisting of the between subject factor Group (experimental, active, passive) and the within subject factors Session (pre-training vs. post-training), Component (C1, C2, C3), and Frequency (high vs. low) revealed a significant triple-interaction Group x Session x Component [$F(4,82) = 3.79, p = .019, \eta_p^2 = .16$], due to the significant Group x Session interaction [$F(2,41) = 4.03, p = .025, \eta_p^2 = .16$] for C3, but not C1 and C2 [$F_s < 1.85, p_s > .171, \eta_p^2_s < .09$] which was due to more positive-going VEPs in the post-training session in the experimental group (Exp. 1), but not in the passive (Exp. 2) or active (Exp. 3) control groups. The four-factorial ANOVA revealed no further interactions involving the factor Group [$F_s < 1.32, p_s > .280, \eta_p^2_s < .07$]. The main effect Group was trending [$F(2,41) = 2.60, p = .087, \eta_p^2 = .11$] due to somewhat lower VEPs in the active control group (Exp. 3). For the consistency data, each main effect, interaction, and the triple

interaction of the factors Group, Session, and Letters reached significance [$F_s > 4.56, p_s < .017, \eta_p^2_s > .15$] due to the marked increase in consistency for the trained letters in the experimental group (Exp. 1) which was not the case in the passive (Exp. 2) or active (Exp. 3) control groups. For the Stroop / priming data, again each main effect, interaction, and the triple interaction of the factors Group, Session, and Consistency reached significance [$F_s > 3.40, p_s < .043, \eta_p^2_s > .14$] due to the substantial increase in the interference effect in the experimental (Exp. 1) and active control group (Exp. 3) after the training, but not in the passive control group (Exp. 2).

4. Discussion

Taken together, our data reveal that overtraining letter-color associations results in a profile of neurophysiological changes and behavioral performance characteristic of those seen in genuine synesthesia, accompanied by striking subjective reports of synesthesia-like phenomenon in all participants. We found higher cortical excitability and enhanced visual perceptual processing after participants engaged in an extensive cognitive training battery in which they had learnt 13 specific letter-color associations. Notably, the magnitude of these effects are comparable to those found in genuine synesthesia (Barnett et al., 2008b; Terhune et al., 2011). These neurophysiological changes corroborate subjective reports and additional (but separate) behavioral markers, providing strong evidence that participants have indeed acquired novel synesthesia-like phenomenon as a consequence of training. Hence, our results support the notion that genuine synesthesia involves a substantive developmental component (Witthoft and Winawer, 2006, 2013; Witthoft et al., 2015), possibly underpinned by a genetic predisposition (Asher et al., 2009; Barnett et al., 2008a; Baron-Cohen et al., 1996; Tomson et al., 2011; Ward and Simner, 2005), which determines the synesthetic phenotype (Bor et al., 2014; Rothen and Meier, 2014). Our results also extend previous reports of perceptual plasticity (e.g., Yan et al., 2014) to show dramatic changes in phenomenonology, underwritten by accompanying neurophysiological modifications.

4.1. Factors affecting training efficiency

Although our study does not compare different training procedures (besides the inclusion of the active control study), the observation that all participants who underwent letter-color association training (Exp. 1) reported color-experiences after training highlights the efficacy of the training regime used. In comparison to previous training procedures which were not successful in inducing synesthetic phenomenonology (see Rothen and Meier, 2014 for a review) and in line with one previous study which was successful in inducing synesthetic phenomenonology (Bor et al., 2014), four aspects emerge as important in promoting the acquisition of additional phenomenonology: a) long training sessions, both in terms of individual sessions as well as the overall duration of the program, with multi-week training likely essential b) adaptive tasks which become more difficult as individual task performance improves c) relatedly, the use of diverse and changing tasks over the training period is helpful in maintaining participant motivation, and d) presenting a preponderance of (or exclusively) to-be-learned (target) associations, rather than a mixture of target and distractor associations (compare e.g., Meier and Rothen, 2009). Future training studies are needed in order to determine the relevance of these different factors, individually and in various combinations, to explore whether training can be made more efficient and less time demanding (for a discussion of different training aspects see also Bastian and Oberauer, 2014).

4.2. Phenomenological specificity: the special status of color

Despite comparable training procedures, only the letter-color association training (Exp. 1), and not the letter-symbol training (Exp. 3,

with 3 exceptions), led reliably to additional phenomenological experiences. Might there be something special about color in this regard, as compared to symbols? Interestingly, occurrences of genuine synesthesia involve synesthetic color experiences more often than any other concurrent synesthetic experience, such as sound or flavors (<http://www.daysyn.com/Types-of-Syn.html> retrieved on 10th November 2017), indicating a predisposition for color phenomenology associated with synesthesia. Some authors have suggested a genetic basis for such a predisposition (e.g., Asher et al., 2009; Barnett et al., 2008a; Tomson et al., 2011). It is also noteworthy that synesthesia with symbols as concurrents does not appear to occur naturally (<http://www.daysyn.com/Types-of-Syn.html> retrieved on 10th November 2017).

