Physiology of abnormal movements*

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Summary

The units of the central nervous system controlling voluntary movement are described and the roles of the motor and sensory cortex, of the basal ganglia and cerebellum and of the final common loop are outlined.

The pathophysiology underlying disturbances of movement, power and tone of the limbs is discussed, with particular reference to the more common dyskinesias.

Introduction

Although major advances have been made recently in neurophysiology, our knowledge of the pathophysiology of movement disorders is still very limited. For the present we can best understand the physiology of the abnormal by seeing where the deviation from normal occurs.

Any physiological discussion of the central nervous system ultimately involves a description of the way that nerve impulses travel through the relevant areas, that is, axon transmission by ionic interchange and synaptic transmission, be it excitatory or inhibitory, by chemical transmitters. Since transmitter chemistry is dealt with in another paper (Curzon, 1977), this paper, therefore, concentrates on the pathways and centres involved, their relationships and interactions. Ultimately it is the chemical interactions that are the important current aspect, especially from the therapeutic point of view.

In the limited time available an attempt will be made to show how the units interact to produce controlled voluntary movement and how abnormalities can develop. Specifically, to concentrate on the actions and interactions of four parts of the motor system: the final common path; the cerebral cortex; the basal ganglia and related structures; the cerebellum.

The final common path

All influences in the central nervous system, excitatory or inhibitory, from local reflex arcs or

higher centres can, through the final common path, only result in the muscle fibres supplied contracting or remaining relaxed. Integration lies at the level of the anterior horn cell or above.

Strictly speaking, the final common *path* must now be looked on as a final common *loop*. The muscle consists of the powerful contracting fibres—the extra-fusal fibres supplied by α motor nerves and, between them, supplied by γ motor nerve fibres, the muscle spindles, composed of two types of intrafusal muscle fibres, the nuclear bag and the nuclear chain cells. There are usually about two bags and four chain fibres in a spindle. The spindle cells have an afferent (sensory) and efferent (motor) supply. The sensory endings are of two types: (a) primary or annulo-spiral endings. The fibres (Ia) are thick and myelinated but lose their myelin sheath near the spindle so that the bare fibre is wrapped round the belly of the intrafusal cells. They innervate both chain and bag cells but mainly bag; (b) secondary or flower-spray endings innervate mainly the nuclear chain cells nearer the polar region. Their efferent fibres (type II) are smaller.

The motor innervation, in the form of small myelinated γ fibres from the central horn supply the striated portions at each end of the intrafusal cells. They are of two types— γ_1 fibres with discrete large endings to nuclear bag cells and γ_2 fibres with trial or plate endings on the chain cells.

The muscle spindle receptors can be stimulated by passive stretch of the ensheathing muscle, or by the contraction of the terminal contractile elements of the intrafusal fibres. Muscle spindles measure their length relative to the ensheathing muscle. The primary receptors respond instantly, then the rate of firing falls off rapidly and settles down to a slower, more steady firing rate. The first phasic signal shows the rate of change of length, the second tonic response the length of the fibre. The secondary receptors require several milliseconds to reach full response, their tonic response showing the length of the receptor and not the velocity of the change.

These receptors are utilized for the production of a reflex contraction of the related extrafusal muscle fibres to maintain postural tone in a muscle, e.g. in

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the upright posture or to form a servo-mechanism for control of muscle contraction.

The primary endings appear to be the most important. Recent evidence (Marsden, Merton and Morton, 1972) suggests that although the Ia fibres connect direct to the anterior horn cells supplying the α motor neurones, the stretch reflex arc by which stimulation of the spindle causes contraction of the equivalent extrafusal fibres lies through a cortical path.

The present view (Marsden *et al.*, 1972) is that muscle contraction arises by α/γ co-activation (Fig. 1). Some excitation reaches the muscle via the servo loop (the γ route) while some reaches the extrafusal fibre directly via the α motor neurones. Thus there is both a direct component of muscle contraction and a servo-assisted control. Local anaesthesia of the portion of the body surface related to the muscle depresses the servo response leading to the need for a greater conscious effort to initiate movement (Marsden *et al.*, 1972).

It appears that in a voluntary movement, cortical motor neurones connecting to both α and γ spinal neurones are partially activated. With local tactile sensibility afferent signals from the muscle spindles are given access to the α cortical motor neurones, thus completing the servo loop, perhaps by an effect through the reticular activating system.

