

Article

Sex-dependent social and repetitive behavior and neurochemical profile in mouse model of autism spectrum disorder

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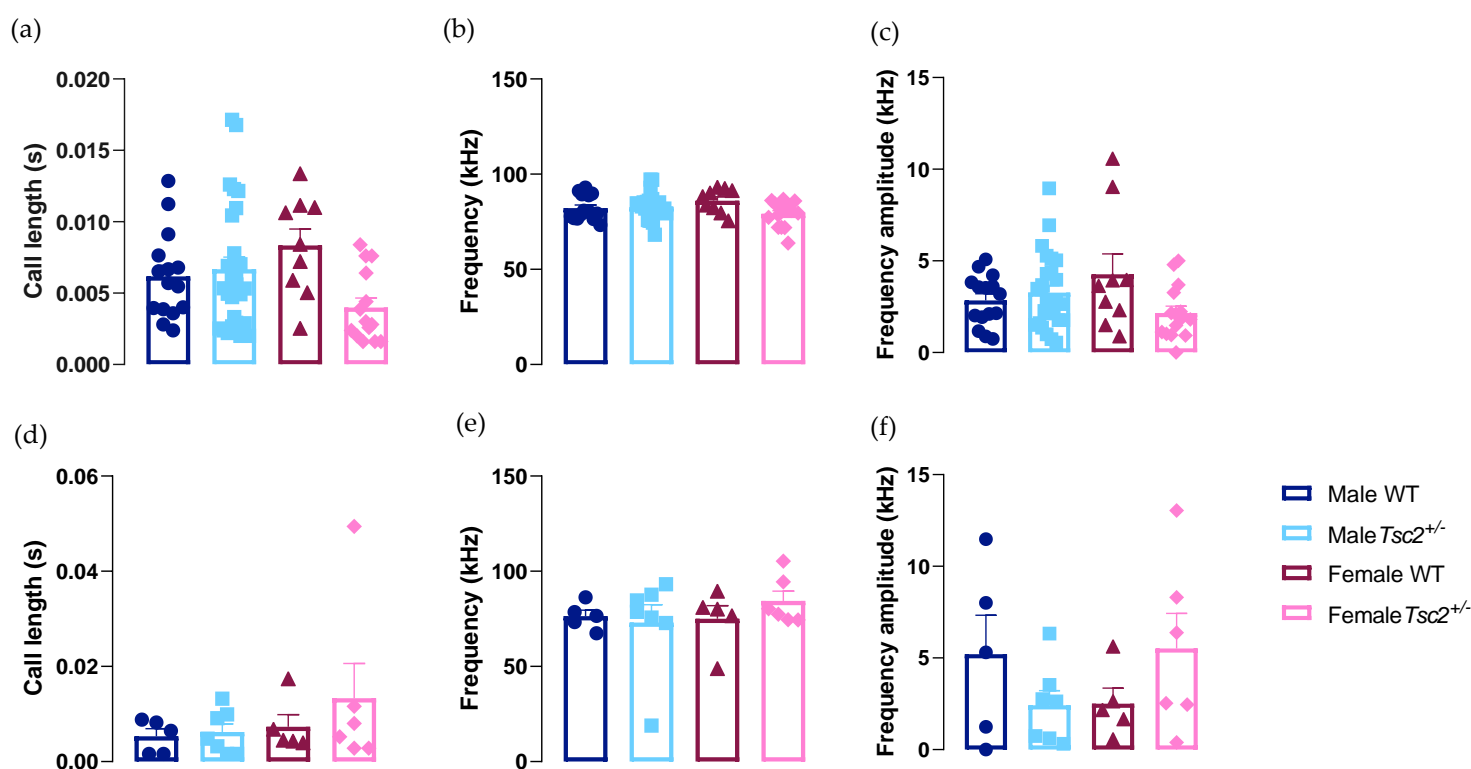
Supplementary Table S1. ¹H-magnetic resonance spectroscopy (MRS) analysis of cortical neurochemical profile.

