he had mild limb and gait ataxia. There was no muscle atrophy nor weakness, and tendon reflexes were normal; the plantar responses were flexor. There were no focal neural movements, no sensory nor autonomic disturbances. Electro-oculographic findings were almost identical to that of his brother. 

Our main clinical feature of our patients was adult onset slowly progressive cerebellar ataxia, thought to be hereditary as there were no apparent causes including metabolic diseases. The most conspicuous finding of rare cases was an abnormal ocular movement during eye closure. It was a rapid irregular multidirectional oscillation with no intersaccadic intervals, and appeared to fulfill the criteria of opsoclonus. To our knowledge, the appearance of opsoclonus, only during eye closure, has not been previously described. Opsoclonus can be caused by an abnormal activity of burst cells and pause cells in the brainstem sac-cadic pulse generator. Various cells in the brainstem sac-cadic pulse generator, and increased opso-clonus during eye closure seem to support this speculation.

Square wave jerks, saccadic dysmetria and saccadic pursuit seen in our cases seem to be common oculomotor abnormalities in hereditary cerebellar ataxia. Opsoclonus, however, has not been clearly described in hereditary cerebellar ataxia, in contrast to opsoclonus of opsoclonus at attempted fixation seem to be due to a similar neural dysfunction. Opsoclonus only during eye closure could be explained by the presence of eye-closure related abnormality of sac-cadic pulse generator, and increased opso-clonus during eye closure seem to support this speculation.

Preferential impairment of slow alternating movements in patients with mild cerebellar ataxia

Clinically, it is well known that patients with cerebellar lesions have difficulty pro-
ducing rapid movements. This has been confirmed quantitatively for fast, so-called 'ballistic' movements and is often apparent in ataxic patients. However, slow movements are also impaired in cerebellar patients. We have recently shown, for example, that the time course of slow, accurate step-tracking movements in mildly atactic patients is preferentially impaired compared with movements of the same amplitude but made at higher speeds. The performance of slow, pursuit movements has also been shown to be impaired both in cerebellar patients and following dentate cooling in monkeys. Clinically, slow alternating movements are not usually tested, probably due to the assumption that one could expect more impairment at higher than at lower frequencies of voluntary alternating movements. That this assumption is misleading will be demonstrated by the following study.

Using previously established selection criteria, 9 cerebellar patients (4 women, 5 men; 35-65 years) were chosen for study. Five patients had mild cerebellar degeneration, 4 of whom had an autosomal dominant, inherited hereditary form of the disorder. None—Pierre—Marie type, and 1 had paraneoplastic Purkinje cell degeneration. The remaining 4 patients suffered from a left-sided PICA infarction, right cerebellar hemisphere haemorrhage or removal of a Hippel Lindau tumour and surgical removal of a pilocytic astrocytoma, respectively. All patients showed mild upper limb ataxia with no clinically apparent intention tremor and gave informed consent for the procedures involved. Two age-matched normal subjects served as controls.

Details of the experimental set up are described elsewhere. In brief, subjects held a manipulandum handle pivoted beneath the elbow and made 30° alternating flexion-extension movements in time with an auditory tone (frequency range: 0.5—3.0 Hz). Targets and handle positions were displayed on an oscilloscope placed in front of the subject. Locations (3°) and position (± 15°) about an elbow angle of 90° of the target zones remained constant across all trials. Position of the manipulandum handle was displayed as a thin vertical line. Subjects were instructed to move the handle back and forth between target zones so that reversal of movement direction occurred in the target zone at the time of the auditory tone. Emphasis was placed on making movements as smoothly as possible. A movement trial lasted 24 s for low frequency (< 1.5 Hz) movements and 12 s for high frequency (> 1.5 Hz) movements. Maximum alternating frequency was determined by asking subjects to move as rapidly as possible between the target zones. A 2-minute rest period separated each trial. In 3 subjects, the effects of visual feedback on low frequency alternating movements (0.5—1.0 Hz) were assessed. Following each trial recorded under normal visual feedback, subjects were instructed to close their eyes and make movements of the same amplitude and frequency. Handle angular position and velocity were digitised at 250 Hz.

As expected, the maximum possible frequency of alternating elbow movements made by cerebellar patients was less than that seen in normal, control subjects. This is illustrated in fig. 1 (upper set of records) where, for the cerebellar patient, maximum frequency was approximately 3.0 Hz compared with approximately 5.0 Hz in the control subject. This was a consistent finding in all patients. Mean (SD) maximum frequency was 3.3 (0.4) Hz. Despite a reduction in maximum frequency, however, both movement range and time course were

![Figure 1](http://jnnp.bmj.com/). Velocity records associated with 30° alternating elbow movements. Records on the left were obtained from a control subject, those on the right from a patient with chronic cerebellar degeneration of approximately 3 years. Movements made at maximum frequency are shown in the upper set; middle and lower sets correspond to target frequencies of 1.0 and 0.75 Hz respectively. (1-0 and 0.75 Hz records have been plotted at a higher gain).

![Figure 2](http://jnnp.bmj.com/). Effects of removing visual feedback on low frequency alternating movements. Individual records of velocity and acceleration are shown for a control subject and 2 cerebellar patients (CB1, CB2) performing 30° alternating elbow movements with and without 'eyes open' and 'eyes closed' conditions. Movements made at 0.5 Hz are shown on the left; 0.75 Hz movements on the right. Acceleration was obtained from 3 point digital differentiation of the velocity signal. Velocity and acceleration gains have been arbitrarily adjusted. Duration of each trial was 24 s.
highly regular over consecutive recording periods. Indeed, movements made by patients at maximum frequencies were qualitatively similar to movements made at the same frequencies by control subjects.

