

Evaluating ASD Symptomatology and Developmental Trajectories of Social Motivation in GRIN2B

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Background

- The GRIN2B gene is responsible for encoding subunits of neurotransmitter receptors that are important for brain development¹.
- Disruptive mutations of GRIN2B have been associated with autism spectrum disorder (ASD)²⁻³.
- Unlike ASD, individuals with disruptive *GRIN2B* mutations have recently been characterized with strengths in social motivation⁴.
- This is important to further understand as it may help identify differences in brain biomarkers of ASD responsible for different phenotypic characteristics.

Objectives

- To better understand how social motivation varies among GRIN2B and idiopathic autistic children
- To examine if specific social motivation strengths vary across age and IQ

Method

- Social motivation was measured using the Social Responsiveness Scale-2 (SRS-2) across two different groups: (1) **children with disruptive GRIN2B mutations** (GRIN2B; $n=40$), and (2) **autistic children with no likely gene disrupting mutation** (NLGDM; $n=2,665$).
- Linear models were used to compare groups and evaluate influence of age and IQ on:
 - (1) Full social motivation T-scores
 - (2) Exploratory analysis of individual social motivation items.

	Age (SD)	Sex (M/F)	ASD Diagnosis (Y/N)	NVIQ (SD)	SRS-2 Motivation (SD)
GRIN2B (N = 40)	8.45 (4.64)	20/20	11/8 (n = 19)	42.00(15.11) (n = 16)	63.43(9.89)
NLGDM (N = 2665)	9.07(3.56) (n = 2568)	2323/34	2665/0	85.40(26.19) (n = 2568)	68.37 (11.98)

Table 1. Demographics for samples. Note: n's indicate a subset sample with available data.

