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ASSESSMENT OF EXTRAPYRAMIDAL DISORDERS

C.D. MARSDEN & M. SCHACHTER

University Department of Neurology,
Institute of Psychiatry and King's
College Hospital Medical School,
Denmark Hill, London SE5

Introduction

In the last twenty years the accurate evaluation of extrapyramidal disorders has become essential to assess the efficacy of an increasing number of potentially useful drugs. Not surprisingly, since the introduction of levodopa, Parkinson's disease has attracted the most attention for developing assessment techniques. It is a common condition, producing a complex and varying pattern of disabilities, and effective treatment is available with which new drugs may be compared. Techniques suitable for use in patients with Parkinson's disease are applicable also to patients with other akinetic-rigid syndromes, but different methods have to be employed to assess the severity and impact of other extrapyramidal diseases which cause abnormal involuntary movements (dyskinesias). The many types and causes of the extrapyramidal disorders under consideration are shown in Table 1.

The problem with all these conditions is that there is no simple sensitive technique for quantifying their severity. This is not surprising, for all the diseases in question are characterised primarily by difficulty in movement, which inevitably interferes with a wide range of bodily actions and activities of daily living. To judge the impact of such disorders on function requires a battery of observations or tests. Such an approach gives a satisfactory global impression of the severity of an extrapyramidal disorder, but inevitably it restricts the scope of each individual observation. The time available and the patient's resilience puts a limit on how long a reasonable assessment may take. Many sophisticated techniques have been derived for quantifying individual items of extrapyramidal disorders, for example tremor or rigidity, but frequently the time involved is too great to allow such methods to be included within a general battery of observations designed to obtain a global impression of disease severity.

For these and other reasons, clinical pharmacologists have approached extrapyramidal diseases in two different ways, depending upon the particular questions being asked. On the one hand, simple, rapid clinical scoring systems of symptoms, signs and disability are employed to establish whether a new pharmacological agent is of value in the treatment of a disease. On the other hand, the more sophisticated quantitative techniques are suitable for studies where more specific problems of pharmacology or pathophysiology are to be examined.

This review will attempt a comprehensive summary of existing methods for the assessment of extrapyramidal diseases. The emphasis throughout will be on the applicability of these techniques to the investigation of new forms of treatment for these disorders.

Parkinson's disease

Introduction

There is a very large and growing literature on the assessment of Parkinsonism. Two approaches have been employed:

(a) subjective assessment, generally based on rating scales of symptoms and signs, or of functional disability, or both;

(b) objective methods of two types: relatively simple tests, most often based on the timing of specific tasks, and more complex neurophysiological investigations designed to measure particular motor abnormalities (Table 2).

Many investigators have used a combination of subjective and simple objective tests, and it is logical to consider these together. Neurophysiological techniques, on the other hand, usually have been developed independently.

Subjective assessment

Table 3 lists the principal subjective rating systems described in studies on Parkinson's disease. Most were developed when levodopa was introduced and the need for such techniques become a matter of urgency.

Assessment systems which concentrated on functional disability usually were developed separately.

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Table 1 Extrapyramidal disorders and their causes

A. Kinetic-rigid syndromes

'Pure Parkinsonism
- Idiopathic Parkinson's disease
- Post-encephalitic Parkinsonism
- Drug-induced Parkinsonism

Parkinsonism of early onset, with other signs
- Wilson's disease
- Huntington's disease (rigid type)
- Hallervorden-Spatz disease
- Progressive pallidal atrophy

Parkinsonism of late onset, with other signs
- Progressive supranuclear palsy
- Strio-nigral degeneration
- Shy-Drager syndrome
- Olivo-ponto-cerebellar degeneration

} Multi-system degenerations

Parkinsonism of late onset, due to diffuse brain disease
- Alzheimer's disease
- Pick's disease
- Multi-infarct dementia
- Creutzfeldt-Jakob disease

Parkinsonism, onset at any age, with diffuse brain damage
- Trauma
- Cerebral anoxia (including carbon monoxide poisioning)
- Manganese poisoning
- Neurosyphilis

B. Dyskinesias

1. *Chorea*
   - Huntington's disease
   - Senile chorea
   - Sydenham's chorea
   - Chorea gravidarum
   - Thyrotoxicosis
   - Systemic lupus erythematosus
   - Polycythaemia rubra vera
   - Encephalitis lethargica
   - Drugs (neuroleptics, phenytoin, contraceptive pill)

2. *Dystonia*
   - Idiopathic dystonia musculorum deformans
   - Paroxysmal dystonia (paroxysmal choreoathetosis)
   - Dystonia with marked diurnal variation
   - Wilson's disease
   - Huntington's disease (juvenile type)
   - Lesch-Nyhan syndrome
   - Athetoid cerebral palsy
   - Hallervorden-Spatz disease
   - Drugs (neuroleptics, metoclopramide)

3. *Tremor*

   Rest tremor
   - Parkinsonism (idiopathic, post-encephalitic, drug-induced)

   Postural tremor
   - Physiological (exaggerated in thyrotoxicosis and anxiety states, and by alcohol and drugs)
   - Benign essential (familial) tremor
   - Wilson's disease
   - Severe cerebellar lesions
   - Neurosyphilis

   Intention (action) tremor
   - Brain stem or cerebellar disease (multiple sclerosis, spinocerebellar degenerations, vascular disease, tumours)

4. *Myoclonus*
   - Idiopathic benign essential (familial) myoclonus
   - Idiopathic epilepsy
   - Progressive myoclonic epilepsy (familial, Lafora body disease, lipidoses, spinocerebellar degenerations)
   - Metabolic disturbances (with or without seizures) (renal failure, hepatic failure, respiratory failure)
   - Drug withdrawal (alcohol, barbiturates)
   - Structural brain disease (without seizures) (post-anoxic, subacute sclerosing panencephalitis, Creutzfeldt-Jakob disease, encephalitis lethargica)

5. *Tics*
   - Simple benign tics of childhood
   - Simple persisting tics
   - Complex tics
   - Complex tics with vocalisation
   - Complex with coprolalia

} Gilles de la Tourette's syndrome

C. Drug-induced syndromes

Parkinsonism
- Reserpine and tetrabenazine; phenothiazines and other neuroleptics

Tremor
- As for Parkinsonism, and β-adrenergic receptor agonists, tricyclic anti-depressants, lithium

Akathisia
- Reserpine and tetrabenazine; neuroleptics

Acute dystonia
- Neuroleptics, metoclopramide, diazoxide

Tardive dyskinesia
- Neuroleptics

Table 2 Features of Parkinson's disease and appropriate modes of assessment

	Subjective assessment	*Simple objective assessment*[1]	*Complex objective assessment*[2]
Major motor signs and symptoms			
Tremor	+		+
Rigidity	+		+
Akinesia	+	+	+
Postural abnormalities	+		+
Other motor signs and symptoms			
Dysarthria	+	+	
Dysphagia	+		
Autonomic signs and symptoms			
Hypersalivation	+		+
Seborrhoea	+		
Postural hypotension		+	
Constipation	+		
Urinary frequency/ incontinence	+	+	

[1] Simple objective assessment requiring no specialised apparatus beyond stopwatch, tape-measure, pegboard, sphygmomanometer, tape-recorder, etc.
[2] Complex methods requiring specialised mechanical, electrical or electronic devices and sometimes requiring computing facilities for analysis.

Karnofsky's scale (Karnofsky, Burchenal, Armistead, Southam, Bernstein, Craver & Rhoads, 1951), originally used in evaluating the response to cancer chemotherapy, rated normality as 100% with proportional decrements for increasing disability. Riklan & Diller (1956) described a 98-item scale listing various activities of daily living, but this did not prove reliable, or feasible. By contrast the North-Western University Disability Scale (Canter, de la Torre & Mier, 1961) has been used very widely; it consists of 5 or 10 point rating scales for walking, dressing, hygiene, feeding and speech, based on clearly defined criteria (Appendix 3). A popular and very simple method of staging Parkinson's disease was described by Hoehn & Yahr (1967) (Appendix 1). The scale provides a generally accepted basis for assessing the severity of Parkinsonism, and Lieberman, Dziatolowki, Gopinathan, Kopersmith, Neophytides & Korein (1980) have noted a good correlation between Hoehn & Yahr's (1967) staging and more detailed scoring systems. However, such staging is relatively insensitive to changes in the patient's clinical state. McDowell, Lee, Swift, Sweet, Ogsbury & Tessler (1970) described a combined rating scale for symptoms and signs and for functional disability which was unusual in assigning weighting factors for each item in the scale; for instance, akinesia was given a weighting of 9, seborrhoea 2, walking difficulties 10, and difficulty in bathing 5. Treciokas, Ansel & Markham (1971) also employed weighting, but the concept has not been adopted widely.

