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24.6 Disorders of the special senses CONTENTS 24.6.1 Visual pathways 5913 Sara Ajina and Christopher Kennard 24.6.2 Eye movements and balance 5922 Michael Strupp and Thomas Brandt 24.6.3 Hearing loss 5931 Linda Luxon 24.6.1 Visual pathways Sara Ajina and Christopher Kennard ESSENTIALS Visual disturbances may be caused by diseases of the optic disc, optic nerve, optic chiasm, optic tract, lateral geniculate nucleus, optic radiations, and occipital lobe of the brain, as well as other brain areas involved in complex visual processing. Diagnosis of disturbances of the visual pathways requires both knowledge of their anatomy and physiology, and the ability to carry out a thorough neuro-ophthalmological examination which should enable (1) documentation of the character and extent of the visual disturbance, and (2) topographic localization of the lesion, so that the relevant investigative techniques, such as radiological imaging, can be appropriately requested. Visual disturbances typically produced by particular lesions (1) Retina—peripheral field constriction as in retinitis pigmentosa and a central field defect as in age-related macular degeneration. (2) Optic nerve—‘relative afferent pupillary defect’; defect of colour vision; central scotoma or arcuate defect (lesions just prior to the chiasm produce a junctional scotoma). (3) Optic chiasm—bitemporal hemi- anopia. (4) Optic tract—incongruous hemianopic defects. (5) Lateral geniculate nucleus—wedge-shaped homonymous field defects. (6) Optic radiations—homonymous quadrantinopia or hemianopia depending on the extent and location of the lesion (upper quadrant, temporal lobe; lower quadrant, parietal lobe). (7) Occipital lobe of the brain—(a) striate cortex—homonymous hemianopia, sometimes with macular sparing, particularly with vascular disturbances; (b) su- perior or inferior bank of the striate cortex—inferior or superior alti- tudinal defects, respectively. (8) Extrastriate areas involved in higher visual processing—can produce a

wide variety of defects, including specific loss of a visual modality such as colour (achromatopsia) or movement (akinetopsia), or visual agnosia. Clinical evaluation of visual function Examination of visual function initially requires an accurate assess- ment of the visual acuity. Acuity should be tested separately in each eye using the Snellen or some other optotype chart, which contains rows of letters of diminishing size. If an impairment (>6/6) is noted, the patient should be allowed to wear spectacles or alternatively to view the chart through a pinhole, which eliminates any significant refractive error or optic media distortion. If the acuity does not im- prove, it is necessary to try to distinguish media opacities and ret- inal abnormalities from optic nerve dysfunction using the swinging flashlight test. In a darkened room each eye is alternately stimulated with a bright light, which is moved rhythmically from one eye to the other. When the light is swung from the good eye on to the defective eye, dilatation of the pupil is termed a ‘relative afferent pupillary de- fect’, and signifies optic nerve dysfunction. Another good indicator of an optic nerve disturbance is a defect of colour vision, which may be tested using one of several available booklets of colour plates, such as the Ishihara pseudo-isochromatic plates. The photostress test is a useful test to distinguish a maculopathy from optic nerve dysfunction. The retina of the ‘normal’ eye is bleached by shining a bright light at the pupil for 10 s, and measuring the time for normal acuity to be re- established. The test is repeated in the ‘abnormal’ eye and, if the difference in recovery time between the two eyes is greater than 60 s, the test is considered abnormal, indicating that the impairment is retinal and not due to an optic nerve disturbance. Careful fundoscopic examination of the eye is essential to identify abnormalities of the optic media, retina, and optic nerve head. Finally, examination of the visual fields is essential for topo- graphic localization because, as a result of the invariate ordering of nerve fibres along the visual pathway, lesions at specific sites pro- duce field defects of specific shapes (Fig. 24.6.1.1). Simple confron- tation tests provide a qualitative method of investigating the visual fields. The examiner sits opposite the patient, maintaining a constant

 distance, and each eye is tested separately. With the patient fixating on the examiner’s nose, he or she is asked to count stationary fingers presented on either side of the vertical meridian in each quadrant in turn. If the patient cannot identify the fingers in a particular area, they are gently wiggled, and the hand moved towards fixation until they are visible to the patient, so mapping out the field defect. To examine the central field a red 5- to 10-mm hatpin is moved away from or towards the central point of fixation. The patient is asked to describe any changes in the perception of colour or brightness, and whether or not the object disappears at any point. Perimetry provides a quantitative technique for measuring the fields, but a full description is beyond the scope of this chapter. Abnormalities of the optic disc Optic disc anomalies Optic nerve hypoplasia Hypoplasia of the optic nerve can be mild or severe, unilateral or bi- lateral, and may be associated with normal or impaired visual func- tion. It can occur in isolation, or be associated with central nervous system anomalies, such as the absence of the septum pellucidum in De Morsier’s syndrome (septo-optic dysplasia). If there is a clinical indication, such as an enlarged blind spot or arcuate defect despite a normal disc appearance, optical coherence tomography can be useful at detecting more subtle abnormalities. This noninvasive test will identify thinning of the inner retinal nerve fibre layer corres- ponding to the hypoplastic nerve. Optic nerve dysplasia Optic nerve dysplasia presents with a spectrum of abnormalities, including optic nerve colobomas, optic pits, and the morning glory syndrome, all considered to be associated with abnormal closure of the embryonic optic stalk and cup fissure. They are sometimes associated with basal encephaloceles and other fore- brain anomalies. Optic disc colobomas These are deeply

