Progressive cortical visual failure associated with occipital calcification and coeliac disease with relative preservation of the dorsal 'action' pathway

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Abstract

We describe the first reported case of a patient with coeliac disease and cerebral occipital calcification who shows a progressive and seemingly selective failure to recognize visual stimuli. This decline was tracked over a study period of 22 years and occurred in the absence of primary sensory or widespread intellectual impairment. Subsequent tests revealed that although the patient was unable to use shape and contour information to visually identify objects, she was nevertheless able to use this information to reach, grasp and manipulate objects under central, immediate vision. This preservation of visuo-motor control was echoed in her day-to-day ability to navigate and live at home independently. We conclude that occipital calcification following coeliac disease can lead to prominent higher visual failure that, under prescribed viewing conditions, is consistent with separable mechanisms for visual perception and action control.

Keywords: visual agnosia, visuo-motor control, lateral occipital cortex, human

1. Introduction

Some cases of coeliac disease are associated with bilateral occipital calcification (BOC). All such cases reported have manifested as occipital epilepsy (Gobbi et al., 1992; Gobbi, 2005). We describe below a case of coeliac disease who shows occipital calcification that is indistinguishable from that found for cases of epilepsy, but who developed a gradually progressive cortical visual disorder. We are unaware of any reports of cortical visual failure in such patients. A prominent feature of the visual loss was the preservation of visual processing for 'action', as originally defined by Goodale and Milner (1992).

Paroxysmal visual disturbances have been reported in some patients with BOC, but the symptoms are short-term, non-progressive in severity or type and usually involve low-level sensory disturbances such as flashing lights, spots, blurriness or brief stereotyped complex visual hallucinations due to occipital epilepsy (Pfaender et al., 2004). No reports of progressive and selective loss of higher visual function have been identified, indeed there have been no reports of visual impairment of any kind in this group of patients until very recently when a patient who presented with epilepsy but who was left with a static defect following treatment of the coeliac disease was highlighted (Millington et al., unpublished results). By contrast, patients with structural lesions to the occipital lobe usually present with a homonymous visual field defect; a complete or partial visual field loss in the contralateral half of the visual field of each eye. The visual field loss may be clinically total but there may be residual vision such as blindsight or the Riddoch phenomenon (see Weiskrantz, 1997). Less commonly after an occipital lesion, positive symptoms arise which may be epileptic but also include the filling-in of scotomas, palinopsia, cerebral polyopia and release hallucinations (see Fraser, Newman & Biousse, 2011). Although often present in cases of visual agnosia and optic ataxia, occipital lesions by themselves have yet to be shown to be sufficient for either condition to occur (see Barton, 2011).

The present case of BOC is especially intriguing because the visual failure is most prominent for processes involving perception, while those involving action are relatively preserved. Numerous lines of evidence suggest that visual perceptual and action processes dissociate, at least to some extent, in the human brain (see Goodale, 2014). That is to say, the mechanisms underlying object identification are partly distinct from those underlying object reaching, grasping and manipulation. Some of the most compelling evidence has come from patients who, following brain injury, show evidence under particular viewing conditions of disordered object recognition in the absence of optic ataxia. Perhaps the most well-known case is that of DF (Milner et al., 1991) who, following carbon monoxide poisoning, could not recognise objects but nevertheless was able to reach out, grab and manipulate them in a manner indicative of spared shape and size processing. Only two other patients have been sufficiently characterized as to show a similar dissociation (patient SB - Dijkerman, Le, Demont & Milner, 2004; patient JS - Karnath, Rüter, Mandler & Himmelbach, 2009). However, a handful of other patients have presented with a clearly documented visual form agnosia that, although not formally assessed, seemed to be unaccompanied by visuo-motor disorder (Adler, 1944; Barton, 2004; Benson & Greenberg, 1968; Campion & Latto, 1985; Landis, Graves, Benson & Hebben, 1982). In all these patients, the dissociation emerged suddenly from an acquired brain injury and, in all but one case, involved lesions that extended beyond occipital-temporal cortex. In the current case, it emerged very gradually in the absence of insult and was accompanied by a circumscribed pattern of cortical calcification in lateral-occipital cortex. Below we report the changing profile of the patient's visual function over a period of 22 years. The studies conducted have been clinical in nature so focused on what she cannot do rather than what she can, so tend to involve recognition and matching tasks.

2. Case history

A 48year old English Caucasian female presented with difficulty reading. She was seen by an ophthalmologist who found best corrected distance visual acuity to be 6/9 bilaterally and near vision N5 with full visual fields, but an acquired alexia was demonstrated. She gave a past history that as an infant she had seizures which manifested as going blank for a few seconds and making groping movements with her hands. At 17 she had a generalised seizure and was investigated at the Radcliffe Infirmary in Oxford where investigations were thought to indicate an occipital vascular malformation. Given this past history, the ophthalmologist requested a skull X-ray which revealed bilateral occipital cortical calcification from which it was again assumed that she had either a vascular malformation or a variant of Sturge Weber syndrome. However, there were no cutaneous manifestations of the latter. The alexia progressed until at the age of 59 she was unable to read script and read printed text largely letter-by-letter. She was re-examined at that time and her visual acuity and visual fields were unchanged. It was noted also that she was unable to read the control (i.e. the first) Ishihara plate indicating impairment of the ability to read fragmented numbers. Well into her 70s she was able to write legibly although unable to read what she had written. Her spelling skills were retained throughout this period and she did not notice any difficulty identifying colours or faces.

The patient had a long history of gastrointestinal upset and at age 61 underwent endoscopy and small bowel biopsy which revealed changes of coeliac disease. Later pernicious anaemia was discovered. She has followed a gluten free diet and received regular intra-muscular hydroxycobalamine supplements since that time. At no time was there evidence of folate deficiency.

Representative CT (at age 65) and MR (at age 73) images of the brain are shown below in Figures 1 and 2. There is extensive occipital calcification affecting particularly the posterior temporal, lateral occipital and posterior, superior parietal cortices. Note that there is relative sparing of the *medial* occipital lobe. There is evidence of leukoariosis compatible with age.

