High prevalence of intellectual disability, autism, ADHD and diminished adaptive functioning in Doose syndrome (MAE)

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Introduction and Purpose

- Myoclonic astatic epilepsy accounts for 1 to 5% of childhood epilepsy.
- The epilepsy prognosis is variable and about 1/3 go into remission.
- The neurodevelopmental outcome is unclear and poorly reported.
- We therefore deeply phenotyped MAE cases for neurodevelopmental symptoms of cognitive ability, adaptive behaviour, autism and ADHD symptoms.

Methods

- MAE cases were recruited across UK paediatric neurology centers. Ref : 09/H0713/76
- MAE case definition was based on ILAE 1989 classification:
  1. Usually normal development before onset of epilepsy.
  2. Onset of myoclonic, myoclonic-atonic or atonic seizures between 6 months and 6 years.
  3. Generalised spike wave and/or polyspike wave discharges on EEG.
  4. Absence of related structural cerebral abnormalities on MRI.
- Phenotyping protocol Table 1:

Symptoms	Assessment Tool
Epilepsy	Clinical history and examination
Cognitive ability	WPPSI III, Bayleys III
Adaptive Behaviour	Adaptive Behaviour Assessment system
Autism spectrum disorder	Social communication questionnaire (SCQ), Developmental Diagnostic interview (3di)
ADHD	Conner's Comprehensive Behavioral Rating Scale – Parent and Teacher DSM IV ADHD subscale, T score > 70
Behavioral screening	Strength and Difficulties questionnaire

Results

- 67 UK MAE cases (49 Male, 18 Females) were recruited.
- Median age of onset 35 months (range 6 to 65), 23 (34%) cases had febrile seizures. Family history of epilepsy in 32 cases (47%).
- Seizures: 100% myoclonic-atonic or atonic, 82% GTCS, 83% myoclonic, 64% absence, 22% tonic and 9% focal seizures.
- Seizure remission of > 2 years was seen in 20 (30%) of cases.
- Low cognitive ability (Figure 2) and adaptive behavior (Figure 3).

Figure 2. Cognitive ability in 25 MAE cases

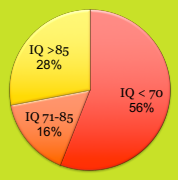
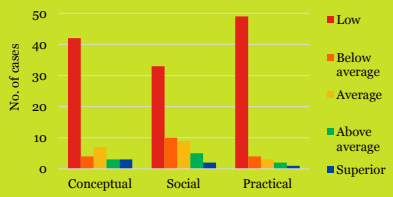
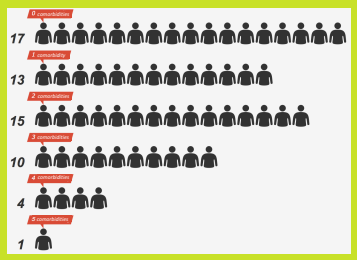


Figure 3. Adaptive behaviour domain scores



- Autism spectrum disorder symptoms were elicited in 20/64 (31%) through the 3di (9/22) and SCQ (16/61).
- ADHD: 21/42 (41%) parents report ADHD with both parent and teacher in 7/52 (13%).
- High scores in behavioural symptoms: emotional symptoms 10/60 (16%), conduct problems 19/60 (31%), hyperactivity/inattention 22/60 (36%), peer relationship problems 29/60 (48%), prosocial behaviour 35/60 (58%). Figure 4 demonstrates multi-morbidity of behavioural symptoms.

Figure 4. No. of behavioural symptoms in 60 MAE cases



Summary:

- One third of MAE patients achieve seizure remission > 2 years.
- MAE patients have significant neurodevelopmental difficulties:
  - 56% have moderate to severe intellectual disability
  - 70% have low adaptive function scores, worst with practical skills
  - 31% have Autism spectrum disorder symptoms
  - 41% have Attention deficit hypertensive disorder symptoms
  - 58% of parents report these difficulties to significant impact on the child and family

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