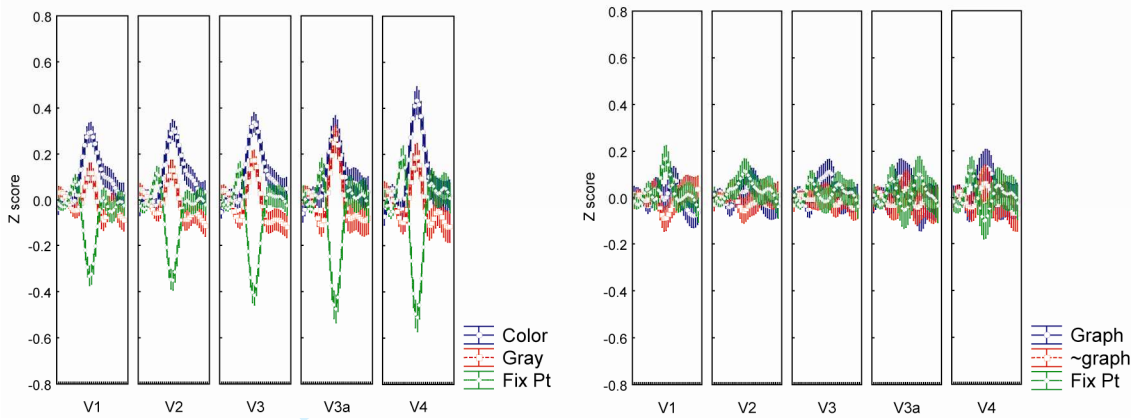
Supplementary Figure S1: Response time course averaged across subjects in retinotopic areas for the Mondrian (left) and the Synesthesia (right) protocols.



Data averaged on both sides (we did not observe any difference) and 10 synesthetes. Error bars represent 95% confidence intervals. Timeline: 4s before to 12s after the beginning of the presentation of the stimulus.

Supplementary Text S1: Definition of Synesthesia

Many kinds of synesthetic associations exist. In the paradigmatic case of colored audition, auditory stimuli induce experiences of color. Almost any combination of senses can be associated in this way, although there is a dominance of visual synesthetic sensations of color (Day 2005; Flournoy 1893). Our formal definition of synesthesia (based on phenomenology alone) is a condition in which a mental experience, which may be perceptual, emotional or imaginative, is a sufficient automatic cause of an arbitrary, idiosyncratic experience in a sensory modality, which is the same as or different to that the original mental state may be in (Macpherson 2007). Examples of types of synesthesia that fulfill this definition include not only canonical ones like colored hearing, but, and much more frequent, colored graphemes, number-

lines (Galton 1883) and personifications of numbers and letters (Flournoy 1893). (It however excludes both 'ticker-tape synesthesia', where speech is experienced as subtitled in the mind's eye, and mirror–touch 'synesthesia' (Blakemore et al. 2005) because in both cases associations are not arbitrary. Note that some grapheme-color associations are found more often than predicted by chance - e.g. (Rich et al. 2005; Simner et al. 2005) - and are therefore not completely random; but to rather add color or texture to a grapheme is arbitrary, and no two synesthetes share the exact same code.) These frequent synesthetic associations are not cross-modal. However, we note that synesthetes who do have cross-modal synesthesia also often possess such symbolic synesthesia – an empirical argument in favor of such a wide definition. Synesthetes often possess several types of synesthesia, and that was the case of our synesthetes. Compared to metaphorical or learned associations, synesthetic associations are considered to possess an additional phenomenological quality. Such qualitative experience also differentiates the direction of the association: when a synesthete reports that a precise color perceived in the environment reminds her or him of a number or a letter that has precisely that synesthetic color, such reciprocal association is however usually implicit, even though it may be demonstrated with objective methods (Cohen Kadosh and Henik 2006; Rothen et al. 2010).

