Cybernetic methods in clinical neurophysiology

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This paper gives a short review of some of our recent activities which have been developed in our collaboration with the Institute of Clinical Neurophysiology at Ljubljana.

A part of our work was concerned with the development of new computer-oriented research techniques to implement the methods of electromyography (EMG) and microelectromyography (micro EMG).

In the second part of our paper we wish to present some of the results of our attempts to study memory and learning in simple neural networks in man.

Frequency analysis of EMG

EMG (Fig. 1) is an important diagnostic tool in clinical neurophysiology. As is well known, it shows a complex series of electrical events in the millivolt range produced by depolarization of muscle fibre preceding their contraction. It is an empirical knowledge that the time course and amplitudes of these voltage changes reflect the spatial and temporal patterns in which the muscle fibres are arranged in the motor units; and from these patterns conclusions can be drawn as to the normal or pathological innervation types.

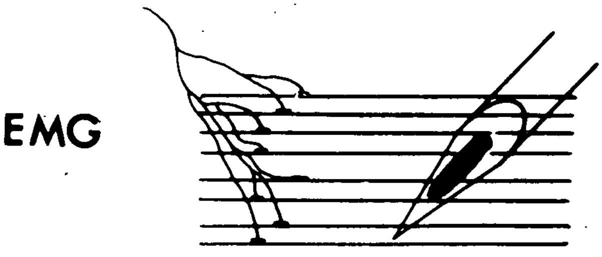

Fig. 1
Coaxial needle electrode recording motor unit action potentials

While it is usually not difficult to recognize clearly abnormal cases, there is a large range of borderline changes which are left to subjective interpretation.

Frequency analysis based on several principles has already proved to be valuable in such cases.

Our aim was to develop an improved method of frequency analysis of the EMG signals.

We have chosen the principle of pattern recognition whereby the frequency content of the EMG signals is represented by a set of twelve-dimension vectors. The EMG signals are fed to twelve band-pass filters covering the whole frequency range; the output of these filters constitutes the components of the pattern vector (Fig. 2). We use a general purpose computer which allows an on-line classification with a pattern recognition method.

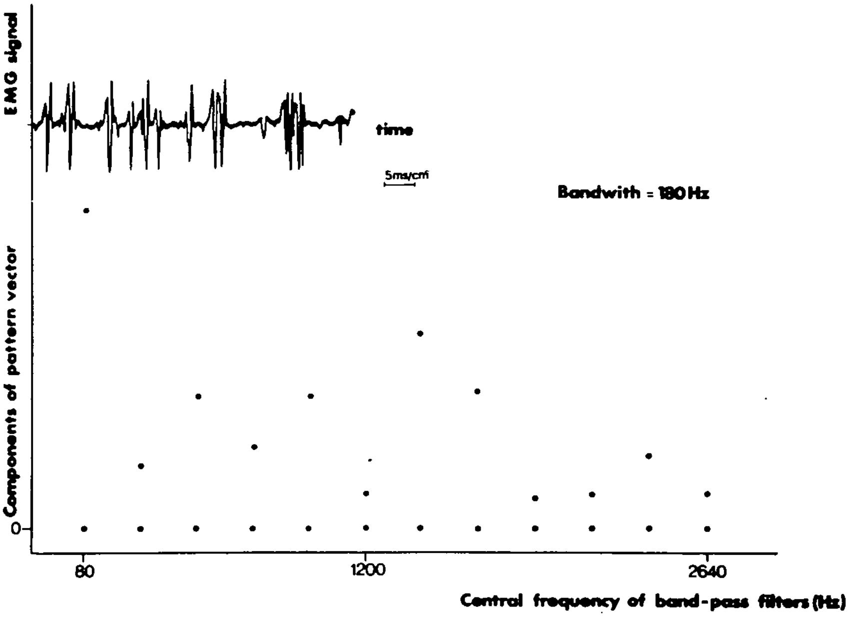

Fig. 2
Recorded EMG and its pattern vector

We have chosen a linear discriminant function

$$g(x, w) = w_1x_1 + w_2x_2 + \dots + w_nx_n + w_{n+1}$$

where w_i are the weights of the threshold logic unit and x_i are components of the pattern vector.

A nonparametric training was used for determination of the weight vector W

$$W' = W + cX$$

where W' is a new value of W and c is the correction coeffcient.

This method is still under evaluation. Nevertheless it seems to be rather promising.

Computerized Micro EMG

Micro EMG is another method in clinical neurophysiology which has been improved by the introduction of on-line statistical calculations performed by a digital computer.

The basic method here is micro EMG which allows the study of the action potentials of single muscle fibres as well as of several muscle fibres innervated by one motor neurone. The interesting parameters in this method are the time intervals between the individual spike potentials, as well as their respective amplitudes, which serve for their recognition.

