

# Pupillary responses to coloured and contourless displays in total cerebral achromatopsia

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**In two patients with total acquired cortical colour blindness and in six control subjects we studied the binocular pupillary response to a variety of sharply defined coloured and grey displays that either had the same mean luminance as the background (isoluminant) or were of greater mean luminance. Despite their complete inability to identify or to discriminate between colours the patients, like the control subjects, showed a pupillary response to the structured coloured displays, even when they were masked by dynamic luminance changes. However, and unlike the control subjects, the patients showed no pupillary response when the coloured displays lacked sharp chromatic borders, as in Gabors or Gaussians. The results indicate that although chromatic processing still occurs in cortical colour blindness its function is solely to give rise to the detection of sharp boundaries which, in their case, can provide the perception of shape but not hue. In accordance with this, the patients could no longer describe the isoluminant borderless figures, which were often totally invisible to them despite their strong chromatic contrast with the background.**

**Keywords:** colour; cerebral achromatopsia; pupillometry; awareness

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## Introduction

Cerebral achromatopsia, or cortical colour blindness, is the loss of colour vision as a result of brain damage. Despite their colour blindness the patients retain three functional cone mechanisms (Mollon *et al.*, 1980), as shown by the increment threshold technique of Stiles (1978), and the deficit is clearly of cerebral, not retinal, origin. Typically, patients cannot match, discriminate, sort or name colours and they perform randomly on the Farnsworth–Munsell 100-Hue test which requires placing isoluminant coloured chips in chromatic order, 20 chips in each of the red, green, yellow and blue parts of the colour circle. But they are able to sort grey chips in order of luminance. The deficit exists in varying degrees of severity, almost certainly related to the extent of the cortical damage, but the present report is restricted to two cases of complete cortical colour blindness.

It is now evident that even patients with dense achromatopsia can, at first sight paradoxically, use wavelength variations to determine other aspects of the visual scene. An early example was provided by Mollon *et al.* (1980), who discovered that patient M.S. was unable to read the Ishihara pseudoisochromatic plates at conventional reading

distance but could do so when they were presented at 2 m. The test involves recognizing a numeral defined by coloured dots embedded in similar dots of varying lightness. At reading distance, the chromatic border which defines the numeral is masked by the luminance contour of all the individual dots. But at distances where the latter are no longer individually resolvable or when the display is optically blurred (Heywood *et al.*, 1991) patient M.S. could detect the now dominant chromatic boundary and identify the hidden figure. Subsequently (Heywood *et al.*, 1991) he was shown two rows of identical isoluminant coloured patches but in one row they were in chromatic order and in the other they were jumbled. When the colours in each row touched each other he could do the task but not when they were a few millimetres apart. Presumably he could tell the difference between jumbled and ordered arrays when the stimuli abutted by detecting, and distinguishing the salience of chromatic boundaries, where, in the jumbled array, adjacent isoluminant hues would inevitably be more widely separated in colour space and give rise to greater chromatic contrast. Chromatic borders between isoluminant hues are therefore visible to M.S. even when the two

hues cannot be perceptually distinguished. But when the colours are a few millimetres apart, the chromatic border is replaced with an identical and conspicuous white border between all adjacent colours and the discrimination becomes impossible for him. This possible ability to detect chromatic boundaries would also explain how M.S. can perceive shape derived solely from colour even when the display is luminance masked (Heywood *et al.*, 1994). A similar dissociation was reported in cases of incomplete achromatopsia (Barbur *et al.*, 1994). Finally, despite his colour blindness M.S. has a photopic spectral sensitivity that is characteristic of opponent-colour mechanisms (Heywood *et al.*, 1991), indicating that wavelength signals are being processed by the brain but cannot be used to generate the perceptual experience of hue.

Such paradoxical abilities of someone with cortical colour blindness have never been systematically studied with chromatic displays in which no sharp chromatic boundary exists, for example coloured targets, isoluminant with their background, which have a Gaussian chromatic profile and appear as coloured blobs, varying in chromaticity from edge to centre. We therefore tested two achromatopsic subjects and six visually normal controls with a variety of luminance and chromatic displays and measured their pupillary responses as well as recording their perceptual judgements.

