

# Myoclonus

Myoclonus can occur in many different settings and in a range of neurological disorders, as well as being seen physiologically when falling asleep in lectures for example! The essential feature of the condition, which makes it instantly recognisable is the sudden, brief and shock-like nature of the movement (and equates to EMG bursts of activity of about 10-50msec). There are different ways in which it is defined according to: what provokes it; where it is; and what it is associated with neurologically as well as pathophysiologically. As with all movement disorders it can be associated with other involuntary movements.

In this short review I will briefly discuss the different types of myoclonus and their salient features and present a pragmatic approach to the patient with this type of movement disorder.

### Clinical evaluation of myoclonus

The initial evaluation is undertaken to decide whether the myoclonus is spontaneous, and this may require a relatively prolonged period of observation. If not present then it is worth trying to provoke it. In the first instance this involves getting the patient to move (such as putting their hands out in front of them) which typically provokes action myoclonus, and in some cases holding the hands out in front causes them to flap (asterixis) which reflects negative myoclonus (which equates to a brief loss of EMG activity). Finally in order to see whether there is any stimulus sensitivity, one should flick the distal finger joints and/or make a sudden loud noise (clap hands) to see if either of these manoeuvres provokes a reflex myoclonus.

This having been achieved the next question is to decide the distribution of the myoclonus and this may provide clues as to aetiology and pathophysiological origin. In particular is the myoclonus confined to one area (i.e. focal such as a jerking limb for example); is it segmental (adjacent body parts- shoulder), multifocal (widely distributed, unpredictable and not synchronised) or generalised (synchronised jerks affecting most of body).

Finally one examines the patient to see whether there are other associated systemic or neurological abnormalities which are associated with the myoclonus.

Defining the pathophysiological basis is not necessary although focal myoclonus is normally of focal origin - so involves the cortex or spinal cord, whilst subcortical sites of origin produce generalised or multifocal myoclonus.

### Investigation of myoclonus

*History and examination* is followed by a series of investigations that may help identify the cause, although the nature of the tests will to some extent be determined by the duration and type of myoclonus and whether it is associated with other neurological or systemic abnormalities.

*Full biochemical screen* looking for major electrolyte, renal or hepatic abnormalities and consider arterial blood gases.

*Autoantibody screen* in particular looking for coeliac disease; paraneoplastic syndromes and anti-GAD for jerking stiff man syndrome.

*Imaging* to exclude cerebrovascular, neoplastic or obvious neurodegenerative condition as well as focal lesion in patients with focal myoclonus, especially in spinal and propriospinal myoclonus.

*EEG* to see whether there is evidence that myoclonus is part of an epileptic syndrome or whether the patient has epilepsy partialis continua as well as looking for CJD.

*SEPs*, which are giant in cortical myoclonus, and is therefore most consistently found in the rare group of patients with progressive myoclonic epilepsy

More sophisticated neurophysiology can also be undertaken such as jerk-locked EMG to EEG back averaging, but this is not routinely available in most hospitals.

### Other tests to be considered

- Genetic tests – looking for DRPLA and mitochondrial disease
- Skin biopsy – looking for neuronal ceroid lipofuscinosis (NCL).
- Axillary skin biopsy – looking for Lafora body disease and Unverricht-Lundborg disease
- Muscle biopsy – looking for mitochondrial disease as well NCL, Lafora body disease
- Enzyme assays in urine and blood – looking for sialidosis, gangliosidosis and Gaucher’s disease
- Systemic investigation looking for a primary malignancy – CT chest/abdomen; whole body PET scan etc
- Brain biopsy – looking for vasculitis and possibly to confirm the nature of a neurodegenerative disorder

### Treatment of Myoclonus

In many cases treatment is not necessary, as there is either a clear underlying aetiology that needs rectifying; the myoclonus does not cause any major disabilities; or the myoclonus is in the presence of advanced neurodegenerative disease.

If drug therapy is required the most successful are:

- Clonazepam for all forms of myoclonus
- Sodium valproate for most forms of myoclonus
- Piracetam for post-anoxic myoclonus
- Levetiracetam for post-anoxic myoclonus
- Tetrabenazine is said to be helpful for segmental myoclonus
- Botulinum injections for some forms of focal myoclonus, especially hemifacial spasm
- Other drugs that may have a role include primidone for cortical myoclonus and fluoxetine in postanoxic and action myoclonus.