The success of letter-color training may also relate to the functional and structural organization of human cortex. In particular, the visual word form area (VWFA, responsible for the processing of letters) is located adjacent to V4 and in vicinity to other ventral occipital regions associated with color perception (Cohen and Dehaene, 2004; Jiang et al., 2007; Lueck et al., 1989; Zeki et al., 1991). Indeed, while early studies showing V4 activation to achromatic graphemes (Hubbard et al., 2005; Sperling et al., 2006; e.g., Weiss et al., 2000) in individuals with genuine grapheme-color synesthesia have proven difficult to replicate (Hupé et al., 2012), a recent imaging study found that the V4 activation, in such cases, was more likely for synesthetes experiencing more vivid ‘projector’-like phenomenology (Gould van Praag et al., 2016).

Motivated by data showing this kind of co-activation, one prominent hypothesis proposes that grapheme-color synesthesia emerges as a result of cross-activation between these two areas due to insufficient neural pruning (Ramachandran and Hubbard, 2001; cf. also Hubbard et al., 2011). In one elaboration of this view, all humans are born with “genuine synesthesia” which is gradually lost as developmental neuronal pruning proceeds (Maurer and Mondloch, 2005; Wagner and Dobkins, 2011; see also Ludwig et al., 2011; but see Deroy and Spence, 2013 for an opposing view). On this view, training letter-color associations may re-instantiate these lost neural connections by the growth of new synapses. By contrast, letter-symbol training may evoke activity preferentially within the VWFA for both types of stimuli, but would not re-instate any lost connections (because they never existed in the first place), precluding the kind of regional cross-talk putatively involved in letter-color training. While between-area and within-area connectivity changes are both consistent with the development of automaticity, it may be the re-instatement of lost connections (and experiences) which explains why the former, but not the latter, should be associated with additional phenomenology. To further probe this account, future studies could examine whether color phenomenology can be acquired as a result of training symbol-color associations.

Moreover, it has been suggested that letter-color synesthesia develops because synesthetic concurrents can aid the acquisition of reading skills (Watson et al., 2017, 2014). For instance, colors might be exploited to master the tasks involved in becoming literate (Asano and Yokosawa, 2013). Other stimulus features seem less useful in this regard: movement is likely to be too distracting, and texture too complex. Although direct evidence for this hypothesis is lacking, it has been shown that colored letters can help children to differentiate between letters which are otherwise difficult to distinguish (Jones, 1965). Notably, this explanation is also in line with the development of color perception, literacy and synesthesia (Simner and Bain, 2013; Simner et al., 2009; cf. also Watson et al., 2017).

4.3. Novelty of experiences: altering a lifetime of experience

It is worth emphasizing that letter-color training (Exp. 1) was able to alter perceptual phenomenology despite a life-long (pre-training) history of no previous letter-induced color experiences. Before the experiment, participants had always perceived letters (and graphemes

more generally) only in the colors in which they were rendered. Our data therefore highlight the powerful potential of learning or training to influence conscious perceptual experiences, even when such training is trivially short in relation to a lifetime of prior learning and experience. In other words, learning does not only influence our actions and other higher cognitive functions, but can shape how we consciously perceive the world. This dramatic potential for phenomenological and perceptual plasticity, in the adult brain, may have potential in the treatment of phobias where specific inducers trigger unwanted experiences (cf. Nakataki et al., 2017). Specifically, similar training paradigms might be developed to alter the experience induced by a stimulus which is initially perceived as fearful, by acting on underlying neurophysiological properties of cortical excitability and perceptual processing. Most generally, our data underline the potential for individual diversity in how we each encounter the world in our conscious experience, since we all have different histories, and different futures.

4.4. Modality-specific cortical changes and memory performance

Our data show that training-induced synesthetic color experiences are associated with enhanced modality-specific cortical excitability, in line with previous studies of genuine synesthesia (Terhune et al., 2011). Acquired color experiences in response to letters are accompanied by increased excitability within visual areas, but not by changes in excitability within motor areas. Furthermore, letter-color training also enhances visual perceptual processing in response to stimuli which do not trigger the novel acquired experiences and which were not involved in training (e.g., checkerboard patterns). This is noteworthy as enhanced visual perceptual processing has been proposed to account for the specific profile of enhanced memory performance associated with genuine synesthesia (e.g., Pritchard et al., 2013; Radvansky et al., 2011; Rothen and Meier, 2010; see Rothen et al., 2012 for a review). This raises the intriguing possibility that enhancing cortical excitability, via associative training, could lead to memory advantages (for similar accounts see for instance Bao et al., 2010; Jaeggi et al., 2008; Jaeggi et al., 2011; Yan et al., 2014). If so, this would have far-reaching implications for restorative therapies in relation to age-related memory decline and dementia (e.g., Berry et al., 2010).