Some investigators developed combined subjective rating scales with simple objective tests of motor function (for example, Godwin-Austen, Tomlinson, Frears & Kok, 1969; Parkes, Zilkha, Marsden, Baxter

Table 3 Rating scales in Parkinson's disease

	Subjective rating		*Objective assessment*	
	Symptoms and signs	*Functional disability*	*Simple*	*Complex*
Webster (1968)	+			
Alba *et al.* (1968)[1]	+			
Duvoisin (1969)[2]	+			
Klawans & Garvin (1969)	+			
Parkes *et al.* (1970a,b)[3]	+	+		
Cotzias *et al.* (1970)	+			
Rinne *et al.* (1970)	+	+		
McDowell *et al.* (1970)	+	+		
Anden *et al.* (1970)	+	+	+	+
Treciokas *et al.* (1971)	+	+		
Birkmayer & Neumayer (1972)	+	+		
Lhermitte *et al.* (1978)	+	+		
Lieberman *et al.* (1980)	+	+	+	

[1] New York University Rating Scale, but may be superseded by Lieberman *et al.* (1980) rating system from the same institution.
[2] Columbia University Rating Scale.
[3] King's College Hospital Rating Scale.

& Knill-Jones, 1970b). The most frequently used tests involved peg-boards, the measurement of walking speed and of the time taken to put on mittens or socks. In a series of papers Schwab and his colleagues (Schwab & Prichard, 1951; England & Schwab, 1956; Schwab, 1960) described a similar approach, and also used a rating scale for functional disability but not for symptoms and signs.

Others have been even more ambitious. Anden, Carlsson, Kerstell, Magnusson, Olsson, Roos, Steen, Steg, Svanborg, Thieme & Werdinius (1970) used a wide-ranging scheme of assessment, intended to evaluate the effects of treatment on severely disabled in-patients. While noting changes in tremor, rigidity and functional disability as well as the time taken to perform specific tasks, these workers recorded standardised movement patterns on cine film, and a tracking device was used to quantify akinesia. Probably the most elaborated combination of objective tests, both simple and complex, was that described by Potvin & Tourtelotte (1975). This was designed for general neurological assessment, rather than specifically for evaluating Parkinsonism. The full examination was said to take 2.5 h for a moderately disabled patient, and it has not been considered suitable for routine use.

Most of the methods described so far were applied successfully to demonstrate the therapeutic action of levodopa and other anti-Parkinsonian drugs in the late 1960s and early 1970s. At that time it was sufficient to assess a patient at any time of day, at infrequent intervals during therapy. Benefit was more or less sustained, so the timing of assessment was not particularly critical. Long-term treatment with levodopa, however, has led to a problem that was not foreseen when these techniques were devised. An increasing number of patients on levodopa have developed 'on-off' phenomena of 'swinging', terms which refer to fluctuations in response (Marsden & Parkes, 1976). Periods of normal mobility often with dyskinesia ('on'), alternate with periods of severe akinesia ('off'). The timing of each of these phases may be related to when the drugs are administered, but is often random and unpredictable; in the most extreme cases these fluctuations can occur within minutes or even seconds. This phenomenon must be distinguished from the well-known variation in Parkinsonian symptoms with emotion, and from the sudden 'freezing episodes' (akinesia paradoxica) which Parkinson described in his original account. To assess new drugs it is now essential to quantify 'on-off' effects. Several methods have been devised in an attempt to do this.

Frequent ratings by a doctor can be used, but these necessarily give only a general impression of the patient's clinical state, and are exceptionally time-consuming. The alternative is to ask the patient, with the help of his family if necessary, to score their own mobility and side-effects. This is done either at fixed intervals throughout the day, or when the patient detects some change in his own condition. Several similar self-rating scales have now been described (Kartzinel & Calne, 1976; Lees, Shaw, Kohout, Stern, Elsworth, Sandler & Youdim, 1977; Lieberman *et al.*, 1980; Schachter, Marsden, Parkes, Jenner & Testa 1980). Kartzinel & Calne (1976) calculated mean daily Parkinsonism and dyskinesia scores, while Lees *et al.* (1977) and Schachter *et al.* (1980) used mean hourly mobility and dyskinesia scores. Lieberman *et al.* (1980) and Schachter *et al.* (1980) both emphasised the importance of the total time each day occupied by 'off' periods, that is, the time spent immobile during the average day.

Objective and neurophysiological methods

Techniques have been developed for the assessment of each of the major clinical features of Parkinsonism.

(a) *Tremor* The earliest devices for the recording and measurement of tremor were designed in the 1880s by Charcot and several German neurologists (reviewed by Boshes, Wachs, Brumlik, Mier & Petrovick, 1960). The apparatus, known as a tambour, transmitted tremor in one plane to a recording device through a number of pneumatic and mechanical components. Optical recording systems were developed some forty years later (Beall, 1925). These techniques have been largely superseded in recent years by methods based on EMG recordings and accelerometry, frequently combined with computer analysis such as Fourier frequency analysis. For example, Schwab & Prichard (1951) and Burns & de Jong (1960) used EMG recordings, while Calne & Lader (1969) analysed similar recordings with a computer, as more recently did Teravainen & Calne (1979). The latter, however, commented that this approach was better suited to the analysis of neurophysiological problems than to the evaluation of drug therapy.

Accelerometry was introduced by Agate, Doshay & Curtis (1956), and has been employed frequently since then (Wachs & Boshes, 1961; Owen & Marsden, 1965; Velasco & Velasco, 1973; Potvin & Tourtelotte, 1975; Oppel & Umbach, 1977). Accelerometry is relatively simple, it is reliable, and causes little inconvenience to the patient. However, the method as originally described has two major limitations. Firstly, tremor is only measured in a single plane, and the 'total' tremor therefore can be considerably underestimated. Clarke, Hay & Vas (1966) and Salzer (1972) described methods for recording tremor in three dimensions, but their techniques have not been used widely. More recently, several investigators have devised apparatus for computerised triaxial accelerometry (Dietrichson, Langbretson & Houland, 1978; Teravainen & Calne, 1979; Stuart, Gopinathan,

Teravainen, Dambrosia, Ward, Sanes, Evarts & Calne, 1980; Jankovic & Frost, 1980). Secondly, there is considerably variability of all types of tremor, and particularly that of Parkinson's disease which is notoriously susceptible to stress and to other emotional influences. Prolonged recording therefore is desirable, but difficult to achieve with most of the systems mentioned. Owen & Marsden (1965) and also Cowall, Marsden & Owen (1965) used single-plane accelerometry combined with telemetry to obtain several hours of recording from each patient so as to assess the effect of β-adrenoceptor blockers on tremor. Although triaxial accelerometry and telemetry have not yet been combined, advances in electronics now make such studies feasible.

(b) *Rigidity* The earliest methods measured the force required to flex a voluntarily relaxed limb through a fixed distance (Boshes *et al.*, 1960). Measurements usually were made in the horizontal rather than the vertical plane (la Joie & Gersten, 1956). A constant velocity of limb movement was employed subsequently to eliminate inertial factors. Thus, Agate *et al.* (1956) measured the torque by which the patient passively resisted a constant-velocity extension of the elbow joint. Boshes *et al.* (1960) and Brumlik & Boshes (1960) used an electric motor to move the forearm alternately through a fixed distance of flexion and extension. Webster refined this technique by designing a servo-controlled electronic device to perform this manoeuvre at a constant angular velocity (Webster, 1959, 1964, 1966). His studies also established that the area of the hysteresis loop of torque versus displacement of the forearm, averaged over several cycles of flexion and extension, was a more accurate measure of rigidity than the torque required to extend the arm. Webster & Mortimer (1977) used this method, with computer analysis, to evaluate the effect of levodopa on rigidity. A somewhat similar approach, with passive movement of the finger rather than the forearm, was described in the early 1960s (Wright & Johns, 1960; Long, Thomas & Crochetiere, 1964), but apparently has not been developed further.

There has been considerable interest in the relationship between Parkinsonian rigidity and stretch-reflex responses, especially those of long latency (Marsden *et al.*, 1978). Lee & Tatton (1975) and Tatton & Lee (1975) reported that the long latency responses to sudden stretch of the wrist flexors and extensors of Parkinsonian patients were increased in amplitude. Mortimer & Webster (1979) have reported similar findings in the biceps and triceps brachii. They also demonstrated a linear relationship between the magnitude of the biceps long-latency response and the degree of activated rigidity (that is, rigidity measured while the limb was performing a voluntary movement). Lee & Tatton (1978) showed that the amplitude of the reflex diminished when rigidity was alleviated by levodopa. However, Teravainen & Calne (1980) found considerable overlap between responses in normal and Parkinsonian subjects on testing the biceps reflex, and Marsden, Merton, Morton & Adam (1978) were unable to find any change in the long latency responses evoked by fast stretching of the long thumb flexor of Parkinsonian patients. It is clear that long-latency responses to stretch, while of great neurophysiological interest, are not a substitute for more direct measurements of rigidity.