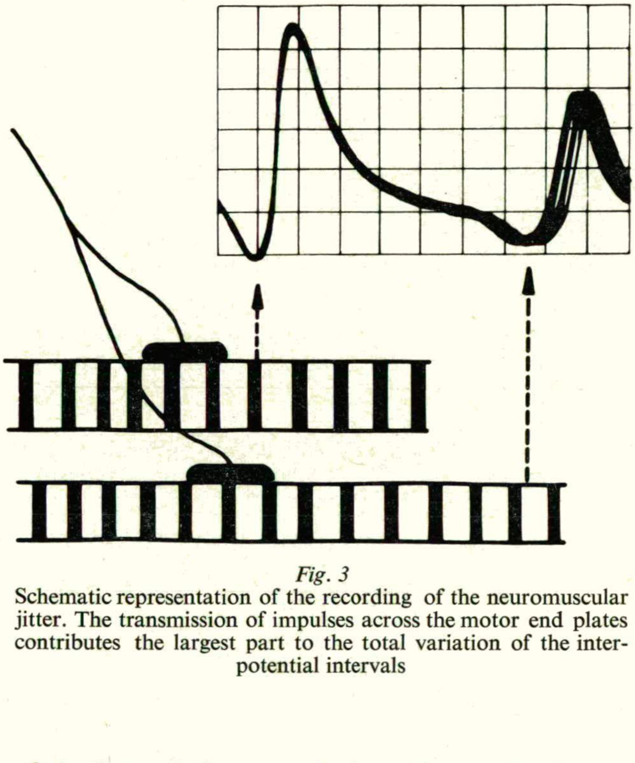

Fig. 3

Schematic representation of the recording of the neuromuscular jitter. The transmission of impulses across the motor end plates contributes the largest part to the total variation of the interpotential intervals

Variation of the intervals between the individual spikes known as the neuromuscular jitter or the variation of the latency time of the spikes following a stimulus can provide an important information about the functions like the neuromuscular transmission, conduction of impulses along the nerve and muscle fibres, and synaptic transmission in the central nervous system (Fig. 3, 4).

The problem to be solved here was to identify the potentials and to compute statistical parameters of interspike time variation.

Fig. 5A) shows repetitive discharges of a pair of potentials generated by two muscle fibres. There is a small variation of the intervals between the two potentials, which is in the normal range, i.e. lower than 30 usec. Fig. 5B) shows a similar pair of spikes but with a pathologically large variation of the intervals and intermittent blocking of the second spike.

The computer performs on-line the following statistics

1. histogram of intervals
2. floating average
3. distribution of intervals
4. dependence of the intervals on the discharge frequency and computes the respective numerical values (Fig. 6, 7, 8, 9).

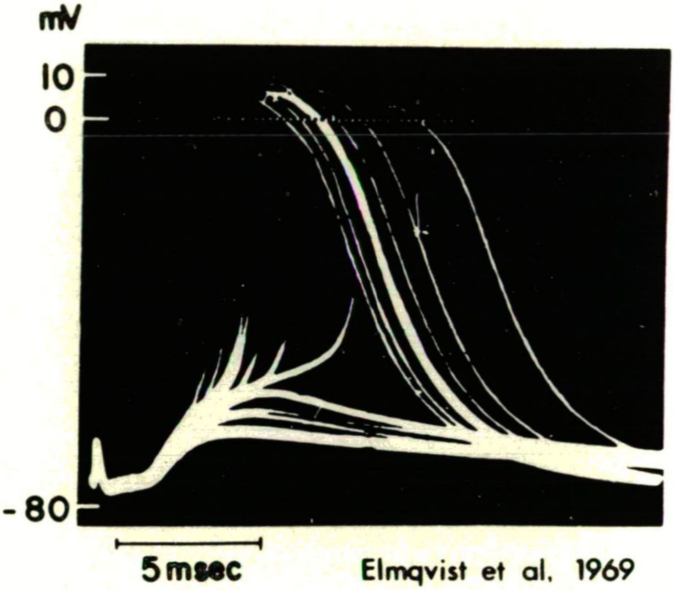

Fig. 4
Intracellular recording near the end plate showing the origin of the neuromuscular jitter. The action potentials of the muscle fibre are triggered when the end plate potential reaches the threshold level

The main difficulty to be solved was presented by the real-time operation which required fast algorithms for the recognition of the potentials and other computations.

We decided to use the distances between the imput pattern and a set of reference vectors as the classification criterion. Suppose that m reference vectors $R_1, R_2, \ldots, R_m$ are given with R_j associated with the pattern class ω_j. A minimum-distance classification scheme with respect to $R_1, R_2, \ldots, R_m$ is to classify the input X from ω_i, i.e. $X \in \omega_i$ if $|X-R_i|$ is the minimum, where $|X-R_i|$ is the Hamming's distance defined between X and R_i.

By the use of these computations we considerably increased the value of micro EMG for both diagnostic and research.