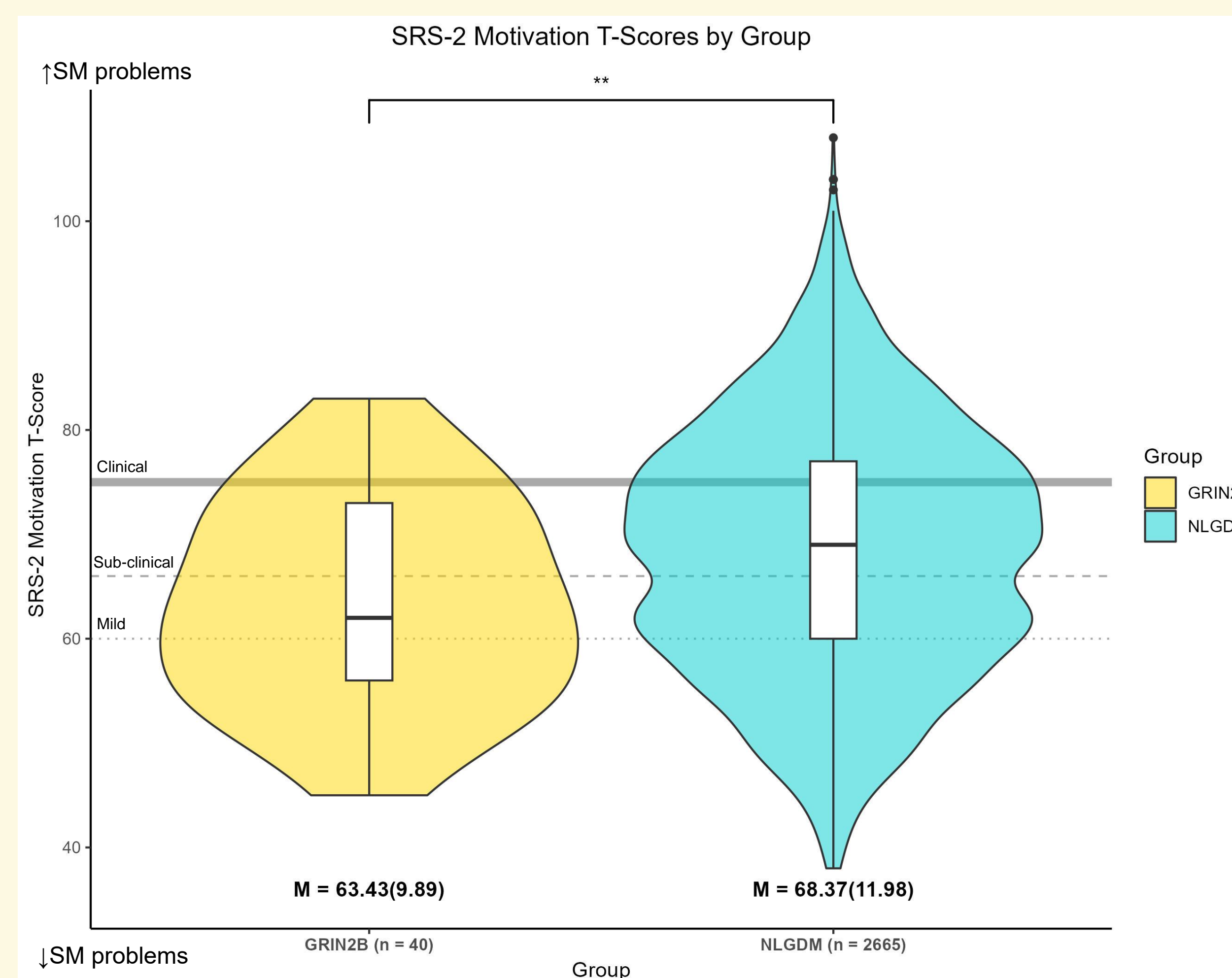


Figure 1. Violin plot of group differences on the SRS-2 motivation subscale. Note: ** indicates significance: $F(1,2703) = 6.74, p < 0.001$

