

Supplementary Materials

Supplementary Table 1: Seizure Frequencies

	T-RTT (N= 504)		A-RTT (N=38)		N-RTT (N=42)	
	Freq. (n)	%	Freq. (n)	%	Freq. (n)	%
Absent	224	44.4%	25	65.8 %	26	61.9 %
< Monthly	94	18.7%	5	13.2 %	7	16.7 %
< Weekly to monthly	57	11.3%	2	5.3 %	1	2.4 %
Weekly	50	9.9%	2	5.3%	1	2.4 %
> Weekly	26	5.2%	3	7.9 %	0	0 %
Daily	53	10.5%	1	2.6 %	7	16.7 %

	CDD (N=49)		FOXG1 (N=37)		MDD (N=42)	
	Freq. (n)	%	Freq. (n)	%	Freq. (n)	%
Absent	6	12.2%	16	43.2%	25	59.5%
< Monthly	2	4.1%	10	27.0%	3	7.1%
< Weekly to monthly	1	2.0%	5	13.5%	2	4.8%
Weekly	5	10.2%	4	10.8%	1	2.4%
> Weekly	3	6.1%	1	2.7%	2	4.8%
Daily	32	65.3%	1	2.7%	9	21.4%

Supplementary Table 2: Investigator Impressions of Reported Seizures

	T-RTT (N= 535)		A-RTT (N= 39)		N-RTT (N=44)	
	Freq. (n)	Percent of total participants	Freq. (n)	Percent of total participants	Freq. (n)	Percent of total participants
Absence	14	2.6%	2	5.1 %	1	2.3 %
Atonic	25	4.7%	2	5.1 %	2	4.6 %
Complex Partial	73	13.6%	5	12.8 %	5	11.4 %
Generalized	144	26.9%	7	17.9 %	8	18.2 %
Infantile Spasm	2	0.4%	0	0 %	1	2.3 %
Myoclonic	12	2.2%	0	0%	0	0 %
Not A Seizure	68	12.7%	4	10.3 %	11	26.5 %
Partial	45	8.4%	1	2.3 %	0	0 %
Rett Spell	86	16.1%	4	10.3 %	0	0 %
Tonic-Clonic	81	15.1%	3	7.7 %	4	9.09 %

	CDD (N=53)		FOXG1 (N=43)		MDD (N=49)	
	Freq. (n)	Percent of total participants	Freq. (n)	Percent of total participants	Freq. (n)	Percent of total participants
Absence	2	3.8%	2	4.7%	5	10.2%
Atonic	8	15.1%	1	2.3%	7	14.3%
Complex Partial	6	11.3%	11	25.6%	6	12.2%
Generalized	22	41.5%	10	23.3%	11	22.5%
Infantile Spasm	24	45.3%	2	4.7%	0	0.0%
Myoclonic	16	30.2%	1	2.3%	4	8.2%
Not A Seizure	4	7.6%	7	16.3%	13	26.5%
Partial	5	9.4%	4	9.3%	1	2.0%
Rett Spell	2	3.8%	0	0.0%	0	0.0%
Tonic-Clonic	21	39.6%	8	18.6%	11	22.5%

Supplementary Table 3: Association between Clinical Variables and Outcomes

Association between HC Z-Score and Age of Seizure Onset (months)							
	Linear Regression				Spearman's Rank		
	N	Model p-value	R ²	Coefficient Independent	95% CI	Correlation	P value
T-RTT	247	0.288	0.0046	-3.986	-11.11, 3.314	-0.0385	0.547
A-RTT	15	0.949	0.0003	-0.605	-20.49, 19.28	0.0286	0.919
N-RTT	13	0.983	0.0000	0.130	-12.87, 13.134	0.0000	1.0000
CDD	49	0.333	0.0199	0.704	-0.744, 2.153	-0.0749	0.609
FOXG1	29	0.717	0.0049	-1.243	-8.21, 5.72	-0.244	0.203
MDD	22	0.0097	0.290	21.307	5.756, 36.858	0.700	0.0003
Association between Clinical Severity Scale (minus epilepsy sub-score) and Age of Seizure Onset (months)							
	Linear Regression				Spearman's Rank		
	N	Model p-value	R ²	Coefficient Independent	95% CI	Correlation	P value
T-RTT	242	0.967	<0.0001	0.0287	-1.32, 1.38	-0.0111	0.863
A-RTT	16	0.987	<0.0001	-0.019	-2.37, 2.34	-0.247	0.356
N-RTT	13	0.0501	0.3054	-1.805	-3.61, 0.001	-0.6997	0.008
CDD	45	0.0024	0.195	-0.449	-0.729, -0.168	-0.165	0.280
FOXG1	24	0.469	0.0241	-0.641	-2.45, 1.16	-0.246	0.247
MDD	20	0.242	0.0503	-2.118	-6.68, 2.43	-0.294	0.209
Association between Age of Seizure Onset and Age of Regression							
	Linear Regression				Spearman's Rank		
	N	Model p-value	R ²	Coefficient Independent	95% CI	Correlation	P value

