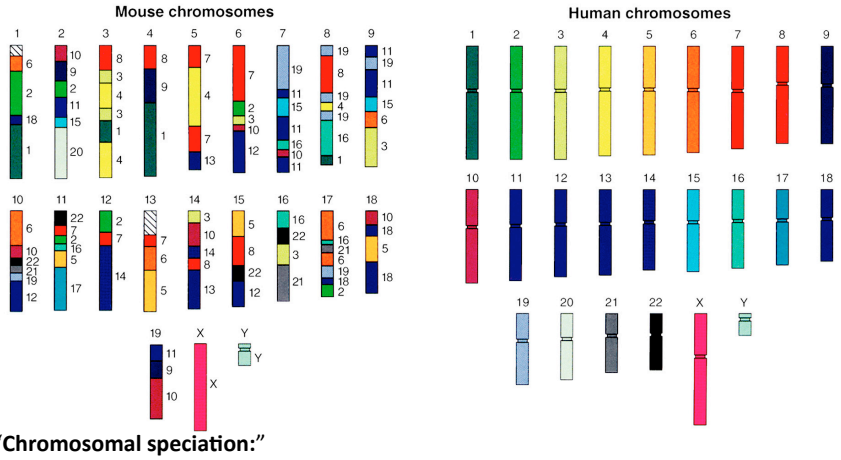
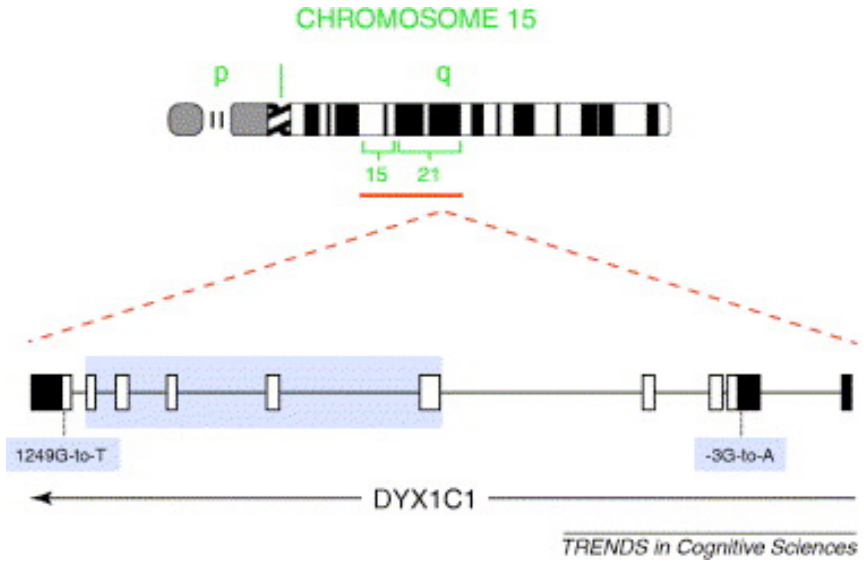
Mouse and Human Genetic Similarities

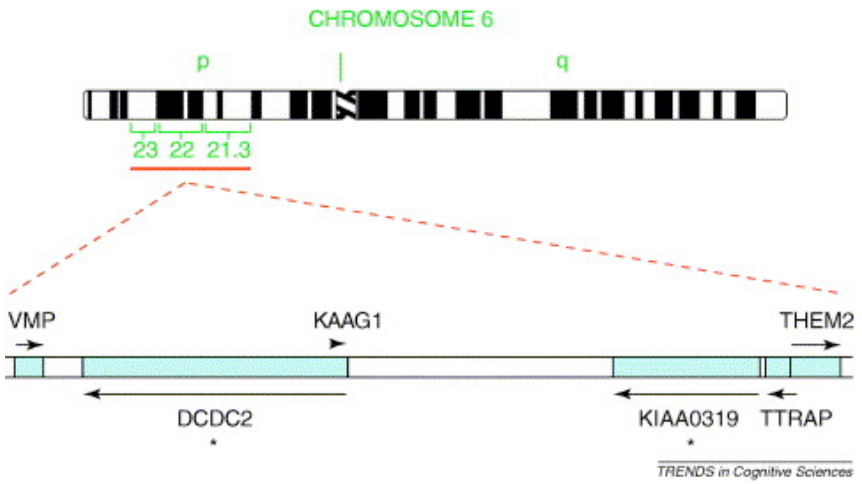


"**Chromosomal speciation:**"
Average *conserved chromosomal length* from moving human to mouse -- as derived by linkage analysis -- is 8.8 cM, suggesting about 150 major rearrangements (via breakage and fusion) occurred along the human or mouse lines as they diverged from a common ancestor that existed 65 million years ago. Note that despite rearrangement, most all human genes have homologous mouse counterparts (located in rather large homologous segments of multiple linked genes), indicating an *amazing conservation of genes*.