4.5. Implications for synesthesia research

Our findings that extensive training can induce phenomenological, behavioral, and neural characteristics of synesthesia provide new support for the notion that genuine synesthesia is not purely a product of genetic predisposition, but has an important developmental or learnt component. In this view, a genetic predisposition may determine only a threshold beyond which learned associations transform into phenomenological experiences (Rothen and Meier, 2014; Seth, 2014, but Albright, 2012; for a review on the perceptual reality of synesthetic experiences see Kim and Blake, 2013). This view is also consistent with findings that some forms of synesthesia can be induced by hypnosis (though presumably without the cortical changes observed in this study and in genuine synesthesia) (Cohen Kadosh et al., 2009). While the developmental trajectory of genuine synesthesia remains largely unknown, some forms (e.g. grapheme-color) are grounded in specific associations highly prevalent in childhood environments (e.g., due to colored letter refrigerator magnets), which become gradually more consistent as a child learns to read (Simner and Bain, 2013; Simner et al., 2009). Thus, it is plausible that some forms of synesthesia depend on specific childhood memories (see Hupé and Dojat, 2015 for the same conclusion from an entirely different perspective).

4.6. Sensory substitution

Similar dramatic plasticity in neurotypical adults can be observed as a result of sensory substitution, in which the input of one modality (e.g.,

visual) is transformed by some specific mapping into input for another sensory modality (e.g., auditory). Neural plasticity is observed after prolonged training with sensory substitution devices under blindfold conditions. For instance, for visual-to-auditory sensory substitution the primary visual cortex starts to respond to auditory signals after training (for reviews see Bach-y-Rita and Kercel, 2003; Maidenbaum et al., 2014; Ward and Wright, 2014). While late blind individuals sometimes start to report visual perceptual phenomenology after extensive use of sensory-substitution devices (Ward and Meijer, 2010), similar reports in congenitally blind individuals must be treated cautiously because of the prior lack of the experience of visual perceptual qualia.

The findings from sensory substitution research corroborate the present study insofar as consistent environmental contingencies can change an individual's sensory response to, and experience of, a physical stimulus. However, there are also marked differences. Sensory substitution in healthy adults is typically conducted under 'blindfold' conditions (i.e., participants are blindfolded during lengthy training sessions with sensory substitution devices) which involve a far more dramatic environmental change than involved in the current training paradigm. Moreover, sensory substitution changes the inducing stimulus (e.g., from visual to auditory) while the modality of the resulting experience is supposed to remain unchanged (e.g., visual). By contrast, synesthetic association training does not change the inducing stimulus, but introduces an additional (concurrent) experience. In contrast to congenitally blind individuals who suddenly report visual qualia as a result of sensory substitution (interpreted with due caution), sighted individuals who develop novel phenomenological experiences due to synesthetic association training are clearly able to judge to what extent their experiences are visual in nature. Another marked difference is that sensory substitution relies on artificial devices (e.g., webcams) to generate mappings from one modality to another, whereas training paradigms continue to rely on the natural properties of the sensory and perceptual systems themselves. It is not only a matter of resolution; a webcam (for example) is a very poor substitute for a fully functioning human visual system. Potentially, these differences may at least partly account for why successful synesthetic association training requires less dramatic environmental changes than sensory substitution.

4.7. Control studies and limitations

Our results are most directly substantiated by inclusion of two control studies, one of which (the active control) also included extensive cognitive training. We designed the active control to test whether extensive training alone could lead to additional synesthesia-like phenomenology and corresponding neural changes, when the trained associations did not reflect a common synesthesia subtype. Indeed, we found that training of letter-symbol associations did not lead to these effects (though a few subjects did report a degree of altered phenomenology). An alternative control study would have been to keep the same letter and color stimuli as in the experimental group (Exp. 1), while frequently changing the associations across the training period. While this design would examine the effects of repeated (unpaired) stimulus presentation in a way that matched the experimental group more closely by stimulus, it would not address the key issue of *training*, since the extent of training would be different across the groups. We therefore decided against running this alternative control in the present study.

When choosing the associations to be trained, we selected non-random letter-color pairings based on associations that are found for some synesthetes, as well as for non-synesthetes when they are forced to select colors for letters (cf. Mankin and Simner, 2017; Simner et al., 2005). This design choice was made in order to maximize the likelihood of training success, in line with (and indeed replicating) our previous study (Bor et al., 2014; see also [Supplemental Results](#)). However, phenomenological experiences were not restricted to semantic associations (e.g., g - green vs. q - purple). A future study could randomize

associations across participants, which would presumably also eliminate any pre-existing biases on the Stroop task.

We demonstrated that synesthesia training affects wider neurophysiological processes which are independent of specific synesthetic experiences. It is important that future training studies also address specific neurophysiological processes which are more directly related to synesthetic experiences. For instance, it would be interesting to see whether synesthesia training can lead to contextual priming effects which have previously been reported for genuine synesthetes who read sentences like "The Coca-Cola logo is white and 2", where '2' elicited a contextually congruent color (i.e., red in this case) or an incongruent color. Consistent with the involvement of perceptual processes, congruity was found to affect early sensory ERP components (Brang et al., 2011). Similar effects in trained non-synesthetes would further corroborate the notion that overtraining synesthetic associations can lead to changes in phenomenological experiences.

