H reflex studies in patients with Parkinson's disease

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SUMMARY The H reflex was studied in 13 patients with Parkinson's disease, and the results compared with those obtained in 22 control subjects. Pairs of identical stimuli near threshold intensity were delivered and the unresponsive period and time course of recovery of the amplitude of the H reflex were determined. The duration of the unresponsive period was significantly shorter in the patients with Parkinson's disease. In 10 patients the studies were repeated after treatment with L-dopa for six months. There was a significant increase in the period of unresponsiveness of the H reflex after treatment. The findings suggest that there is an increase in alpha motoneurone excitability in Parkinson's disease, and that it is reduced by treatment with L-dopa.

The pathophysiology of Parkinsonian rigidity is uncertain. Although some evidence suggests that it results from increased fusimotor activity (Rushworth, 1960), a number of workers have concluded that there is hyperactivity of the alpha motoneurons (Ioku, Ribera, Cooper, and Matsouka, 1965; Olsen and Diamantopoulos, 1967; Takamori, 1967; Yap, 1967; Denny-Brown, 1968). The aim of the present investigation was to investigate the effect of L-dopa on alpha motoneurone excitability in a group of patients with Parkinsonian rigidity by means of H reflex studies.

METHODS

Thirteen subjects with Parkinson's disease, whose ages ranged from 57 to 65 years, were studied. Of these 10 received treatment with L-dopa, and studies were performed before and at six months after commencement of treatment. In all cases, rigidity and akinesia were the prominent clinical features.

Twenty-two control subjects, whose ages ranged from 16 to 73 years, were studied previously and the results reported (McLeod, 1969).

H REFLEX STUDIES The technique and apparatus employed were identical with those previously described (McLeod, 1969). H waves were recorded from the calf muscles with surface electrodes, after stimulation of the medial popliteal nerve in the popliteal fossa. A square wave stimulus of 0.2 msec duration was derived from a Disa Ministim. Muscle action potentials were amplified and displayed on the upper beam of a Tektronix 502A oscilloscope; a time scale derived from a Digitimer (Devices Ltd)

was displayed on the lower beam. Photographic records were made on 35 mm film.

A conditioning shock of intensity less than 1.1 times threshold for the H reflex was followed at intervals ranging from 2 msec to 1 sec by an identical test stimulus. Ten seconds were allowed to elapse between each pair of stimuli. The ratio of the peak-to-peak amplitude of the H wave after the test volley to that of the H wave after the conditioning volley was calculated at each interval of time and a recovery curve plotted.

RESULTS

RECOVERY OF H REFLEX BEFORE TREATMENT WITH L-DOPA Recovery of the H reflex after a near threshold conditioning volley was plotted in 13 patients with Parkinsonian rigidity. The mean curve is shown in Fig. 1, together with that obtained from 22 control subjects. The early phase of facilitation at 0 to 15 msec was less pronounced in patients with Parkinson's disease than in controls. The mean duration and standard deviation of the unresponsive period in the Parkinsonian subjects was 51.5 ± 23.1 msec (range 20 to 100 msec), which may be compared with that of 72.6 ± 18.6 msec (range 45 to 109 msec) found in control subjects. The difference is significant ($P < 0.01$, Student's *t* test). During the later stages of recovery between 200 and 1,000 msec, there was a less pronounced depression of the amplitude of the test response in Parkinsonism patients than in control subjects.

RECOVERY OF H REFLEX AFTER TREATMENT WITH

FIG. 1. Recovery curve of H reflex in control subjects (filled circle, continuous lines) and patients with Parkinson's disease (open circle, interrupted lines). Mean values for 22 control subjects and 13 subjects with Parkinson's disease. Ordinate: Ratio of amplitude of test response to amplitude of conditioning response, expressed as a percentage. Abscissa: Interval between conditioning and test stimuli, in milliseconds. Note change in time-scale, after 100 msec. Vertical lines represent standard error of mean.