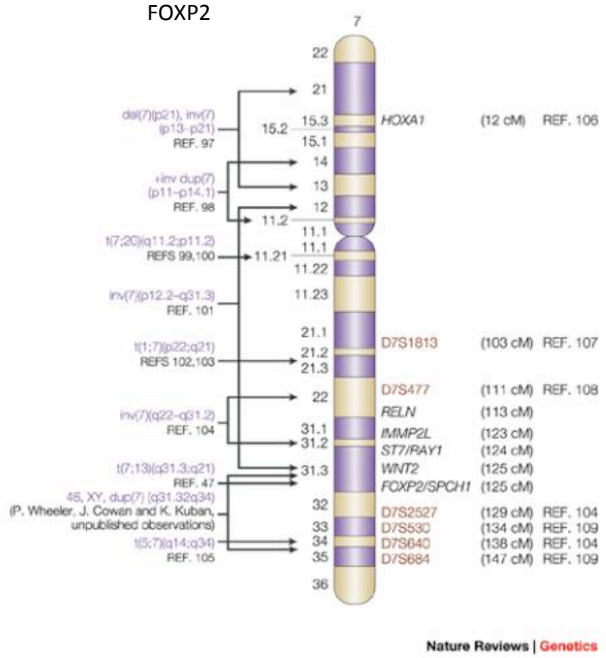
DYX1 region



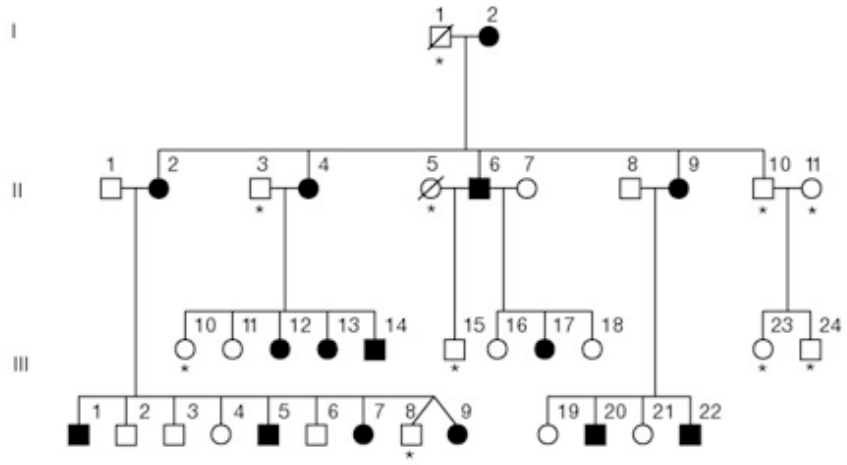
DYX2 region



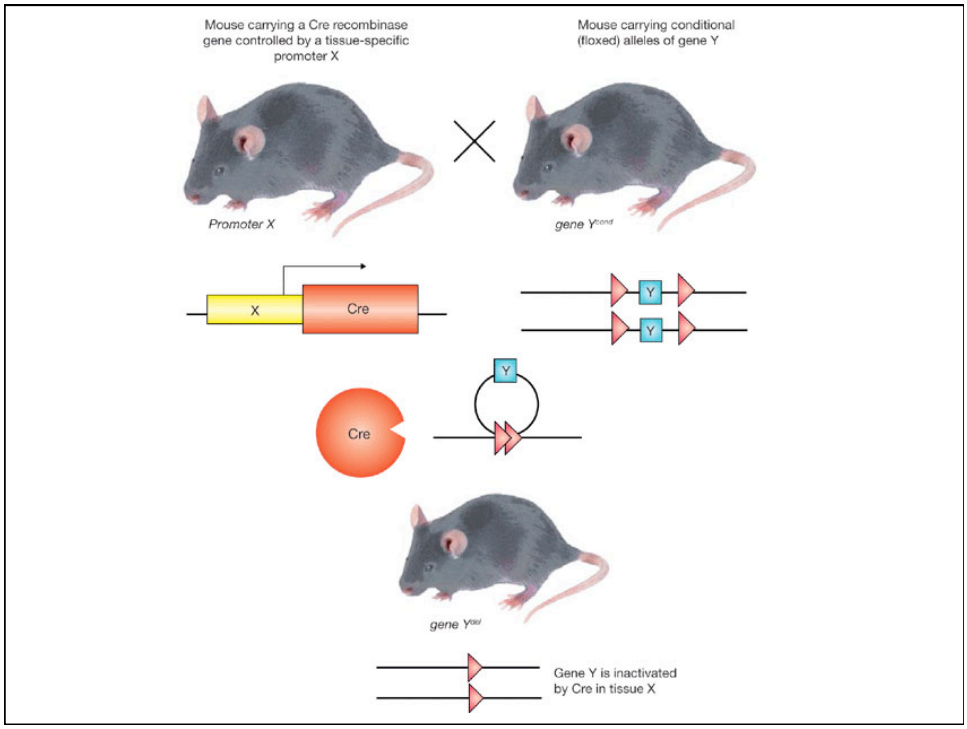
FOXP2

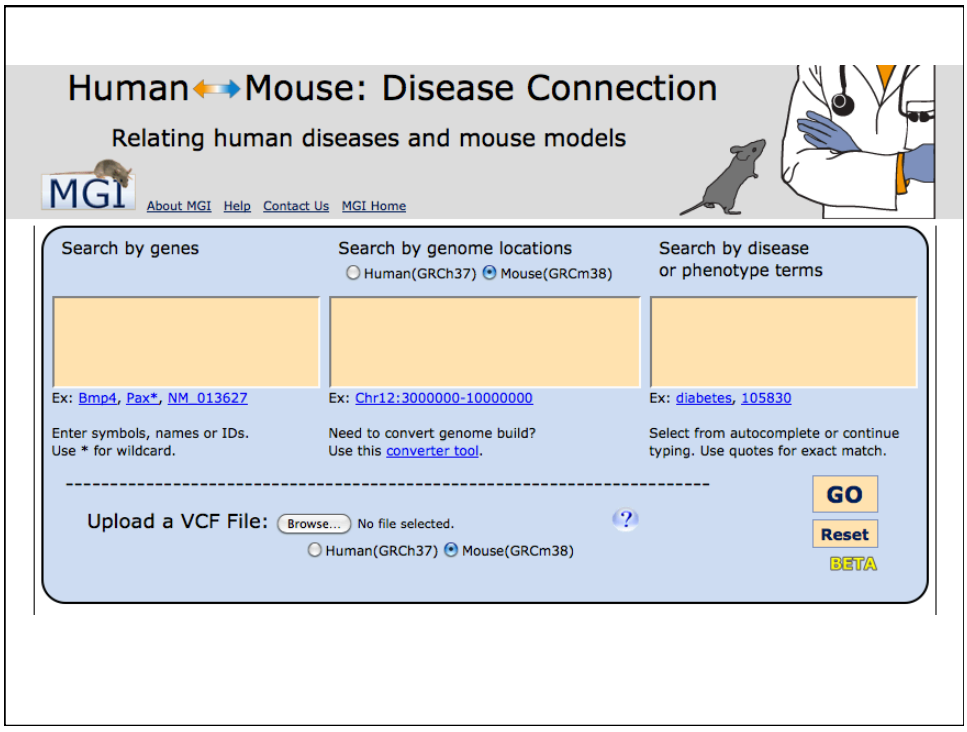


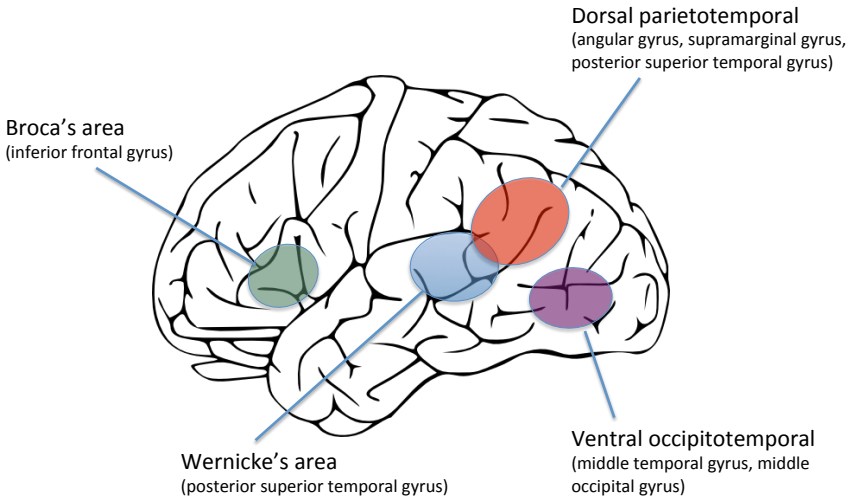
KE family

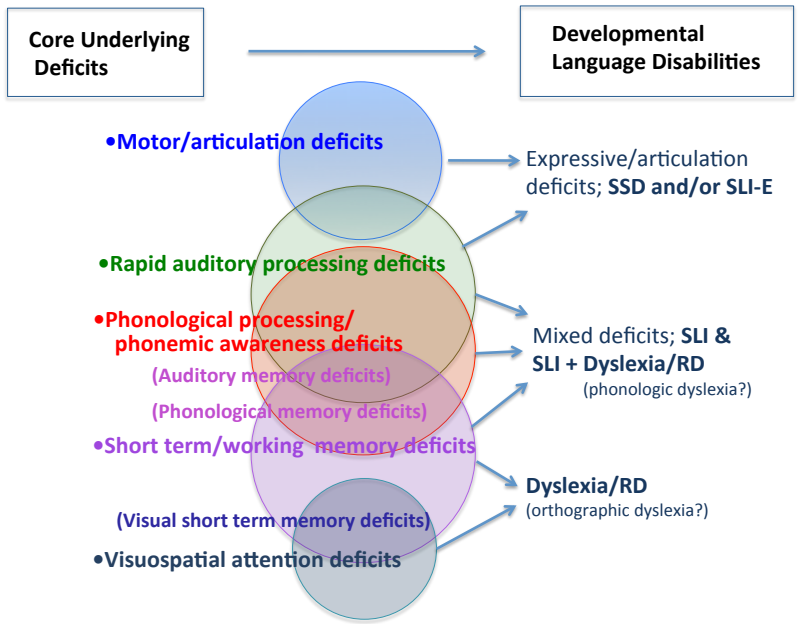


Injection of RNAi into ventricle of externalized rat fetus, followed by application of mild current to promote transfection into migrating Neurons.


Mouse carrying a Cre recombinase gene controlled by a tissue-specific promoter X
