FIGURE 1

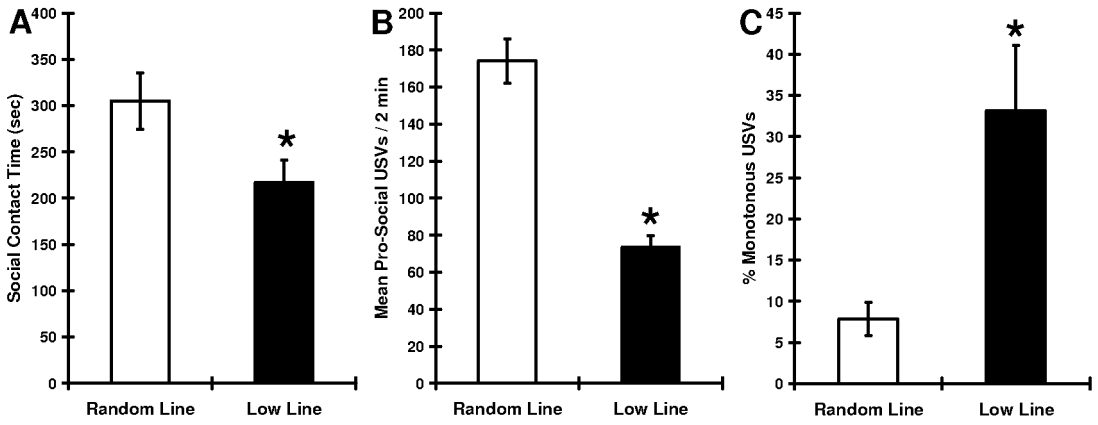

A
Social Contact Time (sec)
400
350
300
250
200
150
100
50
0
*
Random Line
Low Line
B
Mean Pro-Social USVs / 2 min
200
180
160
140
120
100
80
60
40
20
0
*
Random Line
Low Line
C
% Monotonous USVs
45
40
35
30
25
20
15
10
5
0
*
Random Line
Low Line

FIGURE 2

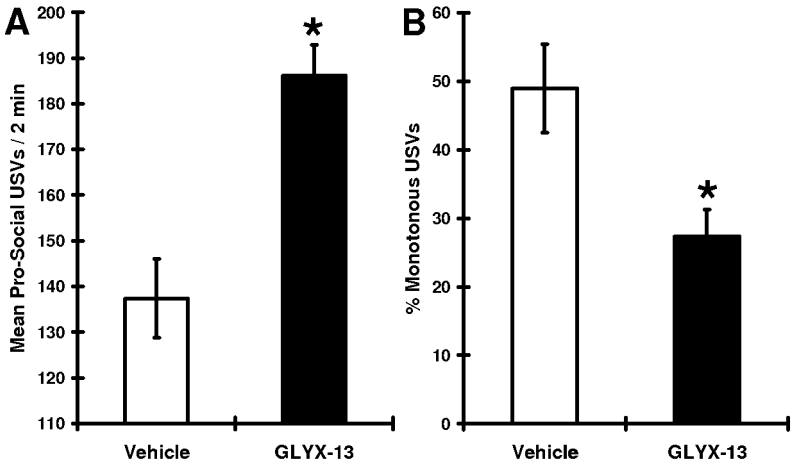

A
Mean Pro-Social USVs / 2 min
200
190
180
170
160
150
140
130
120
110
*
Vehicle
GLYX-13
B
% Monotonous USVs
60
50
40
30
20
10
0
*
Vehicle
GLYX-13