Identification of synesthetic associations is based on first-person reports. Skeptical minds not familiar with synesthesia may consider the possibility that such reports may be delusional or metaphorical. Formal validation of synesthetic associations is usually provided by the 'test of genuineness' (Baron-Cohen et al. 1993), consisting in a surprise retest of associations. Consistency of associations is systematically higher for synesthetes compared to non-synesthetes (Asher et al. 2006; Eagleman et al. 2007). Such validation is in fact a bit superfluous, since in our experience it never revealed any 'fake' synesthete. The evidence of synesthesia as a real phenomenon comes readily from the thousands of independent and converging reports

that have been gathered over more than two centuries (Baron-Cohen and Harrison 1997; Cytowic 2002; Dann 1998; Flournoy 1893; Galton 1883; Suarez de Mendoza 1890), since the first documented and unambiguous description of synesthesia in 1812 by G.T.L. Sachs (Dann 1998; Jewanski et al. 2009; Suarez de Mendoza 1890). Galton indeed did not doubt of the 'authenticity of independent statements [(first person reports)] which closely confirm one another', and he suggested that synesthetes could be detected at a glance: 'every now and then I meet with persons who possess the faculty, and I have become familiar with the quick look of intelligence with which they receive my question' (Galton 1883). Our experience after meeting hundreds of synesthetes is very similar to Galton's.

Supplementary Text S2: Detailed phenomenology

We used questionnaires to identify the types of synesthesia experienced by our subjects. For all our synesthetes, grapheme-color was their main synesthetic association, and it was strong enough, according to their reports, so they could possibly belong to the 'projector' category: most claimed to 'see' the color, not just thinking about it or imagining it, when reading (achromatic) graphemes. However, most of them were ambiguous about what 'seeing' meant in this context. We tried associator/projector questionnaires and obtained what we consider as contradictory answers for most of them (like the synesthetic color being reported both on the page and in the mind's eye). Extensive semi-directed interviews did not help clarifying this issue. Only one subject would have been unambiguously classified as a projector on the basis of every questionnaire and interview (syn04: she was also the one with the strongest associations). For two other subjects, it seemed that they would 'project' the colors of only a few graphemes, but not systematically. These subjects had also among the strongest associations, confirming that

our objective measure of synesthetic strength captured somehow the associator/projector distinction, as proposed by Dixon and colleagues (Dixon et al. 2004) and Ward and colleagues (Ward et al. 2007).

All subjects had other synesthetic associations: colors for the days of the weeks and/or months (8 subjects), personifications of graphemes (8 subjects), colors associated with people or their feelings (5 subjects) but not as strong as taking the form of 'auras' (or only faintly). Several subjects reported multimodal associations like some visual sensation for sounds (4 subjects), tasted words (1 subject), or even touch sensations triggered by colors for our color-blind grapheme-color synesthete. He reported that colors (when imagined for most of them, supposedly) could trigger a touch sensation. Red would feel like fur, green like soft plastic, blue like rubbing, and violet like pressure. This sensation was localized: red on the arms, green on the thumbs and palms, blue on the skull and scalp, violet on the face (especially the cheeks), yellow within the mouth, under the teeth and against the cheeks. Such synesthesia evokes Nabokov's 'color-induced pain, a rare form of visual-tactile synesthesia' (Dann 1998): 'the mere sight of [a golden satin sofa] caused a laciniate shiver to branch from my spine' (p.226) (Nabokov 1966). Only 3 subjects experienced number lines. For at least one synesthete, graphemes were not only colored but had also clear textures. Most subjects seemed to have relatively strong mental imagery. We unfortunately did not have any objective test, but 8 of them claimed to 'see' what they imagine.

