Optic ataxia as a result of the breakdown of the global tuning fields of parietal neurones

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Summary
Optic ataxia is characterized by an impaired visual control of the direction of arm reaching to a visual target, accompanied by defective hand orientation and grip formation. In humans, optic ataxia is associated with lesions of the superior parietal lobule (SPL), which also affect visually guided saccades and other forms of eye–hand coordination. In the last 10 years, anatomical and physiological studies of the SPL have shed new light on the role of parietal cortex in the control of combined eye–hand movements to visual targets, and on the underlying distributed network which links parietal to frontal cortex. A main emerging functional feature of SPL neurones seems to be their capacity to combine, in a spatially congruent fashion, different directional eye- and hand-related information, that any coding scheme so far proposed, considers essential for the composition of motor commands for reaching. This integration occurs within the global tuning field of parietal neurones, is context-dependent and involves eye and hand information that shares the same directional properties. Depending on task demands, this integration of signals can result in the representation of different reference frames for coordinated eye–hand movements. The dynamic operations occurring within the global tuning fields might depend, at least in part, on the reciprocal sets of association connections linking the SPL and the premotor areas of the frontal lobe. From this picture, the SPL emerges as both a main source of visual input to the frontal cortex and a key structure for visuomotor integration based on re-entrant signalling and, therefore, as a crucial node in the visual control of movement. It is hypothesized that in parietal patients, the directional errors that characterize reaching are a consequence of the breakdown of the combination of directional eye and hand information within the global tuning fields of parietal neurones. In these patients, the spatial match among information about target location, eye and hand position, and movement direction would be prevented, so as to impair the composition of visually guided eye–hand movements. This breakdown could be dependent, at least in part, on the failure of a re-entrant frontoparietal signalling, an obvious consequence of the degeneration of the cortico-cortical systems linking parietal and frontal cortex. Cortico-cortical connections are, in fact, essential for shaping the dynamic properties of cortical neurones.

Keywords: optic ataxia; global tuning fields; eye–hand coordination; parietal cortex; frontal cortex

Abbreviations: IPL = inferior parietal lobule; MIP = medial intraparietal area; SPL = superior parietal lobule

Definition and features of optic ataxia: a historical perspective
Rudolf Bálint described optic ataxia within the context of a more general parietal syndrome that also includes ‘psychic paralysis of gaze’, and hemispatial neglect (Bálint, 1909). The post-mortem examination of his case revealed a bilateral softening of the parietal lobe.

As Bálint states, optic ataxia impaired his patient’s daily activities, since, ‘while cutting a slice of meat . . . which he held with a fork in his left hand, . . . would search for it outside the plate with the knife in his right hand’, or ‘. . . while lighting a cigarette he often lit the middle and not the end’. Bálint pointed out the systematic nature of this disorder, which was evident in the patient’s behaviour when searching in space. ‘Thus, when asked to grasp a presented object with his right hand, he would miss it regularly, and would find it only when his hand knocked against it . . .’.

The term optic ataxia was introduced in analogy to tabetic ataxia, which is characterized by a lack of proprioceptive control of movement. It was meant to describe a disorder of
hand reaching movements (Fig. 1A) that, in Bálint’s view, was dependent specifically on a defective visual control. The patient, in fact, correctly performed all movements when these were guided by somatosensory information, such as when reaching with his right hand to different parts of his own body. With eyes closed, he could perfectly imitate, with the right hand, passive postures imposed on his left hand, thus excluding the possibility of apraxic disorders. Crucial to this interpretation was the observation that ‘... all movements performed defectively with the right hand were executed perfectly or with very little error with the left hand’, which excluded the possibility of a disorder of visual attention.

As recently pointed out by Harvey and Milner (1995), in their Introduction to the English translation of the Bálint’s study, this interpretation of optic ataxia has been largely neglected in favour of Holmes’ analysis (Holmes, 1918; Holmes and Horrax, 1919) of this disorder in terms of ‘disturbance of visual orientation’. In modern conceptualizations of the parietal syndrome, Bálint’s interpretation of optic ataxia is gaining consensus, mostly due to converging lines of
evidence coming from behavioural studies in humans (for reviews, see Goodale and Milner, 1992; Milner and Goodale, 1995) and from anatomical and physiological studies in monkeys (for reviews, see Caminiti et al., 1996; Wise et al., 1997; Battaglia-Mayer et al., 1998).

