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Orthoptic treatment and eye movement recordings in Guillain-Barré syndrome

A case report

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Abstract A 50-year-old patient with Guillain-Barré syndrome developed a symmetrical, bilateral sixth nerve palsy which resulted in constant esotropia and diplopia. The patient was treated with both prisms and orthoptics, which eliminated the diplopia. This treatment also improved both fusional divergence amplitudes and vergence adaptation. Objective eye movement recordings revealed subtle abnormalities of fixation, pursuit and saccades, *i.e.*, square-wave jerks and intermittent saccadic dysmetria.

Key words Guillain-Barré syndrome; Miller Fisher syndrome; orthoptics; vision therapy; fusion; diplopia; pursuit; saccades; prism adaptation; vergence adaptation.

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Introduction In 1859, Landry described a condition of rapidly ascending paralysis of unknown etiology which produced acute ataxia and areflexia.[1] In 1916, Guillain and Barré described a similar condition with the added feature of albuminocytological dissociation in the cerebral spinal fluid.[2] The neurological defects in Guillain-Barré syndrome (GBS) are believed to result from lymphocyte-mediated inflammation of the peripheral nervous system. This results in a conduction block due to segmental demyelination of the nerve adjacent to the area of inflammation.[3,4]

Cranial nerve involvement may result in partial or complete ophthalmoplegia with symmetrical sixth nerve palsies occurring most commonly. This simulates a divergence paralysis in which the diplopia or image dissociation is greater at distance than at near.[3] When a third nerve palsy does occur, it usually includes both accommodative and pupillary function. The ophthalmoplegia tends to progress to its worst state within the first few days, with versions often appearing to remain concomitant.[3]

Treatment of GBS has included the use of corticosteroids, plasmapheresis, immunoglobulins, physical therapy, and occupational therapy.[3] Until now, the literature has lacked description of orthoptic intervention for the ocular motor sequelae of GBS. We report the successful orthoptic management of a patient with GBS who had severe residual divergence insufficiency and esotropia after complete bilateral ophthalmoplegia.

History A 50-year-old ophthalmologist (author KZ) became vertiginous early one morning while conducting clinical rounds. Within a few hours, he developed progressive bilateral dysfunction of all cranial nerves with the exception of I, II, and X. He was unable to chew, swallow or speak. Diplopia evolved as a result of complete external ophthalmoplegia. There was an efferent pupillary defect in both eyes. Prior to the onset of diplopia, there was no known oculomotor anomaly, and distance and near phorias were negligible. Normal (40 sec arc) stereopsis was present. An MRI of the brain was negative. Neurologic evaluation revealed generalized weakness and areflexia. Cerebrospinal fluid and electrophysiological studies were also consistent with a diagnosis of GBS. The patient required hospitalization for four months and extended physical therapy for two years.

An orthoptic evaluation was performed two months after hospital discharge. A 40$^{\Delta}$ esotropia at distance and a 35$^{\Delta}$ esotropia at near, combined with 6^ of right hypertropia, were measured. He had been advised to patch one eye to eliminate diplopia. This proved to be unacceptable, since he was unable to work or navigate with the patch. Eventually a 40$^{\Delta}$ base out Fresnel prism, split unevenly between the two eyes (30$^{\Delta}$BO=6$^{\Delta}$BD OD and 10$^{\Delta}$BO OS), was prescribed. This eliminated the diplopia; however, the optics induced both chromatic aberration and reduced visual acuity. Thus, the Fresnel prisms were too disturbing to allow him to resume a full, active professional life.

Diagnostic examination and therapeutic regimen He was examined by one of us (JC) three months after his initial orthoptic evaluation. After removing the prismatic glasses, the cover test revealed a 40$^{\Delta}$ alternating esotropia at distance and a 35$^{\Delta}$ alternating esotropia at near. There was an associated 4$^{\Delta}$ of right hypertropia with 5 degrees of right excyclotorsion at both test distances. Extraocular movements were full. There was no observable nystagmus. Pupillary responses were brisk in each eye without evidence of a Marcus-Gunn pupil. There was incomplete closure of both the right and left eyelids; however, slit-lamp examination was negative for exposure keratitis. With a modified Hess screen, the esodeviation was found to be concomitant, except for a small right hyperdeviation which increased on right head tilt and adduction. This was consistent with the diagnosis of a mild right superior oblique paresis with overaction of the ipsilateral inferior oblique. Dilated fundus examination was unremarkable.