Most striking was the inability of all patients to produce smoothly alternating movements at or below frequencies of about 1-0 Hz (fig 1, middle, lower sets of records). At these frequencies patients became typically irregular with abrupt changes in velocity throughout the movement. The frequency at which this breakdown in movement performance occurred varied among patients, ranging from 1-0 to 0-6 Hz. At 0-5 Hz movements became considerably irregular in all patients with prolonged periods of rapid velocity transients.

"In the present study movement performance and visual feedback was examined. Fig 2 shows velocity and acceleration recordings for "eyes open" and "eyes closed" conditions. As described above, movements became irregular at approximately 0-5-0.75 Hz with periods of abrupt transients, particularly noticeable in the acceleration records. In both patients shown in fig 2, Cerebellar visual feedback during slow alternating movements (0-5-0.75 Hz) did not improve movement performance.

One of the cardinal signs of cerebellar dysfunction is the inability of the cerebellum to produce rapid, alternating movements about a given joint. Movement trajectories are, however, relatively smooth despite a reduction in maximum alternating frequency. The results presented here demonstrate that, despite bradydactylochokinesis, cerebellar patients have more difficulty producing smooth alternating movements when made at low frequencies compared to movements made at higher frequencies. This supports recent findings showing that patients with mild upper limb ataxia have difficulty in performing long duration (>600 ms), discrete movements.

The highly irregular movements at frequencies under 1-0 Hz are similar to those observed during sine wave tracking following dentate cooling in non-human primates and during slow pursuit tracking in cerebellar patients. In these studies pursuit tracking tasks were used. In our study, target zones remained fixed and thus the task did not require moment to moment matching of the hand to a stationary target. Since, in addition, removal of visual feedback did not abolish movement irregularities, it is difficult to attribute the observed breakdown in motor performance to visually mediated corrections arising from a mismatch between actual and intended arm positions. It has been shown that, in cerebellar patients, removal of visual feedback is effective in improving pursuit tracking performance. The results presented here in the "eyes closed" condition, however, suggest that this is not the case for alternating movements made between visual cues. This would support the view originally put forward by Holmes and later confirmed by others that cerebellar dysmetria is not dependent upon visual feedback in fig 2.

In conclusion, these findings underline the importance of clinical evaluation of both slow and rapid movements during routine neurological assessment. In particular, testing the ability to perform smooth elbow pronation and supination may reveal significant upper limb impairment in patients who may otherwise show only minimal cerebellar signs.

S H BROWN
J D COOKE
Faculty of Applied Health Sciences
University of Western Ontario
London, Ontario, Canada

H J FREUND
Department of Neurology,
Humboldt-Universitat,
Dusseldorf, Germany

Correspondence to: Dr Brown, Center for Human Motor Research, Department of Science, University of Michigan, 401 Washington Ave, Ann Arbor, Michigan 48109-2214, USA.

The study was supported by an Alexander von Humboldt Research Fellowship (SHB) and the Deutsche Forschungsgemeinschaft (SFB 194, A5).


BOOK REVIEWS


This volume continues the tradition of excellence which has accrued from the impact of previous editions in this series. The aim of this series is to provide a collection of succinct and timely reviews of an important and particular growing points in clinical neurology written by leading authorities in the relevant subject areas. This aim has always been admirably achieved and the current volume, reviewed here, carries this forward. All the chapters have many strengths and while I feel it would be invidious to single out particular contributions to any great extent I feel compelled to make the following specific comments.

There is something in this book for everybody ranging from junior staff just beginning their training in neurology to the established neurologist who wishes to update his own knowledge. Of the collection of vignettes published in this section, I was particularly pleased to see clear descriptions of the syndromes of chronic paroxysmal hemicrania and chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). In my view, both these conditions are still seriously obscured, and in view of the important therapeutic implications of both disorders, should be more widely known. Indeed, considering the paucity of neurological services in the UK, I could not help feeling that the chapter on inflammatory demyelinating neuropathy should be widely read by general physicians.

The expanding areas of the general role of magnetic resonance in neurological practice and prion related disease are presented in a balanced way, and it is useful to have a current review of expanding impact of mitochondrial pathology in neurological disease. The mechanisms subserving the control of eye movements are notoriously complex, but the editor has found two authors who have been able to give an admirably lucid account of the role of the brain in the control of voluntary eye movements.

All in all, this volume is highly recommended. A copy should be available for day to day reference in all departments of neurology. It will also find a worthy place in the libraries of district general hospitals lacking on-site neurological units and I would, perhaps provocatively, suggest that before being deposited in such libraries, the volume might be inspected by the general practitioners to read the chapter on inflammatory demyelinating neuropathy!

J MITCHELL


Once again Byron Kakulas’ Co-editors and Publishers are to be congratulated on the timely publication of what is now the second in a series of monographs devoted to Duchenne and Becker Muscular Dystrophy. The format is similar to that of their earlier volume (Pathogenesis and Treatment of Duchenne and Becker Muscular Dystrophy; 1990) and consists of a series of lectures given by experts in the field followed by, what appears to be, a verbatim transcription of the discussion which followed each paper.

In Part 1, the localisation, distribution and function of dystrophin is reviewed in the light of developments from their earlier volume. In Part 2, the potential of myoblast transfer as a method for introducing the missing dystrophin into muscle cells is discussed at length and the limitations of such transplantation approaches are identified. The third part is concerned with gene therapy which, at present, is still in its infancy but the possibilities in that field are clearly reviewed.

Once again, following each section, there is a general discussion which provides much of interest to the research worker in the field irrespective of whether he is involved in clinical or basic research. The papers themselves provide a very balanced overview of the situation in respect to the rapidly advancing field of molecular biology up to the time of the meeting.

Roses introduces a measure of clinical realism when saying: “The scientific excitement and experimentation concerning