4.8. Summary

Our results demonstrate that intensive and adaptive training of letter-color associations can alter conscious perceptual experiences. The additional color experiences we found are accompanied by neural changes in cortical excitability and in visual perceptual processing, and by behavioral indicators of the altered phenomenology, which are collectively consistent with well-studied characteristics of genuine grapheme-color synesthesia. The strong similarity between the training induced color experiences and synesthetic phenomenology supports the notion that genuine synesthesia involves a significant developmental component. Control studies excluded the possibility that the acquired synesthesia-like experiences and the accompanying neurophysiological changes could be attributed simply to repetition of the relevant tests, or to engagement in intensive adaptive training. Strikingly, these changes occurred following restricted daily training sessions lasting just a few weeks. While longer than previous training studies, this program is less disruptive than previous demonstrations of altered conscious experience, e.g., through sensory deprivation in blindfolding studies (e.g., Merabet et al., 2004; Pitskel et al., 2007). In summary, relatively short periods of intensive cognitive training, in neurotypical young adults, can generate dramatic perceptual plasticity and altered conscious experiences as evidenced by a coordinated set of phenomenological, behavioral, and neurophysiological changes.

Acknowledgements

We would like to thank Carys Barnfield, Acer Y. C. Chang, Elena Gelibter and Alex Piletska for their assistance with data collection. We would also like to thank Heather M. Iriye for her help with the processing of the Stroop data.

Funding

This work was supported by the Dr. Mortimer and Theresa Sackler Foundation, which supports the Sackler Centre for Consciousness Science, by the Swiss National Science Foundation (Grant Number PZ00P1_154954), which supports Nicolas Rothen, and by the Daphne Jackson Trust and the Biotechnology and Biological Sciences Research Council (BBSRC), which supports Daniel Bor.

Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at <http://dx.doi.org/10.1016/j.neuropsychologia.2018.01.030>.