Higher centres

It is now known (Eccles, 1977) that not only does the motor cortex fire before muscle contraction but so also do the basal ganglia and the cerebellum, while the sensory cortex shows activity after, rather than before, the initial muscle contraction. This implies that the motor cortex, basal ganglia, cerebellum and sensory cortex represent circuits that initiate muscular contraction.

Figure 2 is the imaginative illustration (Eccles, 1976) to explain the activities of the association areas

FIG. 1. Alpha/gamma coactivation and the reflex arc by which stretching the muscle spindle leads to contraction of the main muscle via the cortex.

of the cortex, the basal ganglia, the cerebellum and the motor cortex in the initiation and subsequent control of motor activity.

The current concept is that before execution of the movement by area 4 of the motor cortex, there are two possible planning pathways. Both involve the basal ganglia as an integral part. One however is unlearned and is shown diagrammatically (Fig. 2) as the direct line. For this pathway, concentration on the action is necessary as, for example, in a child first walking. But there is a learned response through the lateral cerebellar cortex in which the movements are pre-programmed and thus need no concentration.

It appears that the basal ganglia are mainly concerned with muscle tone and slow movements, the cerebellum with rapid fine movements.

FIG. 2. Concept of initiation and control of movement. Diagram showing pathways concerned in the planning, execution and control of voluntary movement. Full description in text. (Based on Eccles, 1976.)

It is only after this process that the motor area 4 fires, probably mainly down the pyramidal tract to activate the final common path. In this stage of movement somatosensory information from various parts including eyes and vestibular apparatus and proprioceptive impulses from the limbs feed back to both the cerebellum and motor cortex and enable those areas mutually to control the finesse of the movement.

The entire cerebral cortex, including the somatosensory, visual and auditory regions, sends fibres to both the basal ganglia and the cerebellum, while the cerebellum in addition receives proprioceptive impulses from the muscles and position information from the vestibular apparatus.

The cerebellum pre-programmes and initiates rapid controlled purposive movements, the basal ganglia are concerned with the generation of slow movements and tone, the motor cortex with the extent and pattern of muscle contraction. Thus, the picture emerges of muscle activity through the pyramidal tracts but under the control of three feedback loops—the γ motor path, the basal ganglia loop and the cerebellar loop each with its own specific function.

The interactions and relationships of the various nuclei of the basal ganglia have been reviewed recently by Webster (1975). A simplified diagram of some of the main feedback loops is shown in Fig. 3. Afferents from all areas of the cortex run to the corpus striatum. From the corpus striatum one loop

involves the zona compacta of the substantia nigra which fires back on the corpus striatum via an inhibitory loop in which dopamine is the transmitter substance. A second loop travels via the external pallidum and the subthalamic nucleus to the internal pallidum where it meets a supply direct from the corpus striatum. The internal pallidum is the main area for efferent pathway—the ansal system that conveys its main fibres to the ventro-lateral nucleus of the thalamus and thence back to the motor cortex. There is a topical organization at each area. Other impulses leaving the internal pallidum reach the mid-brain nuclei which, via various polysynaptic tracts, influence the spinal cord ventral horn. Although dopamine has been mentioned as one inhibitory transmitter, numerous excitatory and inhibitory transmitters are found in the region.

The cerebellum contains, as is shown in the simplified diagram (Fig. 4), a pattern of feedback loops remarkably similar to that in the basal ganglia except that proprioceptive and positional impulses are also fed in (Kemp and Powell, 1971). The vertebrate cerebellar cortex has a very uniform structure. Its only output is the projection of large inhibitory cells—the Purkinje cells to the intracerebellar nuclei (including the dentate nucleus), from there to the ventro-lateral nucleus of the thalamus, and thence to the cortex. Like the internal pallidum in the basal ganglia, the intracerebellar nuclei also connect with mid-brain nuclei, notably

FIG. 3. Diagrammatic representation of some important basal ganglia connections.
(—), facilitatory path; (---), inhibitory path.

FIG. 4. Diagrammatic representation of main cerebellar connections.
(—), facilitatory path; (---), inhibitory path.

the nuclei of the reticular formation and the vestibular nuclei which send down facilitatory extrapyramidal impulses to the ventral horn cells.