Figures 1 and 2 about here

The patient was first examined by one of us (MJ-G) in 1990 at age 59 and re-examined extensively at the age of 65 by MJ-G and GTP. Subsequent tests have been repeated periodically until as recently as 2012 (DW) when she was aged 81. Throughout this period, the patient's ability to recognise objects by sight has steadily deteriorated. Yet she has retained the ability to navigate, reach, grasp and perform fine motor acts under visual guidance. She continues to live independently and to help compensate for her failing recognition, many of the objects in her home are colour-coded. For example, tape is attached in bright, primary colours to distinguish items of cutlery or to demarcate handles. In the following section, we report a series of tests that have tracked her perception and recognition failure over the years. The limited data available at her first presentation to us at age 59 is given in Tables 1, 2, 5 and 6. Finally we present data from two recent experiments that more directly compare her visuo-perceptual and visuo-motor skills by controlling for potential methodological confounds.

3. Standard neuropsychological assessment

Method & Results

3.1.Verbal Processing

The following standard tests were performed: Selected verbal IQ subtests of the WAIS-R (performance IQ could not be attempted because of her visual impairment) (Weschler, 1981);

Verbal Recognition Memory test (Warrington, 1984); National Adult Reading test (Nelson & Wilson, 1991); Baxter Spelling test (Baxter & Warrington, 1994).

3.1.1. WAIS-R.

Table 1 shows performance on four verbal subtests of the WAIS-R which remained stable throughout the testing period.

3.1.2. Recognition Memory test

Table 2 shows performance on the Recognition Memory test for words presented orally. Prior to age 69, recognition memory was at the predicted, premorbid level of function for her age (75th percentile), but from age 69 there was a steady decline.

3.1.3. National Adult Reading test

At age 59, the patient was able to read 20/50 words on the National Adult Reading test but used a slow letter-by-letter strategy, spelling the words out to herself to recognise them. When tested at age 65 she identified 15/20 large single printed capital letters, but from age 68 was no longer able to identify any printed letters. Her ability to recognise large, single, wooden letters was therefore tested so that a comparison could be made with both her tactile recognition and the ability to write the same letters to command. As seen in Table 3, her tactile recognition also declined but unlike for vision, did not disappear altogether.

3.1.4. Baxter Spelling test

Spelling was assessed using the Baxter Spelling test and also showed a modest decline (Table 4). This was initially intact for both written and verbal responses although she was unable to read anything that she had written. In later years, written and verbal spelling deteriorated but this was accompanied by a deterioration in handwriting.

Tables 1, 2, 3 and 4 about here

3.2. Early visual processing

The following standard tests were performed: contrast sensitivity, visual field perimetry, single point localization (see Weiskrantz, Warrington, Sanders & Marshall, 1974); Ffookes Symbol test (Ffookes, 1965); Efron 2D Shape Discrimination test (Efron, 1968); Shape Detection and Identification subtests of the Visual Object and Space Perception Battery (VOSP) (Warrington and James, 1991); Farnsworth Munsell 100 Hue Arrangement test (Farnsworth, 1957); Frisby Stereogram test (Saunders, Woodhouse & Westall, 1996). Visual search and illusory contour perception and were also briefly assessed.

3.2.1. Contrast sensitivity and Goldmann perimetry

Contrast sensitivity and Goldmann perimetry were assessed throughout the study period and did not on any occasion reveal a visual field defect under static or kinetic testing. Contrast sensitivity measured to sinusoidal gratings temporally modulated in counterphase was normal across a range of spatial frequencies (0.5, 4, 8, 16 cycles per degree) each tested at 0, 8, and 32Hz temporal modulation.

3.2.2. Single point localization

Single point localisation was assessed by pointing accuracy on an Aimark perimeter. There was no evidence of visual disorientation, although there was a modest deterioration in performance with age. Her average error of pointing to a single point light source on the Aimark perimeter was 1.3^0 at age 65 and 2^0 at age 68 for stimuli presented at eccentricities of 10^0, 20^0, 30^0 and 40^0. A more limited study carried out at 73 revealed a mean error of 4.6^0. These error rates fall below the normative mean error rates reported by Russell and Bharucha (1984).

3.2.3. Ffookes Symbol test

Given her difficulty reading letters, acuity was measured using the Ffookes Symbol test. Best corrected visual acuity (she is emmetropic), remained 6/9 in either eye until the age of 73 after which there was a decline which may partly reflect the appearance of bilateral cataracts.

3.2.4. Efron test

Two-dimensional shape discrimination, as measured by the Efron test, showed initial, mild impairment (Table 5). At 59 there was mild impairment of shape discrimination (controls perform at 100% at all levels on this test) and although there was further deterioration in performance over a period of nearly 20 years, even at 76 years of age (with cataracts) she achieved a reasonable score except at the more difficult discriminations.

3.2.5. VOSP Shape Detection test

Figure/ground discrimination, as assessed by the Shape Detection test from the VOSP, was normal (17/20) at age 59 but she failed the test at ages 65 and 68.

3.2.6. Farnsworth Munsell (FM) 100 Hue Arrangement test

Hue discrimination was assessed using the Farnsworth Munsell (FM) 100 Hue Arrangement test (Table 6). To overcome the problems associated with arrangement tests such as this, a same/different response procedure was also employed. Five sets of swatches were used. Each swatch matched a stimulus (cap) used in the FM 100 hue test and each set (40 trials) was chosen to give a particular separation of the stimuli in the FM 100 hue array, becoming progressively less difficult. Thus set ‘A” consisted of stimuli separated by two FM steps; set “B” 4 steps; set “C” 6 steps; set “D” 8 steps and set “E” 10 steps. It is difficult to equate these scores to the standard F-M test because of the difference in methodology, but it is clear that hue discrimination is severely impaired and deteriorates during the observation period. Even at the latest time of testing, however, the patient was still able to discriminate highly saturated

colours widely separated in colour space, such as those used to colour code cutlery and other objects in her home (see Table 7).

3.2.7. Random dot stereogram

Stereopsis was assessed using random dot stereograms. At the age of 59 she was able to correctly perceive all but the most difficult stereograms in the Frisby test, but by age 68 she was unable to perform any of the tests.