evacuated nerve head anomalies with blood ves- sels exiting from the margins, which are associated with defects in the retinal nerve fibre layer, leading to an appropriate visual field loss. Optic pits Optic pits are crater-like depressions in the optic disc with a dark- grey hue, usually situated in the temporal disc margin with an ac- companying nerve fibre layer defect. The morning glory syndrome In this condition, an enlarged dysplastic disc is associated with an elevated, centrally retained mass of glial, embryonic glial, and vas- cular material, which radiates outwards in a sunburst pattern. Tilted discs An asymmetrically shaped, tilted disc is produced when the optic nerve leaves the globe at an extremely oblique angle. It is often as- sociated with a crescentic zone of exposed sclera along one edge which results in elevation of the superior disc. The disc may appear hypoplastic and patients with this condition often have moderately high myopia and oblique astigmatism. Optic nerve drusen Drusen of the optic disc can give rise to an elevation of the optic nerve head. Drusen are intrapapillary, prelaminar, refractile con- cretions that arise from degenerating nerve fibres (Fig. 24.6.1.2e). Anomalous discs due to drusen are usually smaller than normal, have an absent central optic disc cup, and exhibit an aberrant branching pattern of the central retinal vessels. Initially the drusen are buried with simple elevation of the disc, but become more ap- parent in later years when they seem to give rise to a typical lumpy disc, with a scalloped margin. Myelinated nerve fibres In slightly less than 1% of the population some portions of retinal nerve fibres are myelinated, although normally optic nerve mye- lination stops at the lamina cribrosa. It appears on fundoscopy as a white area, usually adjacent to the disc, which has a centrifugal feathered edge (Fig. 24.6.1.2d). Optic disc swelling Although the terms ‘optic disc swelling’ and ‘papilloedema’ have in the past been used synonymously, it is now usual to refer only to papilloedema as optic disc swelling when it is associated with raised intracranial pressure. Other cases of optic disc swelling are due to either local abnormalities in the optic nerve or orbit, or congenital anomalies as described earlier. A Left eye B C D E F G H Right eye H G F E D C B A Fig. 24.6.1.1 Patterns of visual field loss due to lesions at different locations along the visual pathway: (A) optic nerve lesions result in a central scotoma or arcuate defect; (B) optic nerve lesions just before the chiasma produce a junctional scotoma due to ipsilateral optic nerve involvement with the inferior contralateral crossing fibres (dashed lines); (C) chiasmal lesions produce bitemporal hemianopia; (D) optic tract lesions result in incongruous hemianopic defects; (E, F) lesions of the optic radiation result in either homonymous quadrantanopia or hemianopia depending on the extent and location of the lesion (upper quadrant, temporal lobe; lower quadrant, parietal lobe); (G) lesions of the striate cortex produce a homonymous hemianopia, sometimes with macular sparing, particularly with vascular disturbances; (H) lesions of the superior or inferior bank of the striate cortex result in inferior or superior altitudinal defects, respectively.

 Local causes of optic disc swelling are usually associated with impaired visual acuity and colour vision, central, arcuate, or alti- tudinal field defects, and often an afferent pupillary defect. This con- trasts with papilloedema when the acuity and colour vision remain normal, except in the final stages, and is usually bilateral. Papilloedema The evolution of the disc changes in papilloedema caused by raised intracranial pressure are usually classified into four stages: early, fully developed, chronic, and atrophic. In early papilloedema there is disc hyperaemia, mild disc swelling with blurring of the striations of the fine peripapillary nerve fibre layer, dilatation of retinal veins with loss of spontaneous venous pulsations, and occasionally fine splinter haemorrhages at the disc margin (Fig. 24.6.1.2a). In fully developed papilloedema, disc elevation is moderate to marked, and there is increased venous distension and tortuosity, an increasing number of peripapillary haemorrhages, cotton wool spots, and dilated capillaries on the

