

UC Davis
Pediatrics

Title

The Long-term Characterization of Behavior Phenotypes in Children with Seizures over 36 months

Permalink

<https://escholarship.org/uc/item/5kq2h60q>

Authors

Morales, Karina

Harvey, Danielle

Dunn, David

et al.

Publication Date

2024-04-01

Data Availability

The data associated with this publication are not available for this reason: NA

The Long-term Characterization of Behavior Phenotypes in Children with Seizures over 36 months



Karina Morales BS, Danielle Harvey PhD, David Dunn MD, Jana Jones PhD, Anna Byars PhD, Joan Austin PhD, Bruce Hermann PhD, Temitayo Oyegbile-Chidi MD, PhD

Departments of Neurology and Public Health Sciences, University of California Davis, Departments of Psychiatry and Neurology, Indiana University, Department of Neurology and Public Health, University of Wisconsin, Department of Pediatrics, Cincinnati Children's Hospital

Introduction

Previous studies have documented that children with newly diagnosed epilepsy often exhibit various behavioral comorbidities such as anxiety, depression, aggressive behavior, and attention that affect many aspects of their life including academic performance. Furthermore, these studies have identified distinct behavioral phenotype groups but have not investigated the trajectory of each of these groups over time. In this study we explore the presence and trajectory of behavior and academic performance in children with newly diagnosed epilepsy and their siblings over a 36-month period.

Methods

312 children diagnosed with epilepsy were enrolled within 6 weeks of experiencing their first recognized seizure and the control group consisted of 223 healthy siblings. Each participant underwent assessments using the Child Behavior Checklist (CBCL) and Teachers Child Behavior Checklist (TRF) at three time points: baseline (B) which occurred within 6 weeks of the first recognized seizure, 18 months later (M18), and 36 months later (M36). Additionally, children with epilepsy completed the Multiple Affect Adjective Check List (MAACL) to evaluate anxiety and overall psychological well-being. Academic achievement was evaluated for all children and sibling controls using three subtests of the Woodcock-Johnson Revised Tests of Achievement. Seizure characteristics were evaluated by collecting data on clinical epilepsy features, including age of onset, seizure syndrome, seizure frequency, and antiseizure medication usage, as well as the presence or absence of abnormalities in magnetic resonance imaging (MRI) and electroencephalography (EEG) for children diagnosed with epilepsy. Additionally, sociodemographic information collected at baseline, such as the child's self-identified race, mother's highest level of education, household income, and parental marital status, was combined to create a socio-disadvantage index.