### Some myoclonic syndromes

#### ESSENTIAL MYOCLONUS/MYOCLONIC DYSTONIA

This is a heterogeneous condition, which consists of widespread myoclonus affecting all four limbs, trunk, neck, and face, occurring at about 10 to 50/min, enhanced by action and sensory stimuli. Onset is usually



Roger Barker is co-editor in chief of ACNR, and is Honorary Consultant in Neurology at The Cambridge Centre for Brain Repair. He trained in neurology at Cambridge and at the National Hospital in London. His main area of research is into neurodegenerative and movement disorders, in particular parkinson's and Huntington's disease. He is also the university lecturer in Neurology at Cambridge where he continues to develop his clinical research into these diseases along with his basic research into brain repair using neural transplants.

Table 1. The classification of myoclonus

Clinical Presentation	Clinical Distribution	Neurophysiological Origin	Aetiology
<ul style="list-style-type: none"> <li>● Spontaneous - typically seen normally or in patients with metabolic encephalopathies or CJD</li> <li>● Action - which occurs during active muscular contractions, and is very disabling.</li> <li>● Reflex - which occurs to somesthetic, visual and auditory stimuli.</li> </ul>	<ul style="list-style-type: none"> <li>● Generalised</li> <li>● Multifocal</li> <li>● Segmental</li> <li>● Focal</li> </ul>	<ul style="list-style-type: none"> <li>● Cortical (often associated with giant SEPs)</li> <li>● Subcortical (brainstem and includes hyperekplexia; brainstem reticular myoclonus and palatal myoclonus)</li> <li>● Spinal (typically associated with a focal spinal cord lesion)</li> <li>● Propriospinal</li> </ul>	<ul style="list-style-type: none"> <li>● Physiological</li> <li>● Essential</li> <li>● Symptomatic</li> </ul>

in childhood or adolescence, but disability is strikingly mild in most cases. There is no progression, intellect is normal, fits do not occur, and no other deficit appears. Some patients report that alcohol helps their jerks.

Whilst many cases are sporadic, in some cases there is a positive family history suggesting an autosomal dominant condition with variable penetrance and expression.

In some cases the myoclonus may be associated with dystonia (myoclonic dystonia) – with the latter often being the dominant clinical feature. It often shows a dramatic response to alcohol and is associated in some cases with mutations in the *sarcoglycan* gene, but is genetically heterogeneous with associations with the D2 receptor gene (chromosome 11q23) and a Canadian family linked to chromosome 18p11.

## PROGRESSIVE MYOCLONIC ENCEPHALOPATHIES (PME)

Most of the diseases causing a progressive myoclonic encephalopathy are rare and a discussion of them lies outside the scope of this short review. Those that cause this:

- with cognitive decline and epilepsy include Lafora body disease; neuronal ceroid lipofuscinosis (in the form of Kuf's disease in adults); MERFF, sialidosis; DRPLA
- with minimal cognitive involvement and epilepsy include Unverricht-Lundborg disease and the progressive myoclonic ataxias (e.g. coeliac disease and some of the SCAs)
- with significant cognitive decline and no epilepsy include the neurodegenerative disorders such as CJD, corticobasal degeneration, Alzheimer's disease and in some advanced cases of HD.

## STATIC MYOCLONIC ENCEPHALOPATHIES: POSTANOXIC ACTION MYOCLONUS (LANCE-ADAMS SYNDROME)

This is a distinct entity that may appear after a period of cerebral anoxia, typically respiratory arrests in the context of an acute asthmatic attack. After recovery of consciousness, such patients exhibit muscle jerks affecting face, trunk, and limbs, often provoked by sensory stimuli, and strikingly elicited by willed voluntary action. The condition has been associated with abnormalities of brain 5-HT, as 5-hydroxytryptophan can produce a dramatic response in some patients. However the side-effects of this therapy, in particular the development of the eosinophilia myalgia syndrome (EMS) has meant that other treatments such as clonazepam, piracetam, and more recently levetiracetam are preferred.

## MYOCLONIC EPILEPSIES

In the myoclonic epilepsies, epileptic seizures are the obvious and dominant feature of the illness. There is some confusion in separating the many conditions that may cause this syndrome, which occurs particularly in children. A convenient, if arbitrary, distinction is based on the age of onset and is discussed in ACNR (Mark Manfords series on Epilepsy. See [www.acnr.co.uk](http://www.acnr.co.uk) volume I archive).