## Methods

### Subjects

All subjects gave their consent for the tests, which were conducted with the approval of the regional ethical committee (OxREC C02.304) and in accordance with the code of ethics of the Declaration of Helsinki. The two achromatopsic patients were M.S. and I.E. M.S. was 57 years at the time of the present investigation. His brain damage resulted from idiopathic herpes encephalitis at the age of 22 years. His condition has been reported in detail elsewhere (Heywood *et al.*, 1991, 1994, 2001; Cole *et al.*, 2003; Heywood and Cowey, 2003; Kentridge *et al.*, 2004). He has normal visual acuity and reading ability, and has a verbal IQ of 101. Magnetic resonance imaging (Heywood *et al.*, 1991) revealed extensive damage to the second, third, fourth and fifth temporal gyri in the right hemisphere as well as damage to the right temporal pole. In the left hemisphere damage is confined to the temporal pole, the fourth temporal gyrus and the hippocampal gyrus. The primary visual cortex in the right hemisphere is destroyed, resulting in blindness of the entire left hemifield. In accordance with the damage in other cases of achromatopsia, M.S. also has bilateral ventral-occipital damage to the lingual gyrus and caudal parts of the fusiform gyrus (Brill, 1882; Verrey, 1888; Meadows, 1974; Zeki, 1990 for review). His score of 1245 on the Farnsworth–Munsell 100-Hue test is no better than expected by random sorting of the colours and he cannot read any of the numbers presented on the Ishihara plates when viewed at normal reading distance even though he reads print normally.

Patient I.E. suffered a stroke in 1999 at the age of 69 years, presenting with a left hemiplegia, confusion and problems with his

vision. The hemiplegia recovered rapidly, but not his impaired recent memory and visual problems. At first he could not recognize faces of friends, but this improved. He also lost colour vision, which did not recover. Cognitive assessment with the CAMCOG during the acute stage revealed severe impairment; but this progressively resolved, allowing I.E. to deal with most activities of daily living. Subsequent testing showed no focal deficits of sensory or motor function. Visual fields were full on confrontation testing but he could not identify colours, although he did get 4/6 on Ishihara plates. He was able to identify three out of five overlapping line drawings. Unlike M.S. he had no difficulty recognizing common objects (a key, comb, pen, spectacles). On the Boston Naming Test he was unable to identify several line drawings of common objects: [acorn, volcano, harmonica, whistle, snail ('a saw'), tooth brush, broom ('a paint brush') mushroom ('a lamp'), dart ('a screwdriver'), globe ('a table lamp')]. There was no anomia or aphasia. Like M.S. he could report from memory that grass was green, the sky blue, etc and this remained during the present testing. He could not identify faces of famous people (Prince Charles, Ronald Regan, Elvis Presley). He could remember 2/4 cities and recognize the other two from forced choices.

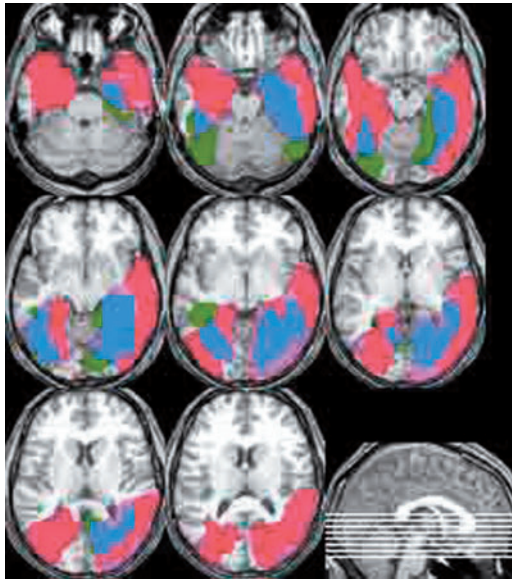
An MRI scan obtained at Ysbyty Gwynedd by Prof. R. Rafal, revealed lacunar strokes in the right basal ganglia and left thalamus. There were also bilateral strokes in the posterior cerebral artery territory. These spared the calcarine cortex, accounting for his full visual fields, but involved the ventral occipito-temporal cortex bilaterally, including the fusiform gyrus on the left and the lingual and fusiform gyri on the right. The infarction destroyed the entire hippocampus on the left, but spared that on the right.