There are two kinds of input to the cerebellar cortex. The mossy fibres have a wide variety of sources including the pontine nuclei which receive the main spinocerebellar tracts and collaterals from the pyramidal tract. The cerebellar granule cells, with which the mossy fibres synapse, send their axons as the parallel fibres to the Purkinje cells either direct or via other inhibitory cells, the Golgi cells, the stellate cells and the basket cells. The second input is via the climbing fibres. Each climbing fibre synapses with only one Purkinje cell and has its origin in the cells of the inferior olive. This receives impulses from many sources, including the small pyramidal cells of the motor cortex. One current theory is that the control memory of rapid purposive movements lies within the cerebellar feedback circuits.

So far, the importance of the cerebellar and basal ganglia feedback via the thalamus to the motor cortex and hence via the pyramidal tracts to the anterior horn cells has been stressed. Less important though still significant downflows from the basal ganglia and cerebellum lie in the excitatory and inhibitory reticulospinal, the tectospinal, the vestibulospinal, the olivospinal and the rubrospinal tracts—the so-called 'extrapyramidal' pathways, which appear to be important in some human motor disorders.

Thus, the final common path has playing on it: the Renshaw cell loop; local reflex arcs; the pyramidal tract (itself influenced by the muscle spindle feedback loop); the basal ganglia; the cerebellar loops; the facilitatory and inhibitory tracts from the brain stem nuclei. The activity in the final common path ultimately depends on an integration by the ventral horn cells of these various stimuli.

Pathophysiology

With this background of the physiology of normal movements we must examine the pathophysiology of abnormal movements. This subject remains in a confused state, particularly when we are dealing with gross fibre tracts and nuclear abnormalities.

The pathophysiology is probably best considered under the headings of the principal individual disturbances of tone and movement (Table 1) for most named disorders consist of composite and complicated variable disturbances of power, posture, tone and voluntary movement. Indeed even if we take one recognized syndrome, chorea, there are numerous possible diseases involved (Marsden and Parkes, 1973).

The pathophysiology of human disorders of movement is shown in Table 1.

Increased tone

Two terms are used clinically for disorders of increased tone—rigidity and spasticity. Rigidity is the

TABLE 1. Pathophysiology of 'movement disorders'

	Possible disorders
Disorders of tone	
Rigidity	Damage to suppressor cortical area (4–6) or its cortico-fugal path. Imbalance between facilitatory and inhibitory extrapyramidal paths. Cholinergic striatal preponderance over dopaminergic. Hyperactivity of α neurone.
Spasticity	Hyperactivity of γ loop.
Reduced movement	
Akinesia	Dopaminergic nigro-striatal cell damage.
Catalepsy	Cholinergic striatal preponderance over dopaminergic.
Abnormal movement	
Tremor*	
(i) Parkinsonian	(i) Cholinergic striatal preponderance over dopaminergic.
(ii) Cerebellar	(ii) Neuronal circuit disturbance. ? from unsuppressed 'tremorigenic' zone in postero-lateral nucleus of thalamus.
(iii) Intention	(iii) Interruption of dentato-fugal activity which influences the postero-lateral nucleus of thalamus.
Chorea (Huntington's)	(i) Striatal small cell damage. (ii) Dopaminergic preponderance over cholinergic. (iii) ? GABA $\uparrow$ -deficiency in caudato-nigral and caudato-pallidal inhibitory pathways.
Athetosis	Putamen or pallidal damage.
Dystonia	(poorly defined).
Torsion movements	Unknown neurophysiology.
Myoclonic movements	Unknown neurophysiology.
Tics	Unknown neurophysiology.
Ballism	Degeneration of subthalamic nuclei (corpus Luysii). Mediated through pyramidal tract.

* N.B. Affected by reticular formation (absent in sleep) and mediated through pyramidal tract; $\uparrow$ γ -aminobutyric acid.

term used to describe the resistance felt by the examiner when the limb of the patient is moved passively. Classically, this resistance is either constant throughout the range (lead pipe) or variable (cog wheel). Such rigidity is usually associated with an increased tone in the muscle—spasticity.

Destructive lesions of the premotor cortex, basal ganglia, mid-brain and cerebellum have all been used to provide animal models of rigidity. In animals, isolated lesions of the motor cortex give rise to a flaccid type of paralysis and of the premotor area a spastic type of paralysis, both of which are reversible. It is only after bilateral removal of the strip that separates cortical areas 4 and 6 that a permanent spastic paralysis results.