3.2.8. Visual search

Visual search performance was measured using stimuli presented on a colour monitor using Macromind Director software. She was asked to detect a salient target presented amongst 0, 3, 11 or 35 distractors at a viewing distance of 57cm. Two types of display were presented: (1) horizontal targets set amongst vertical distracters and (2) red targets set amongst green distracters. She showed mild impairment on the colour detection task and more severe abnormality on the orientation task. An age-matched control subject made no errors on either task (See Table 8).

3.2.9. Illusory contour appreciation

Illusory contour appreciation was tested by asking her to locate an illusory Kanizsa triangle within an array of randomly oriented "PAC men". She was unable to identify the target when first presented at age 59, nor on any subsequent occasion.

Tables 5, 6, 7 and 8 about here

3.3. Higher visual processing

The following standard tests were performed; Oldfield Object Naming test (Oldfield & Wingfield, 1965); object and spatial tests of the VOSP (Warrington & James, 1991). Customised visual/tactile recognition and search tasks were also administered.

3.3.1. Oldfield Naming test

At age 59 she was able to identify 9/14 of the line drawings of objects on the Oldfield Naming test. By age 65 only 1/10 was identified, and at age 68, 2/15 were identified.

3.3.2. VOSP object and spatial perception

Her performance on the object and spatial perception tests from the VOSP was grossly impaired. On the object recognition tests she identified only 1/10 Incomplete Letters at age 59, and 5/20 at age 65. She could not identify any in later years. On the Silhouettes test she identified only 3/30 at age 59. At age 59, she performed at chance on the Position Discrimination test and showed a similar level of impairment on Cube Analysis. She was able to count scattered dots on the Dot Counting test reasonably well at age 59 and 65 but after that time, until she was age 70, she was only able to accurately count small arrays of from 2-5 large dots.

3.3.3. Object identification

Table 9 shows identification of real objects (a custom set of twenty real common objects was assembled, including a cotton reel and pair of scissors) by vision only and touch only. Visual identification was impaired at age 65 and showed further deterioration over time. Identification by touch was less impaired at age 65 but did show decline in the following years. Bedside testing failed to detect any evidence of dyspraxia that may account for this decline, and at age 69 she was still able to mime the use of common objects adequately.

Table 9 about here

4. Comparisons between vision for action and vision for perception

Given the patient's demonstrated ability to navigate, grasp/manipulate objects, and point accurately on the Aimark, at age 81 we administered two experiments based on the classic study of Milner and Goodale (1991) and more recently by Karnath et al., (2009) to more

directly compare the patient's perceptual and visuo-motor function. As described in sections 4.1-4.3 below, the patient continued to show evidence of preserved sensory perception at the time that these two experiments (see 4.4 and 4.5) were carried out. Prior written informed consent was obtained following study approval by the School of Psychology Ethics Committee, University of Kent.

4.1. Contrast sensitivity

The patient scored within the normal range (23/24 correct) on the LEA Paddle Gratings test of contrast sensitivity

4.2. Luminance discrimination

To assess luminance discrimination, 24 computerised images were presented in random order, 12 of which consisted of just a grey background, and 12 of which contained both the grey background (16cd/m^2) and a randomly positioned 6cm x 4cm grey rectangle which differed from the background by a minimum of +/- 1cd/m^2 and maximum of +/- 14cd/m^2. Luminance was measured using a Cambridge Research Systems ColorCal Lightscan device. For each image, participants were asked whether a rectangle was absent or present. Both the patient (88% correct) and 5 age- and gender-matched controls (100% correct) performed the task accurately, producing scores that were not reliably different from one another ($t(23)=2.0$, $p>0.05$).

4.3. Colour discrimination

To assess colour discrimination, the same 24 images were presented as in the luminance task, though the 12 rectangles were now coloured red (CIE 1976: L*= 51 a*= 72 b*= 68), blue (CIE 1976: L*= 38 a*= 49 b*= -99), yellow (CIE 1976: L*= 53 a*= -7 b*= 58), green (CIE 1976: L*= 53 a*= -55 b*= 54), magenta (CIE 1976: L*= 50 a*= 71 b*= -0.1) or orange (CIE 1976: L*= 53 a*= 40 b*= 63. The luminance of the screen background and coloured

rectangles were maintained at 16cd/m^2. Participants were again asked whether a rectangle was absent or present. Both the patient and controls performed the task at 100% accuracy.

4.4. Perceptual orientation matching vs. visually guided reaching towards a slanted surface

In the original Milner et al. (1991) experiment, visuo-motor function was assessed by instructing the visually agnosic patient, D.F., to post her hand through an oblong slot that was oriented at one of several angles. This task was paired with a perceptual version in which she simply had to match her hand orientation to that of the slot without actually posting it. In the present study, it was necessary to amend this task because in pilot testing we found that the patient was unable to discriminate letterboxes from their backgrounds. We therefore devised a similar, but more achievable, task in which she had to place a flat-bottomed object (an iPod) onto the lid of a box that could be oriented at one of several angles. Studies indicate that as this type of reach manoeuvre progresses, the orientation of the object should match the surface on which it is about to be placed (see Jeannerod, 1997). In a perceptual version of this task, we asked the patient to simply hold the iPod to her chest and orient it to the same angle as the box lid. We reasoned that if she is better able to use information about a shape's orientation to guide her actions than her overt perception then, relative to controls, she should perform the reaching task much more accurately than the perceptual judgement task.

Five age-matched, neurologically healthy women with corrected-to-normal vision, aged 75-85 years (mean age = 81) performed the experiment, three of whom also performed the second experiment described in section 4.5.