FIGURE 3-: Gene Expression Changes in Low-Line Animals

Gene Name	Medial Prefrontal Cortex Fold Change	Nucleus Accumbens Fold Change	Gene ID
Autism Candidate Genes			
ABAT	0.80	1.16	4-aminobutyrate aminotransferase
APOE	0.81	1.19	apolipoprotein E
CHRNA4	0.91	0.89	cholinergic receptor, nicotinic, alpha 4
GABRA5	0.67	1.18	gamma-aminobutyric acid (GABA) A receptor, alpha 5
GFAP	0.89	1.15	glial fibrillary acidic protein
GRIN2A	0.86	0.91	glutamate receptor, ionotropic, N-methyl D-aspartate 2A
PDYN	0.90	0.92	prodynorphin
PENK	0.80	1.13	proenkephalin 1
Glutamate Receptors			
GRIA2	0.61	0.66	glutamate receptor, ionotropic, AMPA 2
GRIA3	0.73	0.77	glutamate receptor, ionotropic, AMPA 3
GRIA4	0.82	1.27	glutamate receptor, ionotropic, AMPA4
GRIK4	0.89	1.11	glutamate receptor, ionotropic, kainate 4
GRM1	0.92	1.23	glutamate receptor, metabotropic 1
Potassium Channels			
KCNA4	0.72	1.38	potassium voltage-gated channel, shaker-related subfami
KCNC2	0.94	1.08	potassium voltage gated channel, Shaw-related subfamily
KCND2	0.82	1.22	potassium voltage gated channel, Shal-related family, me
KCNJ1	0.90	0.82	potassium inwardly-rectifying channel, subfamily J, memb
KCNK3	0.92	1.07	potassium channel, subfamily K, member 3
KCNMA1	1.09	1.17	potassium large conductance calcium-activated channel,
Insulin Like Growth Factor Related Genes			
IGF1	1.10	1.10	insulin-like growth factor 1
IGF2	0.83	1.06	insulin-like growth factor 2
IGFBP1	1.27	1.10	insulin-like growth factor binding protein 1
IGFBP3	1.13	0.89	insulin-like growth factor binding protein 3

FIGURE 3 cont

Phosphoproteins			
ATP2A2	0.87	0.92	ATPase, Ca++ transporting, cardiac muscle, slow twitch
ATP2B1	0.90	1.08	ATPase, Ca++ transporting, plasma membrane 1
C3	1.19	1.13	complement component 3
CACNA1C	0.87	1.16	calcium channel, voltage-dependent, L type, alpha 1C su
CALM1	0.90	0.78	calmodulin pseudogene 2; calmodulin 3; calmodulin 2; c
CASP3	1.11	1.14	caspase 3, apoptosis related cysteine protease
CKB	0.77	0.89	creatine kinase, brain
CNP	0.92	1.11	2',3'-cyclic nucleotide 3' phosphodiesterase
DLGAP4	0.93	0.93	discs, large homolog-associated protein 4 (Drosophila)
FAS	0.93	0.92	Fas (TNF receptor superfamily, member 6)
FYN	0.86	1.09	FYN oncogene related to SRC, FGR, YES
GABRA4	0.89	1.09	gamma-aminobutyric acid (GABA) A receptor, alpha 4
GAP43	0.85	0.85	growth associated protein 43
GNAS	0.72	0.86	GNAS complex locus
H3F3B	1.23	1.20	similar to H3 histone, family 3B
HES1	1.35	1.09	hairy and enhancer of split 1 (Drosophila)
HK2	1.19	1.18	hexokinase 2
HMBS	1.33	1.19	hydroxymethylbilane synthase
HSPB1	1.16	1.08	heat shock protein 1
ID1	1.34	0.86	inhibitor of DNA binding 1
ITGB7	1.09	1.07	integrin, beta 7

ITPR1	0.84	0.82	inositol 1,4,5-triphosphate receptor, type 1
LMNB1	1.52	1.13	lamin B1
map2	0.72	0.86	microtubule-associated protein 2
MAPK3	1.08	1.13	mitogen activated protein kinase 3
MBP	0.86	0.90	myelin basic protein
MIF	1.11	0.91	macrophage migration inhibitory factor
MPZ	1.16	0.91	myelin protein zero
NOS2	1.08	0.92	Nitric oxide synthase 2, inducible
NR4A1	1.18	1.10	nuclear receptor subfamily 4, group A, member 1
NTRK2	0.81	1.20	neurotrophic tyrosine kinase, receptor, type 2
NTRK3	0.86	0.86	neurotrophic tyrosine kinase, receptor, type 3
P2RX7	0.92	1.39	purinergic receptor P2X, ligand-gated ion channel, 7
PDGFRA	0.95	0.95	platelet derived growth factor receptor, alpha polypeptide
PLCB1	0.88	1.11	phospholipase C, beta 1 (phosphoinositide-specific)
PPAP2B	0.83	0.86	phosphatidic acid phosphatase type 2B
PRKCB	0.73	0.80	protein kinase C, beta
SCNN1G	0.95	0.88	sodium channel, nonvoltage-gated 1 gamma
SLC6A17	1.08	0.92	solute carrier family 6 (neurotransmitter transporter), member 17
SMN1	1.10	1.07	survival motor neuron 1
SNAP25	0.82	0.83	synaptosomal-associated protein 25
ST13	1.18	1.12	similar to suppression of tumorigenicity 13; suppression of tumorigenicity 13
STAT3	1.12	1.14	signal transducer and activator of transcription 3
STX12	0.95	0.95	syntaxin 12
STX1B	0.86	1.39	syntaxin 1B
SYNE1	0.71	0.74	spectrin repeat containing, nuclear envelope 1
SYT9	0.90	1.15	synaptotagmin IX
VIM	1.24	1.45	vimentin