Supplementary Text S3: Color centers

An area called V4 (or V8, or V4 complex including V4alpha) is often considered as the 'color center' (reenacting somehow the XIXth century localizationist idea that there is a specific area devoted to color perception). Neuropsychological evidence showed indeed that patients could suffer from a specific loss of color perception. Even though the diversity of lesions could not point to a precise area, lesions consistently encompassed the ventral part of the occipital cortex (Bartels and Zeki 2000), where one can also observe stronger BOLD responses to colored stimuli compared to gray ones. Specifically, the majority of retinotopic areas produce stronger BOLD responses to colored Mondrian stimuli, in comparison to gray stimuli of the same average luminance, but with the stronger differential activation consistently appearing ventrally, along the fusiform and sometimes collateral sulci, usually overlapping retinotopically defined V4. However, there is no guarantee that such regions are specifically involved in the building up of color perception, since a 'stronger' activation (that is, practically, lower p-values for a specific experimental design) is difficult to be translated readily in functional terms. Some studies have tried more stringent tests to localize the neural bases of color perception with fMRI, including paradigms on color constancy (Bartels and Zeki 2000), color after-images (Hadjikhani et al. 1998; Sakai et al. 1995) or orientation-contingent color aftereffects (Morita et al. 2004). Also Brouwer and Heeger (Brouwer and Heeger 2009) used multivariate pattern classification techniques to test the decoding power of voxels for specific colors in the visual cortex. Then they applied a principal component analysis to derive color spaces from voxel covariations in the different parts of the visual cortex. Bartels and Zeki (Bartels and Zeki 2000) found that V4 and V4alpha (that they described as a non-retinotopic area anterior to V4, but which may correspond to later retinotopically defined VO1) were specifically involved in color constancy mechanisms. Sakai and colleagues (Sakai et al. 1995) and Hadjikhani and colleagues (Hadjikhani et al. 1998)

observed significant BOLD signal related to color after-images respectively in the posterior fusiform gyrus (anatomically corresponding to 'V4') and in V8 (defined as the area anterior to retinotopic V4 horizontal meridian); Morita and colleagues (Morita et al. 2004) observed that the posterior and anterior parts of the left 'V4' (called that way but not defined retinotopically) color centers were involved respectively in the induction of the color after-effect and in conscious color perception, while the right V4 was modulated by attention to color. Brouwer and Heeger (Brouwer and Heeger 2009) observed that color spaces derived from signal in V4 and VO1 were in agreement with the perceptual color space in some subjects, while that was never the case for lower order areas (their technique did not allow them to test non retinotopic regions, for example anterior to VO1). Single neurons recorded in monkeys also show precise hue tuning in V4 (Zeki 1973), while V1 neurons exhibit only color biases without hue invariance. Interestingly, Conway and colleagues (Conway et al. 2007) showed that color-biased hot spots identified by fMRI and distributed within the posterior inferior temporal cortex of monkeys (that is small parts – they called them globs - of V4, PITd, and posterior TEO) contained cells showing strong luminance-invariant color tuning. Moreover, this neuronal population contained an explicit representation of non-reducible 'unique' hues (red, green, yellow, and blue) corresponding to color perception (Stoughton and Conway 2008). Altogether, these and other studies indicate therefore a broad anatomical agreement between the 'color' areas in and anterior to V4 revealed by yet poorly specific protocols contrasting color and gray stimuli (like our Mondrian protocol that simply picks up the 'tip of the iceberg' of color processing) and areas functionally involved in color perception.

However, we and others (e.g. Brewer and colleagues (Brewer et al. 2005); see also Conway and colleagues (Conway et al. 2007) for monkey data) observed some variability in the precise anatomical (and even functional in terms of retinotopic properties) location and number of

'color hot spots' identified by Mondrian protocols in individual subjects. We observed in our data set that a subject may not have any hot spot in retinotopically defined V4, another subject only in V4, yet another one may have hot spots only on the right side, etc … (of course, a 'hot spot' depends on the statistical power and threshold). Functional localization of the color centers in and anterior to V4 may be correct on average, but it may be more precise and diverse at the individual level. And are three color centers found bilaterally (total = 6) in an individual functionally equivalent to a single, unilateral color center observed in another? Some of the variations across individuals may be artefactual, as the consequence of different noise level, statistical power or magnetic field local heterogeneities (Winawer et al. 2010). But our impression is that individual variability is real, and that the neural bases of color perception may be both more distributed and variable across subjects than suggested by the concept of one or two color centers in and anterior to V4. It may explain, for example, why Brouwer and Heeger (Brouwer and Heeger 2009) could not derive a perceptual color space from signal in V4 and VO1 in every subject. Maybe in those subjects hue perception was achieved only in color hot spots anterior to VO1.