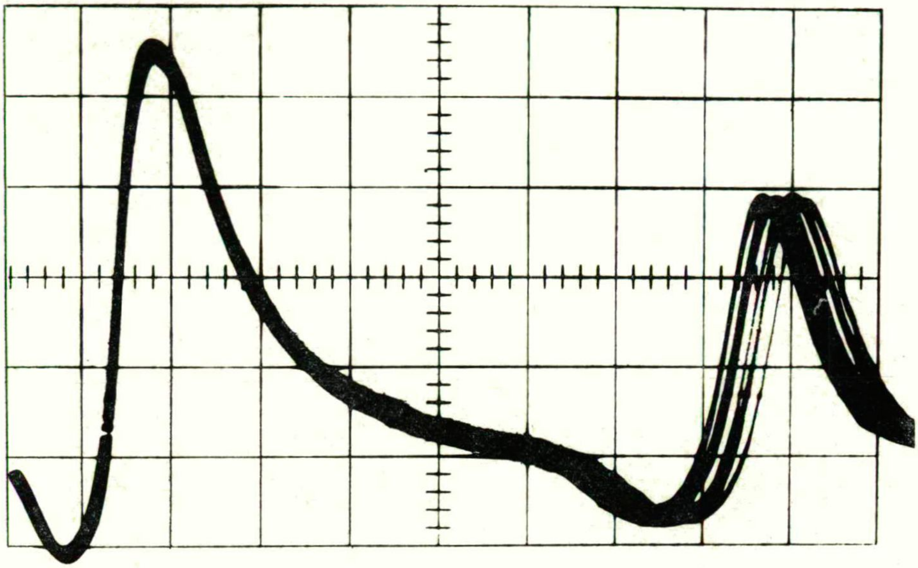

Fig. 5 A)
Action potentials of two muscle fibres of a motor unit;
a normal pair with small variation of interpotential intervals

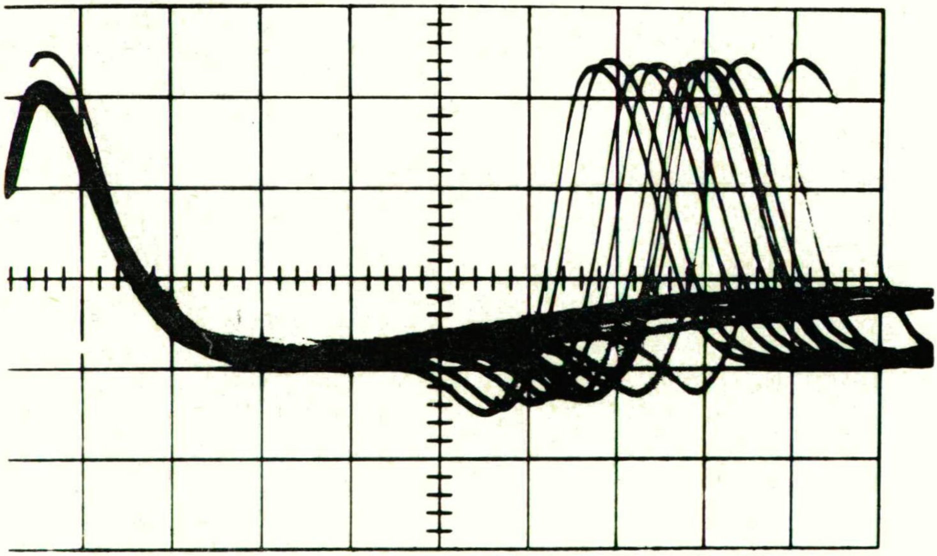

Fig. 5 B)
Action potentials of two muscle fibres of a motor unit;
a pathological pair with a large jitter and occasional blocking of the second potential

The problem of learning in simple polysynaptic reflexes

Initially, our study had a very simple aim: to investigate the properties of human flexion withdrawal reflex, particularly in the paraplegic patient with completely divided spinal cord. A classical definition says that it is a simple polysynaptic reflex subserving withdrawal of the limb from an offending stimulus. This reflex is organized at the level of the spinal cord (Fig. 10), but can be substantially influenced by the descending pathways from the brain. The paraplegic patient retains the flexion reflex, frequently in an exaggerated form, even though his spinal cord is divided from the rest of the central nervous system. The ambition of some research workers has been to use this reflex in the attempts to externally control the paralyzed lower limbs.

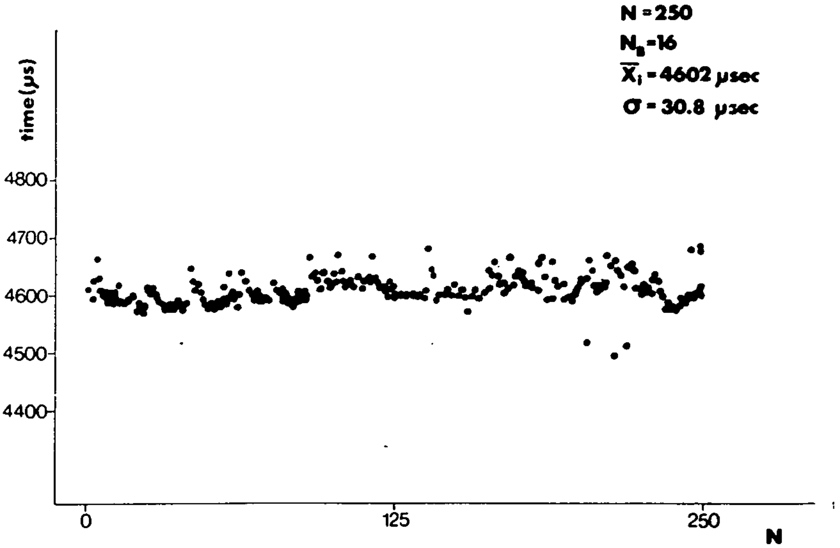

Fig. 6
Sequential histogram of interpotential intervals.
Each dot represents a single discharge of the potential pair