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Figure 3 con't

Other			
ATP1B3	1.13	1.07	ATPase, Na+/K+ transporting, beta 3 polypeptide
B2M	1.18	1.11	beta-2 microglobulin
BMP1	1.10	0.87	bone morphogenetic protein 1
CALB1	0.68	0.86	calbindin 1
CALB2	0.78	1.11	calbindin 2
CALCB	1.22	0.84	calcitonin-related polypeptide, beta
CASP1	1.15	0.83	caspase 1
CD48	1.23	1.12	Cd48 molecule
CITED2	1.12	1.11	Cbp/p300-interacting transactivator, with Glu/Asp-rich carboxy-terminal domain, 2
CPE	0.84	0.74	carboxypeptidase E
GABRD	0.74	1.14	gamma-aminobutyric acid (GABA) A receptor, delta
GFRA2	0.93	0.91	GDNF family receptor alpha 2
GLRA1	0.86	1.09	glycine receptor, alpha 1
GNAO1	0.84	0.93	guanine nucleotide binding protein (G protein), alpha activating activity polypeptide O
HK3	1.35	1.13	hexokinase 3 (white cell)
HPRT1	1.14	1.11	hypoxanthine phosphoribosyltransferase 1
LTP4	1.24	1.15	Non-specific lipid-transfer protein 4
MGAT2	1.18	0.82	mannosyl (alpha-1,6-)-glycoprotein beta-1,2-N-acetylglucosaminyltransferase
NCAN	0.92	1.14	neurocan
PDYN	0.90	0.92	prodynorphin
Penk	0.80	1.13	preproenkephalin 1
PLP1	0.70	0.72	proteolipid protein 1
POU3F3	0.90	1.24	POU class 3 homeobox 3
PTN	0.91	1.11	pleiotrophin
RHEB	0.94	0.93	Ras homolog enriched in brain
SERPINE1	1.20	1.08	serine (or cysteine) peptidase inhibitor, clade E, member 1
SLC32A1	0.83	1.16	solute carrier family 32 (GABA vesicular transporter), member 1
SST	0.82	0.89	somatostatin
STX5	1.12	1.09	syntaxin 5
THRB	0.84	0.91	thyroid hormone receptor beta
VCAM1	0.90	0.90	vascular cell adhesion molecule 1
WNT4	1.14	0.85	wingless-type MMTV integration site family, member 4