References

- Albright, T.D., 2012. On the perception of probable things: neural substrates of associative memory, imagery, and perception. *Neuron* 74 (2), 227–245. <http://dx.doi.org/10.1016/j.neuron.2012.04.001>.
- Asano, M., Yokosawa, K., 2013. Grapheme learning and grapheme-color synesthesia: toward a comprehensive model of grapheme-color association. *Front. Hum. Neurosci.* 7. <http://dx.doi.org/10.3389/fnhum.2013.00757>.
- Asher, J.E., Lamb, J.A., Brocklebank, D., Cazier, J.-B., Maestrini, E., Addis, L., Monaco, A.P., 2009. A whole-genome scan and fine-mapping linkage study of auditory-visual synesthesia reveals evidence of linkage to chromosomes 2q24, 5q33, 6p12, and 12p12. *Am. J. Hum. Genet.* 84 (2), 279–285. <http://dx.doi.org/10.1016/j.ajhg.2009.01.012>.
- Bach-y-Rita, P., Kercel, S.W., 2003. Sensory substitution and the human-machine interface. *Trends Cogn. Sci.* 7 (12), 541–546. <http://dx.doi.org/10.1016/j.tics.2003.10.013>.
- Banissy, M.J., Tester, V., Muggleton, N.G., Janik, A.B., Davenport, A., Franklin, A., Ward, J., 2013. Synesthesia for color is linked to improved color perception but reduced motion perception. *Psychol. Sci.* 24 (12), 2390–2397. <http://dx.doi.org/10.1177/0956797613492424>.
- Banissy, M.J., Walsh, V., Ward, J., 2009. Enhanced sensory perception in synaesthesia. *Exp. Brain Res.* 196 (4), 565–571. <http://dx.doi.org/10.1007/s00221-009-1888-0>.
- Bao, M., Yang, L., Rios, C., He, B., Engel, S.A., 2010. Perceptual learning increases the strength of the earliest signals in visual cortex. *J. Neurosci.* 30 (45), 15080–15084. <http://dx.doi.org/10.1523/JNEUROSCI.5703-09.2010>.
- Barnett, K.J., Finucane, C., Asher, J.E., Bargary, G., Corvin, A.P., Newell, F.N., Mitchell, K.J., 2008a. Familial patterns and the origins of individual differences in synaesthesia. *Cognition* 106 (2), 871–893. <http://dx.doi.org/10.1016/j.cognition.2007.05.003>.
- Barnett, K.J., Foxe, J.J., Molholm, S., Kelly, S.P., Shalgi, S., Mitchell, K.J., Newell, F.N., 2008b. Differences in early sensory-perceptual processing in synesthesia: a visual evoked potential study. *NeuroImage* 43 (3), 605–613. <http://dx.doi.org/10.1016/j.neuroimage.2008.07.028>.
- Baron-Cohen, S., Burt, L., Smith-Laittan, F., Harrison, J., Bolton, P., 1996. Synaesthesia: prevalence and familiarity. *Perception* 25 (9), 1073–1079. <http://dx.doi.org/10.1068/p251073>.
- Baron-Cohen, S., Harrison, J., Goldstein, L.H., Wyke, M., 1993. Coloured speech perception: is synaesthesia what happens when modularity breaks down? *Perception* 22 (4), 419–426.
- Bastian, C., Oberauer, K., 2014. Effects and mechanisms of working memory training: a review. *Psychol. Res.* 78 (6), 803–820. <http://dx.doi.org/10.1007/s00426-013-0524-6>.
- Berry, A.S., Zanto, T.P., Clapp, W.C., Hardy, J.L., Delahunt, P.B., Mahncke, H.W., Gazzaley, A., 2010. The influence of perceptual training on working memory in older adults. *PLoS One* 5 (7), e11537. <http://dx.doi.org/10.1371/journal.pone.0011537>.
- Bor, D., Rothen, N., Schwartzman, D.J., Clayton, S., Seth, A.K., 2014. Adults can be trained to acquire synesthetic experiences. *Sci. Rep.* 4 (7089), 1–8. <http://dx.doi.org/10.1038/srep07089>.
- Brang, D., Edwards, L., Ramachandran, V.S., Coulson, S., 2008. Is the sky 2? Contextual priming in grapheme-color synaesthesia. *Psychol. Sci.* 19 (5), 421–428. <http://dx.doi.org/10.1111/j.1467-9280.2008.02103.x>.
- Brang, D., Kanai, S., Ramachandran, V.S., Coulson, S., 2011. Contextual priming in grapheme-color synesthetes and yoked controls: 400 msec in the life of a synesthete. *J. Cogn. Neurosci.* 23 (7), 1681–1696. <http://dx.doi.org/10.1162/jocn.2010.21486>.
- Cohen Kadosh, R., Henik, A., Catena, A., Walsh, V., Fuentes, L.J., 2009. Induced cross-modal synaesthetic experience without abnormal neuronal connections. *Psychol. Sci.* 20 (2), 258–265. <http://dx.doi.org/10.1111/j.1467-9280.2009.02286.x>.
- Cohen, L., Dehaene, S., 2004. Specialization within the ventral stream: the case for the visual word form area. *NeuroImage* 22 (1), 466–476. <http://dx.doi.org/10.1016/j.neuroimage.2003.12.049>.