4.4.1. Method

A black, cardboard box (29cm long, 25cm wide, 28cm deep) was fashioned with an adjustable lid that could be oriented, via a hinge, to 0º, 15º, 30º or 45º (see Figure 3). The box was positioned on a desk, and participants seated at a distance of 30cm. For recording

purposes, a marker was affixed to the desk to indicate midway between the box and edge of the desk. In the action condition, participants were required to pick up an Apple iPod device that was positioned on the edge of the desk, and to reach out in a smooth movement and place it on top of the oriented lid (a small lip prevented the iPod from sliding off). In the perception condition, participants were again required to pick up the iPod, but this time were instructed to hold it against their sternum and simply tilt it until its orientation matched that of the box lid. Using 3 cameras and the gyroscopic function of the iPod and iRotate™ software, it was possible to record the orientation and spatial location of the iPod in real time (acquisition rate = 6Hz). In the perception task, this information was taken at the moment when the participant indicated that she was happy, via either head-nod or verbal utterance, with her judgement. In the action task, this information was recorded at movement onset, when the iPod was half-way between the start point and the box, and at the point where the leading edge of the iPod crossed the front edge of the box. For both the action and perception tasks, each of the four box lid orientations was presented 4 times in pseudo-random order. All participants performed the trials in the same order. Three practice trials were given before the start of each task.

Figure 3 about here

4.4.2. Results

For each task, each participant produced a mean error score (i.e. angular degrees over- or under-rotated) calculated from all 16 trials (see Figure 4).

Figure 4 here

A modified independent samples *t*-test, which treated the normative scores as sample statistics rather than population parameters (see Crawford & Howell, 1998), indicated that in the perceptual task the patient produced a higher mean error (48º) than the controls (mean =

9º, SD =5.6º), (*t*=6.4, p=0.003). In the reaching task, the iPod showed comparable mean rotational error in the patient (21º) and controls (mean = 13º, SD = 8º) as it crossed the front edge of the box (*t*=.96, p=0.39). Likewise, the mean rotational error at the intermediate marker between start point and box edge also failed to reach significance (patient = 24º vs. control mean = 13º, SD=11), (*t*=0.9, p=0.4). Additional paired sample *t*-tests confirmed that while the patient found the reaching task easier than the perceptual task (*t*(d.f=15) =2.4, p=0.03), the controls showed no difference (*t*(d.f=15) =1.4, p=0.2).

4.5. Perceptual matching vs. grasping of irregular shapes

Based on the experiment conducted by Goodale et al. (1994), we administered a grasping task to further assess the ability of the patient to use shape information to guide perception and action. When grasping an object, neurologically healthy participants typically place their fingers on opposite points on the surface that when connected via a straight line run through (or very near) the object's centre of mass. Such a strategy requires accurate coding of contour and boundary information that in the present experiment could also be used to tell apart objects. If the patient is able to use this information to guide her actions but not overt perception then we would expect her grasping to be significantly less impaired then her perceptual matching.

4.5.1. Method

2x12 grey, irregular clay shapes, were manufactured to resemble the shape and dimensions of those originally used by Goodale et al. (1994) (see Figure 5). For the grasping task, each shape was placed, one shape per trial, on a glass desktop 20 cm away from the edge nearest the participant. Participants were instructed to pick up the shape using their thumb and index finger, and to then place it on a nearby marker. The 12 basic shapes each appeared 4 times, in fixed pseudo-random order, once at 0º, 90º, 180º and 270º from their canonical orientation.

A camera was positioned on the floor directly beneath the shape and recorded the grasping movement. Subsequent frame-by-frame analysis allowed video capture of the initial point of contact between shape, thumb and index finger. As in Karnath et al. (2009), a grasp line between thumb and index finger could then be digitally superimposed on the image, and by calculating the shortest perpendicular distance between the grasp line and the shape's centre of mass, a deviation score (in mm) was produced for each trial. In the perceptual task, two shapes were positioned 10cm apart on the desktop. The two shapes were rotated to 0º, 90º, 180º or 270º from their canonical orientation, and always differed in orientation from one another. Each shape appeared in two 'same' trials and four 'different' trials making 8 appearances overall, and was equally as likely to appear in position 1 and position 2. There were 48 trials for the perceptual and grasping experiments, the order of which was pseudo-randomised but fixed for all participants. Participants were told to say whether the two shapes were the same or different. They were told to treat shapes as the same if they appeared at different angles but otherwise looked identical. Three practice trials were given before the start of each task, and the perceptual task was always performed first.

Figure 5 here

4.5.2. Results

In the perceptual task, the patient was unable to discern any of the shapes from the background so could not provide a task response. By contrast, the controls produced a mean accuracy of 21/24 (SD=1.2) correct. In the grasping task, the patient showed no difficulty in reaching out and picking up the shapes. The mean distance between the grasp line and centre of mass shapes was 2mm for the patient, and 2.3mm (SD=0.5) for the controls (see Figure 6). A modified *t*-test indicated that this difference was not reliable (t=0.4, p=0.75).

Figure 6 here

5. General Discussion

5.1. Occipital calcification and coeliac disease

Although occipital calcification has been commonly associated with coeliac disease there has until very recently been no clear indication in the literature that this can be associated with visual impairment of any kind. Magaudda et al. (1993) described 20 patients with bilateral occipital cortical and subcortical calcification. 95% had epilepsy and, in 8 of 16 cases studied, intestinal biopsy had shown evidence of coeliac disease. There is no mention of visual failure in any case, all of whom were aged less than 23 years (range 6-23). Patients with severe intractable epilepsy were said to have mild mental retardation, and one was noted to have constricted visual fields. The results of a detailed visual assessment are not given in the article. Similarly in a series of 27 cases showing the combination of coeliac disease, epilepsy and parieto-occipital calcification there was no mention of visual impairment other than at the time of seizure (Gobbi et al., 1992). As far as we are aware, the current patient is the first reported case who shows evidence of progressive, higher visual cortical disorder in the presence of these co-morbidities. A case with a visual deficit that has been static since treatment for coeliac disease was instituted has been described but not with the specificity of impairment reported here (Millington et al., unpublished results). In the present case we cannot be sure whether the progressive deterioration occurred because of the late diagnosis of coeliac disease or because of a difference in the underlying pathological process. This will only become clear as further cases of visual deficit in BOC are described.

