CHAPTER 9 - TREMOR AND OTHER DISTURBANCES OF VOLUNTARY MOVEMENT

Prelude

Up until now, each chapter has tried to give the relevant background physiology necessary for the sort of clinical problem-solving approach so strongly advocated in the introductory chapters. Moreover, the central nervous system is one where we can well illustrate the principle of inter-dependence of diagnostic categories, particularly the Functional and Anatomical ones, because our knowledge of neurophysiology and its relation to neuro-anatomy allows us to pinpoint many lesions anatomically in the brain to within a few millimetres, especially in areas such as the brain stem and spinal cord.

Having demonstrated some of the principles involved, I leave you to broaden your own approach along these lines.

In practice, we sometimes cannot always solve problems solely with our physiological approach to anatomical diagnosis, and have to supplement it with pattern-recognition methods. Some such important areas are tremor, abnormal bodily tone and movement addressed in this chapter, and nystagmus in the next. In doing so, we can at least the appreciate the importance of adopting our hierarchic approach to diagnosis.

INTRODUCTION: RELEVANT NEUROPHYSIOLOGY

We have already discussed some aspects of the neurophysiology of motor control, both at the level of the lower motor neurone anterior horn cell, and higher cortical and subcortical centres feeding into the pyramidal tract. But to understand the way in which disturbances of voluntary control come about, we need a more detailed examination of some of the sub-cortical nuclei, particularly the basal ganglia and the cerebellum, and their interactions with other centres, both higher (e.g. motor cortex) and lower (e.g. brain stem and anterior horn cell).

Motor Cortex

This not only directly innervates the anterior horn cell for fine movement of the fingers, but makes three other types of connection, (i) to brain stem nuclei, including the red nuclei, which themselves give rise to descending motor fibres; (ii) to the cerebellum; and (iii) to the basal ganglia. Through these sub-cortical pathways, the cortex can inform key regions of the brain of the way in which particular movements need to be planned. In turn, most of these centres feed back to the motor cortex to let it know how they, in turn, have responded.

Basal Ganglia

Includes the <u>caudate nucleus, putamen, and globus pallidus</u>; also sub-thalamic nucleus and the substantia nigra. Evidence that the basal ganglia have a role in the control of movement comes from finding pathological lesions in one or several of these centres in patients with aberrations of voluntary control, such as tremor and/or muscle rigidity and/or difficulty in initiating or maintaining movement, e.g. Parkinsonism, Huntington's chorea and hemiballismus.

The caudate nucleus and putamen receive information from the cortex, process it, and pass most of it on to the globus pallidus. This information in turn is sent to lower centres such as the sub-thalamic nucleus, the red nucleus, and other brain stem and cerebellar nuclei. Through these pathways, the basal ganglia are connected both directly and indirectly to the anterior horn cell of the spinal cord, so as to allow the fairly automatic performance of basic bodily movement and postural control. At the same time there is feedback of information from the basal ganglia to the motor cortex (largely via the thalamus) so that the higher centres can super-impose their input whenever the lower centres do not lead to the desired control.

Cerebellum

The main action of the cerebellum is to correct errors in motor activity elicited by the motor cortex. In this respect, the cerebellum is best seen as a comparator of information derived from three sources namely; (i) command signals from the motor cortex; (ii) signals from inter-neurones in the spinal cord; and (iii) information from peripheral receptors. From these various inputs, the cerebellum is in an ideal position to compute and make appropriate corrections so as to ensure that there is accuracy to movement initiated by the motor cortex. The cerebellum is also involved in initiation of movement and the learning of certain skilled movements.

MUSCULAR MOVEMENTS

These are determined by all of the above. The ones we want particularly to consider here are as follows:

Posture: Reflex mechanisms involving the spinal proprioceptive apparatus are particularly important, but they require supra-spinal control to be effective, especially from nuclei subserving vestibular mechanisms, which have a close association with the cerebellum, brain stem nuclei, and basal ganglia. Feedback also plays an important part in the automatic corrections necessary for the maintenance of posture. In man, for example, the gamma loop is known to be active in postural control. Cerebellar disorders lead to particularly severe disturbances of posture.

