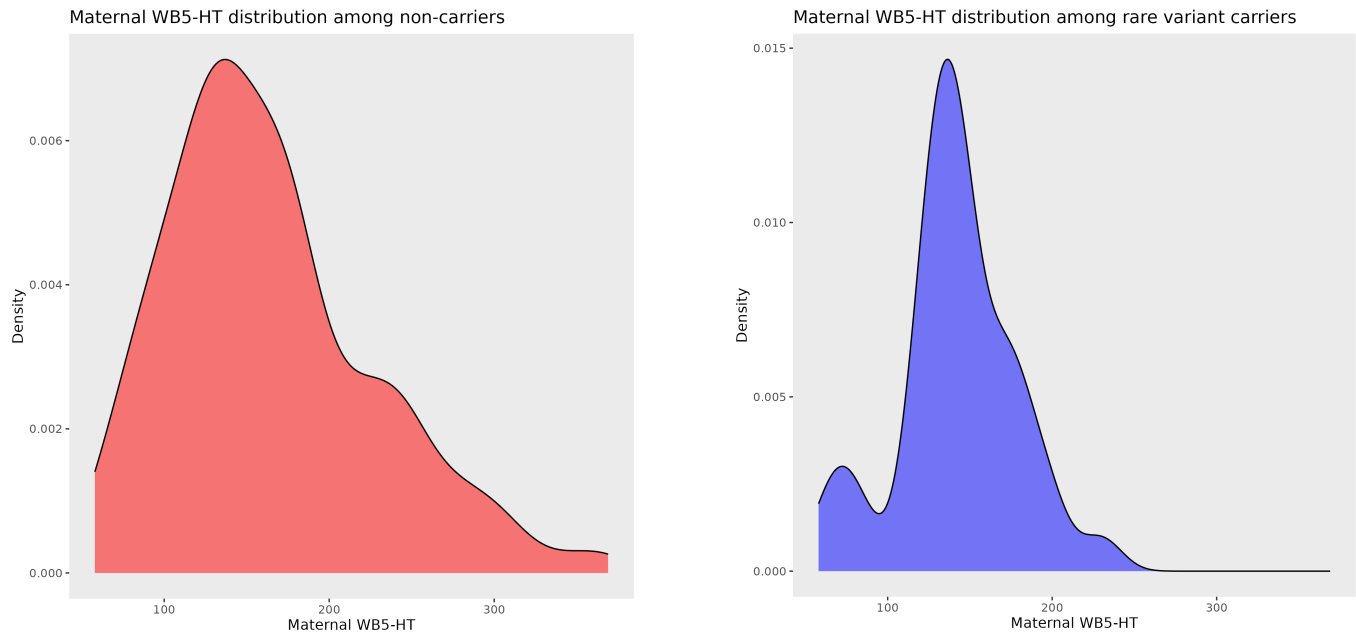


Supplemental Figure 1

We calculated the skewness of the maternal WB5-HT distribution in each group (n = 35 probands with a rare variant and n = 276 without) using the standard formula

$$\frac{n}{(n-1)(n-2)} \sum \left(\frac{x_i - \bar{x}}{s} \right)^3$$
. Non-carriers showed a pronounced right skew (0.80) and rare variant carriers showed a slight left skew (-0.10).

To assess whether skew in non-carriers was significantly greater, we used a resampling method to generate 10,000 bootstrap samples for each group, calculating skewness for each sample. We then calculated the 95% confidence interval (CI) of the skewness distribution for each group (rare variant carriers, 95% CI -0.82 – 0.70; non-carriers, 95% CI 0.53 – 1.05). Although these CIs overlap, the lower bound of the CI for rare variant carriers was smaller than the upper bound of the CI for non-carriers, supporting our directional hypothesis that maternal WB5-HT skewness was greater among non-carriers than carriers.



Supplemental Table 1

Genes and CNVs included in the rare variant group.

