European Journal of Paediatric Neurology 65 (2026) 1–7

Contents lists available at ScienceDirect

European Journal of Paediatric Neurology

journal homepage: www.journals.elsevier.com/european-journal-of-paediatric-neurology

Original article

Treatment responses to antiseizure medication in children with Angelman syndrome

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ARTICLE INFO

Keywords:
Angelman syndrome
Epilepsy
Anti-Seizure medication

ABSTRACT

Background: Angelman Syndrome (AS) is a rare neurodevelopmental disorder with epilepsy affecting up to 90% of the children. Although several studies have examined antiseizure medications (ASMs) in children with AS, preferred ASMs vary between countries and while new ASMs have become available in clinical practice in recent years, their impact on epilepsy treatment in children with AS remains unclear. We report on the frequency of most prescribed ASMs, responder rates and rate of severe side effects of ASM in a natural history cohort. Epilepsy and epilepsy-related parameters were analyzed including differences between genetic subgroups.
Methods: A total of 101 children with AS who visited the Angelman center Munich between 2019 and first quarter of 2025 were included in this retrospective analysis. Epilepsy characteristics, frequency of prescribed ASMs, responder rate and severe side effect rate were recorded.
Results: Epilepsy was present in 75%, with a higher incidence in the deletion genotype. Most patients experienced seizures rather rarely, but one in five had daily or weekly seizures. Seizure frequency was higher in early childhood. Therapy-refractory epilepsy was observed in 34% of AS children with epilepsy. Rate of therapy-refractory epilepsy and seizure burden was higher in the deletion group. Among the most prescribed ASMs (ethosuximide, levetiracetam and valproate), ethosuximide and valproate demonstrated the highest responder rate (>50% reduction of seizures) in 78% and 75% of patients, respectively, closely followed by levetiracetam (64%). The reported side effect rate of ASM did not differ between the most prescribed medications.
Conclusions: The three most prescribed ASMs (valproate, ethosuximide and levetiracetam) in our cohort showed high responder rates in children with Angelman Syndrome. Overall seizure burden and rates of therapy-refractory epilepsy were lower than previously reported, suggesting that combining new and established ASMs may improve seizure outcomes in this population.

1. Background

Angelman syndrome (AS) is a rare neurogenetic disorder, most caused by a deletion of the maternal allele in the chromosome 15q11.2-q13 region. The estimated incidence is 1 in 15 000 live births. Other genetic mechanisms include uniparental paternal disomy (UPD), imprinting defect and pathogenic variants in the maternal *UBE3*A gene [1], [2]. Patients with AS typically present with severe

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https://doi.org/10.1016/j.ejpn.2026.09.001
Received 23 January 2026; Received in revised form 30 June 2026; Accepted 6 September 2026
Available online 7 September 2026
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Open access funding enabled and organized by Projekt DEAL.

neurodevelopmental delay with absence of speech, sleep disturbances and behavioral disorders, gastrointestinal problems and epilepsy [1]. Epilepsy usually begins in early childhood and is more prevalent in the deletion subtype compared to those with UPD, imprinting defects or pathogenic *UBE3A* variants (non-deletion subtype) [3]. Seizure semiology comprises absences, atonic, myoclonic and tonic-clonic seizures as well as focal impaired awareness seizures [4]. Seizures in early childhood are frequently triggered by fever [5], [6]. Non-convulsive status epilepticus (NCSE) is relatively common, particularly in children with deletion subtype [7]. Frequently used antiseizure medications (ASMs) include valproate, clobazam, levetiracetam and lamotrigine. However, preference of used ASMs varies between countries, such as the US and European countries like the Netherlands [8], [7]. In recent years, newer medications like cannabidiol have become available for treatment-resistant epilepsy, though we are lacking data on their use in children with AS [9]. In the present study, we aim to provide an overview of epilepsy characteristics, commonly prescribed ASMs including new treatment options, treatment responses and severe side effect rates. Differences between deletion and non-deletion subtype will be highlighted.

2. Material and methods

2.1. Study design

This retrospective study analyzed data from children with AS who were seen at the Angelman center Munich (ACM) between 2019 and first quarter of 2025. In cases where children visited ACM regularly, the first documented visit was used whenever possible. The study was approved by the medical ethic committee of the Ludwig-Maximilian-University (23-511) and of the Technical University in Munich (2023-79-S-KK).

2.2. Participants

Data of 106 children with genetically confirmed AS who visited the ACM were screened and data of 101 children were included. Data of 5 children were excluded due to incomplete or atypical genetic results or insufficient collection of epilepsy characteristics. Patients with UPD, imprinting defects and pathogenic *UBE3A* variants were summarized into a non-deletion group. Written informed consent was obtained from all caregivers.