### Structural brain images

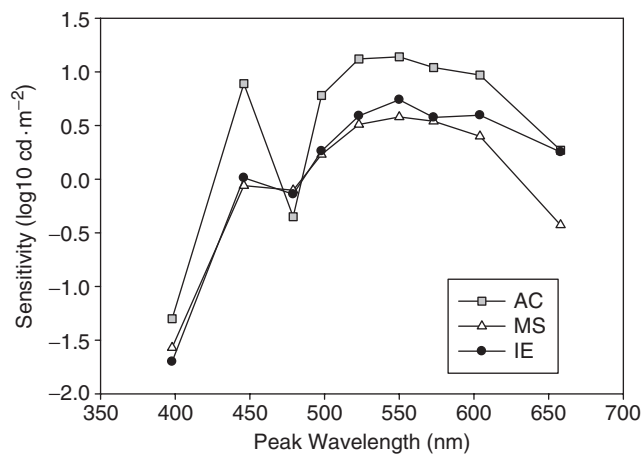
Although M.S. had been scanned in 1989 (Heywood *et al.*, 1991), the resolution and contrast were poor when compared with those of current scanners. He was therefore scanned again in 2004 at the Oxford Centre For Functional Magnetic Resonance imaging of the Brain (fMRIB) with a Siemens–Varian 3T machine. Patient I.E. was scanned with a 1.5T machine at the University of Bangor. The results are shown in Fig. 1.

### Spectral sensitivity

Mesopic spectral sensitivity was measured with a Tübinger perimeter (Sloan, 1971). M.S. was previously assessed 15 years earlier but was re-tested along with I.E. in case his condition had changed. The spectrally narrow-band targets (9–13 nm at half-height) were 2° in diameter and presented binocularly for 500 ms at the fixation point against a white background of 5.5 cd/m<sup>2</sup> while one eye was monitored via the perimeter's telescope. Target luminance was varied systematically via calibrated neutral density filters. One ascending and one descending series of luminance were presented until the first incorrect judgement was given in a descending series and the first correct one in an ascending series. From this point three trials were given at each luminance value until two or three correct responses (ascending series) or incorrect responses (descending series) occurred. The mean of the two types of crossover points was then deemed to be threshold luminance for a particular wavelength. One of the authors, A.C., who has normal colour vision and is older than the two patients, was also tested. Results are shown in Fig. 2.



**Fig. 1** Structural MR images of the brain of patients M.S. and I.E. The eight axial images are taken at the level shown at bottom right. The images from I.E. were transformed on to the template of M.S. Regions of complete destruction are shown in red for M.S. and green for I.O. and in blue for the extensive region common to both subjects. The lesion in M.S. is much more extensive and extends ventrally from the occipito-temporal junction to the temporal pole.



**Fig. 2** Spectral sensitivity in M.S., I.E. and A.C. Increment threshold spectral sensitivity for a 2-degree circular spot presented binocularly for 500 ms at the fixation point against a uniform white background of 5.5 cd/m<sup>2</sup> while one eye was monitored via the telescope of the Tübinger perimeter. The luminance of the coloured targets was varied systematically via calibrated neutral density filters.