Results

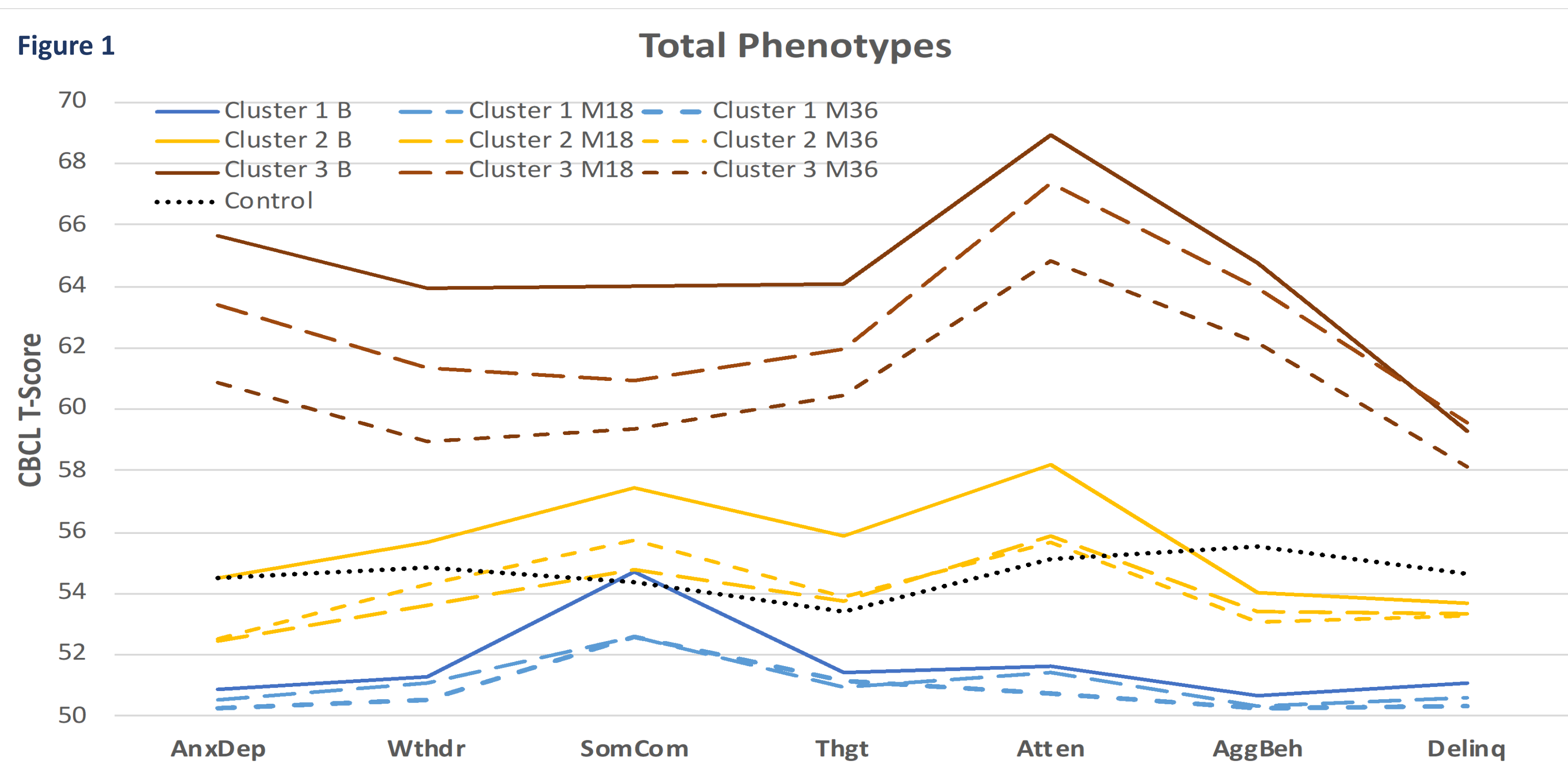


Figure 1. Phenotypes by Behavioral Domains (Parents - CBCL). Cluster 3 exhibited the highest levels of behavior problems in all behavior domains assessing (anxiety/depression (AnxDep), withdrawal (Wthdr), somatic complaints (SomCom), thought problems (Thgt), attention problems (Atten), aggressive behavior (AggBeh), delinquent behavior (Delinq)) consistently over 36 months compared to Clusters 1 and 2.