2.3. Variables/measurement

Seizure data were derived from medical chart review. Seizure types were classified according ILAE classification of 2025 into focal, generalized and unclassified seizures [10]. Present seizure frequency was categorized as follows: daily, weekly, monthly, every 6 months and less often. The responder rate, defined as comparison of seizure frequency before and after start of ASM, was divided into the following categories: no seizure reduction, seizure reduction of 50 – 90% and seizure reduction of > 90%. To assess treatment response, a minimal observation time of 6 months was required (mean observation time: 4.2 years, range: 6 months to 16 years). Since in medical records detailed information about side effects was frequently missing, rate of severe side effects leading to discontinuation of ASM was recorded. Number of mean ASM currently in use and total number of ASM used over patient's lifetime were calculated for AS patients with epilepsy. The percentage of AS patients with monotherapy, polypharmacotherapy and rate of therapy-refractory epilepsy was calculated for subgroup with epilepsy. Missing data of incomplete medical charts were marked as missing and excluded from data analysis.

2.4. Statistical analysis

Descriptive statistics were calculated, including frequencies and percentages for categorical variables and means with standard deviations (SD), confidence interval (CI) and ranges for continuous variables. Group comparisons between deletion and non-deletion group were performed using the independent, two-sided *t*-test and the Mann-Whitney *U* test for continuous variables, as appropriate. The χ^2-Test and the Fisher's exact test were used for categorical variables as appropriate, respectively. P-values (two-tailed) were adjusted for multiple testing using Holm correction. Adjusted p-values <0.05 were considered statistically significant. Data analysis was conducted using IBM SPSS Statistics, version 29.0, and tables were created with Microsoft Excel Version 16.98.

3. Results

3.1. Demographics

Between 2019 and first quarter of 2025, data on epilepsy, ASMs, treatment effectiveness and rates of severe side effects were collected from 101 children with AS during their visit at the Angelman Center Munich. 76 children had a deletion genotype and 25 children a non-deletion genotype. The overall prevalence of epilepsy was 75%. The mean age at epilepsy onset was 1.8 years. Most frequent seizure types included generalized tonic-clonic seizures (63%) and absence seizures (56%), 71% of patients with epilepsy had more than one seizure type. The prevalence of non-convulsive status epilepticus (NCSE) in patients with epilepsy was 34% (Table 1).

3.2. Epilepsy-related parameters

The first seizure occurred in 90.5% of the patients before the age of 5 and no child experienced the first seizure later than age of 8. While most children with AS had seizures rather rarely (i.e. monthly, every six months or even less often), approximately 20% experienced a high seizure burden, with seizures occurring daily or weekly. Children aged 11- 17 years showed a lower seizure frequency than younger children aged 10 years and below (Fig. 1).

3.3. Antiseizure medication in AS children with epilepsy

The mean age at initiation of ASM therapy was 1.77 years. On

Table 1
Demographics of 101 children with AS, who visited the Angelman Center Munich between 2019 and first quarter of 2025.

Characteristics	Value
N	101
Sex male/female, n = , (%)	44 (43.6%)/57 (56.4%)
Age at visit in Angelman Clinic in years, mean [CI] (SD, range)	6.28 [5.42; 7.13] (± 4.332, 17)
Genetic subtype n = , (%)	
Deletion	76 (75%)
Non-deletion	
Total	25 (25%)
Imprinting defect	8 (8%)
Pathogenic UBE3A variant	8 (8%)
UPD	9 (9%)
Epilepsy n = , (%)	76 (75%)
Age at epilepsy onset in years, mean [CI] (SD, range)	1.8 [1.419; 2.252] (± 1.787, 8)
Seizure types, n = , (% of patients with epilepsy)	
Focal seizure	13 (17%)
Generalized seizure	
tonic-clonic seizure	48 (63%)
absence seizure	43 (56%)
myoclonic seizure	31 (41%)
atonic seizure	25 (33%)
Unclassified seizure	17 (22%)
Non-convulsive status epilepticus (NCSE)	26 (34%)
More than one seizure type	54 (71%)