Hence, if one considers that such 'tips of the iceberg' as measured with fMRI Mondrian protocols are functionally important for color perception, specific 'color Regions Of Interest' (ROI) should be defined for each subject. We note that all previous studies on synesthesia used the same ROI for all synesthetes (defined either after a group contrast and spatial smoothing or on the basis of retinotopy).

Supplementary Text S4: Detailed Experimental Procedures

Psychophysics experiments: details of the Synesthetic Stroop procedure and data analysis

We asked synesthetes to name as quickly as possible either the 'real' color ('color of the ink') or the idiosyncratic synesthetic color (the 'photism') of individual graphemes.

Stimuli and procedure

We presented graphemes on a computer screen controlled with a PC running Windows XP and a homemade software written in C++ and using the SDL library for precise control of timing. Graphemes had a maximum diameter of 1.5 deg; they were presented for 160 ms either 5 deg right or left of the central fixation point (7 subjects), or centrally (3 subjects: one of them ran the central and the lateral condition in different blocks). We tailored the tests to each individual subject. We first selected 8 graphemes with easy-to-name colors, if possible red/green/blue/yellow (2 graphemes for each color), also avoiding first-letter interference (for example excluding the letters 'R' and 'B'). Graphemes were presented either with their exact synesthetic color (congruent condition) or with the exact synesthetic color of one of the other selected graphemes (incongruent conditions). Since color choice was dependent on each subject, luminance, contrast and saturation were not the same for different subjects. Absolute response times were therefore not comparable between subjects. The design was however balanced so for each subject the average luminance and contrast were identical in the congruent and incongruent conditions.

In a first block, subjects were asked to name the ('real') printed color as fast as possible. They could correct their response if realizing they were making an error. In a second block and after some delay (usually several hours), subjects were asked to name the synesthetic color of

the graphemes (which we call the 'photism') as fast as possible. Subjects had not been warned before the first experiment that there would be such a task change. Stimuli were exactly the same in the first and second block, but they were presented in a different random order. There were either 144 (central presentation) or 288 trials for each block. Half of them had congruent colors. The experimenter triggered a stimulus as soon as the verbal response was given for the previous stimulus, but sometimes varying the delay to avoid a rhythmic presentation of the stimuli. Every 20 trials, there was a longer pause, and the experimenter pushed the subject to try to respond faster. The goal was to avoid that the subject delayed his/her response to prevent errors, since in that case Stroop effects are not visible.

Data analysis

Responses were continuously recorded with a microphone connected to the computer. A photodiode was placed on the bottom of the computer screen, where a black square was turned to white as long as the grapheme was presented on the screen. The photodiode signal was recorded simultaneously on the audio channel. Both channels were acquired with Audacity software, amplified independently and analyzed offline in Matlab (Mathworks, Inc., Natick, MA). An interactive homemade software developed in Matlab allowed us to check the accuracy of the responses and measure the exact vocal response time, taken as when the low-pass filtered voice power reached 20% of the max power of each verbal response. Each response time was verified and corrected 'manually' when necessary (for example if there was a loud enough noise before the verbal response – sometimes just opening the mouth in anticipation was enough to reach the 20% criterion) or when the subject corrected a wrong response (typically, subjects sometimes started to name the wrong color and then said the correct color); such trials were considered as 'correct' but had typically a longer latency. This procedure allowed us to include

almost all trials in the latency analysis. The inverse of the response times were analyzed within an ANOVA model (we verified that the residuals were approximately normally distributed; that was not case without any transformation or with a LOG transformation of RTs). We did not find any effect of the stimulus position (left, central or right: for such a study on a larger population, see Ruiz, M. J., & Hupé, J.-M.: "Synesthetic colors in grapheme-color synesthesia are probably not lateralized". Society for Neuroscience Abstracts, 380.384, 2009).