Walking: Much of the basis of walking in each individual s eventually enabled by the spinal cord and hind brain. Its detailed programme however comes mostly from the frontal cortex (hence "gait dyspraxia" in frontal lobe lesions).

Voluntary Movement: Not understood completely, but obviously involves the motor cortex, which in turn is probably stimulated by the parietal lobe cortical association areas. Once these have completed their planning, and as movement proceeds, the basal ganglia and cerebellum become involved in fine tuning it towards its goals. Some of the sub-cortical centres such as the substantia nigra and the cerebellum are also involved in the planning and initiation of movement (witness the bradykinesia of Parkinsonism - see below).

Consciousness

N.B. It is emerging that , although we are conscious of our motor movements, we don't make such movements consciously. I have discussed elsewhere how, given this, the brain may control things in relation to consciousness in an article entitled: **The Body, its Emotions, the Self and Consciousess**. Perspectives in Biology and Medicine Vol 55, No 3, Summer edition, in press 2012

A. TREMOR

As defined by clinical neurophysiologists, there are three broad types of tremor.

1. Postural (Action) Tremors

These are seen when the patient is asked to put the part concerned in some position and to actively maintain it, e.g. outstretching the hands and separating the fingers. It is usually of fairly rapid rate, approx. 9-12 cycles/sec. It has various causes, but a frequent thread is an increased activity of the (beta) sympathetic nervous system. For example, it is commonly seen with anxiety states, salbutamol administration (beta-adrenergic agonist), and also in thyrotoxicosis, in all of which conditions it can be improved by beta-blocking agents. Similarly, it is seen in alcohol withdrawal where there is may be a markedly increased sympathetic stimulation. Finally, it is characteristic of so-called 'essential' tremor.' This is usually hereditary, is seem most in the elderly, but may even be seen in children. It may be improved by beta-blockers (also by alcohol).

A quite separate form of postural tremor is so-called "metabolic flap" or asterixis. This occurs with many metabolic disorders, including hepatic, renal, and pulmonary (CO_2 retention) failure, and is best seen by asking the patient to outstretch his hands and hyper-extend his wrists. It is quite different from the regular and rapid fine physiological postural tremor above, because it occurs intermittently and sometimes quite irregularly, (the limb must be viewed for at least 30 seconds before it can be excluded); characteristically, the hyper-extended position of the wrists and fingers is

maintained for some seconds, but then is suddenly lost with resultant transient flexion or drooping of the hands, often associated with a side-to-side tremor, giving the hand the momentary appearance of a fluttering bird's wing.

2. Intention Tremors

Mostly due to cerebellar problems. One of the important roles of the cerebellum is to determine the duration of neuronal excitation after stimulation, as well as the coordination of agonist and antagonist motor neurones in the anterior horn through both alpha and gamma motor neurones. In patients with cerebellar disease, initial stimulation time is sometimes too long, and so movement is correspondingly prolonged, causing"overshoot"; on other occasions, the inhibitory phase is lengthened, producing "undershoot". The poor co-ordination of agonist muscles with antagonists also gives rise to the characteristic intention tremor, which, as we might expect from the above, gets worse as the finger approaches its target, when maximal co-ordinationof agonists and antagonist muscles is required. Closely related is the gait ataxia of cerebellar disturbance ("drunken gait"), and incoordination of speech producing a "staccato" or "scanning" speech, where each syllable is pronounced separately and with great deliberation.This dysarthria is associated with difficulties in making rapid alternating movements of the protruded tongue. Impairment of rapid alternating movements can be seen in the hands and fingers, particularly noticed by the patient as difficulty in writing and other fine limb movements. Similar disturbances of fine eye movement control produces nystagmus (Ch 11).