disc surface. The retinal blood vessels and disc margin become increasingly indistinct (Fig. 24.6.1.2b). In chronic papilloedema, there is resolution of the haemor- rhages and exudates leaving a dome-shaped (‘champagne cork’) disc swelling, which often contains hard exudates. White refractile bodies may appear on the disc surface, known as corpora amylacea. As time goes on there is increasing nerve fibre attrition, leading to progressive visual field loss. Finally, there is postpapilloedema (consecutive) atrophy, in which the disc acquires a milky opalescence and the retinal vessels are sheathed. Clinical features Usually papilloedema is bilateral and there is an absence of visual symptoms. However, unilateral or bilateral transient visual obscurations may occur, which last a few seconds and are often associated with postural changes. Although it has been suggested that such obscurations herald permanent visual loss, there is no evi- dence to support this view. The longer the papilloedema persists, the more likely there is to be progressive visual field loss, which usually starts as a peripheral field constriction. Occasionally, sudden visual loss occurs in a patient with papilloedema due to ischaemic optic neuropathy. Pathogenesis Papilloedema is due to impairment of axonal transport in the ret- inal nerve fibres, leading to axonal distension, which is seen as disc swelling at the level of the prelaminar optic nerve. Aetiology There is a vast array of different causes leading to increased intracra- nial pressure, in particular space-occupying lesions such as tumours (Table 24.6.1.1). Management Treatment primarily depends on the underlying cause of the raised intracranial pressure. If it is due to a mass lesion that cannot be Fig. 24.6.1.2 (a) Mild papilloedema: note several features of papilloedema including blurring of the optic disc margins, hyperaemia and elevation of the optic nerve head, and oedema of the retinal nerve fibre layer. (b) Severe papilloedema: the optic disc here is markedly swollen, with several surrounding splinter and flame haemorrhages present, as well as a few cotton wool spots representing nerve fibre layer infarcts. (c) Optic atrophy: in optic atrophy, the loss of capillaries in the connective tissues among the prelaminar nerve fibre layer accounts for the pale appearance of the optic disc. (d) Myelinated nerve fibres: the abnormal myelination of fibres in the peripapillary nerve fibre layer gives them an opaque, white appearance with feathery edges. Lesions are often continuous with the optic disc, and may be associated with retinal vascular abnormalities. (e) Optic nerve drusen: the optic disc is usually smaller than normal, with an absent central optic cup. The edge of the optic disc is also irregular and lumpy, and there is often an aberrant branching pattern of the central retinal vessels. Table 24.6.1.1 Causes of papilloedema Mass lesions: tumours, aneurysms, granulomas, parasitic cysts Intracranial haemorrhage: subdural haematoma, epidural haematoma, subarachnoid haemorrhage Arteriovenous malformations Intracranial infections: brain abscess, meningitis, encephalitis Obstructed cranial venous outflow: dural venous sinus thrombosis, dural venous sinus infiltration, jugular vein compression, dural venous sinus arteriovenous malformation Obstructive hydrocephalus Brain oedema following trauma Spinal cord tumours Idiopathic intracranial hypertension (i) idiopathic (ii) secondary to metabolic and endocrine disorders: Addison’s disease, diabetic ketoacidosis, thyrotoxicosis, hypoparathyroidism, chronic uraemia (iii) secondary to toxic causes: tetracycline, nalidixic acid, steroid therapy, lithium, hypervitaminosis A Guillain–Barré syndrome Craniostenoses Mucopolysaccharoidoses Systemic illness: Behçet’s syndrome, status epilepticus, Reye’s syndrome, Whipple’s disease, systemic lupus erythematosis, systemic hypertension, chronic respiratory insufficiency

 completely removed, or a nonsurgically remediable cause, a shunting procedure or medical measures (e.g. osmotic agents or diuretics), such as acetazolamide may be used. In idiopathic intracranial hyper- tension, initial management would

also include weight loss. Ischaemic optic neuropathy Ischaemic optic neuropathy (Fig. 24.6.1.2c) is the result of infarc- tion of the optic nerve head, and can either be arteritic, as part of giant cell arteritis, or nonarteritic (idiopathic ischaemic neuropathy, anterior ischaemic optic neuropathy), which is the more common form of the condition. Nonarteritic anterior ischaemic optic neuropathy (NAION) This tends to occur in patients aged between 50 and 80 years, but 23% are under 50 years old. It is characterized by abrupt, painless, and generally nonprogressive visual loss, associated with an arcuate or altitudinal visual field loss. Acuity may worsen over days or even weeks in 35% of patients. In almost all cases, there is optic disc oe- dema, often associated with one or more splinter haemorrhages at the disc margin. Although previously considered irreversible, as many as 40% of patients may show some improvement. There is a 40% chance of involvement of the fellow eye within five years and only a 5% risk of having a second event in the same eye. Optic atrophy rapidly ensues after the ischaemic event. The cause of nonarteritic anterior ischaemic optic neuropathy remains obscure but is thought to result from vascular insufficiency of the posterior ciliary circulation affecting the distal optic nerve. It is often presents on awakening in the morning, which has suggested that nocturnal hypotension, sometimes related to medication for hypertension, may be a risk factor. There is often a small cup-to-disc ratio. There is also increasing evidence for vascular risk factors playing a part, including diabetes mellitus, hypercholesterolemia, and hyperten- sion: 60% of patients with nonarteritic ischaemic optic neuropathy have at least one vascular risk factor. There is no treatment of proven benefit, with use of systemic steroids remaining controversial but probably the most common treatment tried, and low-level evidence supporting secondary prevention with antiplatelet agents. The most important aspect of management is to exclude the possibility of the arteritic form, because in such cases the fellow eye is particularly vulnerable to similar involvement. Arteritic anterior ischaemic optic neuropathy (AION) The arteritic form of anterior ischaemic optic neuropathy usually oc- curs in giant cell (cranial, temporal) arteritis, but also occurs rarely in lupus and polyarteritis nodosa. Anyone with nonarteritic anterior ischaemic optic neuropathy over the age of 50 should be suspected of having giant cell arteritis. This often occurs in the context of head- ache, malaise, weight loss, anorexia, anaemia, proximal muscle ache or stiffness, temporal artery tenderness, jaw claudication, and fever. These symptoms and signs usually precede the visual loss. The disc infarction is similar to that seen in nonarteritic anterior ischaemic optic neuropathy. A high index of suspicion is required for giant cell arteritis and, if suspected in a patient with visual loss, an urgent erythrocyte sedi- mentation rate (ESR) and temporal artery biopsy should be arranged. At the same time as blood is taken for the ESR, the patient should be started on systemic steroids (3 daily doses of 1 g intravenous methylprednisolone, followed by oral 1 mg/kg per day). The oral steroid dose should be slowly tapered to maintain a normal ESR and the patient asymptomatic, and treatment should be continued for at least 12 months. Bone protection and prophylactic proton pump in- hibitors should also be prescribed for gastrointestinal protection. If steroids are withdrawn too early, a relapse of symptoms is common. In most patients the ESR is markedly elevated, as is the C-reactive pro- tein. Occasionally the ESR may be normal. A biopsy of the superficial temporal artery should be obtained as soon as possible after the diag- nosis has been considered. Histologically, the vasculitis is character- ized by mononuclear inflammation often involving the entire vessel wall, with giant cells usually present. The biopsy will not be affected by the use of corticosteroids for at least 48 h, and up to 14 days. A positive temporal artery biopsy confirms the diagnosis of giant cell arteritis, but in 25% of patients skip areas are found in biopsy specimens, and therefore a negative biopsy may sometimes be obtained. Optic atrophy Optic atrophy is the final result of a variety of disturbances to the optic nerve or retina. The disc appears pale, and