(c) *Akinesia and hypokinesia* Tremor and rigidity are relatively easy to assess and quantify, since each is essentially a single variable. This is not true of akinesia and hypokinesia, which are difficult even to define precisely. Several components of akinesia can be measured separately: (i) reaction time (the interval between a stimulus and a motor response), (ii) movement time (the time taken to complete a movement), (iii) the rate of repetition of alternating movements, and (iv) the speed and precision of complex movements using one or both hands. Some of the tests are easy to devise and standardise, while others pose greater difficulties.

Although most studies agree that reaction time is prolonged by 25–30% in Parkinsonian patients, there is an overlap with that of normal subjects. Both visual (Barbeau, 1966; Potvin & Tourtelotte, 1975; Heilman, Bowers, Watson & Greer, 1976) and auditory stimuli (Velasco & Velasco, 1973) have been employed as cues for releasing a switch. More commonly a tracking task is used. Moving targets on an oscilloscope screen are followed by using the arm or hand to manipulate a lever or joy-stick (Anden *et al.*, 1970; Angel, Alston & Higgins, 1970; Cassell, Shaw & Stern, 1973; Flowers, 1975, 1976; Potvin & Tourtelotte, 1975). A few studies have compared reaction times in Parkinsonian patients before and after treatment (Draper & Johns, 1960; Angel *et al.*, 1971; Velasco & Velasco, 1973). There was a tendency for reaction times to diminish with levodopa therapy in the last two papers cited, but the differences were not statistically significant.

Movement times have been studied by many investigators using the same apparatus as employed to measure reaction times (Barbeau, 1966; Flowers, 1975, 1976). Flowers (1976) noted that movement time in Parkinson's disease is almost always longer than reaction time in individual subjects, that movement velocity is reduced for all amplitudes of movement, and that tracking error increases disproportionately as the velocity of the target is increased. As might be expected, movement time is more abnormal when the amplitude of movement is large. Velasco & Velasco (1973) reported marked improvement in movement time in some, but not all, patients after levodopa therapy. Teravainen & Calne (1980) con-

firmed these findings, using a test-system which involved greater use of proximal shoulder-girdle muscles (the hand had to be moved between two targets 32 cm apart), and noted little change in reaction time. They found good correlation between movement time and clinical estimates of akinesia, and conclude that proximal movement time was the best index of this feature of Parkinsonism.

Several subjective rating scales include a score of the ease and speed of rapid alternate movements, especially pronation-supination (Webster, 1968; Parkes, Zilkha, Calver & Knill-Jones, 1970a). Pronation-supination has also been timed (Draper & Johns, 1964; Parkes *et al.*, 1970b; Knutson & Mortenson, 1971; Evarts, Teravainen, Beuchart & Calne, 1979; Teravainen & Calne, 1980). Parkinsonian patients generally were slower than normal controls, and the speed of movement increased with treatment. This improvement did not always correlate well with the observer's subjective assessment. Nor is there necessarily a close correlation between the time taken for single movements and that taken for alternating movements (Flowers, 1976; Teravainen & Calne, 1980).

Tests involving rapid tapping also have been used as estimates of alternating movement speed (Velasco & Velasco, 1973; Cassell *et al.*, 1973; Potvin & Tourtelotte, 1975), but are considered less satisfactory indicators of clinical state than those involving pronation-supination. More complex tapping tasks have been employed to assess the precision of movements rather than their speed (Perret, 1968; Perret, Eggensberger & Siegfried, 1970; Cassel *et al.*, 1973). Peg-board tests have been devised for the same purpose (Godwin-Austen *et al.*, 1969; Parkes *et al.*, 1970b; Cassell *et al.*, 1973; Velasco & Velasco, 1973). The use of timed tasks such as putting on socks and drawing circles, has been described in the previous section. The time taken to walk a set distance, and the number of steps taken, also appear to be accurate indices of hypokinesia; Stuart *et al.* (1980) have automated this test by using a mat with sensors on which the patient walks.

It is reasonable to ask to what extent these ingenious procedures provide a helpful estimate of functional disability, superior to that obtained by simpler methods. In general, they offer few advantages from this point of view, and most are likely to remain within the scope of investigative neurophysiology rather than clinical pharmacology. Nevertheless, a battery of simple largely automated tests, such as that describe by Jankovic & Frost (1980) may become more widely used, though even this was employed in conjunction with subjective scoring methods.

Conclusion

In designing a protocol for the evaluation of an anti-Parkinsonian drug, we recommend the following methods of assessment:

(a) The Hoehn & Yahr (1967) staging system (Appendix 1)

(b) The Webster rating scale for symptoms and signs (Appendix 2)

(c) The North-Western University Disability Scale (Appendix 3)

It may also be necessary to use one of the 'on-off' self-rating schemes (for example, that of Lees *et al.*, 1977) and a dyskinesia rating scale (to be discussed below). A small number of simple objective tests also may be added; for example, the time taken to walk a measured distance; the time to sit down and stand up a number of times, and a pegboard-test. As a simpler alternative to the latter, the patient may be asked to pile plastic counters on top of one another in a measured period. Taken together, the above procedures give a very comprehensive estimate of the severity and impact of Parkinsonism.

Dyskinesias

Introduction

Less attention has been given to the development of techniques for assessing the various dyskinesis encountered as a result of extrapyramidal disease. This reflects the great difficulty in characterising the many bizarre abnormal movements encountered in these conditions, and lack of knowledge as to their basic pathophysiology. In general, two approaches have been adopted. On the one hand, some workers have utilised subjective assessment of the intensity and distribution of the dyskinesias. Others, in contrast, have concentrated on more objective methods of recording abnormal movements.

Subjective techniques

The severity of a dyskinesia may be expressed in very simple terms, for example as mild, moderate or severe, or may be defined by more extensive and complex rating scales. The latter can take into account not only the severity of the abnormal movement at a given site, but can also document the movements at various sites throughout the body. Both approaches have been used to rate a number of dyskinesias, but there is no general agreement as to whether complex rating scales are more efficient or sensitive than simpler techniques. However, our own experience would suggest that rating dyskinesias at different body sites (face, neck, trunk, each arm and each leg) on a simple 0–3 scale (nil, mild, moderate and severe) is the most satisfactory way of approaching the problem. Such subjective rating takes little time and is relatively easily accomplished.

Such a simple subjective rating scale, however, does not take into account one of the major difficulties in assessing dyskinesias, namely the fact that they may occur intermittently. This problem may be approached by rating dyskinesias at each body site not only for their severity, but also for the frequency (occasional, frequent or continuous). Multiplication of the severity factor by the frequency factor gives a score for overall dyskinesias at each body site, which may be summed for all the sites examined to give a global subjective rating score for the severity of a given abnormal movement.

Another question to be considered is whether to rate abnormal movements with the patient in front of one, or whether to take a filmed or videotaped record of the patient for subsequent analysis. Both techniques have advantages and disadvantages. To have the patient in view makes it easier to decide on the significance of the given abnormal movement, and enables the observer to prolong the interview or instruct the patient to undertake certain acts which may resolve ambiguity as to whether a movement is abnormal or not. Unfortunately, it is often difficult to avoid picking up clues as to what treatment a patient may be taking in the course of such a live subjective assessment. Even the timing of the assessment in the course of a known clinical trial may give some clue as to the nature of the treatment being administered at that instant.

Filming or videotaping avoids many of these problems but introduces others (see Table 4). It is much easier to ensure that the raters are quite 'blind' as to treatment at the time when they undertake their assessment, and of course it is possible for a number of raters to examine a given patient's filmed or videotaped record on a number of occasions. The difficulty, however, is in deciding from film or videotape alone whether a given movement really is abnormal or not! Unless a sound-track is available, impromptu speech closely resembles oro-facial dyskinesias, and expressive gesticulation may be misinterpreted as abnormal movements of the limbs. Even with a sound-track it is often difficult to be certain as to the nature of what one witnesses.

Unfortunately, as yet there have been few useful studies comparing the various techniques of rating dyskinesias for inter-rater reliability, reproducibility, and sensitivity to change. Until such information is available, it is impossible to decide on whether to rely on live interview or videotaped recording.

Functional assessment

As in the case of Parkinson's disease, subjective, or even objective assessment of the incidence, frequency and severity of abnormal movements may give little information on their functional impact. This is what disturbs the patient, in terms of therapeutic gain, and changes in functional disability produced by treatment are much more significant than changes in the intensity of abnormal movements. For this reason, most investigators are now supplementing assessments of the dyskinesias with functional assessments of disability. By analogy with Parkinson's disease, rating scales of function have been developed for Huntington's disease and dystonia. Furthermore, again akin to Parkinson's disease, simple systems of staging the severity of illness have been developed for these two conditions.

