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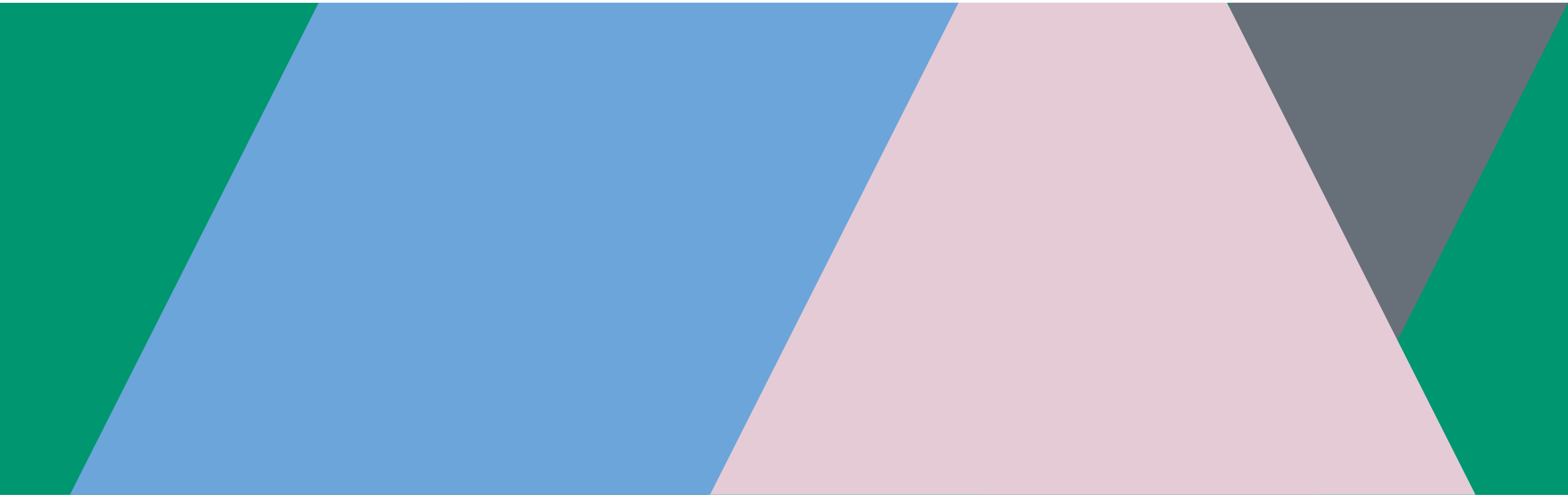
OMS History: with a tribute to Marcel Kinsbourne

10 April 2025. Andrea Klein, Pediatric Neurologist, Bern, Switzerland



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The history of

Ospsoclonus Myoclonus Syndrome
Kinsbourne Syndrome
Opsoclonus Myoclonus Ataxia Syndrome
Dancing Eyes Syndrome
Dancing Eyes und Feet Sydnrome

Polish neurologist Kazimierz **Orzechowski** (1878-1942) and the pediatrician Stanislaw Goździewski (1886-1940) initially presented the term “opsoclonus” in their description of a patient with disorganized conjugate eye movements, at a scientific meeting organized in December of 1924 in the town of Lwów (currently Lviv in western Ukraine), publishing this short report in the chronicle section of the journal *Lwowski Tygodnik Lekarski* (Lviv Medical Weekly)

Yale S, Tekiner H, Yale ES, Gonçalves MVM. Etymology of the Medical Terminology ofOpsoclonus Myoclonus. J Neurol Neuromedicine (2020)
Orzechowski K, Gozdziewski S. Lwowski Tygodnik Lekarski Nr 17 XXXVIII pos nauk z dn 19 XII 1924. Lwów Towarzystwa Lekarskiego Lwowskiego; 1924.
Mikulowski W. Syndrome rare opso-myoclonique observé chez un enfant au cours d’une encéphalite. Arch de méd d enf. 1926; 5: 279-84.