An immediate observation in our studies was that the flexion reflex, when repetitively elicited by electrical noxious stimuli in paraplegic patients, exhibits an unexpectedly large variation in size, even though stimulation parameters and other controllable experimental conditions are kept as constant as possible. Another regular finding was the tendency towards gradual decline of the size of the responses followed by their eventual cessation (Fig. 11). Closer study revealed all features of typical habituation[1], which, according to some authors[2], can be regarded as a primitive form of learning. Others, however, object against this view and rather tend to interpret habituation as a passive process of synaptic fatique[3].

Considering that the flexion reflex probably is one of the simplest systems capable of habituation we became aware of the opportunities which it offers in the

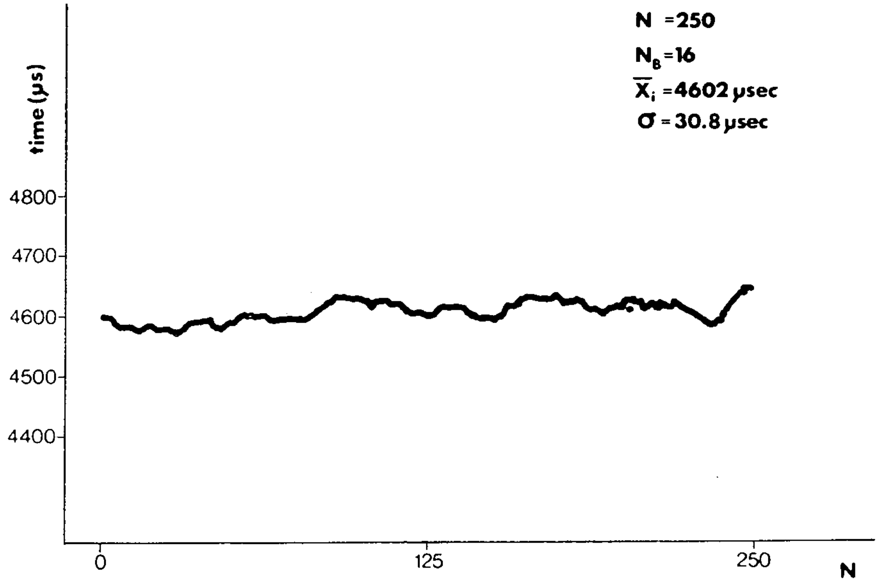

Fig. 7
Floating average of the intervals in Fig. 6

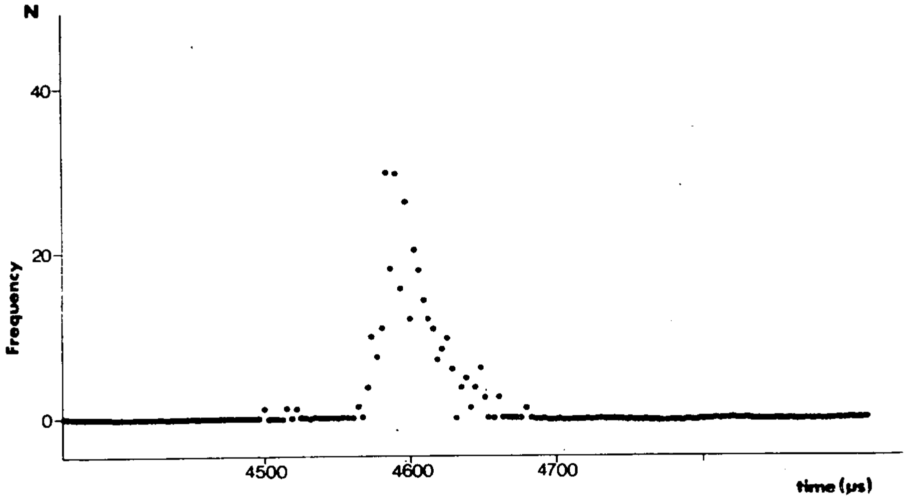

Fig. 8
Distribution histogram of the intervals in Fig. 6

studies of habituation, particularly in the basic neurophysiological problem: whether or not habituation is true learning.

Approaching this problem we first attempted to influence the process of habituation by stochastically changing parameters of stimulation[4] (Fig. 12). This method always resulted in slowing or precluding habituation. A most striking result is illustrated by Fig. 13, which shows responses to a series of equal stimuli, followed by a series of stimuli with stochastically changing amplitude, which however never exceeded that used in the first series. It can be easily seen that habituation was very effectively suppressed in the stochastical series.