5.2. Characteristics of the visual impairment

The patient shows entirely normal threshold detection throughout her visual field. Performance on Goldmann perimetry remained normal throughout the testing period and visual acuity and contrast sensitivity were also normal whenever tested. Verbal IQ remained

preserved, and tactile recognition did not decline at the same rate as visual recognition. The only evidence of significant non-visual decline was on the orally-presented Warrington word recognition memory task. We cannot exclude a more general process leading to cognitive decline in this patient. For example this could explain why she has continued to deteriorate despite starting a gluten free diet at age 61. However this does not militate against the extraordinary specificity of the resulting visual deficit which is likely to be primarily due to BOC. The initial presentation of the patient was as an acquired alexia but from the earliest assessment at age 59 there was evidence of severe visual perceptual deficits in basic shape perception and object recognition. There was also evidence for dyscalculia but this was not marked and it is likely that the alexia partly resulted from the globally impaired form perception. The coincident decline in reading and spelling ability is consistent with the extension of occipital-temporal calcification into the visual word form area (see Purcell, Shea & Rapp, 2014). Most notably, the visual perceptual deficits were not accompanied by comparable problems in either gross or fine visuo-motor coordination.

How might the specificity of the patient's visual loss be explained? Her normal visual threshold detection is in keeping with the absence of calcification in primary visual cortex, and points to a higher-level, cognitive impairment. The sparing of visuo-motor function may rest on intact projections from striate cortex to dorsal stream mechanisms in posterior parietal cortex (Zeki & Shipp, 1988) that for the most part bypass calcified brain. Visuo-motor capacity may also be supported by direct retinal-collicular projections to parietal lobe (Kentridge, Heywood & Weiskrantz, 1997). The specificity with which these subcortical afferents link to dorsal, rather than ventral, visual areas was recently demonstrated in a study in which transynaptic retrograde tracer was injected into macaque V2, V3, V4 and V5. While the V3 and V5 injections left robust levels of disynaptic label within superficial superior colliculus neurons (and inferior pulvinar), injections into V2 and V4 showed no such label

(Lyon, Nassi & Callaway, 2010). Unfortunately, the patient is claustrophobic and unable to undergo more radiological scanning to further investigate the anatomical basis of her preserved function.

By contrast, the patient's profound failure to identify visual stimuli is in keeping with a deleterious effect of calcification on her lateral occipital cortex. This region is known to play an integral role in the recovery of shape and contour information during visual recognition and scene-based perception (see Grill-Spector, Kourtzi & Kanwisher, 2001; Milner, 2014). The present patient is notable for being only one of four who show a visual perception/action dissociation under central, immediate vision. Of these other patients, JS (Karnath et al., 2009) shows the most circumscribed lesion which is confined to ventral medial occipital-temporal lobe. Given that the broader lesion territory seen in patient SB (Dijkerman et al., 2004) encompasses this area, and that DF may also show subtle ventral-medial degeneration, (Karnath et al., 2009) it might be inferred that this region is critical for recovering shape and contour information for object recognition. However, the circumscribed pattern of calcification seen in the present patient indicates that more lateral areas of occipital cortex are likewise critical and that, accordingly, no single area is responsible.

In recent years, the distinction between vision for action and perception has become blurred following the absence of new, corroborative cases and the results of functional imaging studies that have highlighted functional overlap rather than separation (McIntosh & Schenk, 2009). More detailed neuropsychological assessments also indicate that patients with a seemingly pure agnosia show unusual patterns of visually-guided reaching when performing tasks outside of central vision or from memory (See Pisella, Binkofski, Laske, Toni & Rossetti, 2006). While this emphasis on overlap has refined an initially crude distinction between visuo-motor and perceptual processes, it should not however eclipse the striking,

albeit rarely observed, distinction between vision for action and vision for perception within central, immediate vision. The current case provides rare neuropsychological endorsement of this distinction, and further indicates that it is does not simply arise from the complex pattern of neural reorganisation that follows traumatic brain injury. Rather, the capacities to use vision for action versus perception derive from processes that are differentially sensitive to the long-term calcification of occipital lobe, implying that they have, at least partly, distinct cortical origins.

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Figure Legends

Figure 1. Non-contrast axial CT examination of the brain demonstrating symmetrical florid calcification involving the cortices of the posterior temporal and occipital lobes. There is relative sparing of the medial occipital cortices. Note is made of periventricular white matter symmetrical hypodensity in the frontal lobes as well as central white matter volume loss.

Figure 2. Coronal FLAIR (a) and axial T2 weighted (c) sequences demonstrating confluent T2 weighted hyperintense signal within the subcortical and periventricular white matter of the cerebrum in addition to cortical and subcortical volume loss. There is an impression of selective disproportionate cortical volume loss affecting the posterior temporal and lateral occipital regions in a symmetrical fashion. The axial T2*-weighted Gradient Echo sequence (b) illustrates marked gyriform susceptibility involving the posterior temporal, lateral occipital and posterior superior parietal cortices, suggestive of mineralisation (calcification) as seen on the CT study in Figure 1.

Figure 3. Schematic of apparatus used in the visually guided reaching experiment.

Figure 4. Polar plots from the visually guided reaching experiment illustrating the accuracy of (a) perceptual orientation judgments and (b) reaching movements for the patient and controls. Each line represents an individual trial (averaged across participants in the control group). The orientations of individual trials have been normalised to vertical so that a trial with 0^0 error is represented by a vertical line and a trial with 90^0 error is represented by a horizontal line.

Figure 5. Irregular shapes presented in the irregular object grasping experiment.

Figure 6. Frequency distribution showing the range and number of deviations between grasp line and centre of mass for patient and controls.