A more accurate picture of the severity of diseases causing dyskinesias is obtained by rating the abnormal movements themselves, the functional disability they produce, and the stage of severity of the disease.

Objective assessment

Many dyskinesias interfere with manual dexterity and gait, so simple objective timed tests of motor acts

Table 4 Audiovisual recordings in the assessment of dyskinesias

Advantages	*Disadvantages*
Permanent record	Cost of apparatus
Opportunity for repeated assessment by several observers	Time needed to set up apparatus and record
Observers can be truly ignorant of treatment and side-effects	Difficulty in distinguishing normal from abnormal movements or speech
Sequences can be randomised to ensure blind rating	Impossible to prolong observation period in case of doubt
Sequences can be used to train raters and validate rating scales	Impossible to ask patient to undertake tasks which may resolve ambiguities or provoke dyskinesias
	Visual recording in two dimensions only

such as finger tapping, performance on a peg board, and walking have been employed.

More complex methods of objectively recording dyskinesias have not been developed to any great extent. The tambours used to record tremor (described above) also were employed to record abnormal movements of other kinds, and subsequently accelerometers have been employed for the same purpose. Unfortunately, the unpredictability of most dyskinesias and their considerable variability from moment to moment have not encouraged extensive use of techniques such as these for pharmacological research. Nor have other methods such as the use of flash lights attached to the body combined with time lapse photography, or electromyographic recording of individual muscle contractions responsible for abnormal movements, gained widespread favour. Technical advances in the future may improve the reliability and sensitivity of objective methods of recording abnormal involuntary movements, but at present clinical pharmacologists rely mainly upon subjective assessment perhaps coupled with very simple timing tests.

Huntington's disease

Introduction

The concept of neurotransmitter imbalance, which has proved so rewarding in the treatment of Parkinsonism, has greatly encouraged therapeutic research in Huntington's disease (Urquhart, Perry & Hansen, 1975; Enna, Stern, Wastek & Yamamura, 1977). Only the motor aspects of the disease will be considered here; the neuropsychiatric manifestations have been reviewed recently elsewhere (see Chase, Wexler & Barbeau, 1979).

Assessment

The simplest assessments have been by rating scales. A relatively crude global rating of the characteristic movements as worse, unchanged, moderately improved and/or markedly improved in response to treatment has been used by some workers (Swash, Roberts, Zakko & Heathfield, 1972; Perry, Wright, Hansen & Macleod, 1979), supplemented by film and videotape recordings in other studies (Barr, Heinze, Mendoza & Perlik, 1978). Most investigators, however, have preferred more elaborate assessment schemes. Shoulson, Goldblatt, Charlton & Joynt (1978) recorded chorea on a 5-point scale and also scored activities of daily living—eating, dressing, bathing, sleeping and speech to establish the degree of disability. Of course, the latter is influenced by both neuropsychiatric and purely motor problems. Shoulson *et al.* (1978) also counted the number of finger taps performed in a set time, and the time taken to walk a fixed distance. McLellan, Chalmers & Johnson (1974) supplemented global and regional rating scales with tests of manual dexterity (such as handwriting, a peg-board test, and the time taken to pile up a given number of counters).

In the study of Barr *et al.* (1978), elements of all these approaches were combined. The patients' movements were filmed and rated 'double-blind'. Handwriting, a peg-board test, finger tapping and bead-stringing were used to assess aspects of manual dexterity. The degree of disability in walking and bathing were also noted. Shoulson & Fahn (1979) have proposed a scheme for staging the severity of Huntington's disease based upon functional disability (Appendix 4). By allocating scores to the individual items of functional capacity in everyday affairs, the same authors have provided a functional disability scale for Huntington's disease (Appendix 5).

Fahn & Lhermitte (unpublished observations) also have devised a scoring scale for the severity of chorea in Huntington's disease, a scale which we have modified in the light of our own experience (Appendix 6). While this scale will give a reasonable estimate of the severity of chorea, other psychological tests are required to estimate the severity of associated personality change and cognitive impairment in Huntington's disease.

Klawans, Rubovits, Ringel & Weiner (1972) employed a very different approach to assessment, which Klawans & Rubovits (1974) have also used in tardive dyskinesia research (see below). The duration of sustained tongue protrusion and eye closure were recorded. The patient was asked to draw an Archimedes screw, and time-lapse photographs were taken in a darkened room, with flashlights attached to the patient's hands. However, it is difficult to present such photographic records in quantitive terms.

Instrumental methods have played little part in the assessment of Huntington's chorea. Petajan, Jarcho & Thurman (1979) have recently suggested that the degree of control of single motor unit activity, using an audiovisual feedback technique, may be a predictive test in Huntington's disease. However, this claim has not been substantiated by adequate follow-up, and the advisability of predictive tests in this disease, at the present time, is questionable. Witzman *et al.* (1976) quantified abnormal movements in Huntington's disease by power spectrum analysis of the EMG. There appear to be no tracking studies in this disease, analogous to those in Parkinsonism, and very little use of accelerometry (Falek, 1969).

Conclusion

Shoulson & Fahn's (1979) staging system (Appendix 4) and the disability scale derived from it (Appendix 5) are sensitive indicators of functional impairment,

while Marsden and Quinn's chorea rating (Appendix 6) is a reasonable estimate of the severity. A simple timed test, such as the duration of tongue protrusion, may be added to the evaluation. Separate tests for personality and cognitive change also are required to assess the full severity of the illness.

Torsion dystonia

Introduction

Torsion dystonia presents in many ways. In children the disease frequently is hereditary, especially among Ashkenazim Jews. When the illness begins in early life it commonly spreads to involve most parts of the body to produce the disabling generalised torsion dystonia known as dystonia musculorum deformans. In adults, the illness usually is sporadic and remains localised to one particular body part. Such focal dystonias include spasmodic torticollis, writer's cramp, and cranial dystonia in the form of blepharospasm and oro-mandibular dystonia.

All types of this illness are difficult to treat. The problem is that drugs have a very variable effect, and no particular therapeutic agent can be relied upon to be of benefit in an individual patient (Marsden & Harrison, 1974). It is necessary to try a range of drugs in sequence to discover which, if any, may help. Frequently, such drug trials are confused by the great tendency for the severity of this disease to wax and wane spontaneously. The intensity of dystonic muscle spasms is very variable, and is influenced considerably by the emotional state of the patient. This introduces considerable difficulty in assessment of any new form of treatment. In fact, there has been little formal clinical pharmacological study of this group of illnesses, and as a result there have been few attempts to develop standardised, reliable means of assessment.

Assessment

Marsden & Fahn (unpublished observations) have developed a staging system, and a rating scale for assessing the severity of generalised dystonia and its functional impact (see Appendix 7, 8 and 9). Like other rating scales for assessing extrapyramidal disease, this is based on scoring the severity of movement at different sites of the body, severity being judged on the basis of the product of the intensity of the movement and the circumstances in which it occurs. In addition, functional capacity is rated subjectively. We have found this scoring system reasonably reliable and sensitive in the assessment of drugs in generalised dystonia, although modification with future experience may become necessary.

With regard to the various focal dystonias, even less information is available on their assessment. Couch (1976) has described a simple arbitrary rating scale for the frequency and severity of spasmodic torticollis, grading frequency as absent (0), occasional (1), intermittent, occurring less than 50% of the time (2), intermittent, occurring 50–80% of the time (3) and continuous (4). Severity was graded as absent (0), mild (1), moderate (2), severe (3), and very severe and incapacitating (4). Such rating was undertaken during a 10–15 minute interview, and subsequently was supplemented by similar rating of filmed records. Korein, Brodny, Grynbaum, Sachs-Frankel, Weisinger & Levidow (1976) have been one of the few groups to explore objective electromyographic techniques for the measurement (and treatment) of spasmodic torticollis. However, they too relied upon rating of videotape recordings for evaluating the response to therapy.

Recently Marsden, Sheehy & Lang (unpublished observations) have introduced subjective assessment scales for rating two other focal dystonias, namely cranial dystonia (Brueghel's syndrome or Meige's disease) (Appendix 10) and dystonic writer's cramp (Appendix 11).

There have been few other studies of the objective measurement of torsion dystonia, and further work is necessary to explore such methods.