### Pupillometry

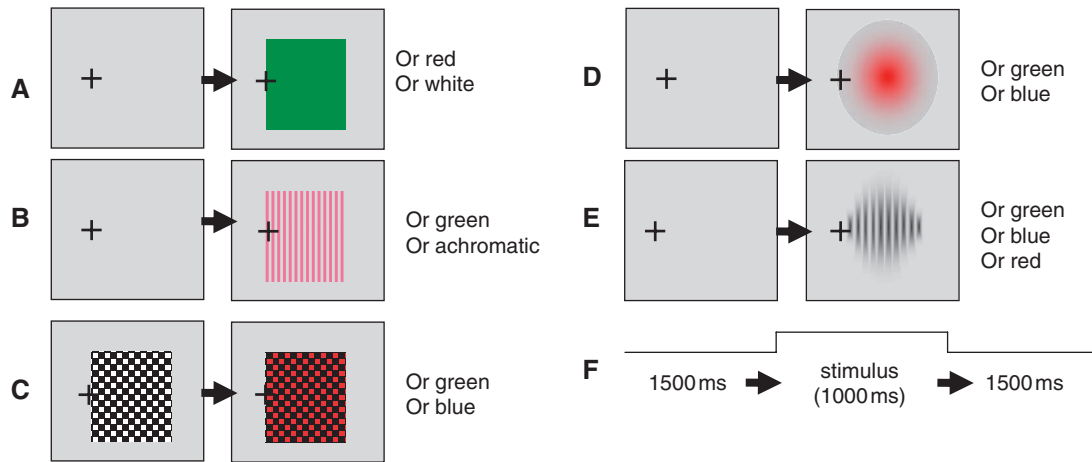
All pupillometric measurements were made with a P\_SCAN-100 system (Barbur *et al.*, 1987; Wilhelm *et al.*, 2002), which simultaneously records pupil size and eye movements, the latter ensuring that fixation is maintained. The measurement precision is sufficient to allow mean changes in pupil diameter of as little as 1% to be recorded (Alexandridis *et al.*, 1992). All measurements were binocular and the results from the two eyes were pooled.

The illumination of the iris was provided by a 5 ms pulse of invisible infrared light, and the images registered by two vertically aligned infrared sensitive cameras mounted below the eyes but viewing their reflection through a 45° glass screen directly in front of the eyes. The pupil diameter was continuously measured at a sampling rate of 50 Hz. Typically 40 trials were delivered in each block of trials and the results for each block were saved and subsequently analysed off-line with P\_scan software, when records from trials in which the eyes moved or blinked were deleted. The viewing distance was 57 cm. The white high-contrast fixation cross could be placed anywhere on the screen.

The first set of measurements used a 10° uniform white or coloured square as the stimulus. The white 20 cd/m<sup>2</sup> square was brighter than the 10 cd/m<sup>2</sup> background, whereas the coloured squares were either isoluminant with the background or 10 cd/m<sup>2</sup> brighter than the background. All the squares had a sharp and therefore prominent chromatic border with the surround. For the second set of measurements grating stimuli of two kinds were presented. The first was a simple achromatic sine-wave grating whose space averaged luminance was the same as the surround. The second was a d-isoluminant chromatic grating (see later), again isoluminant with the surround. They had a spatial frequency of 0.5 cycles/degree. All stimuli were generated on a 19" Sony Trinitron Multiscan monitor (Model 20sf II) driven by a 10-bit graphics card. Initial measurement of the spectral radiance output of each phosphor was made by the P\_Scan suppliers with a telespectroradiometer (Gamma Scientific Model 2030-31, USA). Subsequently the gamma function of each phosphor was also measured with an Optical OP200-E (Cambridge Research Systems, UK). Stimulus luminance was also checked regularly on each testing session with a chromameter (Minolta CS-100, Japan). All measurements of displays were made through the partially silvered glass screen in front of the subject's eyes. With respect to coloured gratings as stimuli, the generated colours had zero scotopic contrast, in order to prevent their possible detection by the scotopic channel, as well as being photopically isoluminant. Such a grating is termed d-isoluminant (Young and Teller, 1991) but is unavoidably restricted to only two hues, which are pinkish or greenish and of low saturation.

In the third set of experiments, using Gaussians or Gabors as stimuli, or checkerboards with or without random luminance masking, the displays were presented on a 19" Eizo Flexiscan, model T660, driven at a frame rate of 100 Hz and calibrated with the Optical and the chromameter. Examples of the above displays are shown in Fig. 3. The Gaussians were 7.5° SD Gaussian. The purpose of the achromatic Gabor (Fig. 3E) was to present a sinusoid of the same type as in the square envelope used earlier but with smooth modulation to eliminate all sharp boundaries and minimize high spatial frequencies. The stimulus was a Gaussian blob which was further modulated so that its colour varied sinusoidally between background colour and that of the original Gaussian according to the equation: Gauss( $x, 0, SD$ ) \* sin( $f x + \pi/2$ ) + Gauss( $x, 0, SD$ ), where  $x$  is spatial position and  $SD$  and  $f$  are constants specifying the standard deviation of the Gaussian envelope and the spatial frequency of the sinusoidal modulation. Gauss( $x, m, s$ ) is a Gaussian with mean  $m$  and standard deviation  $s$ .