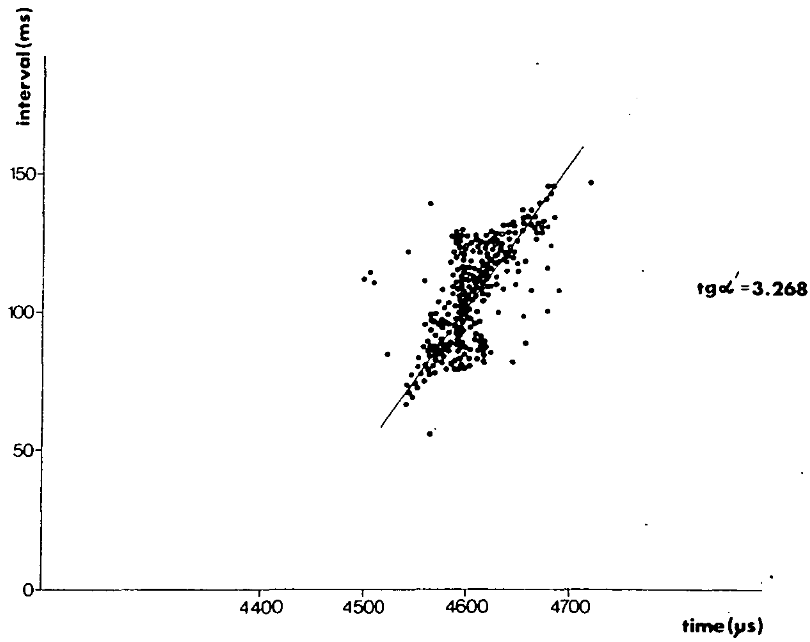

Fig. 9
Relationship between the interpotential intervals and the interdischarge intervals

This observation is a strong argument against the model of habituation based on passive synaptic fatigue. In this model, which incidentally has evolved from a similar experimental situation, i.e. flexion reflex in the spinal cat[5], dishabituation is only achieved with an extrastimulus, or a stronger stimulus, which activates additional interneurones with fresh synaptic endings (Fig. 14). Evidently this logic cannot be applied to our case; weaker stimuli should excite less afferents and less interneurones. Instead, we interpreted this finding to be due to some kind of recognition of stimulus strength, with a consequence that even a weaker stimulus acquires the meaning of a novelty necessary to interrupt the process of habituation. This concept implies the existence of another two functions in the system of the flexion reflex: classifying and memorizing the incoming information.

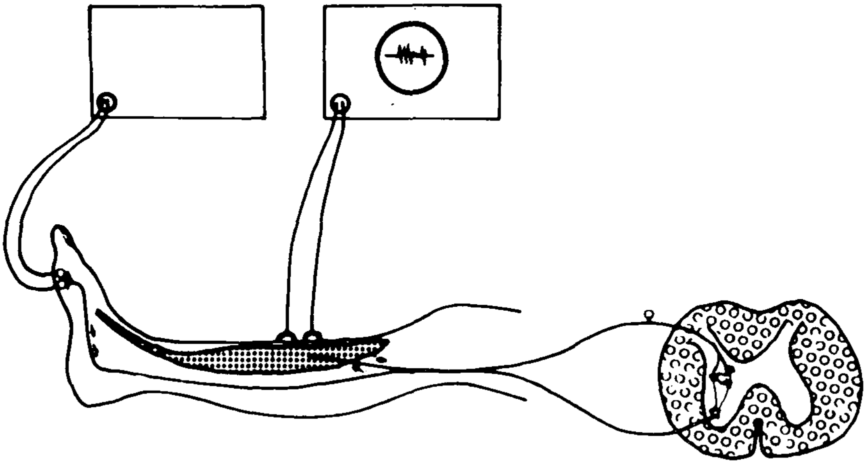

Fig. 10
Schematic representation of the reflex arc of the flexion reflex

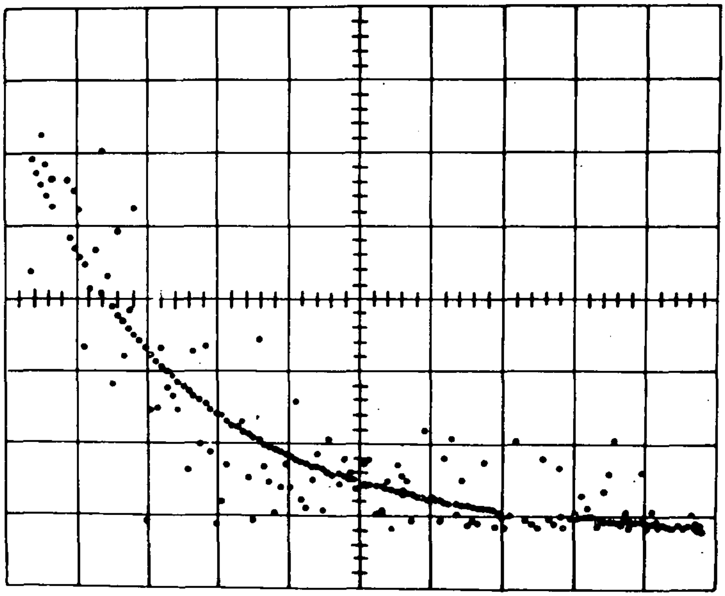

Fig. 11
Decline of the magnitude of [the] repetitively elicited flexion reflex responses. The line in the histogram is the minimum square error exponential curve