Distance fusional divergence amplitudes were x/-30/-36 (blur with fusion/disruption of fusion/recovery of fusion), and near fusional divergence amplitudes were x/-25/-36; blur was not reported, and the negative values indicated grossly abnormal binocular fusion. With a corrective prism in place, he was able to detect 40 sec arc of horizontal retinal disparity (Titmus stereo test). The patient was given the following prescription: OD – 1.50

D=18.5$^{\Delta}$ BO=1.25$^{\Delta}$ BD. OS -3.50D=18.5$^{\Delta}$ BO=1.25 BU$^{\Delta}$ with a near add of +1.75D. The prescription was fabricated in a high index, plastic progressive lens with a small 45mm eye size to minimize thickness and weight. The prismatic correction consisted of the least amount of prism required to maintain bifoveal alignment at all fixation distances. In addition, he was advised and highly motivated to begin an orthoptic treatment program despite the guarded prognosis. The patient refused surgical intervention or Botulinum toxin injections.

Active orthoptic therapy was begun with the goal of increasing both fast reflexive fusional divergence amplitudes and slow vergence adaptation[5-7] (Fig. 1). Stimulus presentation was consistent with an approach previously described by Kertesz and Kertesz,[8] and Cooper.[9,10] Fusional targets were initially large (45 degrees), spatially-complex stimuli presented with a slow, constant velocity (ramp) divergence demand of 0.25$^{\Delta}$/sec. In addition, random-dot stereograms were used in an operant conditioning paradigm to eliminate the possibility of responses based solely upon monocular cues, as well as to provide positive reinforcement to the patient.[11] These targets were presented on the commercially available video-based Computer Orthopter VTS3 system (RC Instruments). Office therapy also incorporated use of prism bars, stereoscopes (Keystone) and variable disparity vectograms (Bernell). In-office therapy was supplemented with daily home therapy for reinforcement, which included a variety of fusional and anti-suppression procedures.

As soon as divergence amplitudes improved by more than 7$^{\Delta}$, the amount of prism in the spectacles was decreased by 10$^{\Delta}$ to foster increased fusional effort and slow vergence adaptation.[12] As fusional divergence amplitudes