The widespread area of injury that will give rise to increased tone demonstrates the broad interplay of the nuclei involved. The physiological process ultimately consists of the imbalance in the facilitatory and inhibitory extrapyramidal pathways that affect the final common path. It appears that the most powerful inhibitory pathway is that from the reticular formation. In contradistinction, the most powerful facilitatory pathway appears to be the vestibulospinal. The inhibitory reticular area is supplied by pathways from the suppressor area of the premotor cortex but the facilitatory vestibular area is not. Hence the typical human cerebral catastrophe which interrupts the pathway in the internal capsule produces a spastic paralysis. It is important to stress that recovery can be complete after section of the pyramidal tract and the spastic extensor paralysis of the so-called pyramidal syndrome is in fact due to destruction of the inhibitory pathway.

Some of the tracts exert their influence direct on the α motor neurones, some indirectly via the γ loop. In this latter group extensor muscle hypertonia predominates and the increased tone can be reduced by dorsal root section. Strictly speaking, only those affecting the γ loop produce true spasticity but in practice it is difficult to be certain in many clinically named disorders. For example, in some cases of Parkinsonism γ -blocking with procaine reduces the tone while in others, clinically indistinguishable, this procedure has no effect (Rushworth, 1960).

Reduced movement

The disorders of reduced movement are akinesia and catalepsy. The pathophysiology is shown in Table 1 but in another paper (Curzon, 1977) the balance of the dopaminergic and cholinergic fibres in the basal ganglia is discussed.

Tremor

The central mechanism for the production of tremor may be regarded either as a rhythmicity of discharge within a neuronal circuit or as a phe-

nomenon of regular unsuppressed discharge arising at a so-called 'tremorigenic site'. Tremor is only encountered if the pyramidal tract is intact, hence the downflow of the rhythmical discharge must come ultimately from the pyramidal area of the motor cortex. Units discharging with tremor-frequency can be recorded from the cortex, but the ventro-lateral nucleus of the thalamus, which feeds back to the motor cortex shows a similar tremor-frequency discharge and surgical destruction of the ventro-lateral nucleus usually dispels the tremor. However, rhythmical discharge of the same rate can also be found in the cerebellum. Despite the evidence for specific unsuppressed tremorigenic centres, neuronal circuit disturbance is currently more in vogue. The reticular activating system appears to be involved in the circuit, as tremor normally disappears during sleep. The caudate nucleus head and the globus pallidus are also involved, because destruction of both of these also stops the tremor.

Clinical experience has always suggested that proximal muscle tremors are cerebellar in origin and distal muscle tremors result from disease of the basal ganglia or mid-brain but recent animal experiments cast doubt on this rather simplistic approach.

Other dyskinesias

Finally, there are the other abnormal movements not related to Parkinsonism.

Choreic movements may be exemplified by *Huntington's disease*. It is the exception to find single discrete brain lesions in this type of dyskinesia. However, a loss of the small nerve cells of the caudate nucleus is a fairly constant feature. Here is seen a pathological manifestation of an abnormal balance of dopaminergic and cholinergic pathways in the striatum.

Athetosis (mobile spasms and dystonia) is also poorly understood. Experimental studies designed to reproduce the disorder have been singularly unrewarding. The basis of our present concepts rests on a very limited number of correlated clinical and pathological reports showing lesions in the putamen or pallidum.

Ballism is one of the few involuntary movements for which a clear somatotopic localization has been established. In the monkey, destruction of the subthalamic nucleus results in ballistic movements involving the contralateral limbs. In man, a variety of lesions involving this nucleus or its neural pathways also produces these movements. It is suggested that this may be a prime example of a release phenomenon in the nervous system, i.e. destruction of the subthalamic nucleus removes an essential modulating ingredient for orderly motor behaviour. However, with the newer ideas of the feedback loops this may be too simplistic a view.

There is at present no underlying pathology or pathophysiology known for *torsion movements*, nor for *myoclonic movements* or *tics*.

We must conclude that there is currently inadequate anatomical and physiological information regarding the neural mechanisms underlying the various involuntary movements. However, increasing evidence is now accumulating that the whole of this region of the brain has a distinctive biochemical topography.

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