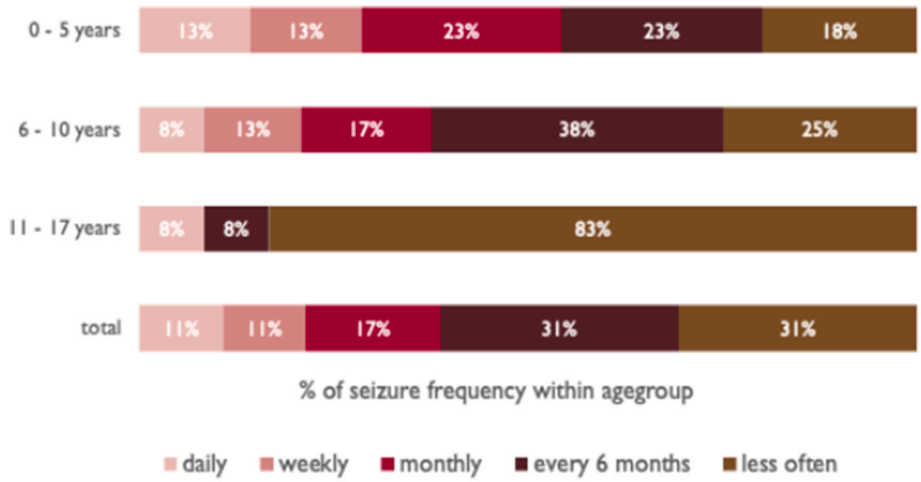

Fig. 1. Seizure frequency (daily, weekly, monthly, every 6 months, less often) per age group (0 – 5 years, 6 – 10 years, 11 – 17 years) and across all age groups (in % of age group).

average, children with epilepsy have been treated with a total amount of 2.01 ASMs throughout their lifetime, while the current number of ASMs in use at the time of data collection was 1.21 ASMs. 37.6% of all children and 17.1% of children with epilepsy were not receiving any ASM at the time of assessment, 48.7% of children with epilepsy were on monotherapy, 34.2% were receiving polytherapy with the highest rate of polypharmacotherapy observed in the 6–10-year-old age group. Therapy-refractory epilepsy (defined as failure of two well-tolerated and appropriately chosen ASMs) was present in 34.2% of AS children with epilepsy (Table 2).

The most frequently prescribed ASMs were levetiracetam (25%), ethosuximide (22%) and valproate (21%), followed by lamotrigine (7%), clobazam (7%), sulthiame (7%) and cannabidiol (6%). The first-line ASMs most commonly used were also levetiracetam (40%), valproate (24%) and ethosuximide (15%) followed by sulthiame (10%). Other ASMs were rarely used as initial therapy (Fig. 2). Interestingly, sulthiame was administered, but no documented continuous spike-wave during slow wave sleep (CSWS) was found in medical records.

Ethosuximide showed a responder rate of 78% (>50% seizure reduction), including 33% with >90% seizure reduction, valproate demonstrated a responder rate of 75%. Levetiracetam had a responder rate of 64% (Fig. 3).

Conclusive statements on efficacy of other ASMs were limited due to a small number of treated children. For instance, cannabidiol was administered to 9 children, with a responder rate of 75% (Fig. 3).

Treatment of NCSE in children with AS included medications as follows: diazepam (n = 10), valproate (n = 4), ethosuximide (n = 3), levetiracetam (n = 3), other benzodiazepines (n = 3) and others (n = 3).

Table 2
Characteristics of use of antiseizure medication in AS children with epilepsy, therapy-refractory epilepsy is defined as use of more than 2 ASMs over patient's lifetime so far.

Characteristics of ASM in AS children with epilepsy	Value
Age at first medication in years, mean [CI] (SD, range)	1.77 [1.388; 2.149] (± 1.366, 6)
ASM total used during patient's lifetime, mean [CI] (SD, range)	2.01 [1.59; 2.43] (± 1.84, 11)
ASM currently in use, mean [CI] (SD, range)	1.21 [1.02; 1.41] (± 0.853, 3)
No medication currently in use n = , (% of all patients; % of patients with epilepsy)	38 (37.6%; 17.1%)
Monotherapy n = , (% of patients with epilepsy)	37 (48.7%)
Polytherapy n = , (% of patients with epilepsy)	26 (34.2%)
Therapy-refractory epilepsy n = , (% of patients with epilepsy)	26 (34.2%)

Responder rate of the three most used ASMs ethosuximide, levetiracetam and valproate on different seizure types were assessed to analyze if responder rate of ethosuximide is caused by high prevalence of absence seizures in children with AS (Table 3). Ethosuximide, valproate and levetiracetam showed a seizure reduction of > 50% on generalized tonic-clonic seizures as well as on generalized absence seizures in most of the patients.

Rate of severe side effects leading to stop of medication did not differ between the three most prescribed ASMs ethosuximide, valproate and levetiracetam (14%, 15% and 15%, respectively). Milder side effects were in line with known side effects of the respective ASMs (to mention examples reported by parents: gastrointestinal problems like reflux for ethosuximide, tremor and elevated liver enzymes for valproate and worsening of behavioral problems for levetiracetam).