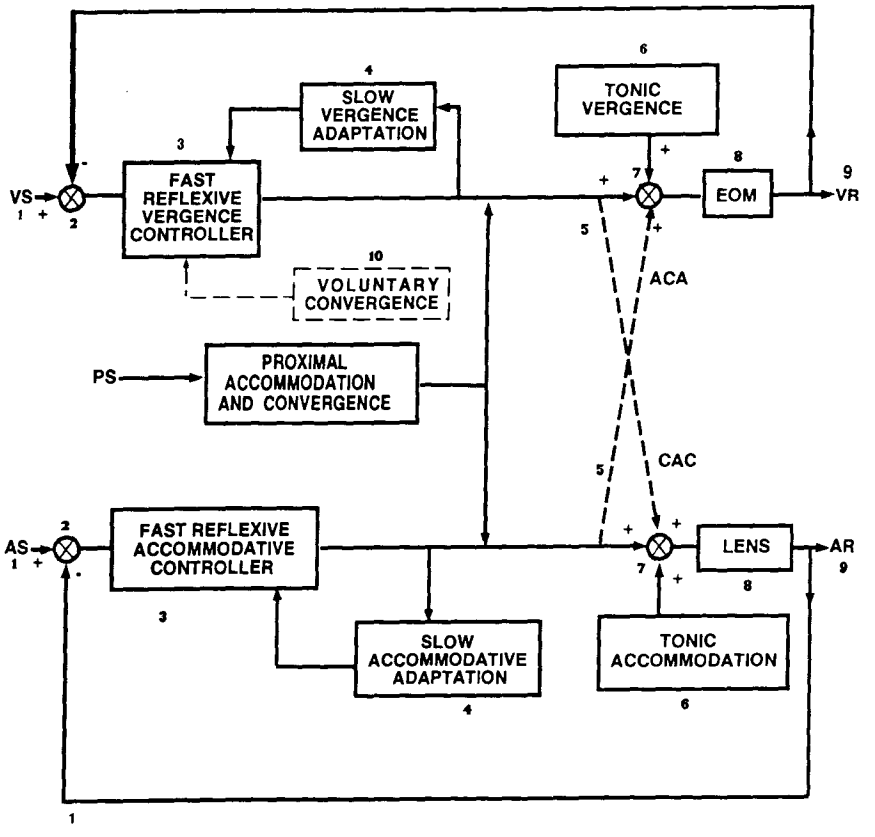

Fig. 1. Model of static accommodation, vergence, and their interactions. The upper negative visual feedback path is for disparity or fusional vergence, whereas the lower negative visual feedback path is for blur-driven accommodation. Each path contains (from left to right): (1) the initial input stimulus value, with VS = vergence stimulus (retinal disparity), PS = proximal stimulus (apparent target distance), and AS = accommodative stimulus (blur), (2) the summing junctions for the initial stimulus inputs and the negative visual feedback pathways: this difference represents the updated or new system error, (3) the fast reflex controllers: they respond to the initial or transient aspect of the new error signal: this gain term multiplies the error signal and thus derives the initial system neural signal, (4) the slow adaptation loops: their input from the controller is converted to an output signal that then acts to modify the controller's dynamics (*i.e.*, transiently increase its decay time constant): the adaptive loops function to sustain the motor response, (5) the crosslink gain terms which reflect accommodative convergence to accommodation (ACA ratio) and convergence accommodation to convergence (CAC ratio), (6) tonic bias inputs that reflect midbrain baseline neural innervation and add non-linearly to the controller signal, (7) second summing junctions, (8) the peripheral neuroanatomical aspects of the controlled system, namely the extraocular muscle complex (EOM) and crystalline lens complex (LENS), (9) the system motor response, namely the vergence response (VR) and the accommodative response (AR), and, lastly, (10) higher-level voluntary vergence control driving the fusional vergence system. Proximal gain inputs to both systems.

continued to improve, additional step-wise reductions in the total amount of prism correction were made, *i.e.*, 30BO, 25BO, 20BO, 16BO, 12BO, 10BO, and 8BO. Initial prismatic changes were large, while subsequent changes were made progressively smaller. With progress, fusional amplitude therapy was made more difficult by slowly increasing the velocity of the vergence stimuli to 5^/sec and/or by reducing the stimulus size to 6 degrees.[12]

As smooth divergence amplitudes improved, more difficult step (jump duction) stimuli were then introduced. Stimulus presentation, vergence demand, and reinforcement contingencies were presented with the VTS3 computerized method of training. Fig. 2 presents both the maximum total fusional divergence reserve and maximum total step amplitude measured at each session. It is readily apparent that both ramp and step fusional amplitudes progressively improved over time.

Over a one-year period of weekly therapy, horizontal divergence fusional amplitudes improved at distance to x/-10/-14 and at near to x/4/2; the more positive post-therapy values demonstrated moderate improvement of fusion ability. Initial occlusion with an alternate cover test resulted in an esophoric deviation of approximately 7^ at distance and orthophoria at near. Upon prolonged repeated alternate cover testing for two minutes, the magnitude of the deviation gradually increased, until it equalled the magnitude found at the initial examination, *i.e.*, 40^ esotropia. Three years after orthoptic treatment, the patient is presently wearing progressive addition lenses without any prism incorporated into the spectacle lens before each eye. After a stressful day, however, the patient often has to revert to his prismatic glasses, which have 2^ BO in each eye.