Throughout pupillometric testing the subjects were asked to describe what they had seen, if anything. This was not done on every trial, which subjects find tedious, but after each batch of 40 trials with a particular stimulus.



Stimuli	Luminance $\text{cd m}^{-2}$	x	y
White Flash	20	0.318	0.335
Red Flash	10	0.596	0.329
Green Flash	10	0.287	0.565
Achromatic Grating	Dark Bar 5	0.318	0.335
	Light Bar 15	0.318	0.335
Red Sine Wave Grating	10 (Pink Bar)	0.350	0.270
	10 (Grey Bar)	0.317	0.333
Green Sine Wave Grating	10 (Green Bar)	0.275	0.418
	10 (Grey Bar)	0.317	0.336
Background	10	0.316	0.330

**Fig. 3** Examples of the stimulus displays. Not all displays are shown. The first box in each pair shows the screen while the subject fixates the cross and waits for the stimulus, shown in the second box. The table beneath shows the luminance and peak C.I.E. values.

## Results

### Structural brain images

Figure 1 shows eight axial images through the brains of M.S. and I.E. at the levels shown at bottom right. The images from I.E. have been transformed on to the template of M.S. Regions of complete destruction are shown in red for M.S. and green for I.O. and in blue for the extensive region common to both subjects. The lesion in M.S. is much more extensive and extends from the occipito-temporal junction ventrally to the temporal pole. In I.E. it is more restricted but includes the posterior fusiform gyrus and rostral lingual gyrus bilaterally, the regions characteristically implicated in cerebral achromatopsia. The sparing of cortex more rostrally presumably explains why I.E., unlike M.S., is not so severely impaired in recognizing faces or objects.

### Spectral sensitivity

Figure 2 shows the mesopic spectral sensitivity for M.S. and I.E. and one of the authors, A.C. The curves are clearly characteristic of normal trichromacy, although both

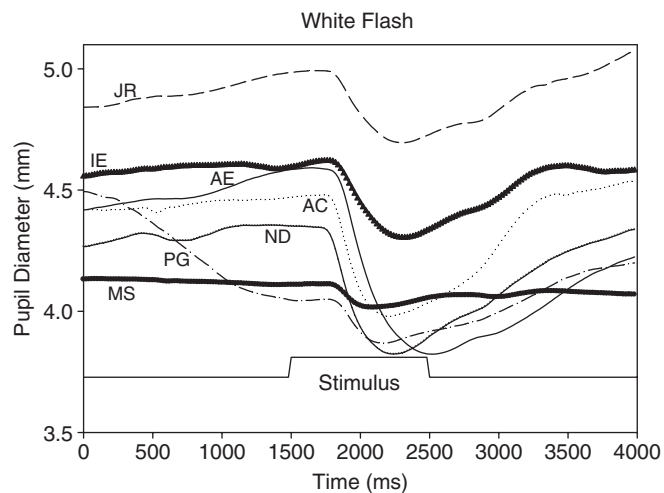
patients are less sensitive than A.C. despite being younger. However, and especially at short wavelengths, the absorption by both the lens and macular pigment varies substantially among normal viewers (because of yellowing of the lens and variations in the yellowish macular pigment) and the variation among the subjects in Fig. 2 is not unusual, although much larger than reported by Crawford (1949). The dip at 480 nm is characteristic of opponency between short wavelength, S, cones and medium plus long wavelength, M+L, cones. There is no prominent dip at 575 nm that is associated with M/L opponency (the Sloan-Crawford notch), but this is always shallow at mesopic levels. But there is a flattening of the curve at this wavelength. Both achromatopsic subjects therefore show good evidence of chromatic processing despite their colour blindness.