In today’s literature, optic ataxia is regarded as an independent disorder, since it can occur in the absence of the other signs of the parietal syndrome. Furthermore, it does not impair only visually guided arm reaching, but also other aspects of visuomotor behaviour, such as grip formation andprehension (Garcin et al., 1967; Rondot et al., 1977; Damasio and Benton, 1979; Jeannerod, 1986; Perenin and Vighetto, 1988; Jacobson et al., 1991).

When tested in central vision, optic ataxia is characterized by variable errors of reaching (Fig. 1A), with no significant constant errors (Jeannerod, 1986; Perenin and Vighetto, 1988; Baxbaum and Coslett, 1998; Milner et al., 1999; Pisella et al., 2000).

In their report of 10 cases of ‘pure optic ataxia’, Perenin and Vighetto have examined patients with unilateral parietal damage (Perenin and Vighetto, 1988). A hemispheric asymmetry was observed: when damage was on the right hemisphere, reaching was affected with either hand in the contralateral visual field (‘visual field effect’), while left-damaged patients, in addition, showed a significant ‘hand effect’, as reaching with the right hand was inaccurate in both right and left visual fields. The parietal lesion disrupted not only the transport of the hand toward the target (Fig. 1A), but also the orientation appropriate to move the hand through a spatially oriented slot (Fig. 1B). In most instances, the lesion responsible for optic ataxia was centred in the superior parietal lobule (SPL).

Other authors have described a unilateral lesion of the SPL as responsible for optic ataxia (Garcin et al., 1967; Ratcliff and Davies-Jones, 1972; Levine et al., 1978; Auerbach and Alexander, 1981). The ‘ataxie optique’ of Garcin and colleagues and the ‘defective visual localization’ described by Ratcliff and Davies-Jones are disturbances of reaching in the contralateral peripheral visual field (Garcin et al., 1967; Ratcliff and Davies-Jones, 1972). The observations that the visual field is generally normal in these patients and that the disorder is bound to the spatial location of objects, rather than to their image on the retina, rule out the possibility that optic ataxia is a consequence of a disorder of visual orientation.

Finally, a recent and intriguing case report (Pisella et al., 2000) has shown that a patient with optic ataxia from bilateral posterior parietal lesions (Fig. 1C) was impaired when making fast automatic corrective movements to a jump in target location. Under these conditions, slower intentional corrections could be made. This patient succeeded in interrupting arm movements in response to sudden changes of target location as quickly as normal controls. However, while normal controls reported that ‘to redirect your movements, you don’t need to concentrate as hard as when you have to interrupt it’, the patient said ‘stopping is easier, because to change direction, you first need to work out the direction of the target jump’. In addition, the same patient was impaired in on-line adjustment of reach-to-grasp movements (Grèa et al., 2002). When a real object jumped from one location to another during arm movement time, the patient made two distinct movements, one to the first and the other to the second target location, instead of smoothly correcting her hand movement trajectory toward the final target location, as normal controls do. This patient had normal saccadic reaction times, which rules out the possibility of a disorder of visual attention. Therefore, optic ataxia can occur in central vision and can be characterized by a deficit of a directional nature that involves on-line control, rather than conscious planning of reaching. This suggests that optic ataxia is a context-dependent disorder.

Damasio and Benton (1979) were the first to report an impairment of visual guidance of distal movements of the hand. A kinematics analysis (Jacobson et al., 1991) of reaching and grasping in a patient recovering from a bilateral occipitoparietal lesion, in addition to directional errors of reaching, has shown a severe loss of anticipatory grip.