- Colizoli, O., Murre, J.M.J., Rouw, R., 2012. Pseudo-synesthesia through reading books with colored letters. *PLoS One* 7, e39799. <http://dx.doi.org/10.1371/journal.pone.0039799>.
- Deroy, O., Spence, C., 2013. Are we all born synaesthetic? Examining the neonatal synaesthesia hypothesis. *Neurosci. Biobehav. Rev.* 37 (7), 1240–1253. <http://dx.doi.org/10.1016/j.neubiorev.2013.04.001>.
- Dixon, M.J., Smilek, D., Merikle, P.M., 2004. Not all synaesthetes are created equal: projector versus associator synaesthetes. *Cogn., Affect., Behav. Neurosci.* 4 (3), 335–343.
- Eagleman, D.M., Kagan, A.D., Nelson, S.S., Sagaram, D., Sarma, A.K., 2007. A standardized test battery for the study of synesthesia. *J. Neurosci. Methods* 159 (1), 139–145. <http://dx.doi.org/10.1016/j.jneumeth.2006.07.012>.
- Esterman, M., Verstynen, T., Ivry, R.B., Robertson, L.C., 2006. Coming unbound: disrupting automatic integration of synesthetic color and graphemes by transcranial magnetic stimulation of the right parietal lobe. *J. Cogn. Neurosci.* 18 (9), 1570–1576. <http://dx.doi.org/10.1162/jocn.2006.18.9.1570>.
- Gould van Praag, C.D., Garfinkel, S., Ward, J., Bor, D., Seth, A.K., 2016. Automaticity and localisation of concurrents predicts colour area activity in grapheme-colour synaesthesia. *Neuropsychologia* 88, 5–14. <http://dx.doi.org/10.1016/j.neuropsychologia.2016.04.016>.
- Howells, T.H., 1944. The experimental development of color-tone synesthesia. *J. Exp. Psychol.* 34 (2), 87–103. <http://dx.doi.org/10.1037/h0054424>.
- Hubbard, E.M., Arman, A.C., Ramachandran, V.S., Boynton, G.M., 2005. Individual differences among grapheme-color synesthetes: brain-behavior correlations. *Neuron* 45 (6), 975–985. <http://dx.doi.org/10.1016/j.neuron.2005.02.008>.
- Hubbard, E.M., Brang, D., Ramachandran, V.S., 2011. The cross-activation theory at 10. *J. Neuropsychol.* 5 (2), 152–177. <http://dx.doi.org/10.1111/j.1748-6653.2011.02014.x>.
- Hupé, J.-M., Bordier, C., Dojat, M., 2012. The neural bases of grapheme-color synesthesia are not localized in real color-sensitive areas. *Cereb. Cortex* 22 (7), 1622–1633. <http://dx.doi.org/10.1093/cercor/bhr236>.
- Hupé, J.-M., Dojat, M., 2015. A critical review of the neuroimaging literature on synesthesia. *Front. Hum. Neurosci.* 9, 103. <http://dx.doi.org/10.3389/fnhum.2015.00103>.
- Jaeggi, S.M., Buschkuhl, M., Jonides, J., Perrig, W.J., 2008. Improving fluid intelligence with training on working memory. *Proc. Natl. Acad. Sci. USA* 105 (19), 6829–6833. <http://dx.doi.org/10.1073/pnas.0801268105>.
- Jaeggi, S.M., Buschkuhl, M., Jonides, J., Shah, P., 2011. Short- and long-term benefits of cognitive training. *Proc. Natl. Acad. Sci. USA* 108 (25), 10081–10086. <http://dx.doi.org/10.1073/pnas.1103228108>.
- Jiang, Y., Zhou, K., He, S., 2007. Human visual cortex responds to invisible chromatic flicker. *Nat. Neurosci.* 10 (5), 657–662. <http://dx.doi.org/10.1038/nn1879>.
- Jones, J.K., 1965. Colour as an aid to visual perception in early reading. *Br. J. Educ. Psychol.* 35 (1), 21–27.
- Kelly, E.L., 1934. An experimental attempt to produce artificial chromaesthesia by the technique of the conditioned response. *J. Exp. Psychol.* 17 (3), 315–341. <http://dx.doi.org/10.1037/h0074963>.
- Kim, C.-Y., Blake, R., 2013. Revisiting the perceptual reality of synesthetic color. In: *Oxford Handbook of Synesthesia*, 283.
- Kusnir, F., Thut, G., 2012. Formation of automatic letter-color associations in non-synaesthetes through likelihood manipulation of letter-color pairings. *Neuropsychologia* 50 (14), 3641–3652. <http://dx.doi.org/10.1016/j.neuropsychologia.2012.09.032>.
- Ludwig, V.U., Adachi, I., Matsuzawa, T., 2011. Visuoauditory mappings between high luminance and high pitch are shared by chimpanzees (*Pan troglodytes*) and humans. *Proc. Natl. Acad. Sci.* 108 (51), 20661–20665. <http://dx.doi.org/10.1073/pnas.1112605108>.