3.4. Epilepsy in deletion versus non-deletion group

A higher prevalence of epilepsy was found in the deletion group (84%) compared to the non-deletion group (48%) (p = 0.009). The mean age at seizure onset was 1.59 years in the deletion group and 3.18 years in the non-deletion group, the age at initiation of ASM therapy was similar (1.6 years in the deletion versus 3.0 years in the non-deletion group). Children in the deletion group had a higher seizure burden with more children experiencing daily or weekly seizures. NCSE was present in 31% of the patients in the deletion group and in 8% of the patients of the non-deletion group. The mean number of ASMs used during the patient's lifetime so far and the current number of ASMs in use were both higher in the deletion group. Polypharmacotherapy in children with epilepsy was more frequent in the deletion group (35.9%) than in the non-deletion group (16%). Therapy-refractory epilepsy in children with epilepsy was more prevalent in the deletion group (31.6%) than in the non-deletion group (8%). 68% of children of the non-deletion group were not receiving any ASM at the time of assessment (Table 4).

4. Discussion

The prevalence of epilepsy in individuals with AS is reported to be up to 90% in several studies [1], [6], [8], [7], [3]. In our cohort, we observed a lower rate of 75%, with a higher prevalence in the deletion group (84%) than in the non-deletion group (48%). The lower overall prevalence in our cohort is likely due to the young mean age of the cohort; some younger children will develop epilepsy in the future. Most patients exhibit multiple seizure types, a finding supported in our cohort: 71% of affected individuals show more than one seizure type [4], [6]. The rate of NCSE in our cohort was 34% of patients with epilepsy