Myoclonus

Myoclonus is a feature of many neurological conditions. It is characterised by generalised or localised, involuntary, very brief muscular contractions. Relatively successful treatment is now available for some forms of myoclonus and has stimulated further therapeutic interest. Electrophysiological techniques have been employed more frequently than in most other extrapyramidal disorders, but rating scales have usually been used in parallel. Chadwick, Harris, Jenner, Reynolds & Marsden (1975) rated co-ordination, speech, gait and handwriting on four-point scales. Van Woert, Rosenbaum, Howieson & Bowers (1977) scored myoclonic jerks on a five-point scale, according to their severity and frequency, and rated speech, handwriting, walking and dressing on similar scales. The patient's movements and speech were recorded on film and tape. Growdon, Young & Shahari (1976) rated the severity of the myoclonus observed when the patient performed certain set movements, such as standing with the arms outstretched, and also used films, surface EMG and accelerometric recordings.

The most comprehensive assessment protocol in myoclonus was described by Chadwick, Hallett, Harris, Jenner, Reynolds & Marsden (1977) (Appendix 12). The ability to sustain a posture (for example, standing with arms outstretched, or on one leg) was assessed. A series of tests of dynamic motor function also were performed (for example, finger-

nose movements, rapid tapping and rising from a recumbent position). All these were rated on a four-point scale. Finally, several electrophysiological recording techniques were employed, including simultaneous EEG and polygraphic EMG studies, as well as somatosensory evoked potentials.

Tics

Gilles de la Tourette's syndrome has attracted much attention from both neurologists and psychiatrists. It is the most complex of the tic syndromes and includes both bodily and vocal tics, the latter often obscene in character (coprolalia) (Fernando, 1967). It is generally believed to have an organic basis (Shapiro, Shapiro & Wayne, 1973a). Assessment has been based on counting the number of bodily tics and vocalisations in a given period (Shapiro, Shapiro & Wayne, 1973b; Feinberg & Carroll, 1979). Sweet, Bruun, Shapiro & Shapiro (1974) converted these counts into scores. Motor tics in each region of the body were counted over a five minute period, with particular emphasis on facial movements. Vocalisations also were counted, with words (obscene or otherwise) and sounds such as grunts and barks being recorded separately. Based on the observed frequency, results were expressed on a scale from 0 to 4.

Tardive dyskinesia

Introduction

Over twenty years ago a syndrome of abnormal involuntary movements associated with prolonged phenothiazine therapy was described (Hall, Jackson & Swain 1956; Sigwald *et al.*, 1959). This is now known as tardive dyskinesia and is recognised as a major hazard of chronic antipsychotic therapy. Estimates of its prevalence in patients at risk range from 4 to 46% (Fann, Davis & Janowsky, 1972; Jus, Pineau & Lachange, 1976; Kane, Wegner, Stenzlek & Ramsey, 1980), although many of the higher figures undoubtedly include patients with minimal or doubtful symptoms. In some cases the syndrome appears irreversible (Crane, 1971). Clinically the condition is characterised by involuntary movements of the limbs, especially the hands. However, any part of the body may be affected (Marsden, Tarsy & Baldessarini, 1975) and in young patients a dystonic picture often occurs. The list of drugs used to treat this syndrome is very long, illustrating that there is considerable individual variation in response to any particular drug (Mackay & Sheppard, 1979). Approaches to assessment have been reviewed by Gardos, Cole & La Brie (1977).

Subjective assessment

Many rating scales have been devised for tardive dyskinesia research. Crude overall assessments indicating an impression of 'better', 'worse' and 'unchanged' have been used (Laterre & Fontetemps, 1975), but more complex rating scales are now more popular, either global (Pryce & Edwards, 1966; Crane & Smeets, 1974), or specific by rating movements of different types at different sites. Villeneuve & Boszormenyi (1970), for example, differentiated between choreiform, buccolingual and buccofaciomandibular dyskinesias and rated the severity of each type, while Gerlach, Reisby & Randrup (1974) divided the body into five areas and ascribed a combined severity/frequency rating to the movements in each area.

Such an anatomical approach to the analysis of dyskinesias has been widely accepted. As early as 1969 Crane, Ruiz & Kernohan devised an 11-item scale in which each symptom was scored on a five-point rating. This method was shown to have high inter-observer reliability and was used by other investigators (for example, Decker, Davis & Janowsky, 1971). An expanded version of this scale was developed by Smith, Tamminga & Haraszti (1977) to include 27 items, combined with a global assessment. More elaborate schemes, also based on anatomical regions, have been developed by others including up to 47 items (Hippius & Logemann, 1970; Simpson, Zoubok & Lee, 1976; Simpson, Lee, Zoubok & Gardos, 1979). Reda, Escobar & Scanlan (1975) used a simpler, 14-item scale, rated according to severity or frequency, as appropriate. Barnes & Kidger (1979) have described a similar system.

The Abnormal Involuntary Movements Scale (1976) (AIMS) devised at the U.S. National Institute of Mental Health, seems likely to gain wide acceptance. It is fairly simple to apply, the terms used are clearly defined, and there is a standardised examination procedure. The scale includes global assessments of severity (both by the patient and the observer) and dyskinesia scores for the face, lips, jaw, tongue and limbs, as well as a functional disability score (see also Kennedy, Hershon & McGuire, 1971).

Audiovisual recordings, especially videotape, have proved very popular in studies of tardive dyskinesia therapy (Reda *et al.*, 1975; Gerlach & Thorsen, 1976; Fann, Stafford, Malone, Frost & Richman, 1977). Since the recordings are themselves rated, this technique is really an extension of those described above (the advantages and disadvantages of recording systems were discussed above).

A different development of the concept of rating has been the use of frequency counts and related techniques. Kazamatsuri, Chien & Colt (1972) counted all orofacial dyskinetic movements for three separate one-minute periods at a fixed time and place

during several drug trials. The patients were unaware that they were being observed. Other investigators have counted lip, tongue and jaw movements separately (Fann & Lake, 1974; Davis, Berger & Hollister, 1975). These methods are simple and objective, but results are subject to rapid fluctuations in the patient's condition and not all patients with tardive dyskinesia have movements that are counted easily. The tongue protrusion test, where the patient protrudes his tongue as long as he can and the duration is noted, avoids the latter disadvantage and may be more widely applicable (Klawans & Rubovits, 1974; Gerlach & Thorsen, 1976).

Objective assessment

Objective assessment methods have not been used extensively in tardive dyskinesia research. EMG recordings have been obtained from facial and buccal muscle groups (Jus, Jus & Villeneuve, 1973), from the limbs (Crayton, Smith & Klass, 1977), or from several anatomical sites (Lonowski, Sterling & King, 1979). Accelerometry of the upper limbs also has been employed in drug evaluation (Alpert *et al.*, 1976; Gardos *et al.*, 1977; Fann *et al.*, 1977).

Since buccofacial dyskinesias are so prominent a feature of tardive dyskinesia, Denny & Casey (1975) designed a pneumatic transducer which was placed in the patient's mouth to record many movements that were not clinically detectable. A similar device was placed between the third and fourth fingers of each hand. Using this system the effects of several drugs were documented. Chien, Chung & Ross-Townsend (1977) found that clinical ratings correlated well with results obtained by this technique.

Finally, Klawans & Rubovits (1974) used a recording method also employed in patients with Huntington's chorea, and first described by Holmes in 1938. The patient was seated in a darkened room and a flashlight was attached to each hand. Time-lapse photographs were then taken at intervals. As noted in the section on chorea, the results obtained cannot easily be quantified.

Summary

Rating scales of tardive dyskinesia, such as the AIMS (Appendix 13) are accurately defined, relatively simple, sensitive and reliable. The tongue protrusion test may be used to supplement any rating scale. Videotape and other audiovisual recording methods are certainly not essential. At present, objective instrumental techniques have no clear advantages in assessing drug responses in tardive dyskinesia.

Other drug-induced syndromes

Two conditions will be considered under this heading, namely dopamine agonist-induced dyskinesia and neuroleptic-induced Parkinsonism.

The occurrence of levodopa-induced involuntary movements was described very soon after the introduction of the drug (Cotzias, van Woert & Schiffer, 1967). Bromocriptine produces similar dyskinesias (Parkes, 1979). Any part of the body may be affected by dystonic or choreiform movements, although orofacial dyskinesia is probably the most common finding (Klawans & Garvin, 1969). Assessment of dyskinesia is now part of the evaluation of all anti-Parkinsonian drugs and there have been increasing efforts to find agents that alleviate dyskinesia without impairing anti-Parkinsonian efficacy of levodopa therapy (Tarsy, Parkes & Marsden, 1975; Miller, 1976; Price, Parkes & Marsden, 1978; Bedard, Parkes & Marsden, 1978; Lees, Lander & Stern, 1979; Lieberman *et al.*, 1980). In all cases subjective four or five-point rating scales were used, with severity of movements scored for each region of the body. The AIMS (see section on tardive dyskinesia) also appears to be suitable for the assessment of dopamine agonist induced dyskinesias, and is being used in some current trials.