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**Fig. 1** Different aspects of optic ataxia. Parietal patients display a defective control of arm reaching, and of hand orientation, since when reaching they miss an oriented slot (A), or are unable to confer to the hand the orientation (B) appropriate to perform the task correctly (modified from Perenin and Vighetto, 1988). (C) This set of figures illustrates the pointing performance of three control subjects compared with Patient I.G., suffering from bilateral optic ataxia, in a location—go (left) and in a location—stop (right) condition. In the first, subjects were required to correct reaching movement toward the new location of a target (target 2), after its jump from the original location of presentation, in the second they were required to interrupt their movement in response to target jump. For each condition, the horizontal bars indicate the 95% confidence intervals of movement time computed for all stationary targets. In the lower part of the figure, the vertical dotted line indicates the upper edge of the 95% confidence interval of movement time computed for all non-interrupted perturbed trials (displayed as a dotted horizontal bar). When requested to correct direction of reaching (location—go), control subjects mostly produced corrections without increasing their movement time with respect to unperturbed trials (horizontal bar), whereas most corrections produced by Patient I.G. were characterized by a large increase of movement duration. When subjects had to stop movement in response to the jump in target location (location—stop), the controls produced a total of ~10% corrective automatic movements, with movement times that were in the range of those of unperturbed trials, whereas the parietal patient did not produce corrective reaches. Under these circumstances, the latency of interrupted reaches of Patient I.G. was identical (vertical dotted lines) to that of controls (modified from Pisella et al., 2000). (D) A defective control of grasping is evident in patients with optic ataxia, since the imaginary lines connecting the point of first contact of the thumb and index finger while grasping different shapes only rarely pass through the centre of mass of the object. This is at variance from what is observed in normal control subjects (E), and results in an unstable grip (modified from Milner and Goodale, 1995).
formation, which reveals a difficulty in sculpturing the hand geometry appropriately to match the shape of the object to be grasped, as also documented by Milner and Goodale (1995) (Fig. 1D). In the patient studied by Jacobson and colleagues, reaching and grasping were accurate in the central part of the visual field (Jacobson et al., 1991). These patients had no major difficulties in their perceptual reports concerning the location and orientation of the objects they were unable to grasp (Milner and Goodale, 1995).

From the data mentioned above, and from the analysis of the literature, it seems that there are three main features of the movement disorder characteristic of optic ataxia. The first is a defective control of the *directional* components of hand movement, which sometimes affects the awareness of the direction in which the movement occurred (Head and Holmes, 1911–1912; Critchley, 1953). The second is that this deficit can affect mostly automatic on-line control, rather than planning *per se*. The third crucial characteristic is that optic ataxia only occurs when visual control of movement is required. These last two features stress the conditional nature of the disorder. These parietal patients do not show any primary motor deficit; elementary movements are executed correctly, as well as reaching movements under proprioceptive control.

Oculomotor disorders in parietal patients (Hécaen and de Ajuriaguerra, 1954; Pierrot-Deseilligny et al., 1987, 1991; Perenin and Vighetto, 1988) are frequent when the lesion involves the dorsal part of the SPL (Vallar and Perani, 1986). These disorders take the form of ‘psychic paralysis of gaze’, and include difficulties in gazing at spatial targets, maintaining attentive visual fixation and tracking a moving visual target. They occur in the absence of paralysis of eye muscles, as also shown by spontaneous eye movements and by saccades to auditory targets, which in these patients are normal in all respects. The dissociation between purposeful and random eye movements is seen constantly in these parietal cases. It has been proposed to define this disorder as ‘gaze apraxia’ (De Renzi, 1982), to stress that the disturbance essentially affects learned eye movements.

While gaze apraxia only rarely occurs in isolation, it has been known since Holmes’ reports that it can be observed in the context of a disturbance of eye–hand movements. In his Case 1, Holmes (1918) reports a parietal patient with a perforating lesion of the skull over the posterior and upper part of the right parietal lobe. The patient displayed severe directional errors in reaching and was also unable to follow, with his eyes, the movement of the examiner’s finger. In such a task, while the finger moved in space, the eyes remained stuck at the origin of the finger movement, or ‘... suddenly jerked toward the direction in which it [the finger] moved’. In contrast, eye movements were accurate when directed toward an auditory stimulus. This difficulty in tracking a moving target with the eye resembles the failure of smooth adjustments of in-flight arm movement necessary to reach at a jumping target (Gréa et al., 2002).