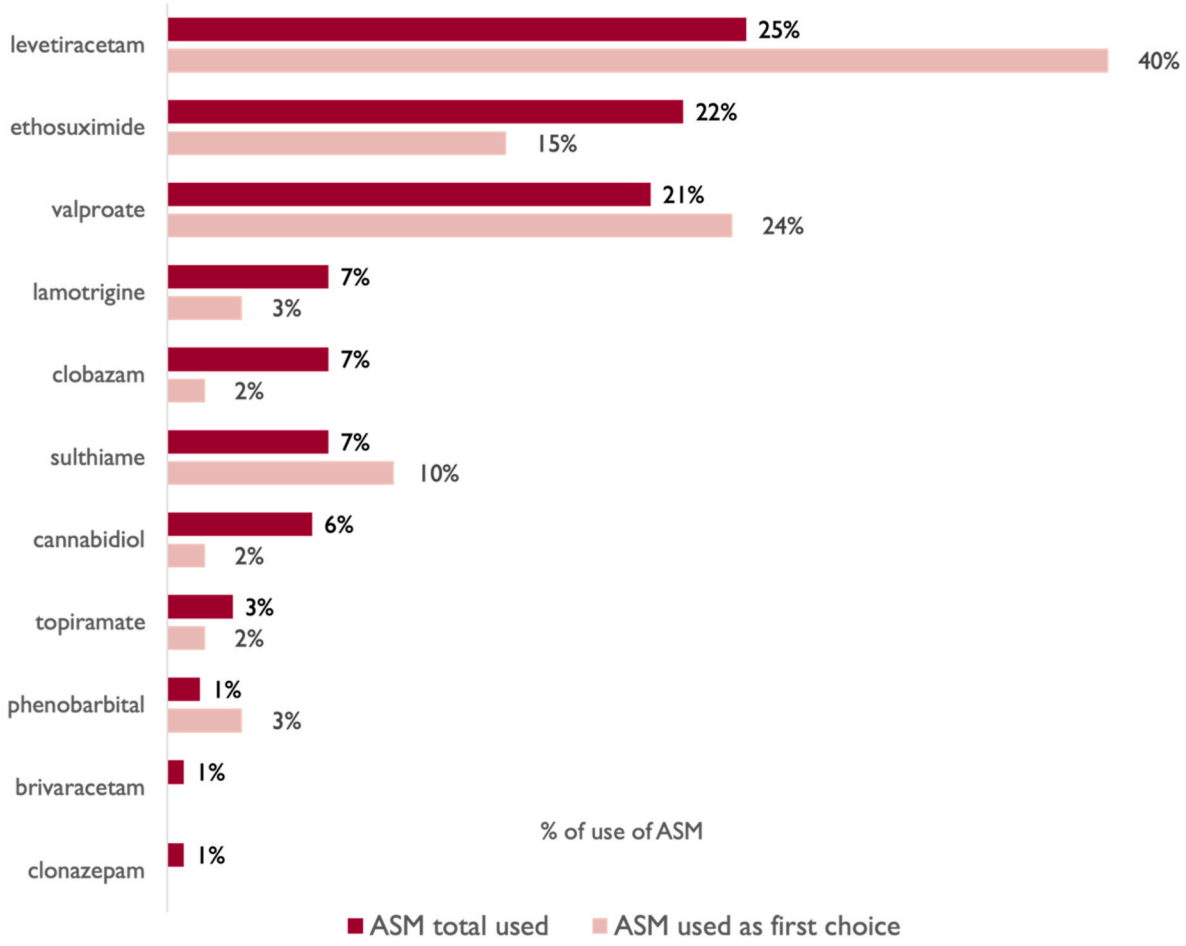

Fig. 2. Frequency of antiseizure medication (ASM) prescribed in children with Angelman Syndrome (AS): ASM in total used in children with AS and ASM used as first choice in children with AS (in %).

(respectively 25% of all patients) consistent with previous data [7], [11]. In accordance with international recommendations we provide education to caregivers about recognizing and managing NCSE, which often presents with subtle symptoms [11], [12]. Outpatient treatment with oral diazepam has been shown to have good efficacy with few side effects [11].

The mean age at first seizure was 1.8 years, most of the children experienced onset before age 5 and no child beyond the age 8, consistent with prior findings [7], [3], [13], [5]. The mean age of medication initiation was higher in the non-deletion group (3.0 years) compared to the deletion group (1.6 years). Interestingly, children in the non-deletion group began medication slightly earlier than their reported age of epilepsy onset, suggesting that some were treated based on suspicious EEG findings rather than clinical seizures.

Seizure frequency varied widely. 11% suffered from daily seizures. However, the majority had monthly or less frequent seizures, aligning with more recent data from the US and contrasting earlier reports that up to 90% of the patients report about previous or current history of daily seizures [3], [4]. Analysis by age group revealed that seizure burden was lower in older age group, particularly in adolescents (11-17 years old) which supports prior findings from longitudinal studies that epilepsy often improves from infancy to adulthood [3], [14], [4]. Nonetheless, epilepsy may persist into adulthood or re-emerge after a seizure-free period during adolescence [15], [13].

The mean number of currently prescribed ASMs in AS children with epilepsy was higher in the deletion group (1.3) compared to the non-deletion group (0.75), in line with data from the US showing means between 1.5 and 1.75 ASMs in the deletion group [3]. Therapy-refractory epilepsy was less frequent than previous reported. While Valente et al. found therapy-refractory epilepsy in 84% of patients [4], 34% of children with epilepsy in our study had therapy-refractory epilepsy. Notably, more than one-third of all children in our cohort and two-thirds in the non-deletion group were not receiving any ASM. Reason might be the young mean age of our cohort. In addition, some parents tolerate low seizure frequencies having in mind the potential side effects of ASMs. Parents sometimes prefer to treat children with exclusively fever-induced seizures with oral diazepam, avoiding chronic ASMs.

Valproate is commonly used as a first-line treatment though concerns over side effects have decreased its use, especially in the US [5], [6], [7], [8]. However, valproate showed excellent responder rates: seizure reduction of $>$ 90% in 67% of the patients and $>$50% in the rest of the patients [8]. In our cohort, valproate showed a 75% responder rate and in only 15% of cases had to be stopped due to severe side effects, indicating a higher retention rate than earlier reports where 60% of the patients discontinued treatment due to adverse effects [8]. Similar good tolerability was observed in a Dutch cohort [7]. Valproate was the second most used first-line ASM in our cohort (24%), behind levetiracetam (40%). In the study of Shaaya et al. levetiracetam was the most used ASM showing a very convincing effectiveness: 86% of the patients had a $>$90% reduction in seizure frequency [8]. Our results did not confirm this excellent effectiveness with a responder rate of 64%, with only 6% archiving $>$ 90% reduction of seizure frequency.