there is an absence of disc vasculature and retinal nerve fibres (see Fig. 24.6.1.1). Optic atrophy occurs after any disease process that results in death of the retinal ganglion cells with a dying back of their nerve fibres. This can, therefore, be due to diseases that directly involve the ganglion cells themselves or from damage to the axons in the pregeniculate visual pathway, resulting in retrograde atrophy. The development of optic atrophy is usually slow, dependent on its cause. In most instances the optic atrophy is bilateral, the disc appearing chalky-white in colour with clearly defined margins. The differential diagnosis of optic atrophy is considered in Table 24.6.1.2.
Table 24.6.1.2 Causes of optic disc atrophy Deficiency states Thiamine (‘tobacco–alcohol amblyopia’) B12 (pernicious anaemia, ‘tobacco amblyopia’?) Drugs/toxins Ethambutol Chloramphenicol Streptomycin Isoniazid Chlorpropamide Digitalis Chloroquine Ethchlorvynol Disulfiram Heavy metals Hereditary optic atrophies Dominant (juvenile) Leber’s Associated heredodegenerative neurological syndromes Recessive, associated with juvenile diabetes Demyelination Graves’ disease Atypical glaucoma Macular dystrophies

 Optic neuritis Optic neuritis is a term used to describe an optic neuropathy due to inflammation, usually due to demyelinating disease but may result from other inflammatory or infectious aetiologies. In most cases the optic disc is normal on ophthalmoscopy and the term ‘retrobulbar neuritis’ may be used. In those cases in which the optic disc is swollen, the terms ‘papillitis’ and ‘anterior optic neuritis’ may be used. Clinical features It is important to distinguish between those features of typical optic neuritis of idiopathic or demyelinating causation and those of atypical optic neuritis. It is more common in women (female:male ratio is 3:1), with an age of onset of 20–50 years (mean age of 30–35 years). In typ- ical optic neuritis there is usually acute unilateral loss of visual acuity and visual field, which may progress over hours or a few days, reaching its maximal effect within one week. Ninety per cent (90%) of patients complain of ocular pain, which is noted especially with eye movement, and which may precede the visual impairment by a few days. The visual loss may range from contrast defects with maintained acuity to no light perception with the associated signs of an optic neuropathy. The optic disc appears normal in about two-thirds of patients and swollen in a third. The patient is usually aged under 40 years, although optic neuritis may occur at any age, and improvement takes place in most patients (90%) to normal or near normal visual acuity over several weeks com- mencing usually within 2–3 weeks of onset. There may be persistent subtle residual defects of colour vision, depth perception, and contrast sensitivity, which may continue for several months. Subsequent disc pallor may occur, but does not correlate closely with the level of visual recovery. An afferent pupillary defect is present in over 90% of patients with acute optic neuritis. Although optic neuritis is generally associated with a central scotoma, a wide variety of field defects may be found, ran- ging from a central scotoma to altitudinal and nerve fibre layer defects. Atypical optic neuritis may involve unilateral or bilateral simultan- eous onset of optic neuritis in an adult patient. There is often a lack of pain and there may be other ocular findings suggestive of an inflam- matory process, such as an anterior uveitis. Other features include a worsening of visual function beyond 14 days of onset, in a patient out- side the 20- to 50-year age span. They may also have evidence of other systemic conditions, particularly inflammatory or infectious diseases (Table 24.6.1.3). The evaluation of patients with optic neuritis rather depends on whether or not it is a typical or an atypical case. Typical optic neuritis probably does not necessitate any additional laboratory investiga- tions, although an abnormal MRI of the brain significantly increases the likelihood of developing multiple sclerosis from around 20% to over 60%. Furthermore, this risk is dependent on the number of lesions identified on MRI; hence it is necessary to take this into consideration when making a decision