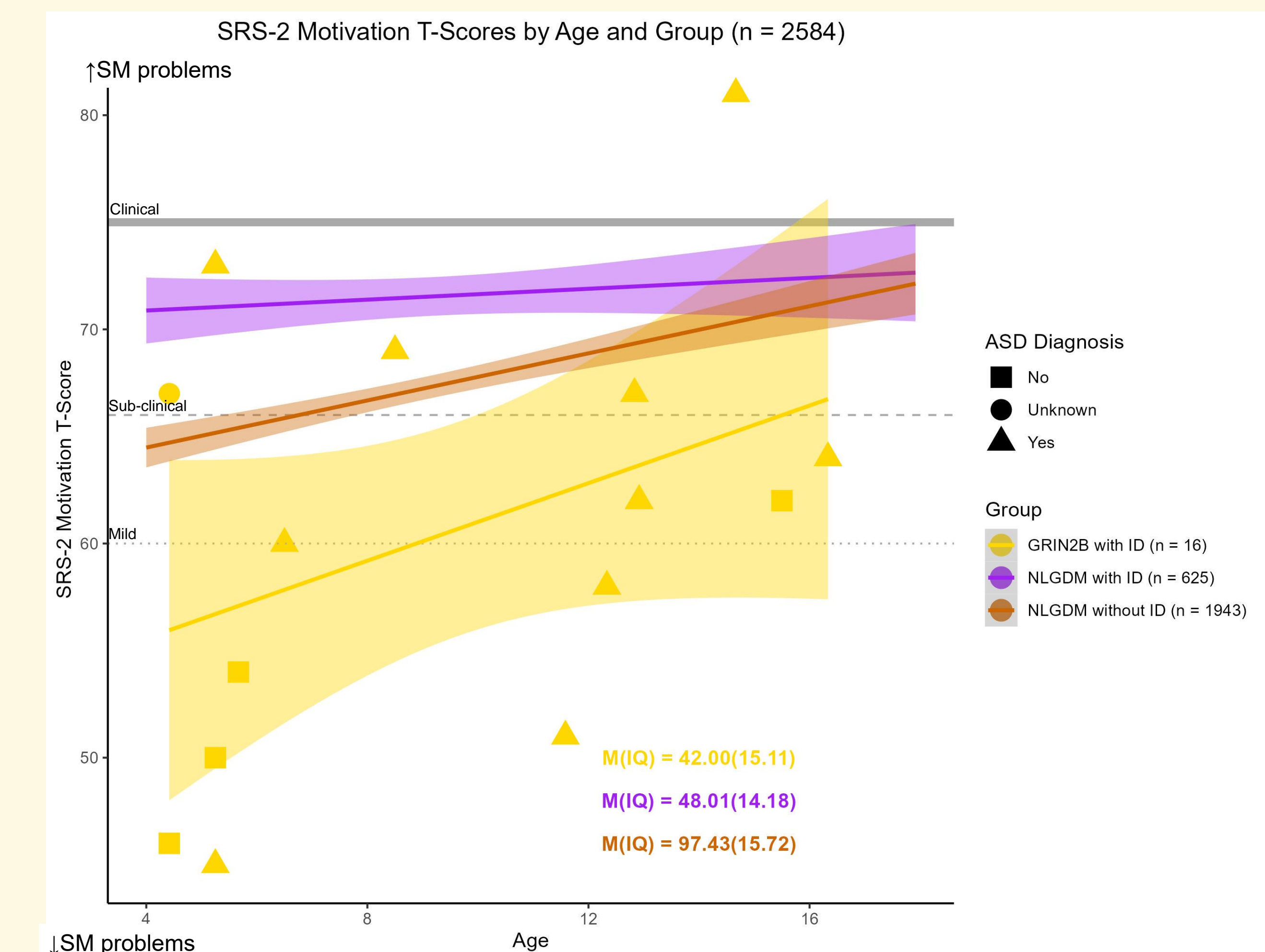


Figure 2. Plot of group differences on the SRS-2 motivation subscale based on age, genetic group, and IQ group. Note: the multiple linear regression model was significant ($R^2 = 0.05, F(5,2578) = 24.96, p < 0.001$) where genetic group ($\beta_1 = 11.43, p < 0.001$), IQ group ($\beta_2 = -4.01, p < 0.001$), and IQ Group x Age ($\beta_6 = 0.42, p = 0.004$) were significant terms.

Children with disruptive *GRIN2B* mutations are more socially motivated than idiopathic autistic children regardless of age and IQ.

Item	Reverse Coded	Motivation Prompt	Genetic Group Term p -value (GRIN2B, NLGDM)	IQ Group Term p -value (ID, No ID)	Age Term p -value
1	No	Seems much more fidgety in social situations than when alone	0.163	<0.001	0.091
3	Yes	Seems self-confident when interacting with others	0.023	<0.001	0.79
6	No	Would rather be alone than with others	<0.001	0.071	0.785
9	No	Clings to adults seems too dependent on them	0.805	<0.001	0.15
11	Yes	Has good self-confidence	0.018	<0.001	0.728
23	No	Does not join group activities unless told to do so	0.001	<0.001	0.073
27	No	Avoids starting social interactions with peers or adults	<0.001	<0.001	0.541
34	No	Avoids people who want to be emotionally close to him or her	0.047	0.006	0.956
43	Yes	Separates easily from caregivers	<0.001	0.005	0.699
64	No	Is too tense in social settings	0.082	0.928	0.882
65	No	Stares or gazes off into space	0.419	<0.001	0.258

Table 2. SRS-2 motivation subscale item level data by genetic group, IQ group, and age. Note: Yellow indicates < mean item score for GRIN2B, Turquoise indicates < mean item score for NLGDM group, Purple indicates < mean item score for group with ID, and Orange indicates < mean item score for group without ID.



Brain Research Across Development Laboratory
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Funding: GRIN2B Foundation, Simons Foundation, NICHD to Dr. Hudac