FIGURE 4

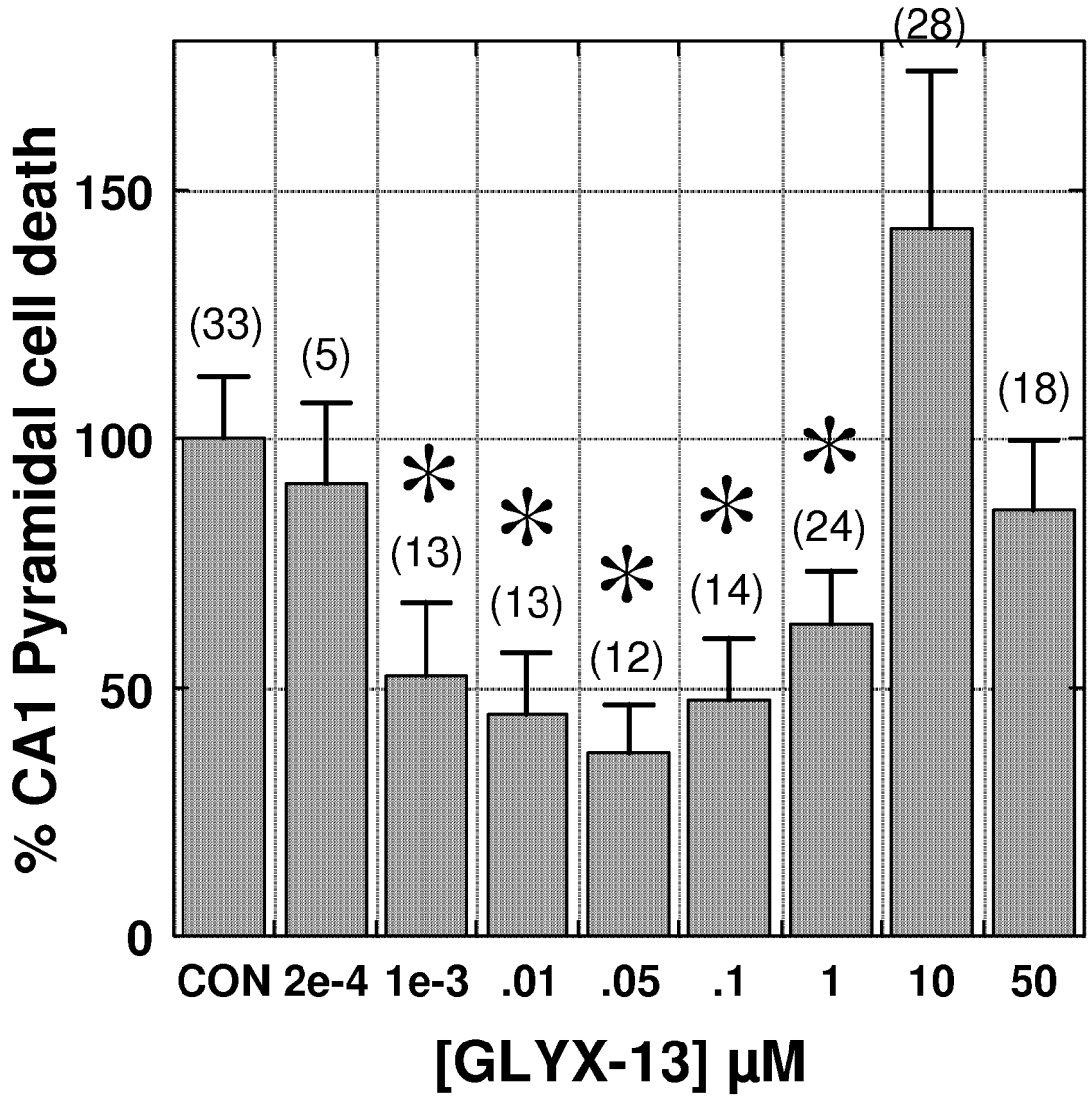

% CA1 Pyramidal cell death
150
100
50
0
(33)
(5)
(13)
(13)
(12)
(14)
(24)
(28)
(18)
*
CON
2e-4
1e-3
.01
.05
.1
1
10
50
[GLYX-13] µM