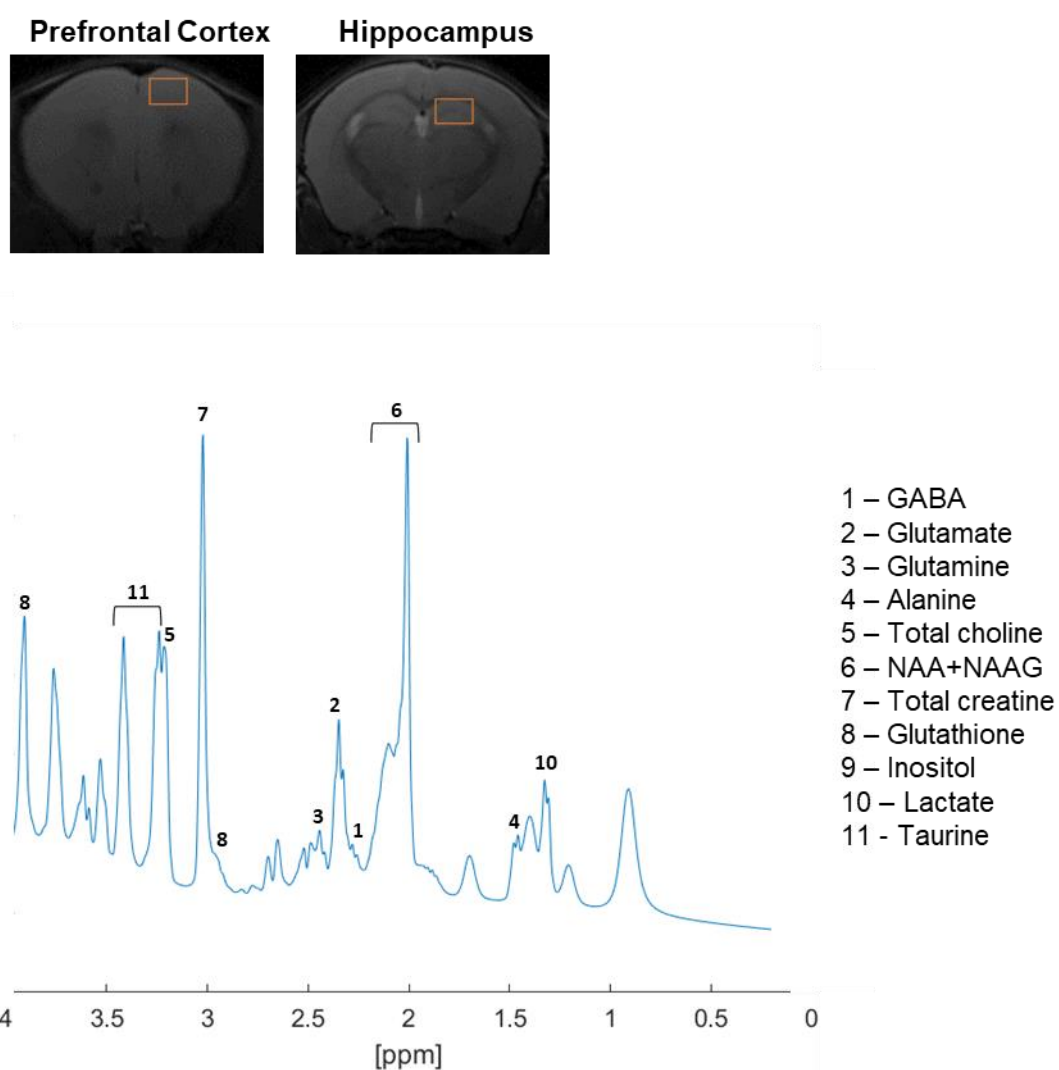
Brain metabolite	Prefrontal cortex			
	Male		Female	
	WT	<i>Tsc2</i> ^{+/-}	WT	<i>Tsc2</i> ^{+/-}
GABA	2.64 ± 0.1132	2.60 ± 0.1167	3.38 ± 0.2118	2.57 ± 0.1685[#]
Glutamate	12.14 ± 0.3246	12.54 ± 0.5710	10.66 ± 0.7597	13.43 ± 0.5382[#]
Glutamine	4.57 ± 0.2307	5.09 ± 0.4838	4.27 ± 0.3094	4.20 ± 0.2505
Alanine	4.52 ± 0.0606	2.43 ± 0.1913[*]	5.31 ± 1.4300	5.69 ± 0.6611⁺⁺
Total choline	1.56 ± 0.0416	1.77 ± 0.0412[*]	1.50 ± 0.0801	1.80 ± 0.0206^{##}
NAA+NAAG	10.42 ± 0.1361	10.29 ± 0.3037	10.24 ± 0.2376	9.91 ± 0.3070
Total creatine	8.97 ± 0.1569	9.06 ± 0.1186	8.62 ± 0.2667	9.21 ± 0.1817
Glutathione	2.50 ± 0.1113	2.11 ± 0.0606[*]	2.76 ± 0.1405	2.39 ± 0.1185
Inositol	4.71 ± 0.2387	4.99 ± 0.1379	5.04 ± 0.4906	6.17 ± 0.2288⁺
Lactate	3.48 ± 0.7489	3.22 ± 0.2109	7.11 ± 1.0330	6.08 ± 1.0610
Taurine	12.26 ± 0.3411	11.65 ± 0.0996	11.75 ± 0.7583	13.07 ± 0.4239⁺