We measured the difference of average response time for congruent and incongruent trials, for each task, as well as the difference of average response time for both tasks in the congruent condition. We reasoned that for a weak synesthetic association, naming the printed color should be fast and only slightly delayed by incongruent synesthetic colors, while naming the synesthetic color should be slower and strongly delayed by incongruent printed colors. The opposite pattern of results is expected for strong synesthetic associations. We did indeed observe such patterns of response that were stable in individual subjects (a couple of subjects ran the same experiment again after a year delay), confirming the group analyses performed by Dixon and colleagues (Dixon et al. 2004) and Ward and colleagues (Ward et al. 2007). We derived from these measures a unique index, based on effect sizes measured on 1/RT, as described in the main text.

MR data acquisition and preprocessing

We acquired high-resolution structural images on a Bruker 3T Medspec S300 whole body scanner using a T1-weighted 3D MP-RAGE sequence, which was optimized based on Deichmann and colleagues (Deichmann et al. 2000). For each subject we acquired 176 sagittal partitions in two segments with an image matrix of 256x112 (read x phase). Further imaging sequence parameters were: TR/TE/TI: 16/4.96/903 ms, excitation pulse angle: 8°, acquisition matrix:

256x224x176 (CC, AP, LR), fast phase encoding direction: AP (112 steps per RAGE train, 2 segments), slow phase encoding direction: LR, isotropic nominal resolution: 1mm, BW= 130Hz/Px, readout direction: CC, number of averages: 1 and total measurement time: 14min 40s. The data for the control group were originally acquired for a functional study investigating primary motor cortex representation (Pizzagali, F., Dojat, M., Troprès-Broux, I. & Delon-Martin, C. Human representation in human M1 revealed using 3T high resolution fMRI and diffeomorphic registration. In: Human Brain Mapping conference, 2010, Barcelona, Spain).

We acquired functional data during retinotopic, color and grapheme stimulus presentations using a 2D, gradient-recalled echo (GRE), multi-slice, EPI MR sequence (TR/TE: 2000/30 ms, excitation pulse angle: 77°, acquisition matrix: 72x64 (AP, LR), isotropic nominal resolution: 3 mm, 30 adjacent contiguous slices, thickness 3 mm). Because assigning functional responses to a surface model of the cortex is particularly sensitive to geometric distortions of the 3D functional data due to static field inhomogeneity (Vasseur et al. 2010), we corrected all the functional images for the geometric distortions and realigned them with respect to the first one of the series. We performed the conjoint field correction and realignment procedure with SPM8 Unwarp toolbox (http://www.fil.ion.ucl.ac.uk/spm). Then, we aligned all EPI data sets to the structural data set using the SPM8 rigid body coregistration procedure. We used the algorithms BET (http://www.fmrib.ox.ac.uk/fsl/bet2/index.html) (Smith 2002) to extract the brain and LOCUS (Scherrer et al. 2009) to segment the gray matter from the white matter. Further processing steps were performed in parallel in BALC (Warnking et al. 2002) and Brain Voyager QX 2.1 (BV). We used the retinotopic maps and statistics obtained in BV for all Region of Interest analyses and time course exportation. Group analyses were performed using DARTEL, SPM8 and SnPM (see below).

We created flat maps of the whole cortex in Brain Voyager using the default pipeline, but skipping BV tissue segmentation since that was already done. Manual editing of the gray/white matter border was often required (most often to remove holes in the frontal regions, around the anterior commissure, that violated the algorithm assumption of a single gray matter surface). We also paid much attention to the segmentation in the ventral cortex around area V4. We noted that small ventral circumvolutions were often lost by BV smoothing process of the gray/white matter border. We used functional activations by colors for each subject in order to help identifying these critical regions, and we tried to expand the gray matter of these circumvolutions so they will be kept on the gray matter surface. We were only partly successful, so we could not guarantee that color functional activations observed in the volume would systematically project on the flat map. Therefore, we used flat maps only to define retinotopic areas. These areas were back projected in the volume in order to identify the location of color activations relative to retinotopic areas (in particular V4).