about commencing disease- modifying therapy. Those patients with atypical optic neuritis should have a chest radiograph, laboratory tests, including a blood count, biochemistry, tests for collagen and vascular disease, and for syphilis serology. Examination of the cerebrospinal fluid is probably justified in this group of patients. Neuromyelitis optica This is a rare but important cause of bilateral or recurrent optic neur- itis that is clinically and pathologically distinct from multiple scler- osis. There is autoantibody-mediated loss of the aquaporin-4 water channel protein on astrocytes, which may cause secondary demye- lination in the central nervous system, including the optic nerves. Antibody testing for neuromyelitis optica (NMO)-IgG has 94% specificity, and sensitivity of diagnosis increases to 99% with the re- vised diagnostic criteria including MRI evidence of a spinal cord or brain white matter lesion. Classically, the disease affects the optic nerves and spinal cord, causing longitudinal extensive transverse myelitis. In general, there is a lower frequency of brain lesions in neuromyelitis optica compared to multiple sclerosis, especially early in the disease, although this is not always the case. The mainstay of treatment is to prevent relapses, and patients with seropositivity at initial presentation are at particularly high risk of developing future episodes of optic neuritis. Although there is little evidence for treat- ment, measures include use of corticosteroids and plasma exchange in an acute attack, and long-term immunosuppression for mainten- ance therapy. Management In typical optic neuritis there is no evidence-based treatment which alters outcome. Although prednisolone or intravenous methylprednisolone may lead to a more rapid visual recovery, at the end of six months the visual acuity is no better than with no treatment. Therefore, steroid treatment of patients with typical optic neuritis is unnecessary, unless there is severe ocular pain that cannot be managed with analgesics, or if there is already poor vision in the fellow eye due to some other disease process. The likelihood of developing multiple sclerosis after optic neuritis is approximately 50% after 13 years. This is strongly related to the presence of white matter lesions on a baseline brain MRI. Where such lesions are pre- sent the evidence on which to base a decision as to whether to raise the issue of disease-modifying treatment is still unclear. Heredofamilial optic neuropathies The hereditary optic neuropathies can either be those that are auto- somal dominant or recessive or those that are due to point mutations in mitochondrial DNA. The autosomal conditions usually present in childhood with impaired vision and pale optic discs. Table 24.6.1.3 Causes of optic neuritis Unknown aetiology Multiple sclerosis Viral infections of childhood (measles, mumps, chicken pox) with or without encephalitis Viral encephalitides Postviral, paraviral infections Infectious mononucleosis Herpes zoster Contiguous inflammation of meninges, orbit, sinuses Granulomatous inflammations (syphilis, tuberculosis, cryptococcosis, sarcoidosis) Intraocular inflammations

section 24 Neurological disorders 5918 Leber’s hereditary optic neuropathy This mitochondrial disorder develops primarily in men (approxi- mately 14% in women) in the second to third decades of life. It is characterized by an abrupt loss of central vision in one eye although vision may progressively worsen over days. Occasionally visual loss may occur simultaneously in the two eyes. There is no associated pain on eye movement, in contrast to acute optic neuritis, and the visual loss is usually permanent with optic atrophy and large ab- solute central scotomas. However, the fundoscopic picture in the acute phase often shows swelling of the papillary nerve fibre layer, circumpapillary telangiectatic microangiopathy, and tortuosity of the retinal vessels. In most cases, visual dysfunction is the only manifestation in Leber’s hereditary optic neuropathy, but rare associations with car- diac conduction abnormalities have been reported and it is appro- priate to recommend a routine ECG. There is a maternal pattern of inheritance and point mutations in mitochondrial DNA, particularly at the 11 778 nucleotide, and less frequently at 3460 and 14 484,

have been identified. The significance of the point mutation at 14 484 is that a much higher percentage (37% as opposed to 4%) of patients show some visual recovery when compared with patients who have a defect at 11 778. Several sec- ondary mutations have also been identified. It is therefore appro- priate to carry out genetic testing in those individuals presenting with atypical optic neuritis of the appropriate sex and age, even if a positive family history is not available. It is also worth noting that there is incomplete penetrance of the disease, with only 50% of males and 10% of females with mutations developing the pheno- type. It is therefore thought that additional factors may play a role, with tobacco smoking and alcohol consumption identified as the two strongest risk factors. There is no effective treatment, although some studies suggest modest results with a derivative of coenzyme Q10, idebenone, which is a potent antioxidant and inhibitor of lipid peroxidation. Dominant optic atrophy Also known as Kjer's optic neuropathy, this is an insidious, slowly progressive optic neuropathy with typical onset in the first decade of life. It is inherited in a dominant fashion. It has an estimated preva- lence of approximately 1:50 000. Patients often present with slowly progressive bilateral and symmetrical visual loss, frequently accom- panied by central or centrocecal scotomas. Dyschromatopsia almost always occurs, with blue–yellow and red–green disturbances being the most common. In 60% of cases, a mutation in the nuclear gene OPA1 was identified as the genetic basis (encoding a mitochon- drial dynamin-related GTPase protein), with most cases mapped to chromosome 3q28-q29. Spontaneous recovery does not usually occur, and there is currently no treatment. Nutritional and toxic optic neuropathies Bilateral, slowly progressive, central visual loss with centrocaecal scotomas, and usually normal or mild temporal atrophic optic discs, characterizes optic nerve failure due to either nutritional de- ficiency or a toxic cause. Once a family history of one of the heredi- tary familial diseases has been excluded, this condition should be considered, and is usually due to a combination of alcohol abuse, deficiencies within the B-vitamin complex, and frequently a high to- bacco consumption. With treatment by abstinence of the likely toxic agents and vitamin supplementation, recovery of vision usually oc- curs, unless the condition is so long standing that optic atrophy has intervened. Recent epidemics of optic neuropathy in Cuba and West Africa have probably been related to multiple dietary deficiencies. Toxic optic neuropathy has been associated with ethambutol, chloramphenicol, amiodarone, linezolid, disulfiram, halogenated hydroxyquinolones, lead, isoniazid, and vincristine. Tumours of the optic nerve Optic nerve sheath meningiomas Although optic nerve sheath meningiomas may arise directly from the optic nerve sheath, usually in the orbital regions of the nerve, they frequently arise from the tuberculum sellae, sphenoid wing, and olfactory groove, leading to secondary invasion or compres- sion of the nerve. Primary optic nerve sheath meningiomas, which arise from the dural sheath of the intraorbital optic nerve, are most frequently found in middle-aged women and are usually unilateral, but if bilateral raise the possibility of central neurofibromatosis type 2 (NF-2). Although most patients will have mild (2–4 mm) prop- tosis and may already have optic disc pallor at the time of their initial consultation, they complain of dimming of vision and de- creased colour vision. Visual loss progresses over years, with optic disc swelling gradually being supplanted by optic atrophy, with or without the evolution of optociliary venous (retinochoroidal anas- tomoses) shunt vessels. The computed tomography (CT) picture in patients with these tu- mours is most often one of diffuse narrow enlargement of the optic nerve, with bulbous swellings of the nerve in the region of the globe and orbital apex (Fig. 24.6.1.3). 'Railroad-track' calcification of the optic nerve sheath in the orbit is a characteristic feature. Use of MRI has enabled optic nerve sheath meningiomas to be distinguished from optic nerve gliomas, where the former but not the latter show that the nerve is readily distinguished from the optic nerve sheath. Fig. 24.6.1.3 CT image revealing a benign left optic nerve glioma. There is classical

fusiform expansion of the optic nerve, causing mild anterolateral displacement of the globe.