L-DOPA In 10 of the patients with Parkinson's disease, the recovery of the H reflex was plotted before and after six months' treatment with L-dopa. In all cases there had been definite improvement in the clinical features of rigidity and akinesia. The results are shown in Fig. 2. It may be seen that, after treatment with L-dopa, there is a longer period of unresponsiveness and

a slower recovery of the amplitude of the test response during the first 200 to 300 msec after the conditioning stimulus. The mean duration and standard deviation of the unresponsive period was 52.0 ± 23.6 msec before treatment with L-dopa, and 75.0 ± 29.4 msec after treatment. The difference is significant ($P < 0.05$). The duration of the unresponsive period before

FIG. 2. Recovery curve of H reflex in 10 patients with Parkinson's disease before treatment with L-dopa (filled circle, continuous lines) and after treatment (open circle, interrupted lines). Results are plotted in same manner as in Figure 1. Vertical lines represent standard error of mean.

and after L-dopa is shown for one subject in Fig. 3, and the results for the group are plotted in Fig. 4.

DISCUSSION

The H wave in man has the characteristics of a monosynaptic reflex. The time-course of recovery of the amplitude of the H wave after a conditioning stimulus has been employed by many

FIG. 3. Unresponsive period in a patient with Parkinson's disease before treatment with L-dopa (A) and after treatment (B). H_1 is the H wave following a near threshold conditioning stimulus, and H_2 is the response to an identical test stimulus at the time interval when the H wave first returns after the unresponsive period. Time scale, 10 msec. Amplitude, 0.5 mV.

workers as a means of studying the excitability of the alpha motoneurone pool in a number of different conditions, including spasticity, Parkinson's disease, and cerebellar disorders (Magladery, Teasdall, Park, and Languth, 1952; Ioku, *et al.*, 1965; Olsen and Diamantopoulos, 1967; Takamori, 1967; Yap, 1967; McLeod, 1969). However, the interpretation of H reflex recovery curves is difficult because the time-course of recovery is influenced by a number of factors including the intensity of stimulus and the effects of muscle contraction. McLeod and Van der Meulen (1967) attempted to analyse the factors which affected the recovery of the H reflex in the cat when identical paired stimuli

FIG. 4. Duration of unresponsive period of H reflex in patients with Parkinson's disease before and after treatment with L-dopa. Results for individual patients are joined by a straight line.

were employed. They found that with low intensities of stimulus the effects of muscle contraction were minimized, and that the initial period of unresponsiveness provided an indication of the state of excitability of the spinal motoneurone pool. More recently, Táboříková and Sax (1969) have employed subthreshold conditioning stimuli in man in order to avoid the effects of muscle contraction and have concluded that long-loop reflexes through the brain-stem and cerebellum contribute to the later phases of facilitation.

In the present study, identical paired stimuli of low intensity were used. The interpretation of the H reflex recovery curve in man using this technique has been discussed elsewhere (McLeod, 1969). The duration of the period of unresponsiveness after the conditioning stimulus was significantly shorter, and the recovery of the H

reflex was more rapid in patients with Parkinson's disease than in controls. The findings indicate that recovery of excitability of the alpha motoneurone pool occurs more rapidly in patients with Parkinson's disease and is consistent with the presence of increased alpha motoneurone excitability in these patients. Denny-Brown (1968) concluded from observations in man and experimental animals that there was alpha motoneurone hyperactivity in Parkinson's disease, and other workers have reached similar conclusions (Stern and Ward, 1962, 1963; Ioku *et al.*, 1965; Olsen and Diamantopoulos, 1967; Takamori, 1967; Yap, 1967).

After treatment with L-dopa for six months there was a significant increase in the duration of the period of unresponsiveness. The finding suggests that L-dopa reduces the hyperactivity of the alpha motoneurone pool, and that this may be a factor in the clinical improvement in degree of rigidity. It is interesting that a similar reduction in alpha motoneurone hyperexcitability has been demonstrated by means of H reflex studies in patients after thalamotomy (Ioku, *et al.*, 1965; Olsen and Diamantopoulos, 1967; Yap, 1967). The present results in man are in accord with the observations of Steg (1964, 1966) in experimental animals. He demonstrated that reserpine-induced rigidity of rats was dependent upon an increase in alpha motoneurone activity, which was reversed by administration of L-dopa. The site of action of L-dopa in causing the alteration of alpha motoneurone excitability is uncertain. It probably has no direct action on the monosynaptic reflex pathway (Andén, Jukes, Lundberg, and Vyklický, 1966), but rather causes an increase in striatal dopamine and influences the spinal motoneurone pool through reticulospinal and other descending pathways.

It is concluded that there is an increased excitability of the alpha motoneurone pool in patients with Parkinsonian rigidity and that this situation is reversed by treatment with L-dopa.

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