Ethosuximide, widely used for absence seizure and known for its favorable side effect profile, was third most prescribed in our cohort, but more frequent than in broad natural history studies from the US (8%)

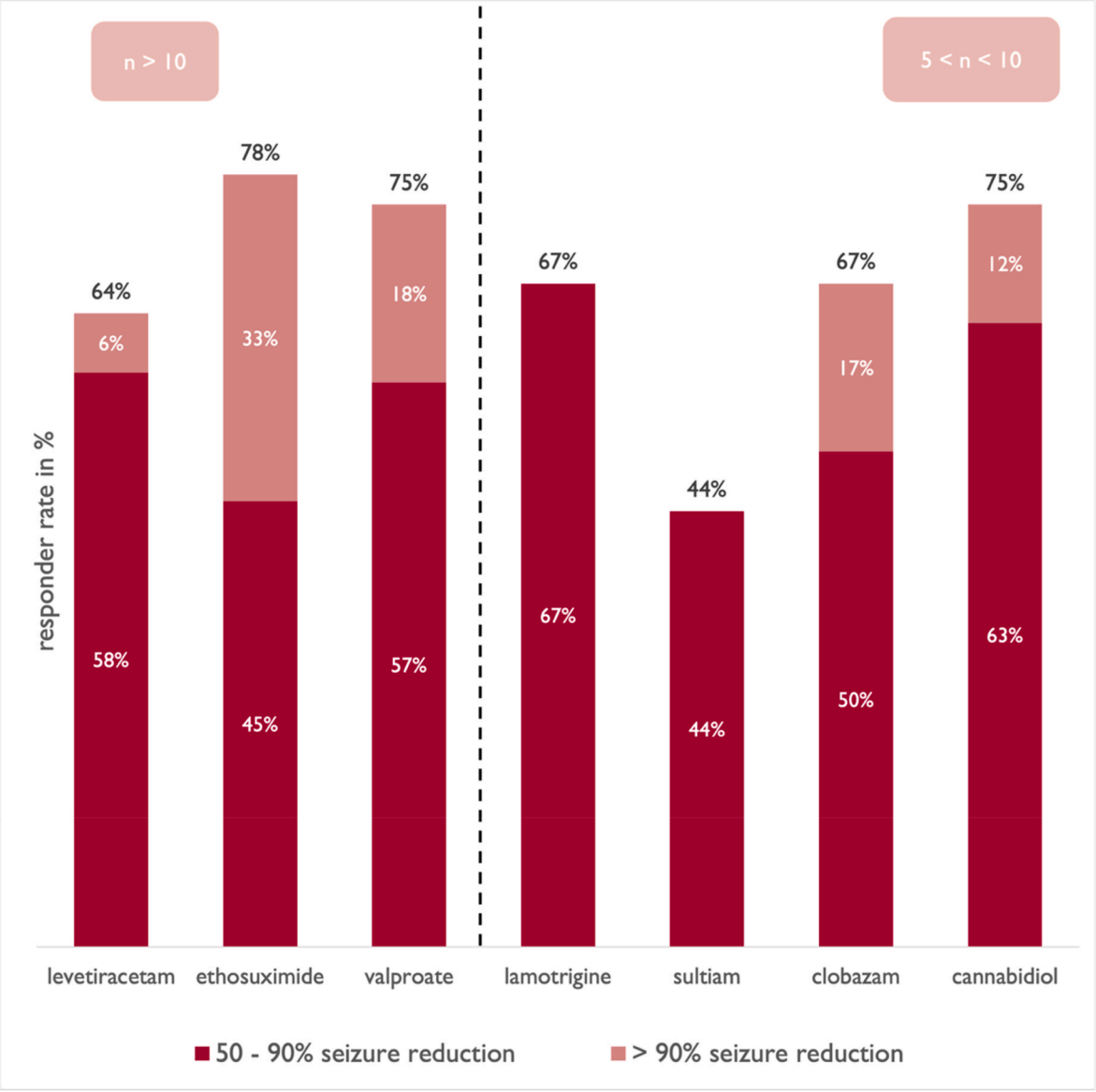

Fig. 3. Responder rate (>50% reduction of seizures) of antiseizure medication used in children with AS (including > 90% seizure reduction and 50 – 90% seizure reduction).

Table 3
Number of non-responders and responders (>50% reduction of seizures) for levetiracetam, valproate and ethosuximide on most frequent seizure types in children with AS.

	Levetiracetam		Valproate		Ethosuximide	
	Non-responder	responder	Non- responder	responder	Non- responder	responder
Focal seizures (n =)	2	3	0	3	0	2
Generalized tonic clonic seizures (n =)	5	18	2	11	0	9
Generalized absence seizures (n =)	3	11	0	15	2	12
Generalized myoclonic seizures (n =)	1	7	0	12	1	12
Generalized atonic seizures (n =)	1	3	0	9	0	7

and the Netherlands (15%) [16], [6], [7]. It demonstrated the highest rate of > 90% seizure reduction with 33%. To assess efficacy to different seizure types was highly challenging, as many patients suffer from multiple seizure types. Although we saw a reduction of generalized tonic-clonic seizures after start with ethosuximide in some individuals, these results have to be interpreted with caution, as ethosuximide might have be used as add on therapy. If the use of ethosuximide can be broadened to generalized tonic-clonic seizures, remains to be elucidated. Interestingly, a positive effect of ethosuximide on EEG abnormalities in a GABAA β3 subunit gene deficient heterozygous mouse model was found. The deletion genotype includes a heterozygous loss of GABAA β3 subunit gene and that might contribute to the more severe affected phenotype of the deletion subgroup [17], [18].