* Male WT vs Male *Tsc2*^{+/-}; [#] Female WT vs Female *Tsc2*^{+/-}; ⁺ Male *Tsc2*^{+/-} vs Female *Tsc2*^{+/-}

Supplementary Table S2. ¹H-magnetic resonance spectroscopy (MRS) analysis of hippocampal neurochemical profile.

Brain metabolite	Hippocampus			
	Male		Female	
	WT	<i>Tsc2</i> ^{+/-}	WT	<i>Tsc2</i> ^{+/-}
GABA	2.66 ± 0.1303	2.75 ± 0.1102	2.88 ± 0.2150	2.78 ± 0.1297
Glutamate	9.91 ± 0.3096	10.10 ± 0.2078	10.14 ± 0.4660	9.88 ± 0.3423
Glutamine	6.05 ± 0.6076	5.18 ± 0.2539	5.21 ± 0.2824	5.60 ± 0.1189
Alanine	2.75 ± 0.0835	2.90 ± 0.3880	2.35 ± 0.1917	2.48 ± 0.1539
Total choline	1.65 ± 0.0099	1.87 ± 0.0698 *	1.93 ± 0.0699 \$	1.82 ± 0.0361
NAA+NAAG	8.85 ± 0.2010	9.48 ± 0.1503	8.918 ± 0.2360	8.603 ± 0.2047 +
Total creatine	9.423 ± 0.2310	9.785 ± 0.1470	9.259 ± 0.1112	9.296 ± 0.0650
Glutathione	2.25 ± 0.1109	2.41 ± 0.1767	2.20 ± 0.1426	2.00 ± 0.0647
Inositol	4.77 ± 0.1217	5.67 ± 0.1246 **	5.42 ± 0.2458	5.47 ± 0.1433
Lactate	3.39 ± 0.1770	4.51 ± 0.2463 *	3.50 ± 0.3303	3.57 ± 0.1376
Taurine	10.81 ± 0.2973	11.79 ± 0.1872 *	10.98 ± 0.2062	10.80 ± 0.1976 +

* Male WT vs Male *Tsc2*^{+/-}; # Female WT vs Female *Tsc2*^{+/-}; \$ Male WT vs Female WT;+ Male *Tsc2*^{+/-} vs Female *Tsc2*^{+/-}**Supplementary Figure S1.** (a) Length, (b) principal frequency and (c) frequency amplitude of USVs produced during social behavior task, and (d) length, (e) principal frequency and (f) frequency amplitude of USVs produced during RRB-eliciting task.



Supplementary Figure S2. Localized ^1H NMR voxel (orange square) in the (a) prefrontal cortex and (b) hippocampus of a 60-days old mouse acquired with 9.4T MR pre-clinical scanner (Bruker Biospec, Billerica MA). Representative fast-spin-echo image of a spectrum was used to show typical location of the volume of interest for spectroscopy.