A constant feature of patients suffering from optic ataxia is the site of the lesion that mainly affects the SPL, at the parieto-occipital junction (Perenin and Vighetto, 1988; Vallar and Perani, 1986). This is a feature distinct from hemispatial neglect, which traditionally has been associated with lesions of the inferior parietal lobule (IPL; Vallar and Perani, 1986) and of the temporoparieto-occipital junction (Leibovitch, 1998). However, different results pose new questions concerning the anatomical substrates of the parietal syndrome. Recently, ‘pure’ spatial neglect in patients free of primary visual field defects has been reported in association with a lesion of the superior temporal cortex rather than the IPL (Karnath et al., 2001). Furthermore, a motor role has been attributed to the IPL (Mattingley et al., 1998), based on the observation that patients with right IPL lesions have problems in initiating leftward movements to visual targets located in the contralateral left part of space. These observations question a strict dichotomy of functions between the SPL and IPL. Finally, ‘visuomotor apraxia’ (optic ataxia; Classen et al., 1995) has been reported after a left thalamic haemorrhage, affecting the most posterior fibres of the caudal limb of the internal capsule, and accompanied by a severe metabolic depression involving, among other structures, the SPL. The authors’ interpretation of this case report pointed to a potential role for parietopontocerebellar circuits as critical for the visual control of limb movements, thus questioning the view of optic ataxia as a disconnection syndrome, consequent to the interruption of cortico-cortical fibres between the parietal and the frontal lobe. Thus, one can conclude cautiously that in the clinical literature optic ataxia emerges when the SPL and its distributed cortical system are damaged. The case report suggesting a role for the parietopontocerebellar loop opens up interesting questions on how different segments of the distributed system (Mountcastle, 1995) of the parietal lobe cooperate for the visual control of movement.

**Lesion studies in monkeys**

Studies of lesions in monkeys have produced conflicting results. In the study of Myers and colleagues, leucotomy of the white matter underlying the parietal lobe did not result in any reaching disorder, after a period of recovery (Myers et al., 1962). The simultaneous ablations of the occipital lobe (ipsilateral to the performing arm) and of the sensorimotor cortex (contralateral to the performing arm) also failed to produce misreaching. Subsequent studies showing a recovery of proximal movements following removal of the motor cortex (Denny-Brown, 1966; Deuel, 1977) are consistent with the original results of Myers and colleagues. They suggest that, with time, plastic changes, which can occur within minutes in the cerebral cortex (Sanes and Donoghue, 2000), might lead to recovery of functions. Since monkeys in the study of Myers and colleagues were tested after a period of post-surgical recovery, it is not surprising that the interruption of the afferent pathways to the frontal lobe did not affect
performance. Haaxma and Kuypers adopted the same type of leucotomy, but used a more demanding behavioural task involving fractionated finger movements, therefore requiring the participation of the primary motor cortex (Haaxma and Kuypers, 1975). The task showed a severe behavioural deficit. In this experiment, the deficit was restricted only to the control of finger movements and did not involve the transport component of the hand, possibly because of the bilateral control exerted by descending motor pathways on the proximal musculature that is responsible for the initial phase of reaching (Brinkman and Kuypers, 1973). The transport component of reaching is, however, clearly affected by posterior parietal lesions in monkeys (Denny-Brown and Chambers, 1958; Bates and Ettlinger, 1960; Ettlinger and Kalsbeck, 1962; Hartje and Ettlinger, 1973; Ratcliff et al., 1977; Faugier-Grimaud et al., 1978; Lamotte and Acuña, 1978; Stein, 1978; Deuel and Regan, 1985; for a review, see Caminiti et al., 1996). An earlier claim (Halsband and Passingham, 1982) that the ablation of the SPL has profound effects on the performance of conditional motor tasks has been abandoned on the basis of more selective experiments (Rushworth et al., 1997a), showing no deficits of arbitrary sensory–motor associations after lesions of different superior and/or inferior parietal areas. A companion study (Rushworth et al., 1997b) has shown, in addition, that these same lesions had profound effects on reaching, and provided an indication that SPL areas, such as area 5 and the medial intraparietal area (MIP), as well as area 7b in the IPL, contain a spatial rather than a purely sensory or motor representation of arm movement. Thus, in monkeys, lesions of the parietal lobe at

**Fig. 2** The distributed cortical system underlying reaching in the monkey. Figurines of the monkeys' brain showing the pattern of cortico-cortical connections linking the parietal and the frontal lobes. In B, parts of the parietal and occipital lobe have been ‘removed’ to show the location of the areas buried in the medial bank of the intraparietal sulcus (MIP, PEa) and in the rostral bank of the parieto-occipital sulcus (V6, V6A; modified from Marconi et al., 2001).
the cortical level mimic the clinical picture observed in humans better than do lesions aimed at disrupting the occipitofrontal connections.