Retinotopic mapping

Stimuli and procedure

We created the visual stimuli in Matlab and controlled their display during the experiment with a PC running Windows XP and a homemade software written in C++ and using the SDL library for precise control of timing. Image presentation was synchronized to pulses sent by the scanner at the beginning of each TR. Stimuli were back-projected using a video-projector (Epson 7250M, Epson Inc., Long Beach, CA) on a translucent screen positioned at the rear of the magnet. Subjects viewed this screen via a mirror fixed on the head coil. Viewing distance was 222 cm. We performed the spectral and luminance calibrations of the display with a PR-650 SpectraScan Colorimeter (Photoresearch).

We acquired four retinotopic functional scans, one for each of the directions of motion of rings (for mapping of eccentricity in the visual field) and wedges (for mapping of the polar angle). Stimulus parameters were the same as described by Warnking and colleagues (Warnking et al. 2002): black and white checkerboards flickering at 4 Hz, 32s cycle period, 3 deg maximum eccentricity. Stimulus presentation started concomitantly with dummy MR excitations about 10 s prior to effective MR data acquisition so as to enable immediate response detection.

In order to help fixation (which was monitored continuously), subjects had to press a button each time the very small (just visible) fixation cross at the center of the display would briefly either change of color (from black to green and back to black) or shape (form + to x and back to +). However we asked subjects to try to span their spatial attention on the whole stimulus, as much as they could.

Data analysis

Once the preprocessing steps were achieved in SPM8, the EPI images were exported to BV software (thanks to Denis Fize at CerCo, who helped us with the tricky exportation procedure into BV non conventional 3D space). We first applied in BV a low trend removal and a high pass temporal filter (2/cycle) to each scan. Then we averaged (using Matlab) the two wedges and rings recordings, one of them being read backwards before averaging. This procedure is convenient to obtain sinusoidally modulated signals within retinotopic areas. Moreover, it gets rid of any variation of the hemodynamic lag across voxels (Warnking et al. 2002). Back in BV, we computed correlation analyses with a sinusoidal function with 16 lags to obtain power and phase maps for both the eccentricity and the polar mapping. Phase maps were thresholded at a correlation of 0.2 and projected on the cortical flat maps. Then we drew by hand the borders between visual areas (identified as phase reversals) on the polar phase maps, with simultaneous

visualization of the eccentricity map to insure that the borders ran perpendicularly to the eccentricity gradient. For every subject and hemisphere, we observed a half-field representation both ventrally and dorsally after the third phase reversal. This easy landmark helped us to identify areas V4 in the ventral cortex and V3a in the dorsal cortex in every subject. Dorsally and next to V3, other retinotopic areas (V3b, LO1, LO2) could have been identified in several but not all subjects unambiguously. Similarly, we observed areas VO1 and VO2 ventrally in a few subjects.

Mapping of color centers (Mondrian protocol)

Stimuli and procedure

We created the stimuli in Matlab and controlled their display during the experiment with a PC running Windows XP and a homemade software written in C++ and using the SDL library for precise control of timing. Mondrian stimuli were presented centrally and extended 8 * 6 degrees (see Figure 2 in the main text). The rectangular field was divided in 23 rectangles of various sizes. The rectangles were either assigned random chromaticities at equiluminance (chromatic event, each rectangle had the same luminance) or random luminance (achromatic event). The only constraint on the choice of chromaticities and luminances for each set is for the average luminance of each stimulus (400 cd/m^2) to be equal to the background. Such stimuli are similar to those used in most color and synesthetic color fMRI studies (Conway et al. 2007; Hadjikhani et al. 1998; Hubbard et al. 2005; Nunn et al. 2002). The protocol was event related, with a random sequence of an equal number (24) of colored, achromatic patterns and fixation points ('Null' condition). We designed the event sequence so as to optimize the efficiencies of the estimation both of the main and of the differential effects (Friston et al. 1999). Images were presented for 1s every 2.5s. Two (3 subjects), four (6 subjects) or even six (1 subject, in 2

sessions over a year) runs each lasted 3.30min (starting with 10s dummy recording and then 10s fixation point, and ending with 10s fixation point). We asked subjects to fixate the cross at the center of the image all the time while paying attention to the whole stimulus. To help controlling attention level, they had to press a button each time another cross (the 'target') appeared briefly at a random position on the stimulus. They were 9 targets within each run, 3 appearing randomly for each condition (fixation point, gray, color), that is 1 out of 8 images.