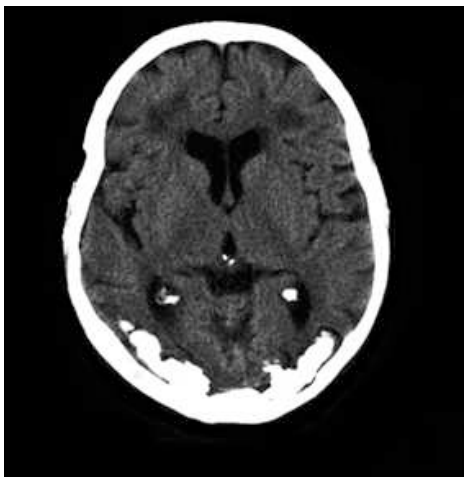


Figure 1

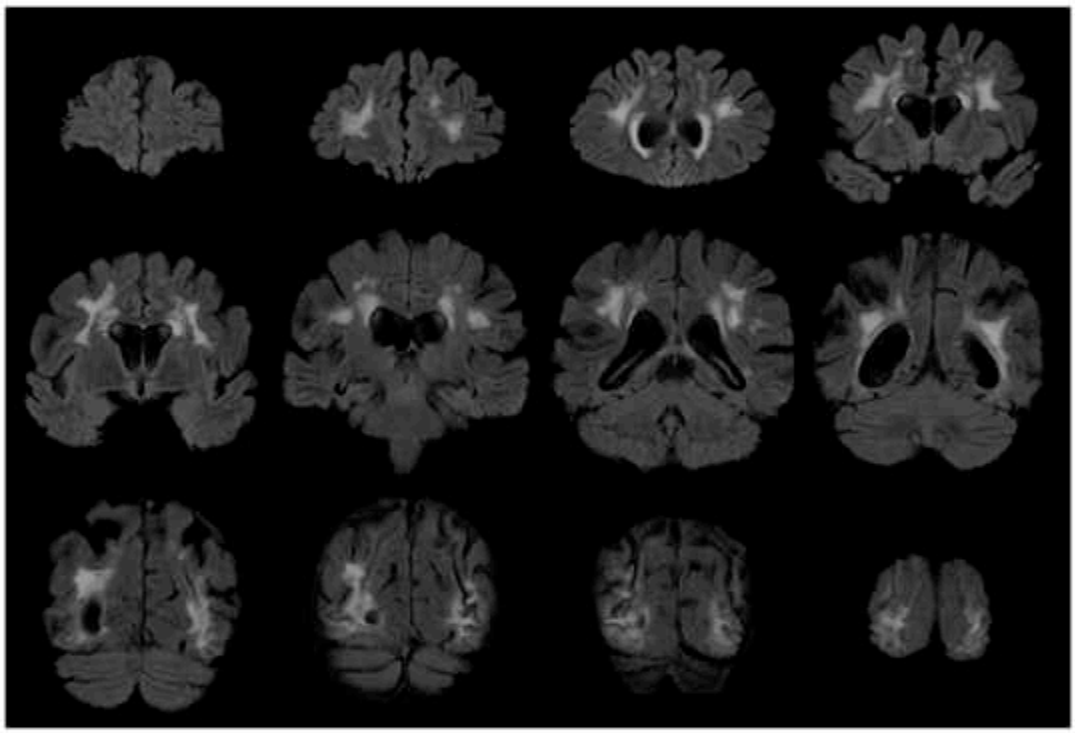


Figure 2a

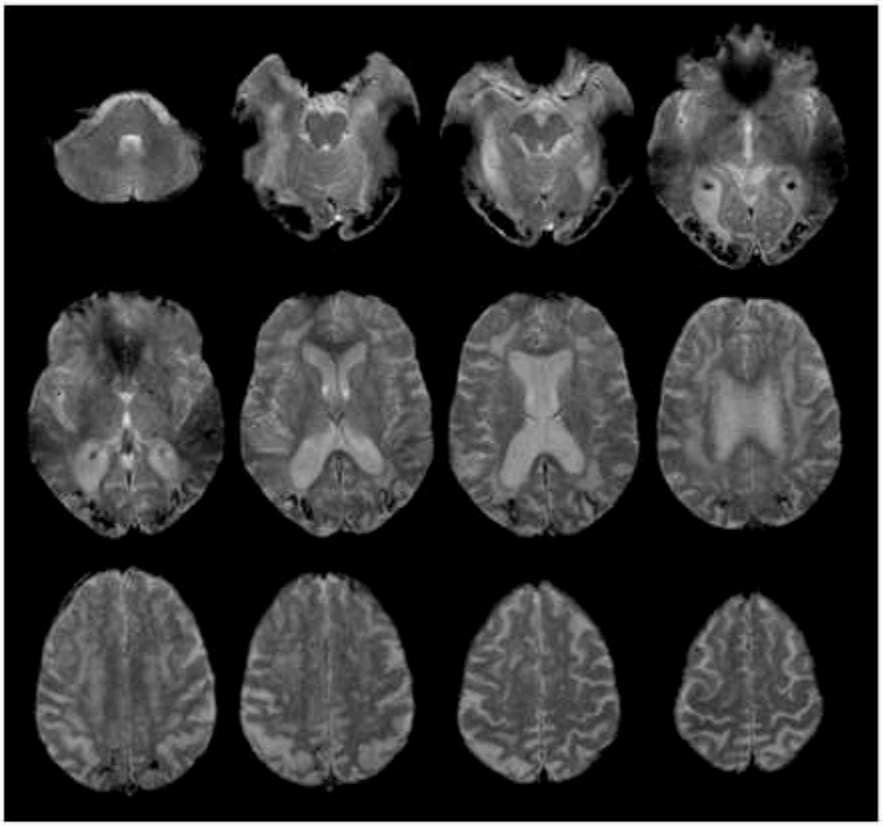


Figure 2b