There are at least three possible explanations for the inconsistency of some of the results of the lesion studies in monkeys. First, in many instances, animals were allowed a post-surgical recovery period, leaving the possibility of plastic changes as the determinant for recovery of functions. Secondly, the complexity of the task was different across studies. Last, but not least, the many parietal and frontal areas involved in the visual control of hand movements, as emerge from today’s literature, delineate a cortical system for reaching (Fig. 2; Caminiti et al., 1996; Battaglia-Mayer et al., 1998) different and more distributed than that probably affected by the experimental lesions performed so far. For instance, the cortical areas of the medial wall of the parietal lobe (7m, PEc; Ferraina et al., 1997a, b, 2001) and those of the parieto-occipital junctions (V6A, PEc; Battaglia-Mayer et al., 2000, 2001; Squatrito et al., 2001), of unknown function until 5 years ago, are now considered as crucial nodes in the early composition of motor commands for coordinated eye–hand movement (Battaglia-Mayer et al., 2001; Marconi et al., 2001). These areas are a major source of association input to the frontal cortex (Johnson et al., 1996; Matelli et al., 1998; Caminiti et al., 1999; Marconi et al., 2001). So far, a complete surgical ablation of all these parietal areas or of their association connections with the frontal lobe has never been performed in lesion studies. Beyond the controversial conclusions of some lesion experiments in monkeys, anatomical and physiological studies of the last 5 years have offered a very coherent picture of the substrata underlying the visual control of movement by cortical circuits.

The anatomical organization of the SPL
The SPL as source of visual input to the premotor areas of the frontal lobe
In monkeys, the SPL (Fig. 2) is composed of different cortical areas. In the dorsolateral aspect, these include PEA, MIP, most of PE and PEc, and part of VIP (ventral intraparietal area). Overall, they correspond to Brodmann area 5. On the medial wall of the SPL, area 5 includes PEci, and the remaining parts of PE and PEc, while area 7m is architectonically similar to the homotypical cortex of the IPL. All these superior parietal areas are homologues of Brodmann areas 5 and 7 of humans. At the parieto-occipital junction, area V6A, which is part of extrastriate area 19, is considered part of the SPL, due not only to the anatomical location, but also to its functional properties.

In the clinical literature (see Critchley, 1953), the SPL has been considered as a somatosensory association area, while the IPL has been regarded as a visual association cortex, crucial for the visual guidance of movement. For many years, this generalization resisted the evidence that no major anatomical projection existed from inferior parietal areas to dorsal premotor and/or motor cortices (for reviews, see Caminiti et al., 1996; Wise et al., 1997; Battaglia-Mayer et al., 1998), as well as the paradox that, in this view, no visual input was available to the frontal motor areas controlling arm and hand movement. The fact that, in humans, lesions of the SPL resulted in optic ataxia did not change this conviction. Within this conceptual framework, optic ataxia remained unexplained, especially when adopting an interpretation in terms of disconnection syndrome.

A new picture emerged when it was shown (Johnson et al., 1993, 1996; Caminiti et al., 1996) that some superior parietal areas, such as MIP and 7m, which are connected to the visual parieto-occipital area (PO) (Colby et al., 1988; Blatt et al., 1990), had significant cortico-cortical connections with dorsal premotor cortex. This result has been confirmed by all subsequent studies (Tanné et al., 1995; Matelli et al., 1998; Shipp et al., 1998), and extended so as to include the dorsal part of area PO, relabelled as V6A (Galletti et al., 1996), and area PEC (Ferraina et al., 2001; Squatrito et al., 2001), among the visually related areas of the SPL linked to premotor cortex (Matelli et al., 1998; Caminiti et al., 1999; Marconi et al., 2001). From these studies, the SPL emerges as the main source of visual input to the premotor and motor areas that control arm and hand movement.

