Ocular contrapulsion in multiple sclerosis: clinical features and pathophysiological mechanisms

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Abstract
The objective was to describe in multiple sclerosis, a cerebellar eye movement syndrome that resulted from an acute episode of inflammatory demyelination. Contrapulsion is an ocular motor disturbance characterised by a triad of (1) hypermetric saccadic eye movements in a direction opposite from a precisely localised lesion within a specific white matter pathway, the uncinate fasciculus, at the level of the superior cerebellar peduncle (SCP); (2) hypometric saccades towards the side of the lesion; (3) oblique saccades directed away from the side of the lesion on attempted vertical saccades.

Infrared oculography was used to demonstrate the characteristic features of contrapulsion in two patients with multiple sclerosis.

Brain MRI showed lesions within the region of the uncinate fasciculus and superior cerebellar peduncle in both patients. Eye movement recordings showed saccadic hypermetria away from the side of the lesion and saccadic hypometria towards the side of the lesion. The hypometricia decomposed into a series of stepwise movements as the eye approached the target. Oblique saccades directed away from the side of the lesion were seen on attempted vertical saccades.

In conclusion, ocular contrapulsion can be seen in patients with multiple sclerosis and results from a lesion in the region of the SCP, involving the uncinate fasciculus.

Keywords: contrapulsion; ipsipulsion; uncinate fasciculus; superior cerebellar peduncle

Contrapulsion is an ocular motor disturbance that results from a precisely localised lesion within a specific white matter pathway, the uncinate fasciculus (also known as the hook bundle of Russell) at the level of the superior cerebellar peduncle (SCP) and is characterised by a classic ocular motor triad of (1) hypermetric saccadic eye movements in a direction away from the side of the lesion; (2) saccades toward the side of the lesion which are typically hypometric and decomposed into a series of steps; (3) oblique misdirection of attempted vertical saccades away from the side of the lesion. By contrast with contrapulsion, ipsipulsion is characterised by hypermetric saccades, most commonly towards the side of a lateral medullary lesion (as seen in the Wallenberg syndrome after a medullary infarct), at the level of the inferior cerebellar peduncle (ICP) in conjunction with hypometric saccades in the direction away from the lesion. In either ipsipulsion or contrapulsion, the eyes under closed lids may be aligned toward the side of the lesion in the former, or away from the side of the lesion in the latter.

Although contrapulsion and ipsipulsion have been described in patients with stroke, these disturbances have not been previously reported in the multiple sclerosis literature. We now describe two patients with multiple sclerosis who presented with a cerebellar syndrome that included ocular contrapulsion in association with a lesion on MRI within the region of the hook bundle of Russell and the SCP.

Case reports
PATIENT 1
A 47 year old woman with a history of relapsing-remitting multiple sclerosis presented with complaints of slurred speech, decreased trunk muscle control, listing to the right, poor control of the right arm, and nausea and vomiting.

A funduscopic examination was normal; however, visual fixation was interrupted by frequent square wave jerks. On direct visual inspection no nystagmus was seen. Pursuit eye movements were mildly saccadic, more prominently to the right than the left. Cancellation of the vestibulo-ocular reflex was diminished to the right.

Saccades were hypermetric to the left while saccades to the right were severely hypometric. The hypermetria of leftward saccades was present during both centripetal and centrifugal saccades to the left. Vertical saccades were seen to move obliquely (in a curved fashion) to the left. Her speech was severely dysarthric. The remainder of the cranial nerve examination was normal.

Examination of coordination showed right upper limb dysmetria with past pointing on finger to nose testing. Dysdiadochokinesis was also evident on the right and there was a positive Barre checking response on that side.

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Figure 1 FLAIR and DWI sequences show a lesion within the region of the right SCP (A and B respectively) from patient 1 (arrows). A T1 weighted coronal MRI with gadolinium infusion shows enhancement of the right SCP (C) (arrow). In D and E respectively, FLAIR and DWI sequences show tegmental lesions on the left extending into the region of the SCP from patient 2 (arrows).
PATIENT 2

A 26 year old woman with recently diagnosed relapsing-remitting multiple sclerosis, presented with new onset vertigo, oscillopsia, nausea, gait ataxia, and poor concentration and attention. There was no history of antecedent illness.

A funduscopic examination was normal; however, during fixation, with ophalmoscopy in the primary position, there was evidence of square wave jerks. In addition there was evidence of bilateral horizontal gaze evoked nystagmus that was more prominent to the right. On attempted downgaze there was minimal downbeat nystagmus. Pursuit movements were saccadic in all directions.

Saccadic eye movements were severely dysmetric with hypometric multistep saccades to the left and hypermetric saccades to the right with obvious overshoots. Rightward hypermetria occurred during both centripetal and centrifugal saccades. On vertical saccades (upward or downward), oblique movements to the right were seen. There was no evidence of ptosis, internuclear ophthalmoparesis, or skew deviation. Examination of coordination disclosed bilateral upper limb dysmetria, which was more prominent on the left. Her gait was extremely wide based, ataxic, and halting.