Neuroleptic-induced Parkinsonism is common; the lowest estimate is 23% (Ayd, 1961), but Kennedy *et al.* (1971) found that 88% of chronic schizophrenics after at least three months of treatment with a phenothiazine had tremor, and 68% had rigidity. Many studies of drug-induced Parkinsonism have employed techniques somewhat different from those in idiopathic Parkinson's disease. Simpson & Angus (1970) developed subjective rating scales for tremor, rigidity and hypersalivation, noted the glabellar tap, and observed changes in the size and form of handwriting. Mindham (1976) described a rating scale in which facial expression, rigidity of the neck and limbs, tremor of the face and limbs, associated movements on walking and a global rating were all scored on a four-point scale. Mindham, Lamb & Bradley (1977) used this scale, together with simple timing tests, and commented that the subjective assessment of clinical signs appeared to show differences between treatments more clearly than the timing tests. It is arguable whether specific rating systems are necessary for drug-induced, as opposed to idiopathic Parkinsonism. Though the pattern of symptoms is somewhat different in the drug-induced disease, the Webster scale (see section on Parkinson's disease) can still be applied. Alternatively, Mindham's (1976) simpler system appears to be suitable.

Design of clinical trials in extrapyramidal disorders

The particular problems involved in the design of therapeutic trials in extrapyramidal disease are worthy of discussion. Most extrapyramidal disorders are chronic and many are progressive. In addition, there may be considerable variation in the severity of symptoms over hours or even minutes. This is evident

most spectacularly in the 'on-off' phenomena occurring in levodopa-treated Parkinson's disease. These problems can be overcome by careful design of the assessment protocol, but otherwise can lead to misleading conclusions.

An important consideration arises from the variable rate of progression of many extrapyramidal diseases. In any population of patients with, say, Parkinson's disease, there will be a very wide range of severity of symptoms and of disability. This makes parallel drug trials at best difficult, and for the rarer conditions quite impracticable; adequate stratification and randomisation will be impossible without unreasonably large populations. This implies that trials of cross-over design almost always will be needed. The disadvantages of such trials, recently examined in detail elsewhere (Vere, 1979; Hills & Armitage, 1979), must be borne in mind in interpreting any such study, but they remain the most practical means of evaluating new therapeutic agents in this group of neurological disorders.

Since these diseases tend to progress, there is always the possibility that drug-induced improvements, particularly small ones, may be masked. Drug trials in extrapyramidal conditions often need to be prolonged for it may take weeks or months for a drug to produce significant benefit even at optimal dosage, and it may require a similar period before that dose is reached. Gradual introduction of new drugs principally is aimed at minimising side-effects. A protracted trial introduces further problems. It must be remembered that many of the patients involved may be severely disabled, and may need to be transported to a hospital or other centre for frequent assessments. Furthermore, the longer the trial lasts the greater is the possibility of intercurrent disease, with consequent clinical deterioration. It is clearly not possible to completely eliminate these problems.

An important concept in the treatment of extrapyramidal disease is that of individualising the dose of the drug for each patient. Frequently there is a large variation in the optimal dose required, as for example with levodopa in Parkinson's disease and haloperidol in Gilles de la Tourette's syndrome. With many new therapeutic agents it is necessary to find the optimal dose for each patient by trial and error, being aware that the tolerated dose may vary tenfold or even more between individual subjects. As a consequence, initial evaluation of most drugs includes an open 'dose-finding' phase.

The individualisation of the drug used is a more recent concept. Mackay & Sheppard (1979) emphasised the value of single-dose drug challenge in an individual patient with tardive dyskinesia, as a guide to which drug would be most likely to be useful in long-term therapy. This can obviously save both the patient and the investigator time and disappointment.

To summarise, the following sequential stages are generally needed in a drug trial in extrapyramidal disease:

(a) If possible, a single-dose drug challenge to establish the most suitable drug for an individual patient

(b) An open, dose-finding study to establish possible efficacy and toxicity

(c) A randomised, double-blind cross-over trial against placebo and/or a standard drug, with appropriate wash-out periods if required, to confirm efficacy. Ideally, the time of cross-over should be randomised from patient to patient so that it is unknown by either the investigator or the patient, but this is rarely achieved in practice.

(d) A large scale multi-centre trial to establish practicability and long-term toxicity. This may provide a large enough population for a parallel study to be carried out, but obviously suffers from the organisational difficulties of any trial where many investigators are involved, and inter-observer reliability of assessment may not prove adequate. In fact, such studies are relatively rare in this field.

(e) Post-marketing surveillance.

Appendix 1

Hoehn & Yahr's (1967) staging for Parkinson's disease

Stage I
Unilateral involvement, usually minimal or no functional impairment

Stage II
Bilateral or mid-line involvement, without impairment of balance

Stage III
First signs of impaired righting reflexes: evident in unsteadiness as the patient turns or demonstrated when he is pushed from standing equilibrium with feet together and eyes closed. Functionally somewhat restricted, but may be able to work, depending on nature of employment. Capable of independent living, with mild to moderate overall disability

Stage IV
Fully developed, severely disabling disease. Can stand and walk unaided, but is markedly incapacitated

Stage V
Confined to wheel-chair or bed without assistance

Appendix 2

Webster's Parkinson's disease rating scale

Directions

Apply a gross clinical rating to each of the 10 listed items, assigning value ratings of 0–3 for each item, where (0) = no

involvement and (1), (2) and (3) are equated to early, moderate and severe disease respectively.

Bradykinesia of hands (including handwriting)

(0) No involvement
(1) Detectable lowering of the pronation-supination rate, evidenced by beginning of difficulty in handling tools, buttoning clothes, and with handwriting.
(2) Moderate slowing of supination-pronation rate, one or both sides, evidenced by moderate impairment of hand function. Handwriting is greatly impaired, micrographia is present
(3) Severe slowing of supination-pronation rate. Unable to write or button clothes. Marked difficulty in handling utensils.

Rigidity

(0) None detectable
(1) Detectable rigidity in neck and shoulders. Activation[1] phenomenon is present. One or both arms show mild, negative[2], resting rigidity.
(2) Moderate rigidity in neck and shoulders. Resting rigidity is positive[2] when patient not on medication
(3) Severe rigidity in neck and shoulders. Resting rigidity cannot be reversed by medication

Posture

(0) Normal posture. Head flexed forward less than 4 inches
(1) Beginning 'poker' spine. Head flexed forward up to 5 inches
(2) Beginning arm flexion. Head flexed forward up to 6 inches. One or both arms raised but still below waist.
(3) Onset of simian posture. Head flexed forward more than 6 inches. One or both hands elevated above waist. Sharp flexion of hand, beginning interphalangeal extension. Beginning flexion of knees.

Upper extremity swing

(0) Swings both arms well
(1) One arm definitely decreased in amount of swing
(2) One arm fails to swing
(3) Both arms fail to swing

Gait

(0) Steps out well with 18–30 inch stride. Turns about effortlessly.
(1) Gait shortened to 12–18 inch stride. Beginning to strike one heel. Turn around time slowing. Requires several steps.
(2) Stride moderately shortened—now 6–12 inches. Both heels beginning to strike floor forcefully.
(3) Onset of shuffling gait, steps less than 3 inches. Occasional stuttering type of blocking gait. Walks on toes—turns around very slowly.

Tremor

(0) None detectable
(1) Less than 1 inch of peak-to-peak tremor movement observed in limbs or head at rest or in either hand while walking or during finger to nose testing
(2) Maximum tremor envelope fails to exceed 4 inches. Tremor is severe but not constant and patient retains some control of hands
(3) Tremor envelope exceeds 4 inches. Tremor is constant and severe. Patient cannot get free of tremor while awake. Writing and feeding are impossible

Facies

(0) Normal. Full animation. No stare
(1) Detectable immobility. Mouth remains closed. Beginning features of anxiety and depression
(2) Moderate immobility. Emotion breaks through at markedly increased threshold. Lips parted some of the time. Moderate appearance of anxiety or depression. Drooling may be present
(3) Frozen facies. Mouth open ¼ inch or more. Drooling may be severe

Seborrhea

(0) None
(1) Increased perspiration, secretion remaining thin
(2) Obvious oiliness present. Secretion much thicker
(3) Marked seborrhoea, entire face and head covered by thick secretion

Speech

(0) Loud, clear, resonant, easily understood
(1) Beginning of hoarseness with loss of inflection and resonance. Good volume and still easily understood
(2) Moderate hoarseness and weakness. Constant monotone, unvaried pitch. Beginning of dysarthria, hesitancy, stuttering, difficult to understand
(3) Marked harshness and weakness. Very difficult to hear and understand

Self-care

(0) No impairment
(1) Still provides full self-care but rate of dressing definitely impaired
(2) Requires help in certain critical areas, such as turning in bed, rising from chairs etc. Very slow in performing most activities, but manages by taking more time
(3) Continuously disabled. Unable to dress, feed or walk alone

[1] Activation phenomenon is an increase in rigidity in involved limb evoked by voluntary movement of contralateral limb

[2] Negative rigidity indicates that the patient aids passive movements performed by the observer, to a greater or lesser extent. Positive rigidity implies involuntary resistance associated with increased tone.