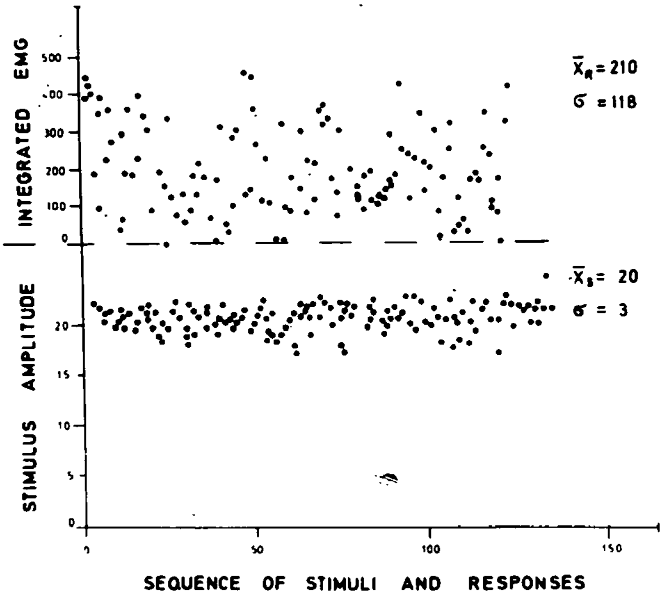

Fig. 12
Stochastically changing stimuli (upper histogram) and the respective responses (lowtoers higram)

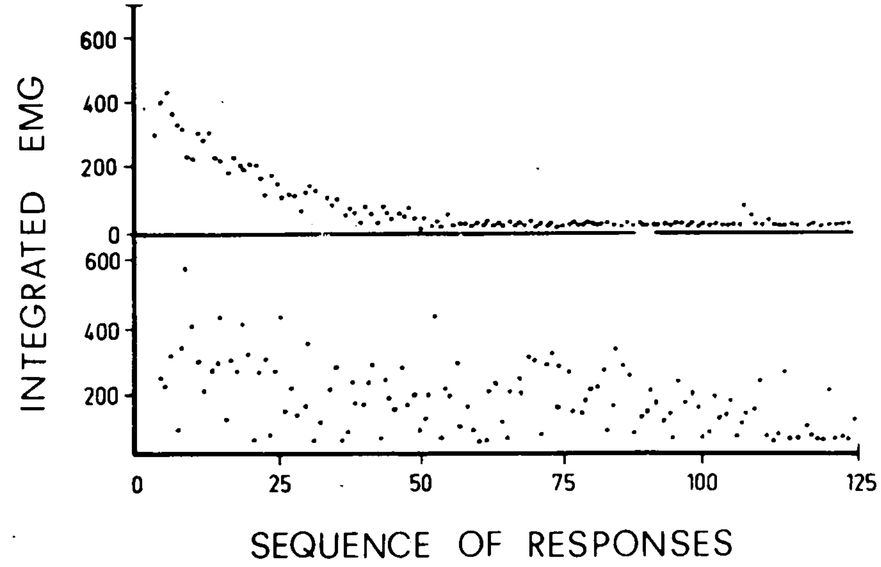

Fig. 13
Dishabituation produced by randomly changed stimulus amplitude (lower series of responses). In the upper series the stimulus amplitude was constant and equaled to the maximum amplitude in the lower series

In a following series of experiments we tried to demonstrate these two functions and estimate their capacities. A difficulty in these studies was the great variability of the responses as well as habituation itself. In order to investigate memory within the system of the flexion-reflex we had to use cross-correlation between stochastically changing stimulus parameters and the size of responses[6]. The cross-correlation coefficient between present responses and preceding stimuli, which ranged from 0.1 to 0.4 (P 0.01), can be regarded as a good evidence of the existence of memory and can also be used as a quantitative estimate (Fig. 15). Because of the rich fluctuation of the size of responses, the testing for the ability of stimulus recognition was even more difficult. An essential requirement was that the comparing patterns of stimulation produced strictly identical afferent volleys. The simplest pair of