24.6.1 Visual pathways 5919 Management of patients with optic nerve sheath meningiomas is controversial. Although there is general agreement that nerve sheath tumours are most aggressive in children and become pro- gressively more indolent with advancing age, there is no con- sensus as to the best way to treat these lesions. Clinical resection, particularly when there is intracranial spread, is usually incom- plete. These patients rarely die from the meningioma and it is probably best just to observe. In some instances radiotherapy has been shown to result in some visual improvement, but should be reserved for those patients in whom there is clear evidence of progression. Optic nerve gliomas Optic nerve gliomas, which may also involve the chiasma, are of two distinct types. By far the more common is the benign glioma of childhood, the other being the malignant glioblastoma in adults. Approximately a quarter of cases occur in the setting of NF-1, where there is a strong female predominence. Benign optic nerve gliomas usually present within the first two decades of life, with a peak incidence from 1 year to 6 years of age. They represent 3–5% of childhood brain tumours. Almost all are histologically World Health Organization (WHO) grade I pilocytic astrocytomas. The usual presenting manifestations are proptosis and visual loss, which may be so mild as to be undetectable, although a profound reduction in acuity is more common. The fundus may show either papilloedema or optic atrophy. MRI is the preferred method of imaging optic nerve gliomas, which usually have a fusi- form appearance, and have an almost pathognomonic appearance, so biopsy is usually not warranted. The clinical course of childhood optic nerve gliomas is highly vari- able. In some, tumour enlargement proceeds very slowly for a time but then reaches a plateau, whereas in others the enlargement proceeds unabated. Optic nerve gliomas are generally managed conservatively with regular follow-up, with evidence of any progression being an indicator for treatment. With evidence of progression some practi- tioners favour radiation therapy for lesions with chiasmal involve- ment and surgery for at least those tumours restricted to the orbit. Optic nerve gliomas of adulthood are malignant gliomas that usu- ally arise in men aged 40–60 years. These patients often present with a rapid onset of visual failure, which on some occasions may mimic acute optic neuritis. The tumour rapidly progresses, and the patient usually dies within a short period. Other optic nerve tumours Metastatic cancer may lead to optic nerve involvement, either as a result of infiltration of the meninges, as occurs with cancer of the breast and lung, or by direct tumour infiltration, as with lymphoproliferative disorders and certain types of leukaemia and non-Hodgkin’s lymphoma. Paraneoplastic optic neuropathy has also been described in patients with small cell carcinoma of the lung. Disorders of the optic chiasm Approximately 25% of all brain tumours occur in the chiasmal re- gion and, as half of these cases initially present with visual loss, an appreciation of the various field abnormalities is important. Although there are several other causes for the chiasmal syndrome, such as trauma and demyelination, these are rare. The neuro- ophthalmological signs of a compressive optic chiasmal lesion are primarily a field defect and deterioration of visual acuity, which de- pend on the relationship of the chiasma to the pituitary. The classic field defect of a chiasmal lesion is a bitemporal hemianopia. This may be complete or incomplete and may or may not be symmetrical. It is unusual to have a bitemporal hemianopia with no reduction in central visual acuity in at least one eye, because the optic nerve is usually compromised in addition to the chiasma. In large series of patients with pituitary tumours the most common field defect is a bitemporal hemianopia (67%); less common are junctional scotoma (29%), homonymous hemianopia (7%), and prechiasmal field loss (2%). Other signs include optic disc pallor, but its absence usually indicates that a virtually complete return of visual function will occur with

successful decompression. Other causes of chiasmal compression, in addition to pitu- itary adenomas (50–55%), include craniopharyngiomas (20– 25%), meningiomas (10%), and gliomas (7%). However, there are other, noncompressive, causes of bitemporal hemianopia, including empty sella syndrome, optochiasmal arachnoiditis, and radionecrosis. Optic tract and lateral geniculate nucleus lesions The optic tract is the first point in the visual pathways where the ip- silateral temporal and contralateral nasal retinal nerve fibres come together, and so the field defect is usually a partial or complete homonymous hemianopia. When partial, there is often gross in- congruity between the visual field defects found in each eye, which may also be found with lesions of the lateral geniculate nucleus and more rarely the optic radiations. The most frequently encountered lesions causing the optic tract syndrome are aneurysms, craniopharyngiomas, and pituitary tumours. Lesions of the lateral geniculate nucleus have been found to pro- duce incongruous wedge-shaped homonymous field defects, but when the aetiology is ischaemic the defect is usually congruous. The optic radiations As the geniculostriate fibres leave the lateral geniculate nucleus, the ventral fibres (subserving the superior visual field) pass anteriorly around the temporal horn of the lateral ventricle to form Meyer’s loop. Lesions in this region usually result in a wedge-shaped, con- gruous, homonymous field defect, mainly affecting the superior quadrant. The visual acuity and pupillary responses are both normal. Lesions involving the optic radiation may be due to vascular occlu- sion, tumours (intrinsic or metastatic), or abscesses. Anterior tem- poral lobe resection is a surgical treatment that may be considered in intractable temporal lobe epilepsy. In about 15% cases this re- sults in a postoperative visual field deficit due to optic radiation damage. On conventional MRI the anterior extent of the Meyer loop (which varies from person to person) is poorly localized and there- fore cannot be reliably used for surgical preplanning. In contrast, MRI diffusion tractography (DTI) is proving increasingly useful for