Gene	Inheritance*	CNV	Type	Inheritance*
ABCA2		chr1:93321461-113327865	Deletion	
ABCA8		chr15:21168391-26113882	Duplication	Maternal
ADCY5		chr15:21235224-26144736	Duplication	
AGO2		chr16:15387380-18085470	Duplication	
AMIGO1		chr16:29470951-30059319	Deletion	
ANK2		chr16:29531748-30107306	Deletion	
ARHGEF16		chr16:29664595-30188229	Deletion	
BRAT1		chr16:6296188-6309514	Deletion	Paternal
BRD4		chr16:8828382-9147487	Duplication	
C9orf57		chr17:6058839-7267958	Duplication	
CACNA1B		chr2:103264154-108718935	Deletion	
CCDC37		chr2:61390488-61873147	Duplication	
CD82		chr3:197219312-198851029	Deletion	
CELF1		chr3:67223272-72356021	Deletion	
CHAT		chr3:67495701-67609694	Deletion	
CHD8		chr7:73331560-74719039	Duplication	
CLCNKB		chrX:1-154900000	Duplication	
COG3				
CPD				
CS				
DHX58				
DLX6				
DYRK1A				
ECEL1				
ELTD1				
EPRS				
FOXP1				
GFRA1				
GLP1R				
GNA11				
GRIK2				
HDAC1				
IL17RA				
ITGA5				
ITPR3				
KDM5B				
KIAA0100				
KIAA1244				
KLHL26				
KMT2B				
KMT2C				
LMTK3				
MAP3K13				
MUC22				
MYH7B				
NF1				
NR2F1				
NUP214				
PAPLN				
PASK				
PLEC				
PLEKHG2				
POLQ				
PPP1R9B				
PQB1	Maternal			
PRKAA1				
RANBP3				
RARA				
REN				
RIMBP3				
RSPH6A				
SCN2A				
SCN2A				
SPEN				
SPG7				
SPTBN1				
SRSF7				
SYNGAP1				
TM4SF18				
TMEM214				
TNPO3				
TTC16				
UGT2B10				
VX2				
VWF				
WIPF1				
ZEB2				
ZFYVE26				
ZNF772				

* All variants were de novo except where otherwise indicated.

Supplemental Table 2

Characteristic	Demographic characteristics of study participants by rare variant carrier status			p-value ²
	Overall, N = 276 ¹	Non-carrier, N = 241 ¹	Carrier, N = 35 ¹	
Age in years	9.42 (4.17)	9.43 (4.12)	9.38 (4.52)	0.69
Study site				0.34
UIC	161 (58%)	138 (57%)	23 (66%)	
Vanderbilt	115 (42%)	103 (43%)	12 (34%)	
Sex				>0.99
Male	229 (86%)	199 (86%)	30 (88%)	
Female	36 (14%)	32 (14%)	4 (12%)	
Race				0.23
Black	33 (13%)	32 (14%)	1 (2.9%)	
White	205 (78%)	176 (77%)	29 (85%)	
Asian	9 (3.4%)	8 (3.5%)	1 (2.9%)	
More than one race	16 (6.1%)	13 (5.7%)	3 (8.8%)	
Ethnicity				0.093
Latine	33 (12%)	32 (14%)	1 (2.9%)	
Non-Latine	231 (88%)	198 (86%)	33 (97%)	

¹ Mean (SD); n (%)

² Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test

Sex as a Biological Variable: Our study's examination of both maternal and paternal WB5-HT is based on biological sex. Biological sex was not otherwise incorporated into our analyses, but, as shown in the table above, sex data were collected from all participants. Our study, consistent with the demographics of autism, included more male than female participants. The sample size of females in the rare variant carrier group was too small to support a sex-specific analysis.

Supplemental Table 3

Maternal WB5-HT by quantile for those probands with a rare variant vs. those without								
QU	<i>N</i> (no variant)	<i>N</i> (variant)	Median (no variant)	Median (variant)	Difference	CI Lower	CI Upper	<i>Adj. p</i>
0.10	241	35	91.04	90.58	0.46	-31.70	23.63	0.956
0.25	241	35	120.51	125.50	-5.00	-19.76	20.65	0.534
0.50	241	35	153.24	140.21	13.03	-5.04	27.76	0.065
0.75	241	35	197.51	164.44	33.07	5.55	64.40	0.002
0.90	241	35	253.23	188.62	64.60	26.65	101.44	0.000