Appendix 3

North-Western University Disability Scale

Scale A: Walking

Never walks alone

0 Cannot walk at all, even with maximum assistance

1 Needs considerable help, even for short distances; cannot walk outdoors with help

2 Requires moderate help indoors; walks outdoors with considerable help

3 Requires potential help indoors and active help outdoors

Sometimes walks alone

4 Walks from room to room without assistance, but moves slowly and uses external support; never walks alone outdoors

5 Walks from room to room with only moderate difficulty; may occasionally walk outdoors without assistance

6 Walks short distances with ease; walking outdoors is difficult but often accomplished without help

Always walk alone

7 Gait is extremely abnormal; very slow and shuffling; posture grossly affected; there may be propulsion

8 Quality of gait is poor and rate is slow; posture

moderately affected; there may be a tendency towards mild propulsion; turning is difficult

9 Gait only slightly deviant from normal in quality and speed; turning is the most difficult task; posture essentially normal

10 Normal

Scale B: Dressing

Requires complete assistance

0 Patient is a hindrance rather than a help to assistant

1 Movements of patient neither help nor hinder assistant

2 Can give some help through bodily movements

3 Gives considerable help through bodily movements

Requires partial assistance

4 Performs only gross dressing activities alone (hat, coat)

5 Performs about half of dressing activities independently

6 Performs more than half of dressing activities alone, with considerable effort and slowness

7 Handles all dressing alone with the exception of fine activities (tie, buttons)

Complete self-help

8 Dresses self completely with slowness and great effort

9 Dresses self completely with only slightly more time and effort than normal

10 Normal

Scale C: Hygiene

Requires complete assistance

0 Unable to maintain proper hygiene even with maximum help

1 Reasonably good hygiene with assistance, but does not provide assistant with significant help

2 Hygiene maintained well; gives aid to assistant

Requires partial assistance

3 Performs a few tasks alone with assistant nearby

4 Requires assistance for half of toilet needs

5 Requires assistance for some tasks not difficult in terms of co-ordination

6 Manages most of personal needs alone; has substituted methods for accomplishing difficult tasks

Complete self-help

7 Hygiene maintained independently, but with effort and slowness; accidents are not infrequent; may employ substitute methods

8 Hygiene activities are moderately time-consuming; no substitute methods; few accidents

9 Hygiene maintained normally, with exception of slight slowness

10 Normal

Scale D: Eating and feeding (scored separately)

Eating

0 Eating is so impaired that a hospital setting is required to get adequate nutrition

1 Eats only soft foods and liquids; these are consumed very slowly

2 Liquids and soft foods handled with ease; hard foods occasionally eaten, but require great effort and much time

3 Eats some hard foods routinely, but these require time and effort

4 Follows a normal diet, but chewing and swallowing are laboured

5 Normal

Feeding

0 Requires complete assistance

1 Performs only a few feeding tasks independently

2 Performs most feeding activities alone, slowly and with effort; requires help with feeding

3 Handles all feeding alone with moderate slowness; still may get assistance in specific situation (e.g. cutting meat in restaurant); accidents not infrequent

4 Fully feeds self with rare accidents; slower than normal

5 Normal

Scale E: Speech

0 Does not vocalise at all

1 Vocalises, but rarely for communicative purposes

2 Vocalises to call attention to self

3 Attempts to use speech for communication, but has difficulty in initiating vocalisation; may stop speaking in middle of phrase and be unable to continue

4 Uses speech in most communication, but articulation is highly unintelligible; may have occasional difficulty in initiating speech; usually speaks in single words or short phrases

5 Speech always employed for communication, but articulation is still very poor; usually uses complete sentences

6 Speech can always be understood if listener pays close attention; both articulation and voice may be defective

7 Communication accomplished with ease, although speech impairment detracts from content

8 Speech easily understood, but voice or speech rhythm may be disturbed

9 Speech entirely adequate; minor voice disturbances present

10 Normal

Appendix 4 Shoulson & Fahn's (1979) Staging of Huntington's Disease

	Engagement in occupation	*Capacity to handle financial affairs*	*Capacity to manage domestic responsibilities*	*Capacity to perform activities of daily living*	*Care can be provided at*
Stage 1	Usual level	Full	Full	Full	Home
Stage 2	Lower level	Requires slight assistance	Full	Full	Home
Stage 3	Marginal	Requires major assistance	Impaired	Mildly impaired	Home
Stage 4	Unable	Unable	Unable	Moderately impaired	Home or extended care facility
Stage 5	Unable	Unable	Unable	Severely impaired	Total care facility only

Appendix 5 Shoulson & Fahn's (1979) functional disability scale for Huntington's Chorea

A. *Engagement in occupation*

3 Usual level: refers to full-time salaried employment, actual or potential (e.g. job offer or qualified) with normal work expectations and satisfactory performance.

2 Lower level: refers to full or part-time salaried employment, actual or potential, with a lower than usual expectation or performance relative to patient's training and education.

1 Marginal level: refers to part-time voluntary or salaried employment, actual or potential, with less than satisfactory work performance.

0 Unable: indicates patient is totally unable to engage in voluntary or salaried employment.

B. *Capacity to handle financial affairs*

3 Full: refers to normal capacity to handle personal and family finances (income tax, balancing cheque book, paying bills).

2 Requires assistance: refers to decline in ability to handle financial affairs such that accustomed routine responsibilities (budgeting, shopping, maintaining chequing account) now require organisation and assistance from family member or financial advisor.

1 Limited: handles pocket money only.

0 Unable: indicates patient is unable to comprehend the financial process and is unable to perform tasks related to routine financial procedures.

C. *Capacity to manage domestic responsibilities*

2 Full: no impairment in performance of routine domestic tasks (cleaning, laundering, dishwashing, table setting, recipes, answering mail, civic responsibilities).

1 Impaired: refers to decline in performance of routine domestic tasks such that patient requires some assistance carrying out these tasks.

0 Unable: indicates marked decline in function with marginal performance requiring major assistance.

D. *Capacity to perform activities of daily living*

3 Full: refers to complete independence in eating, dressing and bathing activities.

2 Mildly impaired: refers to somewhat laboured performance in eating (avoids certain foods which cause chewing/swallowing problems), in dressing (difficulty in fine tasks only, e.g. buttoning, tying shoes), in bathing (difficulty in fine performance only, e.g. brushing teeth); requires only slight assistance.

1 Moderately impaired: refers to substantial difficulty in eating (swallows only liquid or soft foods and requires considerable assistance), in dressing (performs only gross dressing activities and requires assistance with everything else), in bathing (performs only gross bathing tasks, otherwise requiring assistance).

0 Severely impaired: indicates that patient requires total care in activities of daily living.

E. *Care can be provided*

2 Home: patient living at home and family readily able to meet care needs.

1 Home or extended care facility: patient may be living at home but care needs would be better and more easily provided at an extended care facility.

0 Total care facility only: patient requires full-time skilled nursing care.

Appendix 6 Marsden & Quinn's chorea severity evaluation scale

1. *Speech*
   0 Normal
   1 Slight dysarthria
   2 Slurred but understandable
   3 Considerable dysarthria, with interruptions in flow
   4 Dysarthria with considerable 'interruption' in flow
   5 Unintelligible

3. *Gait*
   0 Normal
   1 Increase in choreic movements
   2 Definite 'stuttering, dancing' gait
   3 Pronounced 'stuttering and dancing' gait; tends to be thrown off balance
   4 Walks only with assistance
   5 Unable to walk, even with assistance

3. *Postural stability*
   0 Normal
   1 Decreased postural reflexes
   2 Would fall if not caught, after marked pulls
   3 Would fall if not caught, after mild pulls
   4 Tends to fall spontaneously
   5 Cannot stand alone

4. *Manual Dexterity*
   0 Normal
   1 Occasionally fumbles or drops objects
   2 Difficulty in dressing and/or eating
   3 Requires some help dressing and/or eating
   4 Requires to be dressed and/or fed

5. *Severity of Chorea*
   0 None
   1 Rare to slight
   2 Mild
   3 Moderate
   4 Severe; interferes with some functions
   5 Very severe; unable to function