T-RTT	246	0.941	<0.0001	0.000507	-0.0129, 0.0139	0.029	0.651
A-RTT	14	0.005	0.4969	0.222	0.081, 0.362	0.386	0.173
N-RTT	5	0.432	0.2145	-4.357	-19.677, 10.063	-0.100	0.873
CDD	17	0.662	0.0131	-1.032	-5.96, 3.89	-0.0103	0.959
FOXG1	13	0.655	0.0188	0.0883	-0.335, 0.512	0.142	0.643
MDD	9	0.990	<0.0001	-0.00244	-0.440, 0.434	0.252	0.513

Supplementary Table 4: Clinical Severity Scale Breakdown

Manifestation	Definition
Historical Items	
Age of onset of regression	0: No Regression 1: > 30 months 2: 18 months to 30 months 3: 12 months to < 18 months 4: 6 months to < 12 months 5: < 6 months
Onset of stereotypies	0: ≥ 10 years or no stereotypies 1: 36 months to < 10 years 2: 18 to < 36 months 3: 12 to < 18 months 4: < 12 months
Head growth	0: None to minimal deceleration (0-1 centile) 1: Deceleration > 2 centiles, OFC > 10th after 24 months 2: 2nd - 10th centile after 24 months 3: 2nd - 10th centile before 24 months 4: < 2nd centile by 24 months
Growth	
Somatic growth at this visit	0: No growth failure (26th - 50th % or above) 1: Decrease in BMI (11th - 25th %) 2: Decrease in BMI (5th - 10th %) 3: Decrease in BMI (< 5th %) 4: Decrease in BMI (< < 5th %)
Motor	

Independent sitting at this visit by exam	<ul style="list-style-type: none"> 0: Sits alone acquired < 8 months 1: Sit with delayed acquisition > 8 months 2: Sit with delayed acquisition > 18 months 3: Sit with delayed acquisition > 30 months 4: Lost 5: Never acquired
Ambulation at this visit by exam	<ul style="list-style-type: none"> 0: Acquired < 18 months / Apraxic gait 1: 18 months ≤ walks alone ≤ 30 months 2: > 30 months walks alone 3: > 50 months walks with help 4: Lost 5: Never acquired
Hand use	<ul style="list-style-type: none"> 0: Acquired & conserved 1: Holding of objects acquired on time (by 6-8 months) and partially conserved 2: Holding of objects acquired late (> 10 months) and partially conserved 3: Holding of objects acquired and lost all acquisitions (except, for example, scratching, rubbing nose) 4: Never acquired
Scoliosis	<ul style="list-style-type: none"> 0: None 1: 1° to < 20° 2: 20° to < 40° 3: 40° to < 60° 4: ≥ 60° 5: Surgery
Communication	
Language at this visit by exam	<ul style="list-style-type: none"> 0: Preserved, contextual 1: Short phrases only 2: Single words 3: Vocalization, babbling 4: Screaming, no utterances
Nonverbal communication at this visit by exam	<ul style="list-style-type: none"> 0: Preserved and propositive (points consistently with finger or eyes) 1: Good eye contact maintained (≥30 seconds) 2: Intermittent eye contact (5 seconds to < 30 seconds) 3: Infrequent eye contact (< 5 seconds) 4: Lost and not regained 5: None
Rett Behaviors	

Respiratory dysfunction at this visit by exam	<p>0: None</p> <p>1: Minimal hyperventilation and/or apnea (< 10% of time)</p> <p>2: Intermittent hyperventilation and/or apnea (50% of time)</p> <p>3: Constant hyperventilation and/or apnea without cyanosis (100% of time)</p> <p>4: Constant hyperventilation and/or apnea with cyanosis</p>
Autonomic symptoms at this visit by exam	<p>0: None</p> <p>1: Pink but cool</p> <p>2: Mottled and cold</p> <p>3: Blue-purple and cold hands or feet</p> <p>4: Blue-purple and cold hands and feet</p>
Epilepsy/Seizures at this visit	<p>0: Absent</p> <p>1: < Monthly</p> <p>2: < Weekly to monthly</p> <p>3: Weekly</p> <p>4: More than weekly</p> <p>5: Daily (intractable)</p>