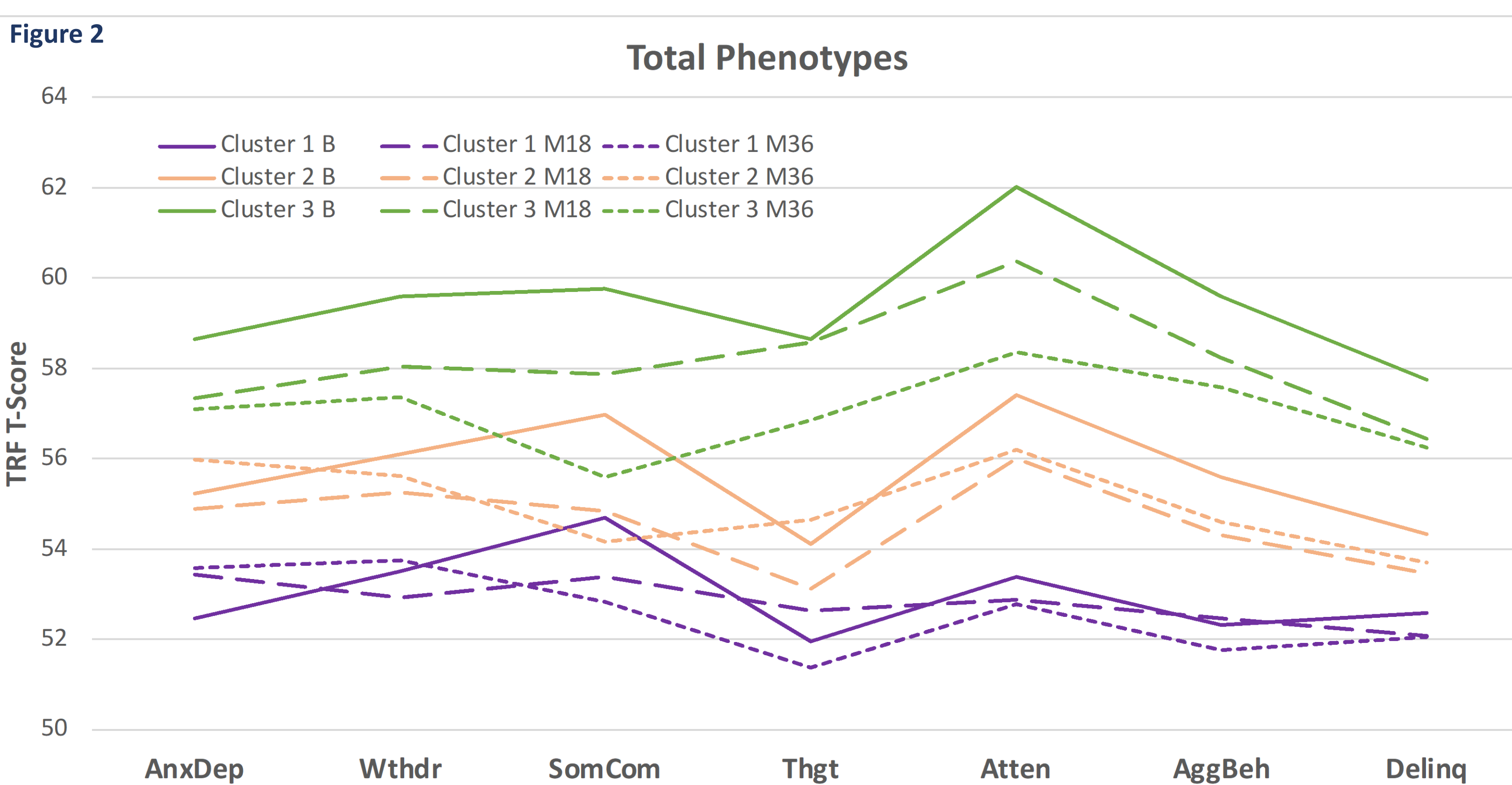


Figure 2. Phenotypes by Behavioral Domains (Teachers - TRF). Cluster 3 exhibited the highest levels of behavior problems in all behavior domains assessing (anxiety/depression, withdrawal, somatic complaints, thought problems, attention problems, aggressive behavior, delinquent behavior) consistently over 36 months compared to Clusters 1 and 2.