There are at least three important features of the organization of the connections between parietal and frontal cortex that deserve consideration. First, all these cortico-cortical connections are reciprocal (Fig. 2), which suggests that in the information-processing flow leading from vision to movement, re-entrant signalling (Edelman, 1993) probably plays a crucial role in the composition of motor commands. Secondly, each individual parietal area is not connected uniquely and reciprocally to a unique frontal area, but to a constellation of them, although with different strengths (Johnson et al., 1996; Matelli et al., 1998; Marconi et al., 2001). Thus, the network of cortico-cortical connections linking parietal and frontal cortex is characterized by a gradient-like architecture, where different signals can be combined on the basis of common features, such as their spatial congruence. Thirdly, in the tangential (anteroposterior and mediolateral) domain of the cortex, the distribution of parietofrontal and frontoparietal association cells is not uniform, but waxes and wanes in a periodic fashion (Johnson et al., 1989; Battaglia-Mayer et al., 2001; Marconi et al., 2001). This arrangement sculptures, in the cortex, bands of different size and shapes, composed of more discrete cell assemblies that take the form of cortico-cortical columns (Jones et al., 1975). Thus, in the reciprocal efferent messages of parietal and frontal cortex, a selection of information seems to occur in a regular and periodic fashion. The question, then, becomes: what is the nature of this information and selection process?
Fig. 3 The global tuning field of parietal neurones. Macaque monkeys made arm and/or eye movements in eight different directions, starting from a common central origin, in different tasks conditions (see also Fig. 4A). Preferred directions (PD, coloured arrows) of cell activity were computed during different epochs of the following tasks: a classical reaching task to foveated targets (red), a reaching task to extrafoveal targets (blue), a saccadic eye movement task (yellow) and an instructed-delay reach task performed in normal light conditions (light green) and in total darkness (dark green). The six circles display the orientation of the PD vectors of six typical individual parietal cells in different epochs (see below for acronyms). The length of each vector is proportional to the firing rate of the cell in that particular task epoch. The circle’s radius is normalized to the vector of maximum length. The mean resultant vector (orange arrow) has variable length (mean resultant length), which varies between 1 and 0, with increasing values indicating an increasing amount of clustering of the PDs. Notice how for each cell, all PDs clustered within a restricted part of the workspace, referred to as field of global tuning (modified from Battaglia-Mayer et al., 2000, 2001). rt (red) = hand reaction time, eye on peripheral target; rt (blue) = hand reaction time, eye fixating the central target; rt (yellow) = eye reaction time in a visual saccadic task; rt (light/dark green) = hand reaction time to a pre-cued target location, eye on peripheral target (light/dark condition); mt (red) = hand movement time, eye on peripheral target; mt (blue) = hand movement time, eye fixating the central target; mt (yellow) = eye movement time in a visual saccadic task; mt (light/dark green) = hand movement time to a pre-cued target location, eye on peripheral target (light/dark condition); tht (red) = hand and eyes holding time on the same peripheral target; tht (blue) = hand holding time on peripheral target, eye fixating the central target; tht (yellow) = eye holding time on peripheral targets in a visual saccadic task; tht (green light/dark) = hand and eye holding time on the same peripheral target (light/dark condition); d1 (green light/dark) = eye reaction time in a delayed reach task (light/dark condition); d2 (green light/dark) = eye movement time in a delayed reach task (light/dark); d3 (green light/dark) = preparation for hand movement to a pre-cued target location in a delayed reach task, hand on central target, eye on peripheral target (light/dark condition).
The functional organization of the SPL: a combinatorial domain for eye- and hand-related signals

**Signal processing in the SPL**

In the last 25 years, the SPL has been the subject of intensive analysis using behavioural neurophysiological studies. After the original contribution by Mountcastle *et al.* (1975), the SPL has been regarded as a complex centre involved in the composition of arm and hand movements, rather than as a purely somatosensory association region, on the basis of both somatosensory and visual information. This view has been confirmed by all subsequent investigations, which have shown how SPL neurones are involved in coding arm movement direction (Kalaska *et al.*, 1983) and position (Georgopoulos *et al.*, 1984) in space, as well as the intention for future arm movement (Seal *et al.*, 1983; Crammond and Kalaska, 1989; Ferraina and Bianchi, 1994; Johnson *et al.*, 1996). Neural activity in the SPL also relates to visual signals about target location, when they instruct the animal about the direction of a future arm movement (Crammond and Kalaska, 1989; Johnson *et al.*, 1996).

Studies addressing the question of the reference frames for arm movement in the SPL have revealed that the dorsal part of area 5, area PE or 5d in the monkey, might be a substrate for egocentric representations of reaching, in either eye-centred (Lacquaniti *et al.*, 1995; Batista *et al.*, 1999) or arm-centred (Lacquaniti *et al.*, 1995) coordinates. The nature of these representations appears to be task dependent, and is probably based on the capacity of neurones in the SPL to combine different information, including eye position signals (Ferraina *et al.*, 1997a, b, 2001; Snyder *et al.*, 1997; Batista *et al.*, 1999; Battaglia-Mayer *et al.*, 2000, 2001).

