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

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-atomic or atomic 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:

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Assessment Tool</th>
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</thead>
<tbody>
<tr>
<td>Epilepsy</td>
<td>Clinical history and examination</td>
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<tr>
<td>Cognitive ability</td>
<td>WPPSI III, Bayleys III</td>
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<tr>
<td>Adaptive Behaviour</td>
<td>Adaptive Behaviour Assessment system</td>
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<td>Autism spectrum disorder</td>
<td>Social communication questionnaire (SCQ), Developmental Diagnostic interview (3di)</td>
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<td>ADHD</td>
<td>Conner’s Comprehensive Behavioral Rating Scale – Parent and Teacher DSM IV/ADHD subscale, T score &gt; 70</td>
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<td>Behavioral screening</td>
<td>Strength and Difficulties questionnaire</td>
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</tbody>
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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-atomic or atomic, 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 behaviour (Figure 3).
- 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.

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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