Face		Upper	_____
		Lower	_____
Neck			_____
Trunk			_____
Limbs		R	L
	Arms	_____	_____
	Legs	_____	_____

Appendix 7 Fahn & Marsden's staging of torsion dystonia

Stage

I Focal: a single segment (e.g. 1 limb; torticollis; blepharospasm; dysphonia; both arms or both legs).
II Segmental: 2–3 continuous (e.g. Meige syndrome, torticollis plus shoulder)
III Unilateral arm and leg
IV Bilateral generalised

Appendix 8 Fahn & Marsden's functional disability scale for torsion dystonia

A. *Speech*
0 Normal
1 Slightly involved; easily understood
2 Some difficulty to understand
3 Marked difficulty to understand
4 Completely or almost completely aphonic or anarthric

B. *Handwriting (tremor or dystonia)*
0 Normal
1 Slight difficulty; legible
2 Almost illegible
3 Illegible
4 Unable to grasp or maintain hold on pen

C. *Feeding*
0 Normal
1 Uses 'tricks'; independent
2 Can feed, but not cut
3 Finger food only
4 Completely dependent

D. *Eating*
0 Normal
1 Occasional choking
2 Chokes frequently; difficulty swallowing
3 Unable to swallow firm foods
4 Marked difficulty swallowing soft foods and liquids

E. *Hygiene*
0 Normal
1 Clumsy; independent
2 Needs help with some activities
3 Needs help with most activities
4 Needs help with all activities

Dressing
0 Normal
1 Clumsy; independent
2 Needs help with some
3 Needs help with most
4 Helpless

G. *Walking*
0 Normal
1 Slightly abnormal; hardly noticeable
2 Moderately abnormal; obvious to naive observer
3 Considerably abnormal
4 Needs assistance to walk
5 Wheel-chair bound

Appendix 9 Fahn & Marsden's dystonia severity evaluation scale

Segments	*Provoking factor*	*Severity factor*	(*Product*)
Eyes			
Mouth			
Speech and swallowing			
Neck			
Right arm			
Left arm			
Trunk			
Right leg			
Left leg			
			Total

Provoking factor
0 No dystonia at rest or action
1 Dystonia on particular action
2 Dystonia on many actions
3 Dystonia on action of distant part of body
4 Dystonia present at rest

Speech and swallowing
1 Occasional either or both
2 Frequent either
3 Frequent one and occasional other
4 Frequent both

Severity factor
0 No dystonia present
1 Slight dystonia, but not causing impairment. Clinically insignificant
2 Mild. Impairment but not disabling
3 Moderate. Disabling, but not eliminating basic function
4 Severe. Preventing basic functions

Appendix 10 Marsden & Lang's cranial dystonia evaluation scale

Rate: *Severity* and *Provoking factor*

Severity	*Provoking factor*
0 nil	0 nil
1 slight	1 reading and viewing, or talking and eating
2 mild (or not interfering with basic function)	2 movement of distant parts
3 moderate (disabling but not eliminating basic function)	3 at rest
4 severe (prevents basic function)	

For: Upper face
Lips
Jaws
Tongue

Also score:

Vision	*Speech*	*Swallowing*
0 normal	0 normal	0 normal
1 rarely troubled	1 slurred	1 occasionally chokes
2 cannot drive or read	2 dysarthric but intelligible	2 frequently chokes but can feed
3 cannot cross roads or leave house	3 dysarthric and difficult to understand	3 significant difficulty in feeding
4 Functionally blind	4 Unintelligible	4 Cannot feed

Appendix 11 Marsden & Sheehy's writer's cramp evaluation scale

Subjective (observe while writing)
0 Normal
1 Curious hand posture which could be interpreted as normal
2 Obviously abnormal hand posture, but abnormalities confined to wrist and/or fingers
3 Abnormal posture involves elbow and/or shoulder as well
4 Abnormal posture involves other distant body parts, for example the neck (specify)

Objective (using affected limb)
1 Gibson's maze traced as accurately and rapidly as possible
2 Number of times the word "sunshine" can be written completely in one minute
3 Number of counters piled on top of one another in one minute
4 Ability to hold a full cup of water with arm outstretched (measured as the percentage of water spilt in one minute)
5 Handwriting sample compared with script prior to illness, using for example the signature, and rated
0 no change
1 slight, uncertain deterioration
2 mild but definite deterioration
3 moderate deterioration, difficult to read
4 severe deterioration, very difficult to read
5 illegible

Appendix 12 Chadwick & Marsden's myoclonus evaluation scale

(a) *Score*[1] *sustained posture*[2]
1 Of outstretched arm
2 Of flexed arm in front of face
3 Of leg elevated from bed while lying
4 Of body while standing on one leg
5 Of face while pursing lips

(b) *Score*[1] *dynamic function*[2]
1 Finger-nose test
2 Rapid hand tapping
3 Rapid pronation-supination hand movements
4 Heel-shin test
5 Gait
6 Speech
7 Handwriting
8 Drawing of Archimedes spiral

[1] Score as 0 = normal
1 = mild abnormality
2 = moderate abnormality
3 = severe abnormality

[2] Where appropriate, an individual score was given for each limb tested

Appendix 13a The abnormal involuntary movement scale (AIMS, 1976): examination procedure

Either before or after completing the examination procedure observe the patient unobtrusively, at rest (e.g. in waiting room). The chair to be used in this examination should be a hard, firm one without arms.

1. Ask patient whether there is anything in his/her mouth (i.e. gum, candy, etc) and if there is, to remove it.
2. Ask patient about the current condition of his/her teeth. Ask patient if he/she wears dentures. Do teeth or dentures bother patient now?
3. Ask patient whether he/she notices any movements in mouth, face, hands, or feet. If yes, ask to describe and to what extent they currently bother patients or interfere with his/her activities.
4. Have patient sit in chair with hands on knees, legs slightly apart, and feet flat on floor. (Look at entire body for movements while in this position).
5. Ask patient to sit with hands hanging unsupported. If male, between legs, if female and wearing a dress, hanging over knees. (Observe hands and other body areas).
6. Ask patient to open mouth. (Observe tongue at rest within mouth). Do this twice.
7. Ask patient to protrude tongue. (Observe abnormalities of tongue movement). Do this twice.
8. Ask patient to tap thumb, with each finger, as rapidly as possible for 10–15 seconds; separately with right hand, then with left hand. (Observe facial and leg movements).
9. Flex and extend patient's left and right arm (one at a time).
10. Ask patient to stand up. (Observe in profile. Observe all body areas again, hips included).
11. Ask patient to extend both arms outstretched in front with palms down. (Observe trunk, legs and mouth).
12. Have patient walk a few paces, turn and walk back to chair. (Observe hands and gait). Do this twice.

Appendix 13b The abnormal involuntary movements scale (AIMS, 1976): Scoring system

Instructions: Complete examination procedure before making ratings
Movement ratings: Rate highest severity observed. Rate movements that occur upon activation one less than those observed spontaneously.

Code: 0 = none
1 = minimal may be extreme normal
2 = mild
3 = moderate
4 = severe

		(Circle one)				
Facial and oral movements	1. Muscles of facial expression e.g. movements of forehead, eyebrows, periorbital area, cheeks; include frowning, blinking, smiling, grimacing	0	1	2	3	4
	2. Lips and perioral area e.g. puckering, pouting, smacking	0	1	2	3	4
	3. Jaw e.g. biting, clenching, chewing, mouth opening, lateral movement	0	1	2	3	4
	4. Tongue Rate only increase in movement both in and out of mouth, *not* inability to sustain movement	0	1	2	3	4
Extremity movements	5. Upper (arms, wrist, hands, fingers) Include choreic movements (i.e. rapid, objectively purposeless, irregular, spontaneous), athetoid movements (i.e. slow, irregular, complex, serpentine) Do *not* include tremor (i.e. repetitive, regular, rhythmic)	0	1	2	3	4
	6. Lower (legs, knees, ankles, toes) e.g. lateral knee movement, foot tapping, heel dropping, foot squirming, inversion and eversion of foot	0	1	2	3	4

Trunk movements	7. Neck, shoulders, hips e.g. rocking, twisting, squirming, pelvic gyrations	0	1	2	3	4
Global judgements	8. Severity of abnormal movements	None, normal				0
		Minimal				1
		Mild				2
		Moderate				3
		Severe				4
	9. Incapacitation due to abnormal movements	None, normal				0
		Minimal				1
		Mild				2
		Moderate				3
		Severe				4
	10. Patient's awareness of abnormal movements	No awareness				0
		Aware, no distress				1
		Aware, mild distress				2
		Aware, moderate distress				3
		Aware, severe distress				4
Dental status	11. Current problems with teeth and/or dentures	No	0			
		Yes	1			
	12. Does patient usually wear dentures?	No	0			
		Yes	1			

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