Data analysis

We performed the statistical analysis in BV once the preprocessing steps were achieved in SPM8. For each subject, we used a conjunction contrast: we considered voxels as active if they responded more to both colored and achromatic Mondrian compared to the fixation point, and more to colored than achromatic Mondrians. We added a predictor based on eye blinks (blink events convolved with a canonical hemodynamic function) as a non-interest factor (see below: eye tracking). For each subject, we first set the threshold at the 0.05 FDR level (False Discovery Rate), which value ranged between t = 3.37 and t = 5.21 (average t = 4.31). At least one cluster of voxels in the ventral cortex reached that threshold in 6 out of our 10 subjects, within or anterior to retinotopically defined V4 ('V4topo'). Then we increased the threshold in order to capture a larger number of color 'hot spots' within the ventral cortex, in or anterior to V4 (threshold values ranged between t = 2 and t = 3.9, average t = 3.18). Other 'hot spots' were sometimes present at these lower thresholds in V1, V2 or V3, in the dorsal visual cortex as well as (rarely) outside of the visual cortex. Their locations were never even approximately consistent across subjects. We ignored these regions, since we were interested specifically in the specialized color regions of the ventral cortex. We verified that the average response to chromatic Mondrians was well above the average response to achromatic Mondrian in each ROI

(average t = 4.59, range [2.76 6.34]). Each subject had between 1 and 7 ROIs. Each ROI comprised between 3 and 330 voxels (72 voxels on average). For most subjects, ROIs lay in V4 and/or putative VO1/VO2. In 2 subjects, a cluster appeared more laterally to V4/VO1 (Brewer et al. 2005), and in 2 other subjects there was a cluster much more anterior, on the right side, in one case in the anterior collateral sulcus and in the other in the sub-hippocampal region.

The peri-stimulus time histogram (PSTH) in Figure 2 (top right) of the main text illustrates the strength of the average response to colors in all the ROIs. Such a PSTH was constructed by first extracting the time course for each run averaged within each ROI, for each subject. Time course was converted to z-score, cut around each event, and the average signal during the 4s before stimulus ('baseline') was subtracted (such a normalization was in fact of little use because all events were well balanced; the curves were similar when not removing the baseline). Event frequency was much faster than the time course of the hemodynamic response, but the optimized and balanced pseudo-random sequence of the 3 events (colored Mondrian, gray one or fixation point) guaranteed little contamination between events (a deconvolution analysis would have been more rigorous but was not necessary for our illustration purpose). Signal decrease for the fixation point is due to z-score normalization. For the Mondrian protocol, we obtained 9465 traces this way, which we analyzed in Statistica 8, allowing us to factor out subject variability. We also regrouped the ROIs as belonging to V4topo or anterior to it, and either on the left or right side (only 8 subjects could be included in these analyses). Time courses to all conditions were very similar in these grouped ROIs.

We also performed a group analysis after registering each brain to the average brain of our population (DARTEL software, see 'Voxel-based morphometry' in the main text). The analysis with either SPM8 or SnPM (Non-parametric Statistic Mapping) revealed no active voxel when controlling strictly for multiple comparisons (Family Wise Error = 0.05), confirming the individual

variability of the individual locations of the color hot spots. Relaxing the statistic threshold revealed a first cluster around V4topo on the right side (MNI X = 23 Y = -78 Z = -9) and then a second cluster around V4topo on the left side (MNI X = -26 Y = -81 Z = -9), confirming the many studies that showed such an average activation when sufficient data are pooled with enough spatial smoothing. But we note that such an average activation does not mean that there is a single 'color' center, or that it lies specifically within V4topo or anterior to it.