### Responses to a white or coloured square

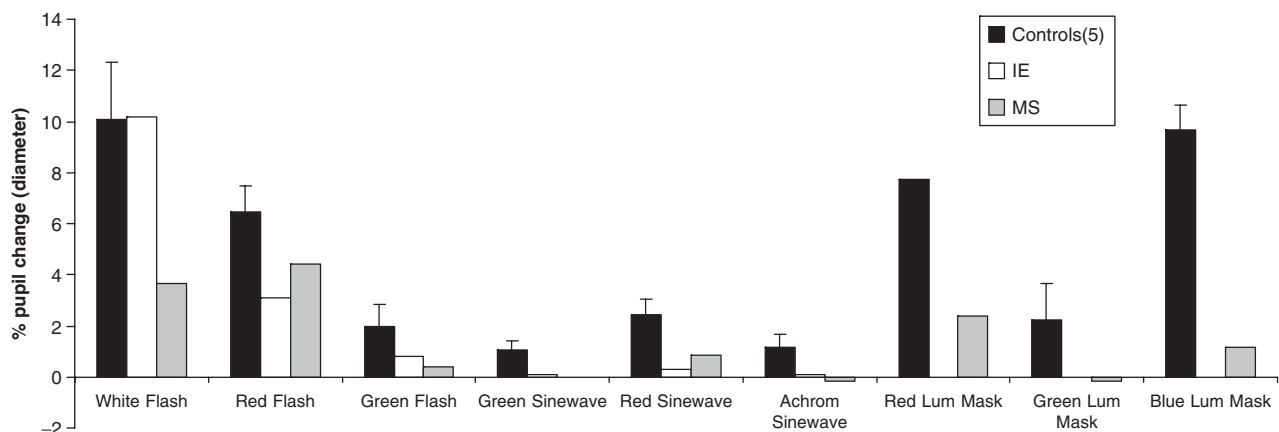
Figure 4 shows averaged pupillary responses for each of the five control subjects, and M.S. and I.E., to a 1 s presentation of the  $10^\circ$   $20 \text{ cd/m}^2$  white square whose left edge was

contiguous with the white fixation cross on the  $10 \text{ cd/m}^2$  background. The response, a contraction of the pupil, began at about 300 ms in all subjects and did not fully recover until about 1 s after the end of the stimulus. The magnitude of the change in pupillary diameter varied from 4.5% to 12% in the controls (mean = 9%) and was 3.75% in M.S. and 10.4% in I.E. There was much more variation among subjects in the latency to the peak of the change but both of the achromatopsic subjects were no different from several of the normal subjects. These differences among subjects with respect to latency of the peak change were not simply a reflection of the variations in magnitude of the pupillary response because they persisted when the traces for individual subjects were scaled to equivalent amplitudes, in a manner similar to that recommended by Barbur *et al.* (1998).

The response to a red square isoluminant with the background was similar to the response to a white square



**Fig. 4** Mean pupillary response to a white  $1.0 \text{ s } 20 \text{ cd/m}^2$  square-wave flash against the white screen background of  $10 \text{ cd/m}^2$  for two achromatopsic subjects (M.S. and I.E.) and five control subjects with normal vision. There is no obvious difference between the records of the two groups.



**Fig. 5** The percentage change in pupil diameter for the different displays. Error bars =  $\pm 2$  SD from the mean.

(mean controls = 8.8%; M.S. = 4.6%; I.E. = 3.4%) except for being much smaller in I.E. than to the white square. In addition, the onset latency was about 20–60 ms later, slightly greater than observed by Barbur *et al.* (1998), but consistent with a cortical contribution to the pupillary response to a colour change. From this point all the results are shown in tables or histograms. Figure 5 shows that all control subjects showed a pupillary constriction to the white and red stimulus, but the change to green was much smaller and not even significant in control subject J.R. and in both achromatopsic patients. However, every control subject was able to correctly describe the green square. In contrast M.S. and I.E. could not reliably describe the colour of the red square, using words like dark or solid, and with the green square they were frequently unsure it had been presented at all. Even when it was subsequently presented for several seconds for inspection they said it was just a square, whose outline they could trace with a fingertip, and that it did differ from the background in this respect.