Orzechowski 2027

The diagnosis can be difficult when the disorders in question appear with very great intensity, going as far as "fury of chaotic movements" (opsochorie); it is only during the regression of the phenomenon, that it is then possible to realize the exact nature of the eye disorders. I think it is useful to remind readers beforehand of what constitutes opsoclonus when it acquires a certain intensity, the eyes are in a state of continuous agitation, they are shaken and displaced by very rapid and uneven movements, which generally occurs in the horizontal plane. Often these movements occur in a series, each ending in a sudden elevation, followed by a fall of the eyes, and then a short pause. In the period of remission, when the phenomenon is less marked, the findings appear mainly at the moment when the eyes change their position, whether this change is intentional or reflexive. The findings are especially intense at the beginning of the movement, and throughout its course, the intensity of the tremors decreases and finally stops when the globes reach the point of fixation. Between the horizontal tremors which always predominate, sudden jolts appear occurring in other directions. Throughout the entire clinical picture we always find a few cerebellar symptoms of low intensity (hypotonia of the extremities, spontaneous deviation of the index during Barany's test, tendency to fall, ataxia); but what dominates the clinical picture here are polyclonies [multiple uninterrupted myoclonic muscle jerks], myokymia and trembling of the fingers, chin, lips, blinking, frowning of the forehead, and even difficulty standing and walking as a result of tremor of the muscles of the trunk and lower extremity.(5, p. 15)

J. Neurol. Neurosurg. Psychiat., 1962, **25**, 271

Myoclonic encephalopathy of infants

M. KINSBOURNE

From the Hospital for Sick Children, Great Ormond Street, London

- 1962 Marcel Kinsbourne described in 6 children in much detail and labeled the syndrome as ‘myoclonic encephalopathy in infants’
- Acute-subacute onset in infancy: Opsoclonus, generalysed myoclonus also affecting the face, normal EEG, normal brain biopsy
- Protracted but non progressive course, flutuating, response to steroids/ACTH with relapse/worsening when stopped or reduced.

Kinsbourne M 1962

It is proposed to report six cases in which mycclonic status produced clinical appearances and took a course differing from any previously described and yet conforming to a consistent and distinctive pattern. The acute onset of myoclonic status (especially involving the extraocular muscles in an unusual manner) was unaccompanied by electroencephalographic evidence of cerebral discharges. This isolated motor disorder pursued a protracted but not progressive course.

The diagnosis is nevertheless not a difficult one, and can be made with confidence on clinical grounds

Case 1

The motor disorder continued a fluctuating course for the next three years. Anticonvulsant treatment was ineffective. During exacerbations there was much dribbling and marked dysphagia. Even in relative remission, involuntary movements were never absent. After three years, however, they gradually cleared, and the patient has now been free from involuntary movement for five years. She remains somewhat clumsy in movement and speech, and intellectually she falls into the educationally subnormal group (I.Q. 60 on the Terman-Merrill scale). In view of the history of slow acquisition of skills in the first year of life (before the onset of the motor disorder) the present intellectual and motor deficit cannot with certainty be attributed to the motor disorder. The long persistence of the disorder, absence of electroencephalographic abnormality, and lack of response to anticonvulsant drugs distinguish it from minor epileptic status, idiopathic or symptomatic. The non-progressive and uncomplicated nature of the disorder, its ultimate spontaneous remission, and the negative cortical biopsy distinguish it from the myoclonic types of progressive cerebral degeneration.

Kinsbourne M 1962

Opsoclonus: irregular, arrhythmic, conjugated and chaotic eye movements that occur in all directions and planes of gaze and exacerbates with pursuit
Visible with closed eyes

Can be mild, intermittent. Can be elicited by saccades

Zee 2015
Mahoney KW, Gold DR, Zhang J. Teaching Video Neuro*Images*: Maneuvers to elicit opsoclonus in opsoclonus-myoclonus syndrome. Neurology. 2017

Diagnostic criteria and long term prognosis

Helv Paediatr Acta. 1979 May;34(2):119-33. **Myoclonic encephalopathy of infants or "dancing eyes syndrome". Report of 7 cases with long-term follow-up and review of the literature (cases with and without neuroblastoma).** Boltshauser E, Deonna T, Hirt HR.