Towards the end of the orthoptic therapy, both horizontal versional (monocular and binocular) and vergence eye movements were recorded using a commercially-available infrared eye movement system (Gulf and Western, Eye Trac Model 200). This system has a bandwidth from DC to 250 Hz, a resolution of 0.2 degrees, and a linear range of ±10 degrees; however, the frequency response of the eye movement traces was limited by the bandwidth of the strip chart recorder (DC to 80 Hz). The target consisted of a small (5 min arc), bright spot of light presented on a display monitor 57 cm from the subject which was controlled by a function generator.

Representative eye movement recordings are shown in Fig. 3. Midline

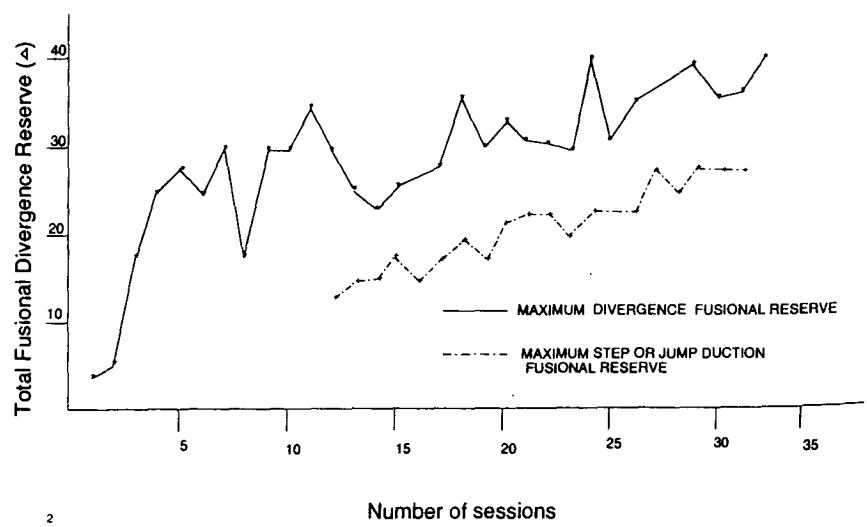

Fig. 2. Total divergence fusional reserve (phoria/tropia plus divergence fusional convergence amplitude measurements minus prism in the spectacles) is presented for each orthoptic therapy session. Measurements are for disparity stimuli moving with a constant velocity (ramp) which is depicted in the upper curve, and jump duction (step) which is depicted in the lower curve. As amplitudes improved, therapy was increased in difficulty by making the vergence stimuli smaller and by increasing the velocity of the target during ramp therapy.

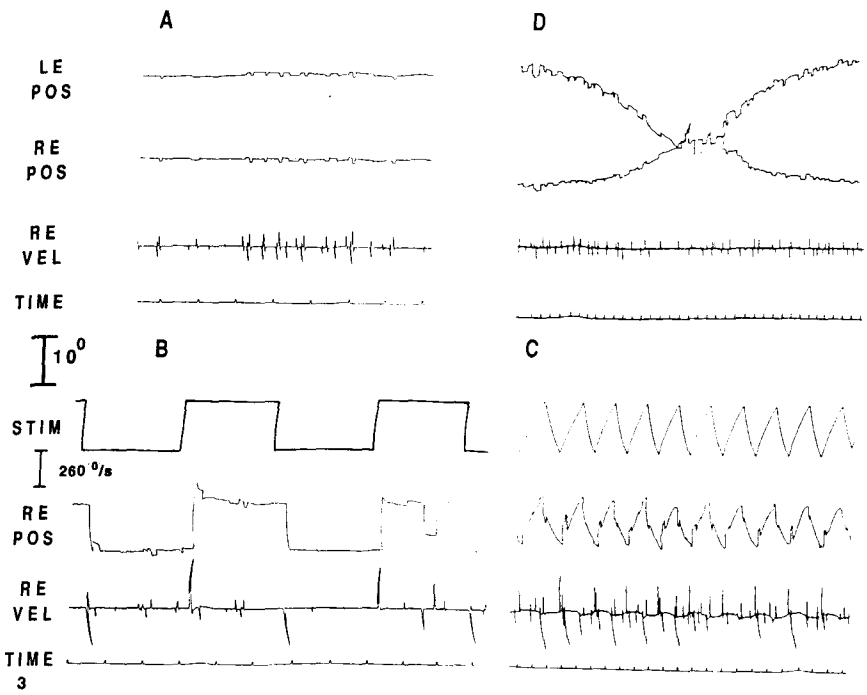

Fig. 3. Representative objective eye movement recordings in our subject during binocular viewing. A. Fixation. B. Saccades. C. Pursuit. D. Vergence. In the position traces, upward deflections represented leftward movement and downward deflections represented rightward movement. Time markers represent seconds.