The combinatorial power of SPL neurones has been studied in detail at the parieto-occipital junction, in areas PEc and V6A (Battaglia-Mayer *et al.*, 2000, 2001; Ferraina *et al.*, 2001; Squatrito *et al.*, 2001), while monkeys made eye and hand movements to visual targets under different combinations and task conditions. Two main results emerged from these studies. First, the activity of individual neurones relates in a directional fashion to a variety of information, including retinal motion, hand and eye position and movement direction, preparation for future hand movement, monitoring of hand trajectory in the visual field, as well as signals about
the spatial correspondence between the position of the hand and that of the fixation point. Secondly, in each individual parietal cell, the preferred directions that are the expression of these neural signals align with another within a restricted part of space, the field of global tuning (Fig. 3), where the depth of modulation is different for different signals. Thus, SPL neurones integrate spatially congruent retinal, eye and hand information of different strength. The global tuning field is therefore an ideal combinatorial domain for all information relevant to eye-hand coordination during reaching.

A final crucial feature of the SPL that deserves discussion is the context dependency of neural activity. Significant differences of cell activity are, in fact, observed (Battaglia-Mayer et al., 2000, 2001) when the same reaching movement is made with or without prior information about the direction of the next arm movement (Fig. 4B). In the SPL, context dependency can also be found in the oculomotor domain (Battaglia-Mayer et al., 2000, 2001). Thus, during saccades to a given spatial location, neurones in area V6A and PEc fire differently depending on whether or not that location is also the target for a hand movement (Fig. 4C). This suggests that neural activity co-varying with saccadic eye movements is often related not to the eye movement per se, but to the prediction of a future correspondence between eye and hand position on the fixation point.

**Distribution of signals in the superior parietal cortical domain**

Knowing the distribution of eye- and hand-related information in the tangential cortical domain is crucial to understand the operations performed by the SPL. These cannot be interpreted by adopting traditional topographic criteria. In fact, studies on receptive field properties indicate that there are no fine-grain maps of the somatosensory (Duffy and Burchfield, 1971; Sakata et al., 1973; Mountcastle et al., 1975; Burbaud et al., 1991) and visual (Galletti et al., 1999; Battaglia-Mayer et al., 2000; Squatrito et al., 2001) peripheries in the SPL. Similarly, the distribution of movement-related cells does not seem to obey any strict somatotopic pattern.

A key to interpreting the role of the SPL in the visual control of movement probably resides in the analysis of the distribution of dynamic (neural activity types), rather than static (receptive field location) properties of neurones in the cortex. This approach has offered results that are relevant to the issue treated in this review. Johnson and colleagues examined the distribution of different signals, concerning the processes of target localization in space, planning and execution of hand movement, and static position of the hand in space, in areas PE, PEA and MIP of the SPL, as well as in dorsal premotor and primary motor cortices of the frontal lobe (Johnson et al., 1996). They found that in parietal cortex, these different activity types were distributed in a trend-like fashion, with visually derived signals represented mainly in the posterior part of the parietal cortex and movement-related information, concerning planning and execution of movement, and arm static posture, at progressively more anterior locations. This trend was mirrored by a similar one found in the frontal cortex, where visual signals predominate in dorsal premotor cortex, and movement-related activity is more common in the motor cortex. Furthermore, this same study showed that regions of similar activity types in parietal and frontal cortex were linked by association connections. The study of the relationships between distribution of anatomical and functional properties in the SPL has been extended recently to areas PEC and V6A (Battaglia Mayer et al., 2001). Again, an orderly periodic arrangement of different activity types was found, with a strict correspondence between patterns of activity types and sets of parietofrontal connections. This suggests that in the parietofrontal network, eye- and hand-related activity types are probably shaped thanks to a re-entrant signalling operated by ipsilateral cortico-cortical connections. This interpretation is consistent with recent results (Chafee and Goldman-Rakic, 2000) showing that ipsilateral cortico-cortical connections play a crucial role in shaping common activity types in pre-frontal and inferior parietal cortex.

**A hypothesis on the origin of optic ataxia**

The advances in understanding the anatomical and physiological organization of the SPL, achieved in the last years, shed new light on the operations underlying the early coding of visual reaching in the cerebral cortex and, therefore, allow an interpretation of optic ataxia from a physiological perspective, i.e. in terms of failure of mechanisms. To our knowledge, this has never been attempted in the neuropsychological literature. We will treat this subject at three different levels: cellular, network and contextual.