Journal of the Royal Society of Medicine Volume 76 June 1983

Michael C G Stevens
Department of Paediatrics
John Radcliffe Hospital, Oxford

The most comprehensive review of this condition (Boltshauser *et al.* 1979) defined four criteria for its diagnosis: (1) marked motor incapacity related to ataxia and myoclonus; (2) opsoclonus (defined as irregular, chaotic but conjugate jerking eye movements); (3) acute or subacute onset; (4) no evidence for an infectious aetiology. It is a disease of infancy with a mean age of onset before the second birthday and has an equal sex incidence. Irritability and vomiting are associated features in a large minority of cases and perhaps 50% have a history of respiratory infection in the preceding few weeks. A very few cases have

Forty-One-Year Follow-Up of Childhood-Onset Opsoclonus-Myoclonus-Ataxia: Cerebellar Atrophy, Multiphasic Relapses, and Response to IVIG

Michael R. Pranzatelli, MD,[1]* Elizabeth D. Tate, FNP, MNC,[1]
Marcel Kinsbourne, MD,[2] Verne S. Caviness, Jr., MD, PhD,[3]
and Bibhuti Mishra, MD[4]

[1]*The National Pediatric Myoclonus Center, Departments of Neurology and Pediatrics, Southern Illinois University School of Medicine, Springfield, Illinois, USA*
[2]*New School University and Tufts University, Winchester, Massachusetts, USA*
[3]*Massachusetts General Hospital, Boston, Massachusetts, USA*
[4]*Temple University, Philadelphia, Pennsylvania, USA*

Longterm follow up of case 3 of the original publication by M. Kinsbourne

Neuroblastoma meeting in Genoa 2004: Diagnostic criteria and severity scale

Opsoclonus myoclonus syndrome in neuroblastoma a report from a workshop on the dancing eyes syndrome at the advances in neuroblastoma meeting in Genoa, Italy, 2004

Katherine K. Matthay[a], Franz Blaes[b], Barbara Hero[c], Dominique Plantaz[d], Pedro De Alarcon[e], Wendy G. Mitchell[f], Michael Pike[g], Vito Pistoia[h,*]

Proposed diagnostic criteria:

the presence of at least 3 out of the following four features:

(1) Opsoclonus

(2) myoclonus/ataxia,

(3) behavioral change and/or sleep disturbance,

(4) neuroblastoma

Matthay, K. K., Blaes, F., Hero, B., Plantaz, D., De Alarcon, P., Mitchell, W. G., Pike, M., & Pistoia, V. (2005). Opsoclonus myoclonus syndrome in neuroblastoma a report from a workshop on the dancing eyes syndrome at the advances in neuroblastoma meeting in Genoa, Italy, 2004. *Cancer Letters*

Severity scale: Mitchell-Pike OMS rating scale

Mitchell-Pike OMS rating scale

Table 1 Opsoclonus myoclonus syndrome severity scale developed by Drs. Wendy Mitchell and Michael Pike following the Advances in Neuroblastoma Research (ANR) Meeting in Genoa, 2004.