### Responses to grating stimuli

The pupillary response to achromatic or d-isoluminant sine-wave red and green gratings is shown in Fig. 5. In the control subjects, and unsurprisingly given that no mean luminance changes were present, the responses overall were smaller than to a bright white square. Two of the controls showed no significant response to the achromatic grating. Despite the great increase in the total amount of chromatic contrast the response to the red grating was smaller than to the red isoluminant flash and one control failed to respond to it. However, four of the five control subjects showed a significant response to the red grating. It was presumably smaller than to the red square because the square was a saturated colour, whereas the d-isoluminant grating is necessarily desaturated. The response to the green grating was even smaller and only significant in three of the control subjects. Neither of the achromatopsic patients showed a significant response to any of the gratings. When asked to describe the

stimuli all control subjects described them accurately, irrespective of whether their pupils had responded. But although M.S. and I.E. perceived and described the achromatic grating they often saw nothing, or nothing they could readily describe, with either of the d-isoluminant gratings. Both M.S. and I.E. sometimes said that they thought there was a square, which of course had sharply defined sides, and they could roughly indicate its outline.

### Dynamic luminance masking of patterned stimuli

Although there were clear pupillary responses in both controls and M.S. to an isoluminant red square, it is possible that the response is mediated by retinal M cells which, although non-colour opponent, respond very differently to long and short/medium wavelengths. The pupillary response might therefore have little or nothing to do with colour *per se* but could be a response to a chromatic boundary that is not perceived as coloured in achromatopsia. However, M cells can be saturated by rapid temporal and spatial change and their contribution to pupillary change should be abolished. We therefore presented stimuli such as those in row C of Fig. 3. In the initial black/white checkerboard the luminance of the black and white squares alternated at 5 Hz. The white squares were either 10 cd/m<sup>2</sup> and changed to an isoluminant red or green for 1 s, or they were 7 cd/m<sup>2</sup> and changed to isoluminant blue for 1 s, before returning to dynamic black white. The square checkerboard was therefore dynamically active throughout each trial, which should saturate the M cells. The dynamic display produced illusory motion along its rows and/or its columns. Figure 5 shows that there was a clear pupillary response, but least to green checks, in the control subjects, with the exception of green in subject J.R. M.S. also responded to the red and—just—to the blue, but not to green. He was able to describe the checkerboards but not their colours, i.e. he could see edges but not what lay within the checks. I.E. was unfortunately unavailable for this testing.

### Responses to Gaussian blobs and Gabor patches

Only M.S. and subject A.C. were available for this part of the Experiment. The results are shown in Table 1. Subject A.C. showed a measurable pupillary response to every stimulus, but greatest to the luminance contrast white Gaussian, the isoluminant red Gaussian and the luminance contrast red Gaussian. In striking contrast M.S. showed a measurable pupillary response only to the white Gaussian, which has a luminance change, albeit only prominent at its centre. With the exception of this stimulus the absence of any sharp borders in every stimulus therefore abolished his pupillary response. It is conceivable that his failure either to detect and/or to show a pupillary response to the coloured

**Table 1** Percentage pupil change to Gaussian blobs and Gabor patches in M.S. and control subject A.C.

	Change (%)	
	M.S.	A.C.
Stimulus		
Green Gaussian	–	1.95
White Gaussian	1.62	10.72
Isoluminant red Gaussian	–	8.92
luminance contrast red Gaussian	–	15.95
Blue Gaussian	–	1.97
Achromatic Gabor	1.0	2.35
Red Gabor	–	1.97
Green Gabor	–	1.22

Where there is no entry in the Table the change was <1.0%.

Gaussians simply reflect an elevated threshold for the detection of chromatic contrast (Barbur, 2004). Accordingly, we presented M.S. with a display in which colour, uniformly filling the entire screen, was varied sinusoidally over time at 2 Hz across the largest isoluminant colour range between red and green that the monitor could produce. M.S. could not discriminate between this intense colour-varying display and a static display of the same luminance. He showed a similar inability to detect colour change over time when we used a display in which a large Gaussian blob (10° SD) was sinusoidally modulated between red and green at 2 Hz. He was clearly baffled by these two tasks because for him nothing changed on the screen. As the change was from pure red to pure green, or the reverse, at a chromatic contrast he can easily detect in tasks involving the discrimination of chromatic boundaries of small stimuli (Heywood and Cowey, 2003; Kentridge *et al.*, 2004), his failure on the previous tasks cannot be attributed to severely impoverished detection of chromatic contrast *per se*.