## FOCAL MYOCLONUS

### *Spinal myoclonus*

Repetitive, often rhythmical, myoclonic jerking restricted to a limb, or even to a few muscles of an arm or leg, may occur with a focal myelitis, spinal cord tumour or

Table 2 Causes of myoclonus

### Generalised myoclonus

#### Essential myoclonus

Non-progressive condition in which myoclonus is only or most important neurological symptom and sign.

#### Progressive myoclonic encephalopathies (PME)

Conditions in which there is obvious myoclonus (with or without seizures) as part of a progressive encephalopathy.

- With demonstrable metabolic cause (e.g. Lafora body disease, mitochondrial encephalomyopathy (esp. MERFF); Sialidosis; Neuronal ceroid lipofuscinosis)
- Hereditary myoclonus with no known metabolic cause (e.g. Familial myoclonic epilepsy (Unverricht-Lundborg disease); rarely seen in HD and DRPLA)
- Other sporadic diseases (e.g. Subacute sclerosing panencephalitis (SSPE), Creutzfeldt-Jacob disease, Alzheimer's disease, Parkinsonian plus conditions- especially corticobasal degeneration; paraneoplastic; vasculitis; coeliac disease)
- Metabolic myoclonus (e.g. uraemia, hepatic failure, CO<sub>2</sub> narcosis)

#### Static myoclonic encephalopathies

Condition in which there is obvious myoclonus after some acute and now static cerebral insult. E.g. Postanoxic action myoclonus (Lance-Adams syndrome).

#### Myoclonic epilepsies

Conditions in which epilepsy is the main problem, but myoclonus is present.

#### Focal myoclonus

Conditions in which the myoclonus is restricted to one small discrete part of the body

- Spinal myoclonus
- Propriospinal myoclonus
- Palatal myoclonus (see Case on ACNR website, [www.acnr.co.uk](http://www.acnr.co.uk))
- Hemifacial spasm
- Cortical myoclonus
- Epilepsia partialis continua

angioma, or after spinal cord trauma. The rhythmic muscle jerking occurs spontaneously, at 20 to 180 per minute, is not affected by peripheral stimuli, often persists in sleep, and is not associated with any change in the EEG. Anticonvulsants and tetrabenazine may help, but it is often very difficult to control.

### *Epilepsia partialis continua*

Encephalitis, tumour, abscess, infarct, haemorrhage, or trauma to the cerebral cortex may rarely cause repetitive, rhythmic muscle jerking once or twice a second, confined to one collection of muscles, persisting even in sleep for days, weeks, or months. Usually the damage involves not only the cerebral cortex, but also deeper structures including the thalamus. Because of its large cortical representations, the most common site of epilepsia partialis continua is the hand and in all cases the focal source may spread to give secondary generalised seizures. Treatment is with anticonvulsants, but may be difficult.

### *Hemifacial spasm*

Hemifacial spasm occurs at a frequency of about 1; 100,000 people, most commonly affects middle-aged or elderly women, and usually appears without obvious cause. Rarely, it may be symptomatic of obvious facial nerve compression. The condition consists of irregular, but repetitive clonic twitching of the muscles of one side of the face with each spasm closing the eye and drawing up the corner of the mouth. At this stage, a mild facial weakness and contraction becomes evident, but a frank facial palsy never develops. Facial sensation is normal and there are no other physical signs in idiopathic hemifacial spasm.

Treatment with drugs is usually unrewarding. Posterior fossa exploration has been advocated especially if there is evidence of facial nerve compression but injection of botulinum toxin into the facial muscles, repeated every 3 to 4 months, is a simpler and usually effective treatment.

## References

- Barker RA (2003) Disorders of movement excluding Parkinson's disease. In: Warrell DA, Cox TM, Firth JD, Benz EJ (eds). *Oxford Textbook of Medicine*. Volume 3. Pp1058-1068. OUP. Oxford
- Obeso JA (1997) Classification, clinical features and treatment of myoclonus. In: Watts, R.L. and Koller, W.C. (eds) *Movement Disorders. Neurologic principles and practice*. Pp541-550. McGraw-Hill, New York.
- Agarwal P, Frucht SJ (2003) *Myoclonus*. *Curr Opin Neurol*. 16:515-521

## Correspondence to:

Dr Roger Barker  
Cambridge Centre for Brain Repair, Cambridge, CB2 2PY  
E-Mail. [rab46@cus.cam.ac.uk](mailto:rab46@cus.cam.ac.uk)