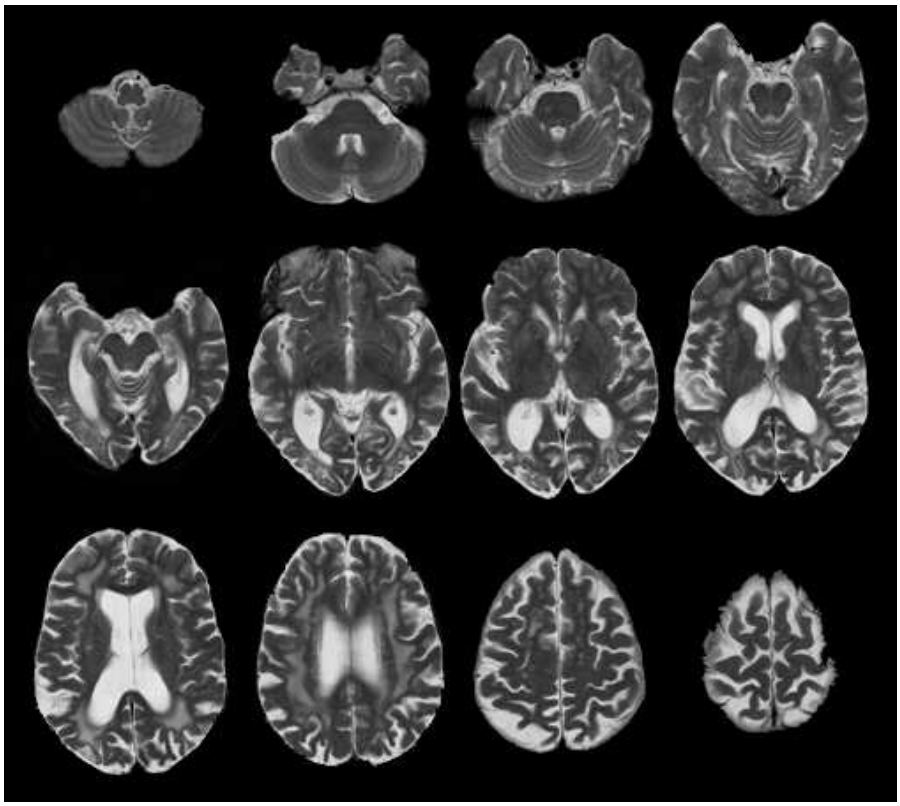


Figure 2c

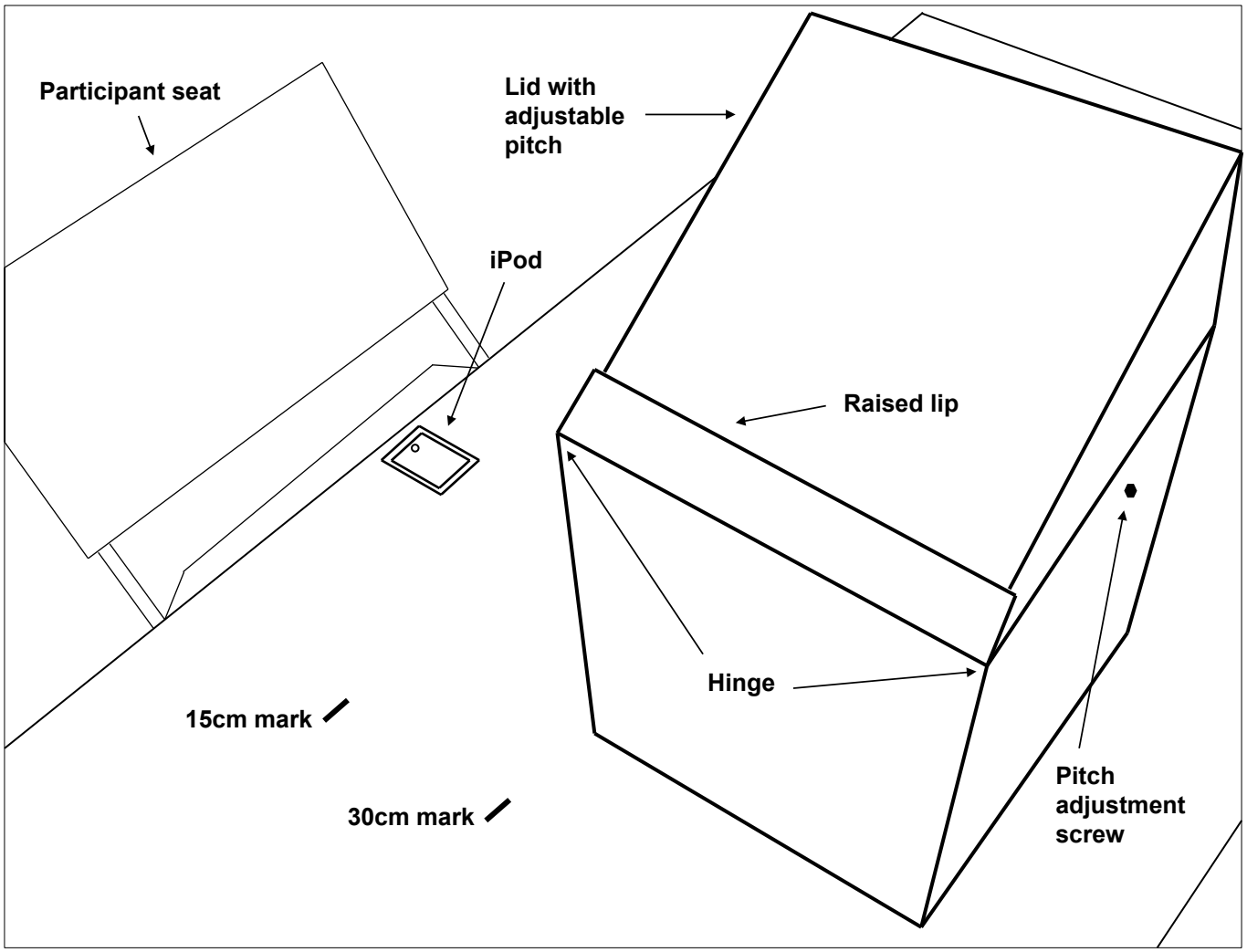
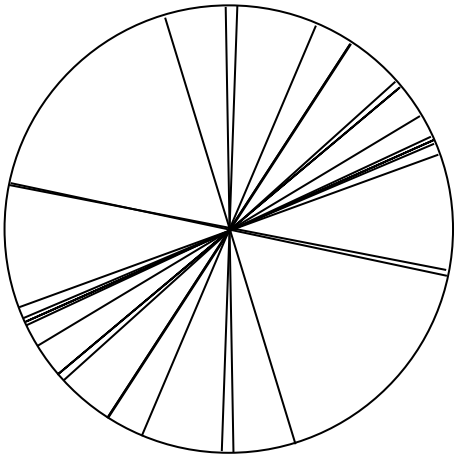
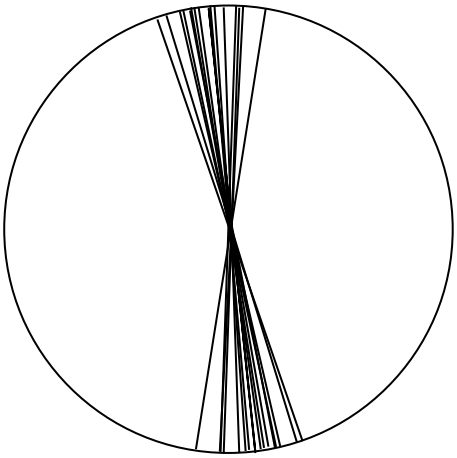