fixation revealed mostly rightward directed square-wave jerks. They had a mean amplitude of 0.5 degrees, a mean inter-saccadic interval of 185 msec, and a variable frequency ranging from 0.5 to 2 Hz with intermittent 3 to 4 Hz bursts. These square-wave jerks became more prevalent as testing continued. Saccadic tracking (10 deg amplitude, 5 deg left and right of midline; temporal randomization) revealed highly variable metrics, at times exhibiting: (1) large (0.5 to 2 deg) dynamic overshoots on rightward gaze; (2) large (0.5 to 2 deg) glissadic overshoots on both rightward and leftward gaze, sometimes following a rightward directed static overshoot; (3) hypometric saccades to the right and left requiring a subsequent one- to two-degree corrective saccade (200 msec later) to attain accurate foveation; and (4) normometric saccades to the left and right.

Mean saccadic latencies were within normal limits (195 msec) for both leftward and rightward directed saccades. Square-wave jerks of 0.5 degree were intermittently present, at times occurring in couplets, during the inter-saccadic fixation periods. Saccades had normal peak velocities in both directions. During constant velocity pursuit (10 amplitude, 5 deg left and right of midline), the patient easily tracked targets ranging in frequency 0.2 to 2 Hz. Pursuit gain was normal (0.93 to the left and 0.88 to the right). There was evidence of prediction to the right but not to the left, with a large initial one- to three-degree saccade embedded in each response in both directions. To the left this consisted of a square-wave jerk, whereas to the right it consisted of a single saccade. Versional movements were similar under both monocular and binocular viewing conditions. When asked to perform symmetrical (midline) vergence tracking of a pencil point moving slowly (*i.e.*, ramp-like) between 57 and 17 cm, the patient easily followed the target in both the convergent and divergent directions. However, numerous rightward directed square-wave jerks of 0.5 degree amplitude with a frequency of 1 Hz were always present.

Discussion This is the first case report describing the use of orthoptic therapy to improve oculomotor vergence control in a patient with acquired bilateral sixth nerve paralysis. One may argue that the strabismic deviation was a result of a divergence paralysis, since the velocities of the horizontal saccades were equal and normal for both left and right gaze, and the deviation was not significantly greater at distance.[13] However, there are several findings which suggest that the origin of his esotropia was a bilateral sixth nerve palsy. First, he had a total ophthalmoplegia, which by definition includes a sixth nerve palsy; second, the deviation at distance was equal to the sum of the individual lateral rectus palsies, *i.e.*, 20$^{\Delta}$ from each eye (divergence paralysis would have a much smaller deviation). Third, it is possible that the initial presentation of a similarly-sized deviation at distance and near was masked by the wearing of prisms and the resultant motor slow vergence (prism) adaptation. And, lastly, GBS is thought to be a disease of peripheral nerve involvement.

Recently, Chiba *et al.*[14] demonstrated that patients with either Miller Fisher syndrome (MFS) or GBS with an associated ophthalmoplegia have the same specific serum anti-GQ1b IgG antibody. They also reported that none of the controls with various neurological conditions had this antibody. In addition, the serum antibodies were only found in peripheral nerves III, IV, and VI. None of the nerve fibers in the spinal cord or brainstem demonstrated serum antibodies. These findings lend credence to the notion that both GBS and MFS are variants of the same disease and mainly affect peripheral nerve function.