Due to small sample sizes (n < 10), conclusions about other ASMs (e.g. topiramate, lamotrigine and cannabidiol) are limited. Topiramate, an ASM broadly used in the US, was used infrequently in our cohort, likely

Table 4
Comparison of epilepsy and epilepsy-related parameters in deletion versus non-deletion group, p-values were adjusted using Holm correction, * statistically significant.

	Deletion	Non-deletion	Adjusted p-value
Epilepsy n = , (% of genetic subgroup)	64 (84%)	12 (48%)	p = 0.009*
NCSE n = , (% of genetic subgroup)	24 (31%)	2 (8%)	p = 0.128
Seizure frequency			
• Daily n = , (%)	8 (13%)	0	
• Weekly n = , (%)	7 (11%)	1 (8%)	
• Monthly n = , (%)	10 (16%)	3 (25%)	
• Every six months n = , (%)	19 (30%)	4 (33%)	
• Less often n = , (%)	19 (30%)	4 (33%)	
Age at epilepsy onset in years, mean [CI] (SD, range)	1.59 [1.195; 1.999] (± 1.583, 8.00)	3.18 [1.623; 4.738] (± 2.316, 8.00)	p = 0.128
Age at first medication in years, mean [CI] (SD, range)	1.60 [1.24; 1.976] (± 1.238, 6.00)	3.0 [1.123; 4.877] (± 1.789, 5.00)	p = 0.128
ASM total used during patient's lifetime, mean [CI] (SD, range)	2.19 [1.71; 2.66] (± 1.901, 11)	1.08 [0.39; 1.77] (± 1.084, 3)	p = 0.265
ASM currently in use, mean [CI], (SD, range)	1.3 [1.08; 1.51] (± 0.849, 3)	0.75 [0.27; 1.23] (± 0.754, 2)	p = 0.246
No medication currently in use n = , (% of genetic subgroup)	21 (27.6%)	17 (68%)	p = 0.009*
No medication currently in use in patients with epilepsy n = , (% of patients with epilepsy within genetic subgroup)	10 (15.6%)	5 (42%)	p = 0.265
Monotherapy n = , (% of patients with epilepsy within genetic subgroup)	31 (48.4%)	5 (42%)	p = 0.759
Polytherapy n = , (% of patients with epilepsy within genetic subgroup)	23 (35.9%)	2 (16%)	p = 0.634
Therapy-refractory epilepsy n = , (% of patients with epilepsy within genetic subgroup)	24 (37.5%)	2 (16%)	p = 0.606

due to its known side effects on cognition and appetite [14]. Lamotrigine - according to international guidelines first choice in treatment for focal and second choice for generalized epilepsy - was prescribed only in some cases. In a case series about five patients with refractory seizures lamotrigine showed convincing effects as add-on therapy [19]. Lamotrigine acts as a sodium channel blocker but also enhances GABAA β3 subunit expression in vitro [20]. It could be considered as add-on therapy in refractory cases in children with AS.

Growing interest in therapeutic cannabidiol was found in our cohort with nine patients receiving cannabidiol. Responder rate of 75% was comparable to the other prescribed ASMs. Cannabidiol is approved for treatment of therapy-refractory epilepsy in Dravet syndrome and Lennox-Gastaut syndrome and preclinical data suggest its potential in AS [21], [22], [23]. A case report on successful NCSE treatment with cannabidiol after valproate and levetiracetam failed is promising, but further clinical trials are needed to assess efficacy and safety in children with AS [24].