 tracking individual optic radiation pathways before resection, thus avoiding postoperative visual field defects. Although lesions of the dorsal optic radiation in the parietal lobe may result in a homonymous hemianopia primarily affecting the lower fields, large lesions usually result in a complete homonymous hemianopia with macular splitting. Damage to the parietal or occipitoparietal cortex may result in the phenomenon in the contra- lateral visual field, called unilateral visual inattention or visual ex- tinction. A test object presented in this field is perceived normally, but, when an identical object is similarly presented equidistant from the fixation point in the ipsilateral visual field, the stimulus in the field contralateral to the parietal lobe lesion disappears. Occipital lobe On reaching the occipital lobe there is a high degree of order in the fibres of the optic radiation and lesions, which usually result from infarction, trauma, or tumour, produce homonymous congruent field defects. The only features of the field defect that help localize the lesion to the occipital lobe, rather than the anterior optic radi- ation, are the presence of sparing of the macula or temporal crescent areas in a homonymous hemianopia. In macula sparing there is preservation of the visual field within a region of 1–2° up to 10° around the fixation point in the hemianopic field. In the more usual situation, the hemianopic field is split along the vertical meridian through the fixation point (macular splitting). Altitudinal (dorsal/ventral) field defects involving either the upper or lower occipital poles may occur as a result of trauma or vascular lesions. Cortical blindness Cortical blindness usually indicates selective involvement of the oc- cipital visual cortex. The essential features are: (1) complete loss of all visual sensation; (2) loss of reflex lid closure to threat; (3) normal pupillary light reactions; and (4) normal retina and full extraocular eye movements. The most common aetiology is hypoxia of the striate cortex. Despite the perception of blindness, so-called ‘blind- sight’ can sometimes be demonstrated in these

patients. This is the ability of patients with clinically blind fields, due to damage to pri- mary visual cortex, to detect, localize, or even discriminate visual stimuli despite not being able to report seeing the stimulus at all. This effect appears particularly strong for highly salient moving or flashing objects. The pathways subserving this function are not clear, although they are believed to involve subthalamic projections via the superior colliculus, or direct pathways bypassing primary visual cortex between LGN and extrastriate areas. Hemianopia and driving In the United Kingdom, the Driver and Vehicle Licensing Agency (DVLA) issues guidelines for drivers with visual field impairments, and this must be consulted when advising people with visual field loss about driving. In general, the minimum visual field for safe driving is a field of vision of at least 120° on the horizontal meridian. There should also be no significant field defect in the binocular field which encroaches within 20° of fixation either above or below the horizontal meridian. By this means, homonymous or bitemporal defects that come within 20° of fixation, whether hemianopic or quadrantanopic, are not accepted as safe for driving. Isolated scotomata represented in the binocular field near to the central fixation area are also inconsistent with safe driving. Following a stroke, patients with homonymous hemianopia are recommended not to drive. They may, however, be able to apply to the DVLA after one year if they can prove that they have learned to compensate for the defect. Rehabilitation of hemianopia Hemianopia is notoriously difficult to treat, with spontaneous re- covery unlikely after six months. There are three main therapeutic aims: attempts to restore the deficit itself, enlarging the field of gaze through compensatory strategies including saccadic eye move- ments, and the use of orthotic devices to increase the angle of vi- sion in intact fields. In most cases such techniques are of limited benefit, although their evidence is arguably getting stronger. With all techniques, patients must practise for many hours to experience the benefits, perhaps with eye movement-based therapies requiring the least amount of exposure. However, because visual field loss can be very debilitating, it is increasingly accepted that some form of visual rehabilitation should be offered to patients. Disorders of higher visual processing In the extrastriate cortex there is parallel processing of different aspects of visual information before an organized synthesis of the visual scene can be generated. Specific lesions in one or other of these areas might be expected to give rise to an appropriate specific loss of a visual modality such as colour (achromatopsia), movement (akinetopsia), or faces (prosopagnosia). Acquired disorders of colour vision due to lesions of the central nervous system are of two types. In one type there is an inability to see colours (dyschromatopsia or achromatopsia). These patients have lesions in the region of the lingual and fusiform gyri, which lie in the antero-inferior region of the occipital lobe. They complain that they cannot see colours and that everything looks grey or various shades of black and white. They are unable to identify the figures on pseudo-isochromatic test plates, although they are able to name the colours of brightly coloured objects correctly. Other functions such as visual acuity, object recognition, and depth perception are all normal, but there is often an associated visual field defect, usually a bilateral superior homonymous quadrantanopia. In the other type of disorder, the colour sense is normal, but the naming and recog- nition of colour are impaired. This can occur as part of an aphasia, such as Wernicke’s or anomic aphasia, in the syndrome of alexia without agraphia, or as one feature of visual agnosia (see next). Rare cases of patients, who exhibit a selective deficit of move- ment perception (akinetopsia) have been reported. The patients have bilateral lesions involving the lateral occipitoparietotemporal junction. Visuospatial and/or visuoperceptual abnormalities can occur with neurodegenerative diseases such as posterior cortical at- rophy, with tumours, or after brain injury or stroke affecting the parieto-occipital lobes. In posterior cortical atrophy, a less common form of Alzheimer’s disease, neuronal loss is initially focused on