– **Stance**
0 standing and sitting balance normal for age
1 mildly unstable standing for age, slightly wide-based
2 unable to stand without support but can sit without support
3 unable to sit without using hands to prop or other support
– **Gait**
0 walking normal for age
1 mildly wide-based gait for age but able to walk indoors and outdoors independently
2 walks only or predominantly with support from person or equipment
3 unable to walk even with support from person or equipment
– **Arm and hand function**
0 normal for age
1 mild infrequent tremor or jerkiness without functional impairment
2 fine motor function (e.g., pincer grip of small object, pencil use) persistently impaired for age but less precise manipulative tasks (e.g., playing with larger toys feeding, dressing) normal or almost normal.
3 major difficulty with all age-appropiate manipulative tasks
– **Opsoclonus**
0 none
1 rare or only when elicited by change in fixation
2 frequent, interfering frequently with fixation and/or tracking
3 persistent, interfering continuously with fixation and tracking
– **Mood/behaviour**
0 normal
1 mild increase in irritability but consolable and/or mild sleep disturbance but easily settled
2 irritability and sleep disturbance, interfering substantially with child and family life
3 persistent severe distress
– **In addition for children aged 18 months or less:**
able to hold head consistently erect when trunk vertical?
☐ yes ☐ no ☐ no information
able to reach and grasp object with each hand?
☐ yes ☐ no ☐ no information
able to roll back to front and front to back?
☐ yes ☐ no ☐ no information
able to finger-feed self?
☐ yes ☐ no ☐ no information

Trials and Registries

COG Trial with 53 patients with neuroblastoma included

OMS DES trial, 100 patients with ad without neuroblastoma. Fully recruited and follow up completed

Oxford-Boston-Zürich long term prognosis study=> POOMAS Registry

OMS life patient reported registry

de Alarcon PA, Matthay KK, London WB, Naranjo A, Tenney SC, Panzer JA, Hogarty MD, Park JR, Maris JM, Cohn SL. Intravenous immunoglobulin with prednisone and risk-adapted chemotherapy for children with opsoclonus myoclonus ataxia syndrome associated with neuroblastoma (ANBL00P3): a randomised, open-label, phase 3 trial. Lancet Child Adolesc Health. 2018

Sheridan A, Kapur K, Pinard F, Dietrich Alber F, Camposano S, Pike MG, Klein A, Gorman MP. IQ predictors in pediatric opsoclonus myoclonus syndrome: a large international cohort study. Dev Med Child Neurol. 2020

Kerr LM, Ryan ME, Lim M, Hearn S, Klein A, Deiva K, Hopkins SE, Bacchus MK, Sokol EA, Waanders AJ, Mitchell WG, Khakoo Y, Lotze TE, Zhang B, Gorman MP. An International Pediatric-Onset Opsoclonus-Myoclonus Ataxia Syndrome Registry and Clinical Research Network: Development, Progress, and Vision. Pediatr Neurol. 2023

Jimenez Giraldo S, Michaelis M, Kerr L, Cortina C, Zhang B, Gorman MP. Inaugural Patient-Reported Registry of Pediatric Opsoclonus-Myoclonus-Ataxia Syndrome: Presentation, Diagnosis, and Treatment of 194 Patients. Pediatr Neurol. 2024

Marcel Kinsbourne

Born in Vienna in 1931, when eight years old, he and his parents escaped to England

Doctor of Medicine and Doctorate of Medicine degree at Oxford University

Following this, he completed his training and worked in the US at Duke University Hospital, starting a pediatric neurology unit, the at the Hospital for Sick Children in Toronto

Early 1960-ties he at Pediatric Neurology at the Great Ormond Street Hospital in London, headed by Prof. Paul Sandifer one of the first official paediatric neurologists in the United Kingdom

This was when he described the 6 Myoclonic Encephalopathy cases with the encouragement of P. Sandifer

1964 he changed to the Psychology Faculty in Oxford before relocating to the USA

He had Professorships in neurology and psychology at Duke University in Northern Carolina and the University of Toronto.

He headed the Behavioral Neurology Research Division at the Shriver Center in Boston Massachusetts

He also served as Presidents of the International Neuropsychology Society and the Society of Philosophy and Psychology

He published >400 Manuscripts, book chapters ect. and was active untile he died in April 2024, at the age of 92.

Marcel Kinsbourne is described as an original, profound, and knowledgeable intellect, but a loving and generous family man and mentor, with a wonderful sense of humor. He loved talking to graduate and medical students and postdoctoral fellows who took any opportunity to question him eagerly about difficult clinical and theoretical issues.

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Thank you for your attention