The signs of cerebellar dysfunction include muscle hypotonia, with pendular reflexes (poor damping of reflexes because of poor agonist/antagonist co-ordination). Midline cerebellar lesions affect that part of the cerebellum most connected with the vestibular nuclei, and hence cause ataxia of stance and gait and nystagmus more than incoordination of movement and speech. Because of this, it is often only detectable when the subject is asked to walk or turn quickly. More laterally placed cerebellar lesions cause ipsilateral hypotonia with intention tremor and past pointing as well as difficulty in initiating and repeating movements. The same is true of lesions on the input (e.g. spino-cerebellar pathways) or output (cerebellar-spinal pathways) side of the cerebellum. All of these conditions result in an inability to accurately execute signals to the anterior horn cell agonist/ protagonist neurons; the corrections when made are too large, too late, and too prolonged.

Occasionally, the tremor of cerebellar lesions involves the head (titubation), but this is more characteristic of senile or essential tremor; it is most unusual in the static or rest tremor of Parkinson's disease.

3. Static Tremor (i.e. tremor at rest)

Classically, this occurs in <u>Parkinson's disease</u> and is a moderately slow, uniform movement occurring at a rate 3-7 c/s, e.g. the classical "pill rolling" between fingers and thumb. The movement is characteristically coarse and rarely involves the head. It does not necessarily occur synchronously

throughout the body. It is most prominent when the part is at complete rest (to achieve this, quietly watch the part without allowing the patient to know you are doing so). It tends to be aggravated by voluntary movement of the involved part. However sometimes voluntary action, such as carrying a newspaper may reduce the degree of tremor, probably by reducing the embarrassment which aggravates it. Oddly enough, the tremor is absent during sleep. Its pacemaker partly involves the brainstem and thalamus, but the substantia nigra is the primary nucleus concerned.

Because it involves other centres in the extra-pyramidal system, Parkinson's disease is characterised not only by tremor, but also by other abnormalities of bodily movement and posture. These are also seen in other disturbances of the basal ganglia / extra-pyramidal system. Therefore we now turn to consider the disturbances or aberrations in bodily movement.

B. ABERRATIONS IN CONTROL OF BODILY MOVEMENT

We will refer here particularly to <u>clinical disorders associated with the extra-pyramidal system</u>, which involve, in varying degree slowness in initiating movements, bradykinesia (slow movements once started), and abnormal movements, including tremor, chorea, athetosis, ballism, and various dystonias.

Parkinsonism

Pathologically, this is characterised by degeneration of the substantia nigra and fibres linking it with the corpus striatum of the basal ganglia. This pathway normally uses dopamine as its neurotransmitter, and reduced levels of dopamine occur in Parkinson's disease (hence improvement by L-dopa which is converted to dopamine by the brain). Clinical features include the tremor described above, and difficulty in initiation of movement (one of the key functions of the substantia nigra), rigidity, associated hypokinesia, and disturbances in posture control. Rigidity can be either "lead pipe" or "plastic" on the one hand, or "cogwheel" on the other. The latter is not, as you might think, entirely due to the super-imposition of tremor on rigidity. There is usually some weakness but no consistent alteration in reflexes.

Rigidity

Rigidity of either "lead pipe" or 'cog wheel' type occurs in patients with extra-pyramidal disorders, particularly Parkinson's disease. In these conditions there is an increased discharge from the extra-pyramidal system to the gamma motor neurone in the anterior horn cell of the spinal cord. As a consequence, the muscle spindles contract and the "gamma-loop" is activated so as to increase the alpha motor neurone discharge to the main muscle belly and hence increase its tone. A similar situation leads to the spasticity of cortical motor lesions, due to the release of subcortical extrapyramidal nuclei from higher inhibitory control.