24.6.1 Visual pathways 5921 the occipital and parietal lobes rather than the hippocampus and medial temporal lobes, although symptoms classically worsen and pathology becomes more global over time. Dyspraxia and visuoperceptual problems may lead to problems with reading des- pite preserved single-letter visual acuity, as well as difficulty rec- ognizing faces. Detailed cognitive testing using the Addenbrooke's Cognitive Examination (ACE-R) or Queen Square Screening Test for Cognitive Deficits ('green book') should be carried out to assess the degree and localization of impairments. Visual agnosia The term 'visual agnosia' refers to a rare condition in which there is an inability to recognize, name, or demonstrate the use of an ob- ject presented visually, in the absence of a language deficit, general intellectual dysfunction, or attentional disturbances. The patient is, however, able to name the object when using other sensory modal- ities such as touch or sound. Impaired visual object recognition is the prototypical disorder of lesions in the ventral occipitotemporal pathway. When patients are able to copy and match to sample ob- jects that they fail to name or recognize visually, the agnosia is termed 'associative'. If there is an inability to perform all these tasks, the agnosia is termed 'apperceptive'. One classification depends on the specific category of visual ma- terial that cannot be recognized such as alexia, prosopagnosia, and achromotopsia. Alexia is a disturbance of recognition of words, and in the pure form can cause difficulty reading despite an ability to write, good acuity, and intact auditory and language skills. Almost all lesions are localized to the left hemisphere, mostly the medial and inferior occipitotemporal region. A disturbance of face recogni- tion (prosopagnosia) is a specific inability to recognize familiar faces despite a normal ability to recognize everyday objects and is, there- fore, different from visual agnosia. Most cases of prosopagnosia are associated with bilateral damage to the lingual and fusiform gyrus of the medial occipitotemporal cortex, and are due to infarction, head injury, or hypoxia. Absent colour perception (achromotopsia) may occur in isolation or in various combinations, with localiza- tion similar to that for prosopagnosia. The most common cause of achromotopsia is bilateral simultaneous or sequential infarction in the distribution of the posterior cerebral artery. Bálint's syndrome This disorder of higher visual processing encompasses a classical triad of visuospatial dysfunction. These are: (1) an inability to in- terpret complex scenes despite intact perception of the individual elements (simultanagnosia); (2) a failure to accurately reach and grasp components corresponding to an object's characteristics (optic ataxia); and (3) a difficulty initiating voluntary saccades to visual targets (ocular motor apraxia). Optic ataxia is distinguish- able from visual agnosia, as in the latter case patients may be able to perform simple reaches to an object, despite an inability to rec- ognize it. Bálint's syndrome results from bilateral occipitoparietal damage. In particular, simultanagnosia is linked to lesions of the dorsal occipital lobes, whereas optic ataxia is more variably lo- calized, including premotor cortex and occipitoparietal regions. Acquired ocular motor apraxia requires bilateral lesions of the frontal eye fields, inferior parietal lobes, or both. The most common cause is ischaemic, in particular watershed infarcts or vasculitis. Other causes include neurodegenerative disorders or subacute sclerosing panencephalitis, and less commonly tumours, abscesses, and trauma. Visual illusions Visual illusions occur when the visually perceived target appears al- tered in size, shape, colour, position in space, and number of images. The illusory type of defects may occur in the entire field of vision, or affect only the object or the background. The term 'dysmetropsia' indicates the apparent smallness (micropsia), largeness (macropsia), or irregularity of shape (metamorphopsia) of objects. Dysmetropsia usually occurs as a result of retinal disease due to distortion of the relative distance between rods and cones. Visual hallucinations Visual hallucinations occur under many circumstances, most com- monly as impaired visual input which most frequently occurs in age- related macular degeneration. These hallucinations, known as the Charles Bonnet Syndrome, occur in up to 10% of patients with severe binocular visual loss. Other causes include drug

withdrawal, anoxia, migraine, infection, and schizophrenia, in addition to those related to focal neurological disease in the occipital or temporal lobes. Those in the last category may be unformed, consisting of flashes of light (coloured or white), lines, or simple shapes, or they may be complex, highly organized hallucinations of people or objects. Palinopsia Palinopsia is a rare disorder in which there is persistence (persev- eration) or recurrence of visual images after the exciting stimulus has been removed. There are several potential aetiologies for palinopsia, including seizures, cerebrovascular diseases, brain neoplasms, and eye or optic nerve disease. There are also a small number of case reports suggesting a reversible pallinopsia induced by topiramate use. FURTHER READING Apple DJ, Rabb MF, Walsh PM (1982). Congenital anomalies of the optic disc. Surv Ophthalmol, 27, 3–41. Beck RW, ONTT Study Group (1992). A randomized, controlled trial of corticosteroids in the treatment of acute optic neuritis. N Engl J Med, 326, 581–8. Boghen DR, Glaser JS (1975). Ischaemic optic neuropathy: the clin- ical profile and natural history. Brain, 98, 689–708. Chung SM, Selhorst JB (1992). Cancer associated retinopathy. Ophthalmol Clin North Am, 5, 587–96. Cowey A (2010). The blindsight saga. Exp Brain Res, 200, 3–24. de Renzi E (1997). Prosopagnosia. In: Finberg TE, Farah MJ
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