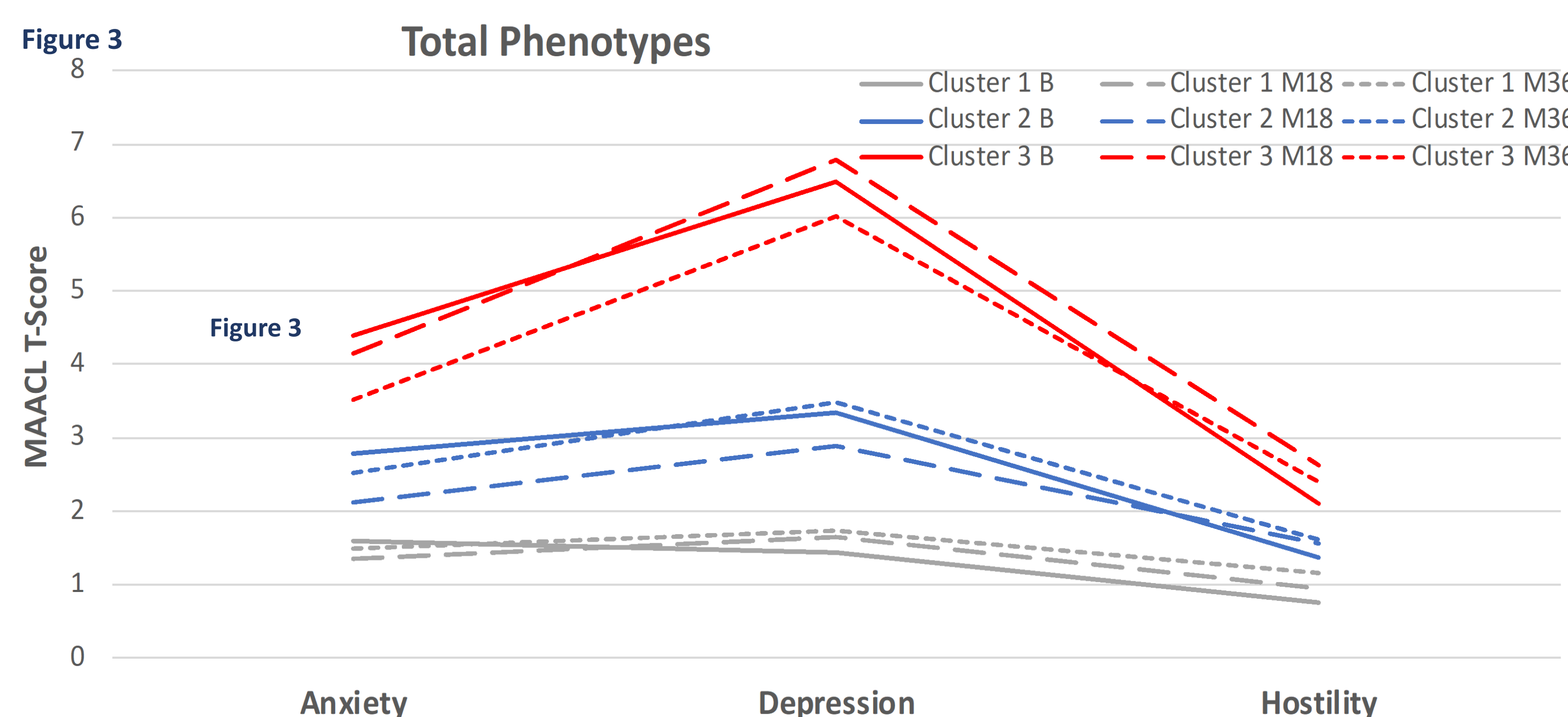


Figure 3. Phenotypes by Behavioral Domains (Child -MAACL): Cluster 3 exhibited the highest levels of behavior problems in all behavior domains assessing anxiety, depression, and hostility consistently over 36 months compared to Clusters 1 and 2.

Behavior phenotypes – 36 Months Later	Cluster 1	Cluster 2	Cluster 3	F	P
<i>Internalizing Phenotype</i>					
Global Intellectual Ability	106.10 (1.80)	100.24 (1.50)*	98.15 (2.26)*	4.69	0.010
Academic Performance: WJ-LET	103.07 (1.94)	100.36 (1.63)	97.09 (2.45)	1.84	0.161
WJ-CALC	101.25 (2.56)	96.04 (2.15)	90.30 (3.24)*	3.58	0.03
WJ-DICT	93.92 (1.74)	89.22 (1.46)	84.94 (2.20)*	5.32	0.006
<i>Externalizing Phenotype</i>					
Global Intellectual Ability	107.38 (1.79)	100.87 (1.44)*	94.73 (2.26)**	9.98	<.001
WJ-LET	104.95 (1.93)	100.32 (1.57)	94.09 (2.46)*	6.03	0.003
WJ-CALC	103.29 (2.56)	95.57 (2.08)*	88.13 (3.26)*	6.90	0.001
WJ-DICT	94.95 (1.75)	88.89 (1.42)*	84.09 (2.23)*	7.83	0.001
<i>Total Phenotype</i>					
Global Intellectual Ability	107.73 (2.05)	101.87 (1.42)*	95.69 (2.00)**	8.84	<.001
WJ-LET	104.00 (2.23)	101.47 (1.55)*	95.48 (2.19)*	4.06	0.019
WJ-CALC	104.05 (2.93)	96.57 (2.05)*	89.33 (2.88)*	6.42	0.002
WJ-DICT	94.66 (2.00)	90.30 (1.40)*	84.43 (1.97)*	6.72	0.001

Table 1. Academic performance and global intellectual ability by internalizing, externalizing and total behavioral phenotypes, 36 months later. Clusters 1 of internalizing, externalizing and total behavioral phenotypes all performed with the highest scores compared to Clusters 3 consistently, and compared to Clusters 2 frequently.