FIGURE 5

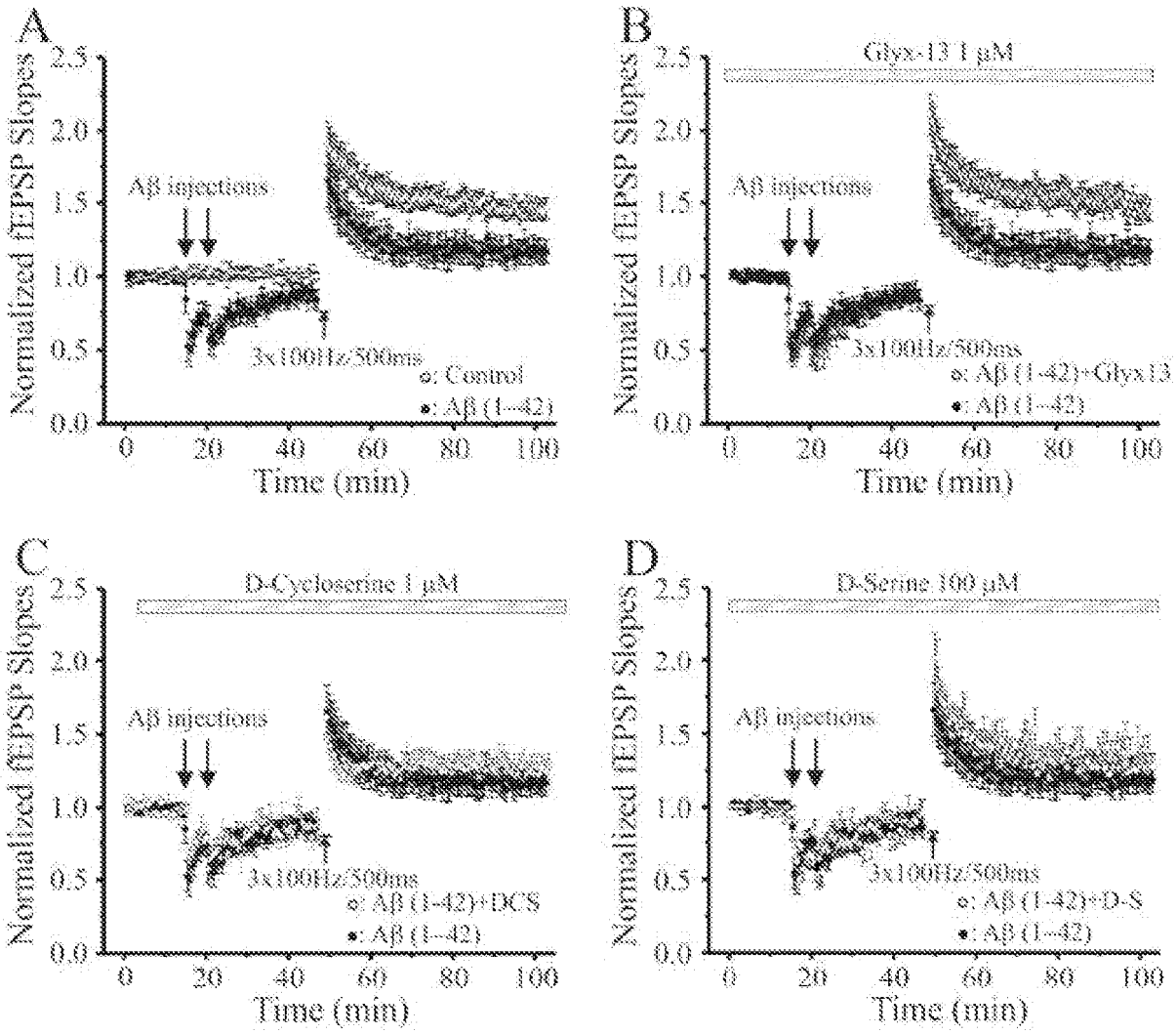
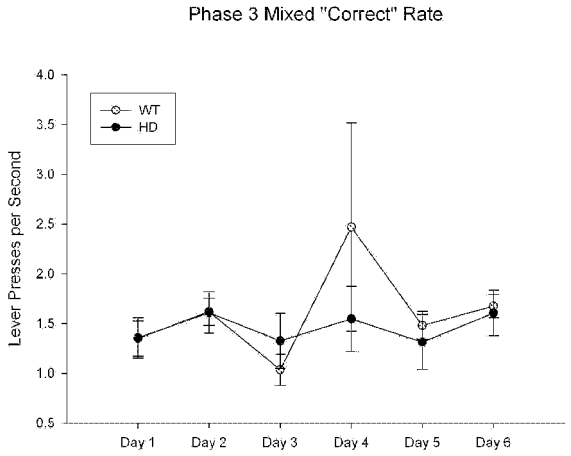
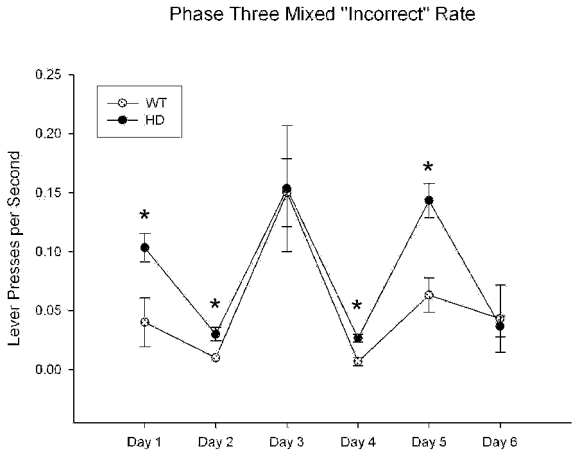

A
Normalized fEPSP Slopes
Aβ injections
3x100Hz/500ms
o: Control
•: Aβ (1–42)
Time (min)
B
Glyx-13 1 μM
Aβ injections
3x100Hz/500ms
o: Aβ (1–42)+Glyx13
•: Aβ (1–42)
Time (min)
C
D-Cycloserine 1 μM
Aβ injections
3x100Hz/500ms
o: Aβ (1–42)+DCS
•: Aβ (1–42)
Time (min)
D
D-Serine 100 μM
Aβ injections
3x100Hz/500ms
o: Aβ (1–42)+D-S
•: Aβ (1–42)
Time (min)

FIGURE 6


Phase 3 Mixed "Correct" Rate
Lever Presses per Second
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
WT
HD
Day 1
Day 2
Day 3
Day 4
Day 5
Day 6

A


Phase Three Mixed "Incorrect" Rate
Lever Presses per Second
0.25
0.20
0.15
0.10
0.05
0.00
WT
HD
*
*
*
*
Day 1
Day 2
Day 3
Day 4
Day 5
Day 6

B