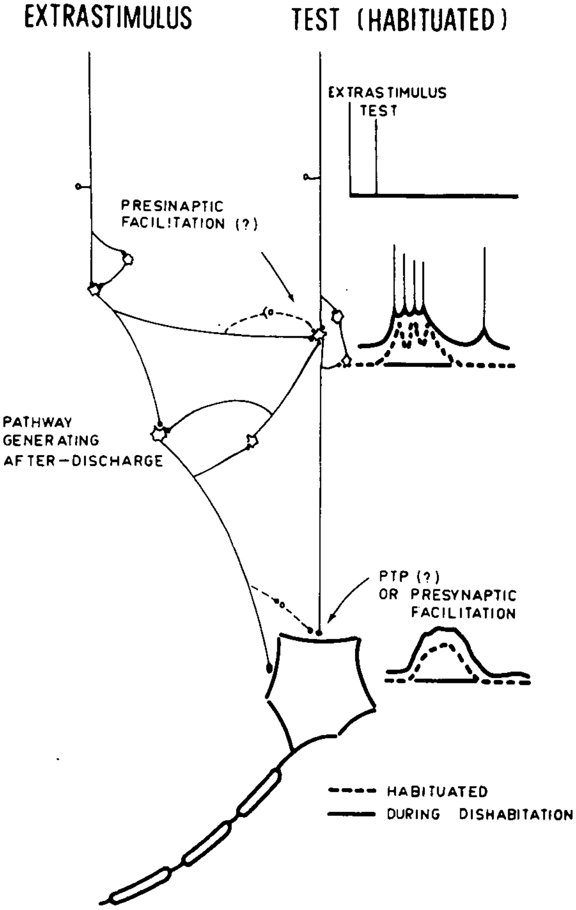

Fig. 14
Postulated mechanism of dishabituation[5]

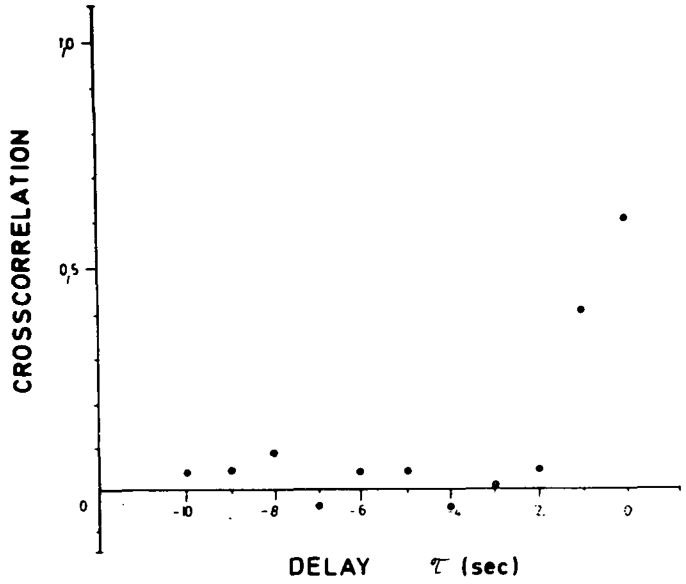

Fig. 15
Cross-correlation between stochastically changing stimuli and the responses

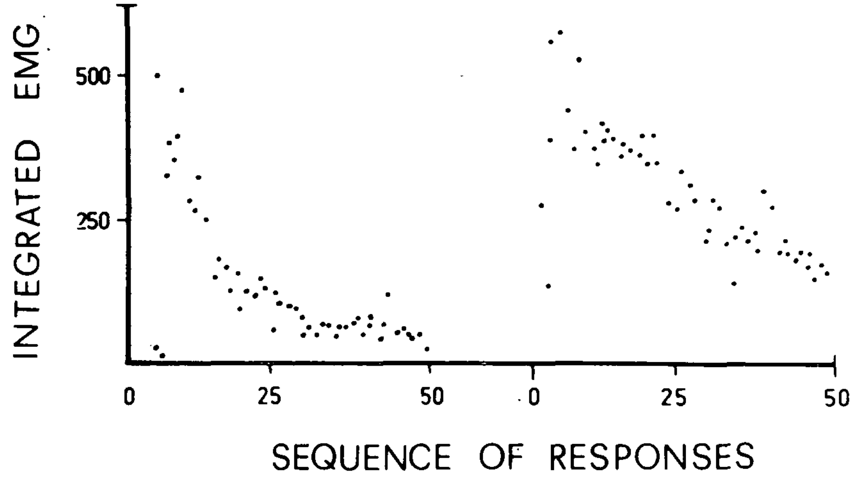

Fig. 16
Stimulation with stimuli of two strengths; shown are only the responses to the weak stimuli. Left: regular alternation of the weak and strong stimulus. Right: random sequence of the weak and strong stimulus

stimulation patterns satisfying this requirement consisted of two stimuli of different strengths, in one pattern alternating regularly while in the other pattern the sequence of the strong and the weak stimulus was random. Fig. 16 shows only the responses to the weak stimuli selected from both series in one of such experiments; habituation is clearly much more expressed in the left series with regular alternation of the strong and the weak stimulus. This finding can be interpreted as a result of recognition of temporal stimulation pattern besed on learning.