Prisms were used to reduce the vergence demand on the fast reflexive fusional vergence system and to eliminate diplopia at all distances. Concurrently, orthoptic therapy was designed to improve fusional amplitudes with the goal of reducing the amount of prism in the spectacles. Initial reduction in the magnitude of the prism placed a new demand on the fast reflex component of the fusional vergence system. However, through appropriate visual feedback and prolonged visual effort, the patient partially adapted to the prism as evidenced by a decrease in the size of the distance esotropic deviation from 40$^{\Delta}$ to 7$^{\Delta}$. This resulted in a decreased demand on reflex fusional vergence.[15] The longer the vergence system maintains fusion, the larger is the slow vergence adaptive contribution, and the smaller is the fast reflexive fusional vergence contribution. This results in a decrease in the standard clinically-measured phoria.[16]

These findings are similar to those previously reported by Ogle and Pragen,[17] and later by Carter,[16] in which vergence adaptation occurred after a patient wore either vertical or horizontal prisms for a considerable period of time. Complete adaptation was demonstrated by similarity of fixation disparity (*i.e.*, small static vergence error), cover test, and fusional amplitude measurements both prior to and while wearing the prisms.[18,19] Removal of an 'adapted prism' usually resulted in diplopia with a slow return (*e.g.*, minutes to several hours) to the position of the eyes prior to wearing the prism.[16] Recovery can be significantly accelerated by slowly decreasing the prismatic value via a Risley prism, while allowing fusion to be maintained continuously. Carter[16] has shown that vergence adaptation is unaffected by sleep. This non-stimulus mediated 'memory' appears to maintain vergence adaptation during non-waking hours, thus preventing the occurrence of diplopia

also explain the apparent decrease in the phoria of our patient which remained stable from day to day.

Horizontal fusional amplitude training was probably effective in decreasing the patient's symptoms in two ways. First, therapy reinforced both the sensory and motor aspects of the vergence system by stimulating the fast reflexive fusional response to eliminate the initial large retinal image disparity and resultant diplopia. Second, either removal or reduction of the fusional vergence demand increased adaptation of the slow fusional vergence system via its internal adaptive loop.[20]

One may argue that the patient would have improved in time without any treatment. This seems unlikely for several reasons. First, prior to the initiation of orthoptic therapy, the patient's oculomotor status, in particular the divergence palsy, had remained stable for the previous six months. Second, orthoptic therapy resulted in large and immediate improvement, with smaller but consistent successive gains (Fig. 2). Third, and most importantly, repeated alternate occlusion increased the deviation from 7$^{\Delta}$ to the original deviation of 40$^{\Delta}$ esotropia. Thus, orthoptic therapy promoted the development of slow vergence adaptation which reduced the phoria/tropia, and concurrently developed a robust fast reflexive fusional vergence response to compensate for any residual, dynamically-changing oculomotor deviation not eliminated by slow vergence.

There has only been one report in the literature involving objectively recorded dynamics of eye movements in patients with GBS[4]. The recordings were obtained within the first two months of symptom onset, and a variety of intra- and post-saccadic fatigue-like effects were documented, including slowed saccades. None of these abnormalities were found in the present case, which was recorded late in the disease and after therapeutic intervention. In addition, the saccadic amplitudes used in the present study (10 degrees) were considerably smaller than those used by Feldon *et al.* (20 to 30 degrees). Thus any relatively modest velocity deficit, being proportional to saccadic amplitude, may not be evident in our patient. In addition to traditional medical/hospital care, our patient received an extended period of intensive and successful office and home orthoptic therapy.

Residual eye movement deficits included square-wave jerks and a moderate degree of intermittent saccadic dysmetria. Square-wave jerks are found in a variety of pathological and non-pathological conditions, and thus may not be of pathognomonic significance.[21] However, the intermittent occurrence of the high frequency bursts suggest residual abnormal neural control of fixation. Further, the intermittent saccadic dysmetria may represent subtle residual deficits in peripheral neuromuscular conduction. However, this does not preclude coexisting central involvement, as both square-wave jerks and ocular dysmetria are also commonly found in such cases.[22] Lastly, the near vergence tracking results confirm and extend the successful clinical orthoptic picture. The vergence findings clearly demonstrate that under naturalistic conditions, in which the full complement of vergence stimuli were present[23] (*e.g.*, disparity, blur and proximity), appropriate and full changes in vergence response dynamics occurred.[24]

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