Although the normal subject A.C. could see and describe every stimulus, even when the pupil response was small, e.g. the green Gaussian, the verbal reports of M.S. were entirely consistent with the response of his pupil. He said that he could see something ‘rather vague’ when the white Gaussian was presented and something that ‘moved from the right’ in response to the achromatic Gabor. To all the other borderless stimuli he either said that he saw nothing or that he thought there might have been something but he could not be sure.

### Discussion

The principal and important result was that when sharp chromatic borders around or within coloured stimuli were removed, the paradoxical ability of totally cortically blind subjects to detect coloured stimuli against isoluminant backgrounds was either severely diminished or abolished. When sharp chromatic borders are present they are presumably detected by chromatic channels that use colour to generate shape without conveying subjective impressions of hue. The latter interpretation of cortical colour

blindness explains why, despite detecting isoluminant chromatic borders, such patients cannot tell whether two colours are the same or different, why they cannot arrange colours in spectral order, why they cannot use surface colour to identify similarly shaped but differently coloured objects like apples, peaches and oranges. Cortical achromatopsia therefore becomes another prominent example of visual processing where the feature that is successfully processed can sustain certain perceptual judgements—in this case form—but not others—in this case hue. It resembles the correct identification of form-from-motion, e.g. Johansson figures, by subjects who are motion blind (Vaina *et al.*, 1990; McLeod *et al.*, 1996), the successful forced-choice discrimination of motion, flicker and orientation in blindsight patients who have no subjective vision (Weiskrantz, 1997; Stoerig, 2006, for reviews), and the many examples of patients with unilateral parietal neglect who fail to consciously notice visual features on the neglected side that can nevertheless influence their judgements, including affective ones, of objects that contain the neglected features (Marshall and Halligan, 1988). However, a prominent difference between all these conditions and achromatopsia is that in the latter the wavelength processing leads to a conscious phenomenal perceptual experience; it just lacks any colour. In other words, it is not ‘blindsight for colour’.

The results also show that, without exception, the response of the pupil parallels the perceptual comments of the two achromatopsic patients. Whenever the pupillary response was insignificant they were unable to describe the visual stimulus accurately, e.g. a green d-isoluminant grating, and were usually even unaware that any stimulus had been presented, e.g. coloured Gaussians. However, it must be noted that the absence of a pupillary response does not of itself infallibly indicate an absence of any awareness. Two of the control subjects showed no significant response to a high-contrast achromatic sine-wave grating with the same mean luminance as the surround despite the fact that it was perceptually one of the most salient displays.

Although patient I.E. was not available for all the tests both his pupillometric results and his subjective reports about the displays were essentially similar to those of M.S., despite the fact that the cortical lesion was much greater in M.S. But M.S. is also densely prosopagnosic and visually agnostic for objects. This difference indicates that I.E.’s smaller lesion, centred on the fusiform and lingual gyri in the middle third of the ventral temporal lobe, is sufficient to abolish the subjective experience of colour and the response of the pupil to colour *per se*. The results from M.S. and I.E. also indicate that the pupil colour response, which is believed to depend on projections from cortex to midbrain (Barbur, 2004) rather than direct retinal input to the latter, is not deriving the information from early extra-striate visual areas like V2 and LOC, which are intact in both patients.

Figure 5 shows that a pupillary constriction of <1.0% was often recorded, yet we have not regarded this as significant in the results despite the absence, with one exception, of a similarly small expansion. The reason for this is that when we tested ourselves with blocks of trials that included catch trials, a small constriction, up to 1.0%, was recorded at the time the subject expected the stimulus. Even though the timing of the stimulus was not precisely related to the verbal warning to the subject not to blink because the trial was about to begin, its appearance was on average 3 s later. Constrictions of <1.0% might therefore simply reflect the subjects’ expectations that a stimulus is about to appear.

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