Hypokinesia and Bradykinesia

These occur in many extra-pyramidal conditions other than Parkinson's disease, and the term includes not only poverty in range of movement, but difficulty in its rapid repetition, and slowness to initiate it. Posture and balance are also defective, because the patient is unable to compensate quickly for any sudden change in position. Correspondingly, gait tends to be slow and shuffling, and if the upper body happens to tilt forwards during walking, the patient has to try his best to chase his centre of gravity to correct this, so resulting in an increasingly rapid number of small steps, i.e. so-called festinant gait (typical of Parkinsonism). Arm swinging is also impaired as part of the hypokinesia.

Chorea is another characteristic disorder in basal ganglia disease. Choreiform movements are brief and jerky, and may be given the appearance of conscious intention by the patient to make it less noticeable to the observer, and therefore less embarrassing. Movements include facial grimacing, rapid protrusion of the tongue, gesturing of the arms, the appearance of fidgeting etc. In Huntington's chorea there is a loss of small neurones in the caudate nucleus, whilst in Sydenham's chorea (one variant of rheumatic fever), neurons are lost in other areas of the basal ganglia as well, including the lentiform nucleus. The latter nucleus is particularly involved in Wilson's disease or hepato-lenticular degeneration, an abnormality of copper metabolism.

Athetosis is yet another disturbance which may occur in extrapyramidal disease, and is closely related to chorea. Athetoid movements, however, are rather slower and, in the case of the hands, often take on a somewhat writhing character. In most cases, lesions seem to particularly involve the putamen and/or globus pallidus. Athetosis probably arises from abnormal excitatory discharges in the subcortico-spinal pathways involved in the control of trunk, girdle and limb movements. The commonest form of athetoid movememts now is therapy with excessive L-dopa in Parkinson's disease, or neuroleptic drugs used in the management of psychotic conditions - in what is called 'tardive dyskinesia.'

Ballism is a sudden involuntary flinging movement of limbs. Usually affects only one limb and is therefore called hemiballismus. Characteristically, the pathological lesion involves the subthalamic nucleus.

Dystonias include two classic conditions.

a) Torsion Dystonia is the name given to slow twisting or turning movements of the head, neck, trunk or limbs. These may be spontaneous or follow the onset of voluntary movement. The movements are powerful and must therefore involve most of the neurones of associated motor neuron pools. Often there seems to be contraction of both agonists and antagonist muscles at the same time. The distribution of the involved musculature suggests that, as with athetosis, that subcortico-spinal motor pathways are involved, but pathological studies usually show disease of the thalamus an deep cerebellar nuclei as well.

b) <u>Spasmodic Torticollis</u>: used to be regarded as an hysterical trait, but is probably mostly a variant of torsion dystonia with particular emphasis on the cerebellar nuclei.

Neurotransmission and Extrapyramidal Disorders:

In many patients with one or other of the movement disorders above, it is difficult to identify degeneration in any single nucleus or tract within the overall extrapyramidal system. But in neurophysiological terms, there are two major pathways in the extrapyramidal system, one dopaminergic and the other cholinergic. In some extrapyramidal lesions such as Parkinson's disease, the balance between these two transmitters appears to be altered in favour of cholinergic transmission. By contrast, in those conditions which include the facial tics, chorea, athetosis, muscle spasms, torsion dystonia, there seems to be a dominance of dopaminergic pathways over cholinergic ones. The classical athetoid syndrome is over-treatment of Parkinson's disease with L-dopa. When such disturbances of movement occur as a late consequence of this or other drug therapy, they are collectively referred to as the 'tardive dyskinesias.'

MCQ Question on Tremor/Aberrations of Voluntary Muscle Control

Mechanisms in Disease:

Cerebellar tremor characteristically includes which of the following features?

1. A rest tremor of 3-7 cycles/sec.

2. Is maximal when the hands are held in outstretched position.

3. Is associated with limb rigidity.

4. Is characteristically improved by alcohol.

5. Is one of the recognised side effects complicating chronic phenothiazine therapy.

Problem Solving Exercise: Not available for this chapter