HOSPITAL COURSE

Both patients were admitted to hospital and treated for a new multiple sclerosis exacerbation with intravenous methylprednisolone (1.5 g daily) for 5 days followed by an oral prednisone taper (200 mg for 4 days, 100 mg for 4 days, then decreasing by 10 mg every 3 days).
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Discussion

The fastigial nucleus is the most medial of the deep cerebellar nuclei and has both ipsilateral and contralateral projections to various brainstem nuclei including the paramedian pontine reticular formation. One important projection involves a pathway from the fastigial nucleus to the contralateral PPRF. This pathway sweeps around the region of the SCP (as the hook bundle of Russell) and can lead to the activation of contralateral saccadic eye movements. As such, stimulation of the fastigial nucleus will typically result in the production of contralateral saccades whereas stimulation of the outflow pathway after the point of decussation results in ipsilateral saccades. By contrast, lesions within the fastigial nucleus result in hypermetric ipsilateral saccades whereas lesions within the region of the hook bundle or SCP produce hypermetric contralateral saccades.

Ocular contrapulsion is an ocular motor syndrome that is characterised by asymmetric saccadic dysmetria with hypometric eye movements toward the side of a lesion within the region of the hook bundle of Russell and the SCP, and hypermetric saccades contralaterally. Vertical saccades are obliquely misdirected away from the side of the lesion.

PATHOPHYSIOLOGICAL MECHANISM OF CONTRAPULSION

The Purkinje neurons within the dorsal vermis of the cerebellum exert an inhibitory influence on the ipsilateral fastigial nucleus. However, the climbing fibres that originate in the contralateral inferior olive and ascend in the inferior cerebellar peduncle produce diminished Purkinje cell inhibition. A lesion within this pathway (for example, with the lateral medullary syndrome) results in increased Purkinje cell inhibition. A lesion within the fastigial nucleus (and thereby diminished activation of the contralateral PPRF) producing hypometric contralateral saccades and hypermetric ipsilateral saccades; or ipsipulsion. Ranalli and Sharpe have described saccadic contrapulsion and ipsilateral limb ataxia in a patient that resulted from a rostral lesion involving the uncinate fasciculus, a region involving the hook bundle.

To our knowledge, we describe the first published examples of ocular contrapulsion that resulted from demyelinating lesions within the region of the hook bundle of Russell and the SCP. Both of our patients had pronounced upper limb ataxia (unilateral in the first patient and bilateral in the second) and cerebellar dysarthria. Limb ataxia likely resulted from involvement of the dentatorubrothalamic projections as they exit the SCP, travelling to the contralateral red nucleus and later to the posterior portion of the ventrolateral nucleus of the thalamus. Both patients exhibited oculographic evidence of frequent square wave jerks, a saccadic intrusion that is commonly seen after cerebellar lesions, although not specific to them.

The demonstration of contrapulsion in patients with multiple sclerosis is not surprising.

Results

Analysis of saccadic eye movements in both patients showed evidence of ocular contrapulsion characterised by hypermetric overshoot saccades in one direction and hypometric saccades in the other (fig 2). Hypermetric saccades were in a direction opposite from the side of the hook bundle of Russell lesion. Correspondingly, hypometric undershoot saccades were in a direction toward the side of the lesion. Hypometric saccades were decomposed into a series of stepwise movements, with the eyes ultimately achieving the target (fig 2). Obliquely misdirected saccades away from the side of the lesion were seen during attempted vertical saccades (fig 2). There was no evidence of saccadic slowing in either the abducting or adducting eye. In both primary position and with the eyes in eccentric gaze positions, we noted frequent square wave jerks (fig 2).

MRI IMAGING

In our first patient, fluid attenuation inversion recovery (FLAIR) imaging and diffusion weighted imaging (DWI) sequences demonstrated a lesion within the region of the right SCP (fig 1). With gadolinium infusion, enhancement was seen in the region of the right SCP (fig 1). In our second patient, FLAIR and DWI sequences showed lesions in the brain stem tegmentum with the left sided abnormality in the region of the SCP (fig 1).

EYE MOVEMENT RECORDINGS

Eye movements were recorded using 2D infrared oculography (EyeLink, SMI, Berlin, Germany). The binocular recordings were at 250 Hz with a resolution of 0.01 degrees. A third camera tracks four infrared markers, mounted to a visual stimulus and provides drift corrections for head movement. Patients were seated 100 cm away from a light emitting diode (LED) board, fitted with a lightweight headband mounted eye tracking system, and their heads were stabilised with a chin rest.

A calibration was performed using LEDs located at straight ahead, +20°, and -20° degrees vertically and +30° and -30° horizontally. Each eye was calibrated separately. The patient was then instructed to make saccades to LEDs that were illuminated in a pseudorandom sequence. The LEDs were located at straight ahead, -30°, -20°, +20°, and +30° along the horizontal axis and -10°, -20°, +10°, and +20° along the vertical axis. Every other saccade was to the straight ahead position. The patients performed about 20 saccades to each eccentric LED location.

Eye movement data were analyzed using an off line interactive program that marked the beginning and end of the saccades.

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given the strong propensity for demyelinating lesions to involve both brainstem and cerebellar pathways, which can result in a broad diversity of ocular motor abnormalities.¹⁰

This work was supported by the National Multiple Sclerosis Society (EMF, MKR), the Yellow Rose Foundation (EMF, MKR), and the Hawn Foundation (EMF).