At the cellular level, optic ataxia can be regarded as the consequence of the breakdown of the combinatorial mechanisms occurring within the global tuning fields of parietal neurones. These fields can be regarded as ideal domains to combine different retinal-, eye- and hand-related information in a simple way, i.e. on the basis of their spatial congruence. Of crucial importance is the observation that all signals encoded and combined within the global tuning field of each individual cell share a common property; they all point in the same direction. In this context, it is worth stressing that combination of retinal, eye and hand signals is regarded as a necessary prerequisite of reaching to visual targets by virtually all coding hypotheses derived from both psychological and neurophysiological studies proposed so far, and, most importantly, that the main feature of optic ataxia is a movement disorder of a directional and conditional nature. Within the global tuning field, different directional eye and hand signals influence individual cells with different strengths. Therefore, neurones in the SPL can be regarded as directional in nature, since they maintain a constant relationship to this parameter, regardless of the nature of the
such coordination is lacking, all directional combinations of eye and hand signals are compromised. This point of view can explain the deficits observed in optic ataxic patients, i.e. their inability to reach accurately in the direction of, or to grasp appropriately, an object under visual control. Like the reaching disorder, the grasping difficulty might be interpreted as a directional disorder. In this case, parietal patients show both a lack of proper hand orientation when reaching toward an object, and a failure in directing the grip toward the optimal point, such as the centre of mass, for grasping it.

At the network level, these eye- and hand-related signals are distributed in a gradient-like fashion across the tangential domains of both parietal and frontal cortex. This suggests that motor commands for reaching in the frontal lobe emerge as a result of a progressive match (Burnod et al., 1992, 1999) of information, thanks to the gradient architecture of the distributed system including the superior parietal and frontal cortex, and their sets of reciprocal association connections. Cortico-cortical connections could be the anatomical substrate of a re-entrant mechanism necessary to match eye and hand information, on the basis of their spatial congruence and relative weight, within the network. These connections undergo degeneration after parietal and/or frontal lesions. The failure of re-entry might prevent the formation of the global tuning field of parietal neurones, since, as discussed above, cortico-cortical connections are essential for shaping the dynamic properties of cortical neurones (Chafee and Goldman-Rakic, 2000).

What remains to be explained is why the movement disorder of optic ataxia occurs only in certain contexts, i.e. when visual control of movement is required. A possible explanation resides in the anatomical and functional composition of a large part of the SPL, which seems to combine different eye and arm inputs on the basis of visual information. This combination probably requires a selection process that is dependent on the conditional nature of cell activity in parietal cortex. The signal composition of the global tuning fields and, therefore, the signal representation in the gradient architecture of parietal cortex, may, in fact, change, depending on task demands. When a target for a reaching movement is localized through vision, in order to move the eye and the hand in the direction of that particular target, a dynamic process probably selects the neural units that can combine visual information with spatially congruent eye and hand signals. In this interpretation, conditionality is regarded as the result of the association of only certain classes of signals, as a consequence of a selection process. What would be lost in optic ataxia is the early and context-dependent combination of certain information, i.e. the combination of visual information with directional eye and hand signals, within the global tuning fields of parietal neurones. The resulting ‘collapse’ of the gradient-like architecture of the network will prevent the progressive match or combination of information necessary for coordinated eye–hand movement, thus disrupting the coordinate transformation necessary for appropriate motor commands. This interpretation can also account for the case report (Pisella et al., 2000) showing that, after parietal lesions, optic ataxia emerges when on-line control of movement is required. As voluntary motor planning, ‘automatic’ control requires and can be achieved through the combination of retinal, eye and arm signals, within the field of global tuning of parietal neurones. This case report provides an additional intriguing example of the context dependency of optic ataxia.

This view on the origin of optic ataxia is an attempt to put into a coherent frame a large amount of anatomical, physiological and clinical data, and, therefore, to offer a ‘positive image’ of this syndrome. For further progress, more detailed information is necessary on the quantitative analysis of movement in these patients, with special reference to eye–hand coordination during reaching, on its characterization in terms of reference frames (Baxbaum and Coslett, 1998), on the analysis of the site and extent of a lesion, including frontal lesions, and on the relationships with anatomical, physiological and lesion studies in animals. Exciting work is guaranteed for the years to come.

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References


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