- Lueck, C.J., Zeki, S., Friston, K.J., Deiber, M.-P., Cope, P., Cunningham, V.J., Frackowiak, R.S.J., 1989. The colour centre in the cerebral cortex of man. *Nature* 340 (6232), 386–389. <http://dx.doi.org/10.1038/340386a0>.
- Maidenbaum, S., Abboud, S., Amedi, A., 2014. Sensory substitution: closing the gap between basic research and widespread practical visual rehabilitation. *Neurosci. Biobehav. Rev.* 41, 3–15. <http://dx.doi.org/10.1016/j.neubiorev.2013.11.007>.
- Mankin, J.L., Simner, J., 2017. A is for apple: the role of letter-word associations in the development of grapheme-color synaesthesia. *Multisens. Res.* <http://dx.doi.org/10.1163/22134808-00002554>.
- Maurer, D., Mondloch, C., 2005. Neonatal synesthesia: a reevaluation. In: Robertson, L.C., Sagiv, N. (Eds.), *Synesthesia: Perspectives from Cognitive Neuroscience*. Oxford University Press, Oxford, UK, pp. 193–213.
- Meier, B., Rothen, N., 2009. Training grapheme-colour associations produces a synaesthetic Stroop effect, but not a conditioned synaesthetic response. *Neuropsychologia* 47 (4), 1208–1211. <http://dx.doi.org/10.1016/j.neuropsychologia.2009.01.009>.
- Merabet, L.B.O., Maguire, D., Warde, A., Alterescu, K., Stickgold, R., Pascual-Leone, A., 2004. Visual hallucinations during prolonged blindfolding in sighted subjects. *J. Neuro-Ophthalmol.* 24 (2), 109–113.
- Muggleton, N., Tsakanikos, E., Walsh, V., Ward, J., 2007. Disruption of synaesthesia following TMS of the right posterior parietal cortex. *Neuropsychologia* 45 (7), 1582–1585. <http://dx.doi.org/10.1016/j.neuropsychologia.2006.11.021>.
- Nakataki, M., Soravia, L.M., Schwab, S., Horn, H., Dierks, T., Strik, W., Morishima, Y., 2017. Glucocorticoid administration improves aberrant fear-processing networks in spider phobia. *Neuropsychopharmacology* 42 (2), 485–494. <http://dx.doi.org/10.1038/npp.2016.207>.
- Odom, J.V., Bach, M., Brigell, M., Holder, G.E., McCulloch, D.L., Tormene, A.P., Vaegan, 2010. ISCEV standard for clinical visual evoked potentials (2009 update). *Doc. Ophthalmol.* 120 (1), 111–119. <http://dx.doi.org/10.1007/s10633-009-9195-4>.
- Pitskel, N.B., Merabet, L.B., Ramos-Estebanez, C., Kauffman, T., Pascual-Leone, A., 2007. Time-dependent changes in cortical excitability after prolonged visual deprivation. *Neuroreport* 18 (16), 1703–1707. <http://dx.doi.org/10.1097/WNR.0b013e3282f0d2c1>.
- Pritchard, J., Rothen, N., Coolbear, D., Ward, J., 2013. Enhanced associative memory for colour (but not shape or location) in synaesthesia. *Cognition* 127 (2), 230–234. <http://dx.doi.org/10.1016/j.cognition.2012.12.012>.
- Radvansky, G.A., Gibson, B.S., McNerney, M.W., 2011. Synesthesia and memory: color congruency, von Restorff, and false memory effects. *J. Exp. Psychol.: Learn., Mem., Cogn.* 37 (1), 219–229. <http://dx.doi.org/10.1037/a0021329>.
- Ramachandran, V.S., Hubbard, E.M., 2001. Synaesthesia: a window into perception, thought and language. *J. Conscious. Stud.* 8 (12), 3–34.
- Rothen, N., Meier, B., 2010. Grapheme-colour synaesthesia yields an ordinary rather than extraordinary memory advantage: evidence from a group study. *Memory* 18 (3), 258–264. <http://dx.doi.org/10.1080/09658210903527308>.
- Rothen, N., Meier, B., 2014. Acquiring synaesthesia: insights from training studies. *Front. Hum. Neurosci.* 8, 109. <http://dx.doi.org/10.3389/fnhum.2014.00109>.
- Rothen, N., Meier, B., Ward, J., 2012. Enhanced memory ability: insights from synaesthesia. *Neurosci. Biobehav. Rev.* 36 (8), 1952–1963. <http://dx.doi.org/10.1016/j.neubiorev.2012.05.004>.
- Rothen, N., Seth, A.K., Witzel, C., Ward, J., 2013a. Diagnosing synaesthesia with online colour pickers: maximising sensitivity and specificity. *J. Neurosci. Methods* 215 (1), 156–160. <http://dx.doi.org/10.1016/j.jneumeth.2013.02.009>.
- Rothen, N., Tsakanikos, E., Meier, B., Ward, J., 2013b. Coloured Letters and Numbers (CLaN): a reliable factor-analysis based synaesthesia questionnaire. *Conscious. Cogn.* 22 (3), 1047–1060. <http://dx.doi.org/10.1016/j.concog.2013.07.005>.