This study has several limitations. Data were collected retrospectively over a period spanning up to 16 years, which might undermine internal validity. Children with AS were not stratified by severity scores or neuropsychological testing results. Seizures were classified according to ILAE. Rate of unclassified seizure types were high, many patients showed multiple seizure types. The effects of individual ASMs could not be isolated and synergistic effects of polytherapy could not be evaluated. Ethosuximide demonstrated a convincing seizure reduction rate. However, whether this reflects its known efficacy in generalized absence seizures or indicates potential efficacy in generalized tonic-clonic seizures requires further investigation. Milder side effects were not recorded in a structured and complete way. In consequence, only rate of severe side effects leading to discontinuation of ASM were addressed in this study, underestimating overall side effect rate. As parents from various treatment centers across German-speaking countries presented their children in the Angelman Center Munich and reported on the use of ASMs in their children, data on dosages and serum levels were frequently missing and could not be reported in this clinical trial. As our clinical study has no prospective and longitudinal study design, lack of longitudinal data limits conclusions about the natural individual evolution of the disease. To address superiority of any ASM to recommend first- and second-line treatments in children with AS a controlled randomized study is needed.

5. Conclusion

In this study, we presented data from a cohort of 101 children with AS from German-speaking countries. Our findings demonstrate that therapy-refractory epilepsy remains a challenge in children with AS but appears to be less common than previously reported. This may reflect the benefits of optimized treatment strategies, combining established and newer ASMs. We could not confirm the high discontinuation rate of valproate, nor support the general skepticism of caregivers towards its use. We found convincing seizure reduction rates for valproate and ethosuximide, closely followed by levetiracetam. In future studies, we would like to address the question of whether the use of ethosuximide can be extended beyond the treatment of generalized absence seizures in individuals with AS. We recommend selecting antiseizure medication according to the individual, clinical indication, in accordance with international guidelines. Close monitoring of treatment response and tolerability, along with clear communication with caregivers about potential side effects is essential for maintaining compliance and optimizing outcome.

Declaration about ethics approval

The study was approved by the medical ethic committee of the Ludwig-Maximilian-University (23-511) and of the Technical University in Munich (2023-79-S-KK). For the study, written consent from all caregivers was obtained. A consent for publication of the caregivers was not required.

Consent for publication

All authors confirm that the article has not been published or submitted for publication elsewhere. All authors confirm that they have read and approved the final version of the manuscript. They confirm that they have read the guidelines about ethical publication of this journal and confirm that this report is in accordance with these guidelines.

Availabilty of data

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declaration about authors contribution

Lena Manssen: data collection, analysis and interpretation of results, writing of the manuscript.

Patrick Pfarrer: data collection, final approval of the manuscript.

Janina Gburek-Augustat: data collection, final approval of the manuscript.

Ilona Krey: data collection, final approval of the manuscript.

Leonie Nicolai: data collection, final approval of the manuscript.

Malin Zaddach: data collection, final approval of the manuscript.

Johannes R. Lemke: data collection, final approval of the manuscript.

Ingo Borggraefe: analysis and interpretation of results, editing text, final approval of the manuscript.

Christine Makowski: data collection, analysis and interpretation of results, editing text, final approval of the manuscript.

Funding

This publication was funded by the German parent association Angelman e. V.

Declaration about conflict of interests

The Angelman Center Munich is funded by the German parent association Angelman e. V. The Angelman Center Munich (Christine Makowski and Lena Manssen) is participating in clinical trials about Angelman Syndrome ("Phase 3 Efficacy and Safety Study of GTX-102 in Pediatric Subjects With AS (Aspire)" and "A Study to Investigate the Pharmacokinetics (PK) and Safety and to Provide Proof of Mechanism of Alogabat in Children and Adolescents Aged 5-17 Years With Angelman Syndrome (AS) With Deletion Genotype (Aldebaran)" and "REVEAL: A phase 3 study of ION582 in Angelman Syndrome"). The Angelman Center Munich receive fundings from the sponsors of these clinical trials. Christine Makowski and Lena Manssen do not receive personal salaries from the sponsors. The Angelman Center Leipzig is funded by the German parent association Angelman e. V. The Angelman Center Leipzig (Janina Gburek-Augustat) is participating in clinical trials about Angelman Syndrome (Phase 1: Study of Safety and Tolerability of GTX-102 in children with Angelman Syndrome, Phase 3: Long-term Extension of GTX-102 in Angelman Syndrome and Phase 3: Study of GTX-102 in Pediatric Subjects With AS (Aspire)). The Angelman Center Leipzig receives fundings from the sponsors of these clinical trials. Janina Gburek-Augustat does not receive personal salaries from the sponsors.

Acknowledgement

We would like to thank the German parent association Angelman e. V. for their great support.

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List of Abbreviations:

AS: Angelman Syndrome
ASM: Anti-seizure medication
ACM: Angelman Center Munich
CI: 95% Confidence interval for mean
CSWS: continuous spike-wave during slow-wave sleep
GABA: Gamma-aminobutyric acid
NCSE: Non-convulsive status epilepticus
SD: Standard deviation
UPD: Uniparental paternal disomy
US: United States of America