Participant seat
Lid with adjustable pitch
iPod
Raised lip
Hinge
15cm mark
30cm mark
Pitch adjustment screw

Figure 3

(a)

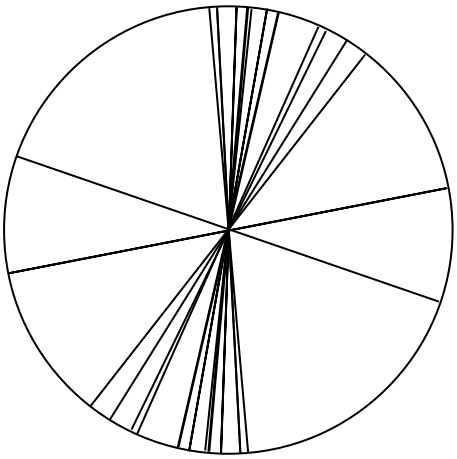


patient perceptual orienting

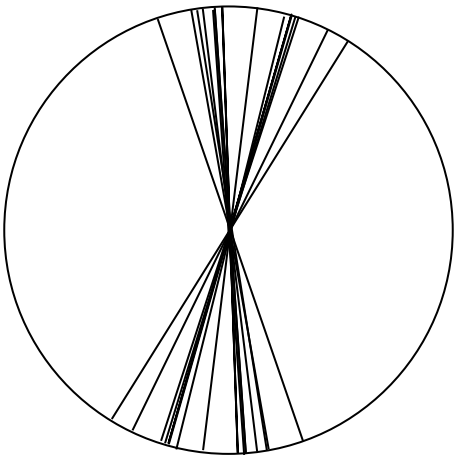


controls perceptual orienting

(b)



patient reaching



controls reaching

Figure 4

Figure 5

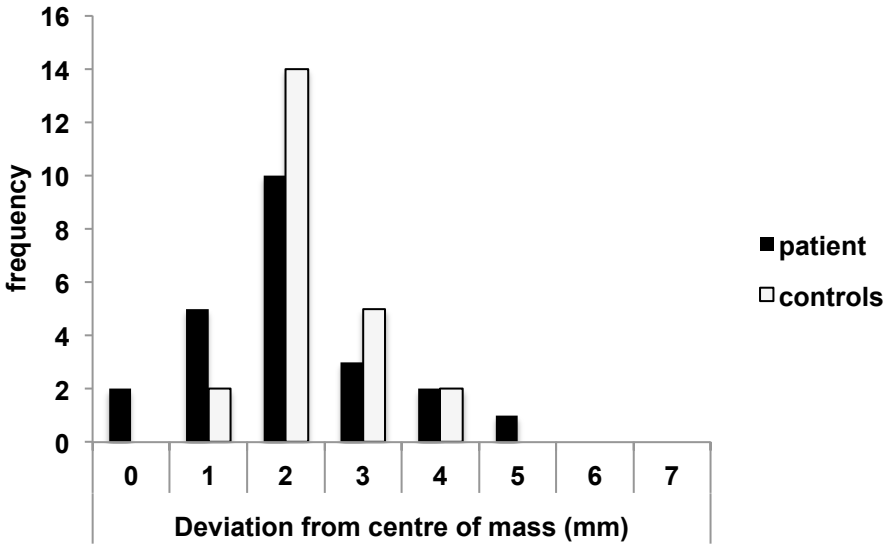

16
14
12
10
8
6
4
2
0
frequency
0
1
2
3
4
5
6
7
Deviation from centre of mass (mm)
patient
controls

Figure 6

Table 1. Verbal sub-test scaled scores of the WAIS-R

	Age						
	59	65	68	70	73	76	80
Digit span	14	11	8	11	9	12	7
Vocabularly	14	14	12	12	13	12	12
Arithmetic	7	7	6	7	6	6	6
Similarities	11	13	14	13	12	11	11

Table 2. Recognition Memory Test Scores (percentiles)

	Age							
	59	65	69	70	73	76	77	80
RMT	75	75	50	50	25	10	5	5

Table 3. Visual/tactile recognition and copying scores (%correct) for single wooden letters

	Age				
	68	70	71	76	77
Visual	35	10	10	0	0
Tactile	40	45	10	10	20
Writing	100	95	100	100	90

Table 4. Baxter spelling test scores (%correct)

	Age							
	65	68	70	71	73	76	77	80
Baxter	75	75	57	63	51	53	48	28

Table 5. Two-dimensional shape discrimination Efron scores (%correct)

		Age					
		59	65	68	71	73	76
F		100	100	100	100	95	100
E		100	100	100	100	85	75
D		100	100	100	95	85	75
C		95	95	80	80	75	75
B2		85	70	75	80	60	60
B		85	60	75	70	0	0

Table 6. Farnsworth Munsell 100 hue arrangement total error scores

	Age		
	59	65	69
FM100	350	450	500

Table 7. Farnsworth Munsell 100 hue arrangement same/different scores

	Age					
	65	68	71	73	76	77
A	70	100	95	95	100	100
B	30	80	65	60	100	100
C	0	55	50	35	45	85
D	0	0	0	10	35	65
E	0	0	0	5	25	40

Table 8. Visual feature search (%correct)

	No. distractors			
	0	3	11	35
Colour				
control	100	100	100	100
patient	100	100	90	90
Orientation				
control	100	100	100	100
patient	100	60	45	50

Table 9. Recognition of real objects (%correct)

	Age						
	65	68	70	71	73	76	80
Vision	61	45	20	12	10	5	5
Touch	90	70	65	85	60	35	40