Externalizing Phenotype Predictors	Standardized β Coefficient	S.E.	p	95% CI Lower	95% CI Upper
<i>Cluster 1 vs Cluster 2</i>					
Age of Onset of Seizures	-.047	.054	.387	.859	1.061
Number of seizures	.001	.001	.101	.997	1.000
Generalized vs Focal Seizures	-1.013	.327	.002	.191	.689
Anti-seizure medications at baseline (yes or no)	.012	.037	.345	-.215	.263
Sociodemographic Disadvantage Score	-.310	.145	.033	.552	.975
<i>Cluster 1 vs Cluster 3</i>					
Age of Onset of Seizures	-.064	.068	.344	.821	1.071
Number of seizures	-.002	.001	.104	.996	1.000
Generalized vs Focal Seizures	-.795	.397	.045	.207	.983
Anti-seizure medications at baseline (yes or no)	.086	.022	.399	.029	.120
Sociodemographic Disadvantage Score	-.664	.170	<.001	.369	.718

Table 2. Predictors of the Externalizing Phenotype Clusters: Children in Cluster 2 and 3 were more likely to have a generalized seizure type and more likely to come from a more disadvantaged sociodemographic background compared to Cluster 1.

Conclusions

This study reveals varied latent behavioral trajectory patterns occurring over a 36-month period in children who develop new-onset epilepsy. As these children exhibited different behavioral trajectory patterns, there are consistent and measurable changes observed in both their cognitive functioning and academic performance throughout the 36-month period. It was seen that not only were disease-related factors influencing the outcomes of these distinct behavioral phenotypic patterns but also social related factors were a contributing factor to the behavioral phenotypic group outcomes that were observed. Future investigations may shed light on whether delivering early targeted interventions can alter these behavioral phenotypic groups to enhance behavioral and cognitive outcomes in children with epilepsy.

References

- Oyegbile-Chidi T, Harvey D, Eisner J, et al. The Relationship Between Sleep, Cognition and Behavior in Children With Newly-Diagnosed Epilepsy Over 36 Months. *Front Neuro.* 2022;13:903137. doi:10.3389/fneur.2022.903137
- Hermann B, Jones J, Sheth R, Dow C, Koehn M, Seidenberg M. Children with new-onset epilepsy: neuropsychological status and brain structure. *Brain J Neuro.* 2006;129(Pt 10):2609-2619. doi:10.1093/brain/awl196
- Vinti V, Dell'Isola GB, Tascini G, Mencaroni E, Cara GD, Striano P, et al. Temporal Lobe Epilepsy and Psychiatric Comorbidity. *Front Neuro.* 2021;12:775781.
- Hunter MB, Yoong M, Sumpter RE, Verity K, Shetty J, McLellan A, et al. Neurobehavioral problems in children with early-onset epilepsy: A population-based study. *Epilepsy Behav.* 2019;93:87-93.
- Fastenau PS, Johnson CS, Perkins SM, Byars AW, deGrauw TJ, Austin JK, et al. Neuropsychological status at seizure onset in children: risk factors for early cognitive deficits. *Neurology.* 2009;73(7):526-34.
- Oostrom KJ, Smeets-Schouten A, Kruitwagen CL, Peters AC, Jennekens-Schinkel A, Childhood DSGoEi. Not only a matter of epilepsy: early problems of cognition and behavior in children with "epilepsy only"--a prospective, longitudinal, controlled study starting at diagnosis. *Pediatrics.* 2003;112(6 Pt 1):1338-44.
- Oostrom KJ, van Teeseling H, Smeets-Schouten A, Peters AC, Jennekens-Schinkel A, (DuSECh) DSoEiC. Three to four years after diagnosis: cognition and behaviour in children with 'epilepsy only'. A prospective, controlled study. *Brain.* 2005;128(Pt 7):1546-55.

Acknowledgments

This research was supported by the National Institute of Neurological Disorders and Stroke (NS22416, J. Austin, P.I. and NS131574, T. Oyegbile-Chidi, P.I.). The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.