Grapheme response in individual subjects (Synesthesia protocol)

We performed the same analyses as for the Mondrian stimuli, looking for voxels that responded more to graphemes than pseudo-graphemes. We found in half of our subjects (5 out of 10) one (or two in one of them, for a total of 6 clusters across 10 subjects) cluster of voxels that each reached both the 0.05 FDR level and a non-corrected 0.001 threshold (conjunction contrast as for the Mondrian protocol). Four of these clusters were in the frontal cortex (3 on the left, one medial), the other two in the left parietal cortex. The anatomical locations were even not consistent across subjects, and none of these areas responded more to colored than gray Mondrian stimuli (at a non-corrected p = 0.05, performed within each ROI). We also identified a total of 20 ROIs that responded more to graphemes at the non-corrected 0.001 threshold (t=3.34) and 13 more at 0.01 (t=2.60; we used such a high threshold in 4 subjects because no voxel was active at 0.001). Only two of these ROIs responded more to colored Mondrian, but another one responded more to gray ones. Importantly, there was no anatomical consistency across subjects, and most of the ROIs were not located in the visual cortex (14 ROIs in frontal cortex, 4 in parietal cortex; most on the left side). Only 3 subjects had a unilateral (2 on the left side) ROI in the ventral part of the temporal cortex, more or less anterior to VO2 (so in a location loosely compatible with a region involved in grapheme processing (Joseph et al.

2006)). Again, there was no response to colored Mondrians. Altogether, we did not have any strong evidence that any region responded more to graphemes than pseudo-graphemes. Those that did (at a high statistical threshold, but more data may have shown that the differences were real) seemed in any case not involved in color perception.

Our lack of identification of any 'grapheme area' may come as a surprise for the reader of Hubbard and colleagues (Hubbard et al. 2005). In fact, the relevant literature is far from being clear-cut on that issue. First of all, since we are not even convinced that 'color perception' is both strongly and precisely localized in the visual cortex (**Text S3**), we should be surprised if the coding of individual graphemes, an exquisite expertise developed by our brains but without any genetic modification (Dehaene et al. 2005), were localized. Indeed, it does not appear to be strictly localized in the visual cortex when contrasting letters with pseudo letters (Longcamp et al. 2003). For example Vinckier and colleagues (Vinckier et al. 2007) observed that only the processing of *strings* of letters might be localized in the ventral cortex (in a 'visual word form area', VWFA). Hubbard and colleagues (Hubbard et al. 2005) had identified their grapheme area anterior and adjacent to V4. They did that by excluding retinotopic areas from their localizer analysis, but their figures showed that in fact most visual areas responded more to graphemes than false fonts – an argument against precise localization. Moreover, anterior and adjacent to V4 lies VO1, an area still much involved in color processing (Brewer et al. 2005; Brouwer and Heeger 2009), and a close inspection of the supplemental data of Hubbard and colleagues (Hubbard et al. 2005) reveals that the average time course of the BOLD response in their 'grapheme area' was very similar for pseudo-graphemes and letters, and only slightly larger for numbers. In fact, if there is any localization for graphemes, it should lie much more anteriorly, since anterior to the VWFA (Joseph et al. 2006).

Eye tracking

We monitored the position of the left eye over the course of all the experiments with an ASL EyeTracker 6000. At the beginning of the scanning sessions, subjects had to fixate red points displayed on a 9 points grid for off-line calibration. We analyzed and inspected visually all the traces at a resolution of 10s / screen width, using interactive software developed in Matlab (Hupé et al. 2009). We devoted much attention to identify blinks faithfully, using pupil size as well as vertical position and speed information. In every subject, we observed blink related activation in the visual cortex whatever the protocol. Peak activations were located in the anterior part of the calcarine sulcus and along the parieto-occipital sulcus (Bordier, C., Dojat, M., & Hupé, J.-M.: "BOLD activation in the visual cortex for spontaneous blinks during visual tasks". Journal of Vision 2010 10(7): 902 [abstract]). We observed very few saccades and systematic deviations from the fixation point, but the relatively poor signal quality prevented us to use eye position and saccades as regressors for functional analyses.

Supplementary References

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