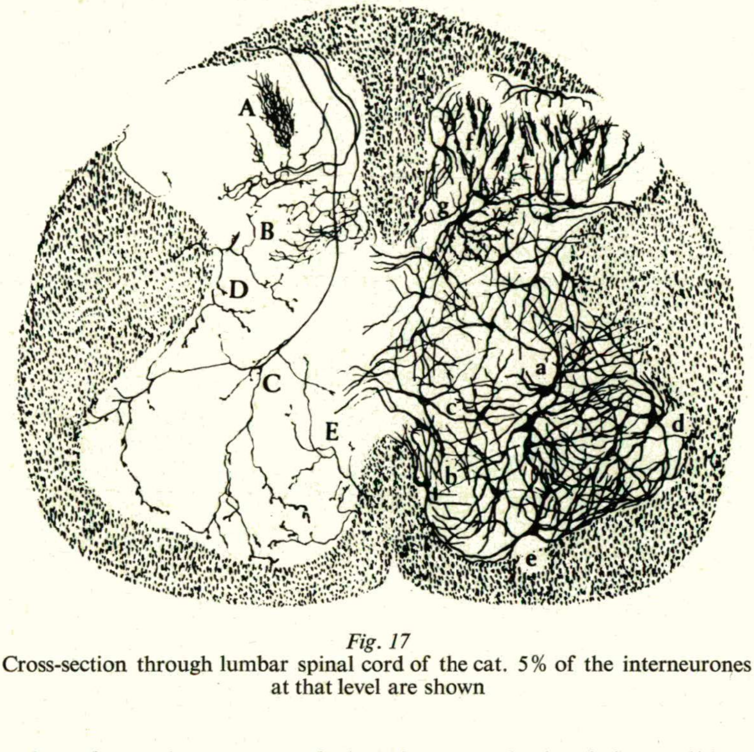

Fig. 17
Cross-section through lumbar spinal cord of the cat. 5% of the interneurones at that level are shown

A number of experiments were designed to see whether it is possible to demonstrate classical conditioning within the system of the flexion reflex in the paraplegic patients. However, statistically significant results indicative of such a possibility were not obtained.

In another series of experiments, the flexion reflex was recorded from single motoneurones with the aid of single fibre electromyography. The purpose of these experiments was to gain more insight in the structure and function of the reflex arc. One of the findings was that the latencies of consecutive responses varied several tense of milliseconds even within the first component, which is 10 to 20 times more than in the case of the monosynaptic *H*-reflex. This implies considerable possibilities for the processing of the afferent information in the way of the well-known neurophysiological processes of spatial and temporal summation as well as facilitation and inhibition. Thus, even though the system of the flexion reflex in terms of a neural network is rather specialized, it nevertheless seems to possess the capacity for some adaptive decisions. On the other hand, it is simple enough to provide interesting possibilities for the basic neurophysiological and biocybernetic studies of habituation and learning.

One might claim that it is too simple to be capable of such functions. To convince you that it is not so, the last two pictures are shown.

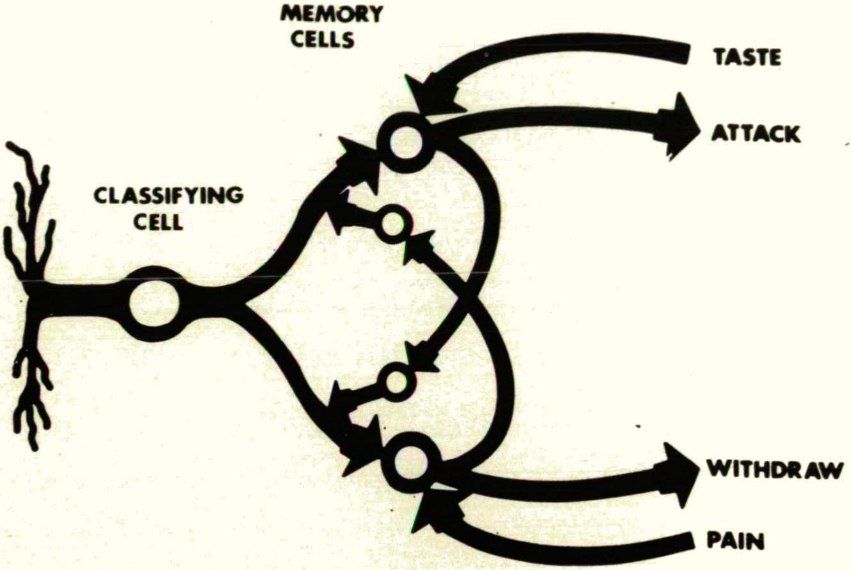

Fig. 18
The "mnemon" of Young. A minimum neural network of octopus capable of learning and adaptive decisions

Fig. 17 shows a cross-section through the spinal cord with the network of interneurones. Only 5% of the total number in that section is shown.

Fig. 18 on the other hand shows the simplest neural network capable of learning and adaptive decisions.

From this comparison it is evident that the structure of our model is rich enough.

Summary

This paper deals with some methods based on statistic theory and pattern recognition, which were used in studies of human reflexes, in the analysis of the electromyogram and in the studies of the single fibre electromyography.

A cybernetic study of the human flexion reflex was performed to see whether elements of learning can be demonstrated to occur in its pathway. Several methods based on stochastically changing input and statistical analysis of input-output relationship were designed. It has been shown that the system of the human flexion reflex is capable of memorizing parameters of stimulation. Experiments were also designed to investigate the ability of this reflex system for adaptive decisions based on learning.

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