- Rothen, N., Wantz, A.-L., Meier, B., 2011. Training synaesthesia. *Perception* 40 (10), 1248–1250. <http://dx.doi.org/10.1068/p6984>.
- Rouw, R., Scholte, H.S., 2007. Increased structural connectivity in grapheme-color synesthesia. *Nat. Neurosci.* 10 (6), 792–797. <http://dx.doi.org/10.1038/nn1906>.
- Rouw, R., Scholte, H.S., 2010. Neural basis of individual differences in synesthetic experiences. *J. Neurosci.* 30 (18), 6205–6213. <http://dx.doi.org/10.1523/JNEUROSCI.3444-09.2010>.
- Seth, A., 2014. A predictive processing theory of sensorimotor contingencies: explaining the puzzle of perceptual presence and its absence in synesthesia. *Cogn. Neurosci.* 5 (2), 97–118. <http://dx.doi.org/10.1080/17588928.2013.877880>.
- Simner, J., Bain, A.E., 2013. A longitudinal study of grapheme-colour synaesthesia in childhood: 6/7 years to 10/11 years. *Front. Hum. Neurosci.* 7, 603. <http://dx.doi.org/10.3389/fnhum.2013.00603>.
- Simner, J., Harrold, J., Creed, H., Monro, L., Foulkes, L., 2009. Early detection of markers for synaesthesia in childhood populations. *Brain* 132 (1), 57–64. <http://dx.doi.org/10.1093/brain/awn292>.
- Simner, J., Ward, J., Lanz, M., Jansari, A., Noonan, K., Glover, L., Oakley, D., 2005. Non-random associations of graphemes to colours in synaesthetic and non-synaesthetic populations. *Cogn. Neuropsychol.* 22, 1069–1085. <http://dx.doi.org/10.1080/02643290500200122>.
- Sperling, J.M., Prvulovic, D., Linden, D.E.J., Singer, W., Stirn, A., 2006. Neuronal correlates of colour-graphemic synaesthesia: a fMRI study. *Cortex* 42 (2), 295–303. [http://dx.doi.org/10.1016/S0010-9452\(08\)70355-1](http://dx.doi.org/10.1016/S0010-9452(08)70355-1).
- Stroop, J.R., 1935. Studies of interference in serial verbal reactions. *J. Exp. Psychol.* 18, 643–662.
- Terhune, D.B., Murray, E., Near, J., Stagg, C.J., Cowey, A., Cohen Kadosh, R., 2015a. Phosphene perception relates to visual cortex glutamate levels and covaries with atypical visuospatial awareness. *Cereb. Cortex* 25 (11), 4341–4350. <http://dx.doi.org/10.1093/cercor/bhv015>.
- Terhune, D.B., Song, S.M., Cohen Kadosh, R., 2015b. Transcranial alternating current stimulation reveals atypical 40 Hz phosphene thresholds in synaesthesia. *Cortex* 63, 267–270. <http://dx.doi.org/10.1016/j.cortex.2014.09.006>.
- Terhune, D.B., Tai, S., Cowey, A., Popescu, T., Cohen Kadosh, R., 2011. Enhanced cortical excitability in grapheme-color synesthesia and its modulation. *Curr. Biol.* 21 (23), 2006–2009. <http://dx.doi.org/10.1016/j.cub.2011.10.032>.
- Tomson, S.N., Avidan, N., Lee, K., Sarma, A.K., Tushe, R., Milewicz, D.M., Eagleman, D.M., 2011. The genetics of colored sequence synesthesia: suggestive evidence of linkage to 16q and genetic heterogeneity for the condition. *Behav. Brain Res.* 223 (1), 48–52. <http://dx.doi.org/10.1016/j.bbr.2011.03.071>.
- Wagner, K., Dobkins, K.R., 2011. Synaesthetic associations decrease during infancy. *Psychol. Sci.* 22 (8), 1067–1072. <http://dx.doi.org/10.1177/0956797611416250>.
- Ward, J., 2013. Synesthesia. *Annu. Rev. Psychol.* 64 (1), 49–75. <http://dx.doi.org/10.1146/annurev-psych-113011-143840>.
- Ward, J., Li, R., Salih, S., Sagiv, N., 2007. Varieties of grapheme-colour synaesthesia: a new theory of phenomenological and behavioural differences. *Conscious. Cogn.* 16 (4), 913–931. <http://dx.doi.org/10.1016/j.concog.2006.09.012>.
- Ward, J., Meijer, P., 2010. Visual experiences in the blind induced by an auditory sensory substitution device. *Conscious. Cogn.* 19 (1), 492–500. <http://dx.doi.org/10.1016/j.concog.2009.10.006>.
- Ward, J., Simner, J., 2005. Is synaesthesia an X-linked dominant trait with lethality in males? *Perception* 34 (5), 611–623. <http://dx.doi.org/10.1068/p5250>.
- Ward, J., Wright, T., 2014. Sensory substitution as an artificially acquired synaesthesia. *Neurosci. Biobehav. Rev.* 41, 26–35. <http://dx.doi.org/10.1016/j.neubiorev.2012.07.007>.
- Watson, M.R., Akins, K., Spiker, C., Crawford, L., Enns, J.T., 2014. Synesthesia and learning: a critical review and novel theory. *Front. Hum. Neurosci.* 8. <http://dx.doi.org/10.3389/fnhum.2014.00098>.
- Watson, M.R., Chromý, J., Crawford, L., Eagleman, D.M., Enns, J.T., Akins, K.A., 2017. The prevalence of synaesthesia depends on early language learning. *Conscious. Cogn.* 48, 212–231. <http://dx.doi.org/10.1016/j.concog.2016.12.004>.
- Weiss, P.H., Toni, I., Shah, N.J., Fink, G.R., Zilles, K., 2000. Color perception in synaesthesia: an fMRI study. *NeuroImage* 11 (5, Supplement 1), S725. [http://dx.doi.org/10.1016/S1053-8119\(00\)91655-0](http://dx.doi.org/10.1016/S1053-8119(00)91655-0).
- Withoft, N., Winawer, J., 2006. Synesthetic colors determined by having colored refrigerator magnets in childhood. *Cortex* 42 (2), 175–183. [http://dx.doi.org/10.1016/S0010-9452\(08\)70342-3](http://dx.doi.org/10.1016/S0010-9452(08)70342-3).
- Withoft, N., Winawer, J., 2013. Learning, memory, and synesthesia. *Psychol. Sci.* 24 (3), 258–265. <http://dx.doi.org/10.1177/0956797612452573>.
- Withoft, N., Winawer, J., Eagleman, D.M., 2015. Prevalence of learned grapheme-color pairings in a large online sample of synesthetes. *PLoS One* 10 (3), e0118996. <http://dx.doi.org/10.1371/journal.pone.0118996>.
- Yan, Y., Rasch, M.J., Chen, M., Xiang, X., Huang, M., Wu, S., Li, W., 2014. Perceptual training continuously refines neuronal population codes in primary visual cortex. *Nat. Neurosci.* 17 (10), 1380–1387. <http://dx.doi.org/10.1038/nn.3805>.
- Yaro, C., Ward, J., 2007. Searching for Shereshevskii: what is superior about the memory of synaesthetes? *Q. J. Exp. Psychol.* 60 (5), 681–695. <http://dx.doi.org/10.1080/17470210600785208>.
- Zeki, S., Watson, J.D., Lueck, C.J., Friston, K.J., Kennard, C., Frackowiak, R.S., 1991. A direct demonstration of functional specialization in human visual cortex. *J. Neurosci.* 11 (3), 641–649.