Mouse carrying conditional (floxed) alleles of gene Y
Promoter X
gene Y
X
Cre
Y
Y
Cre
Y
gene Y
Gene Y is inactivated by Cre in tissue X


Human Mouse: Disease Connection
Relating human diseases and mouse models
MGI
About MGI Help Contact Us MGI Home
Search by genes
Search by genome locations
Human(GRCh37) Mouse(GRCm38)
Search by disease or phenotype terms
Ex: Bmp4, Pax*, NM_013627
Ex: Chr12:3000000-10000000
Ex: diabetes, 105830
Enter symbols, names or IDs. Use * for wildcard.
Need to convert genome build? Use this converter tool.
Select from autocomplete or continue typing. Use quotes for exact match.
Upload a VCF File: Browse... No file selected.
Human(GRCh37) Mouse(GRCm38)
GO
Reset
BETA

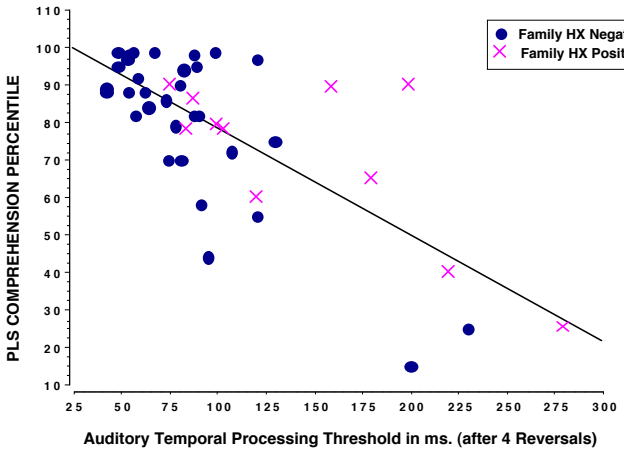




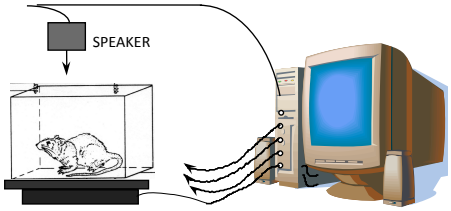
SSD= speech sound disorder; SLI=specific language impairment; SLI-E=specific expressive language impairment; RD=reading disability

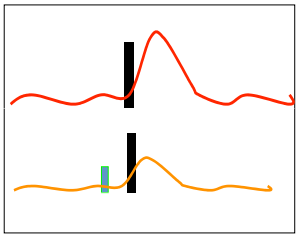
Measures of receptive processing

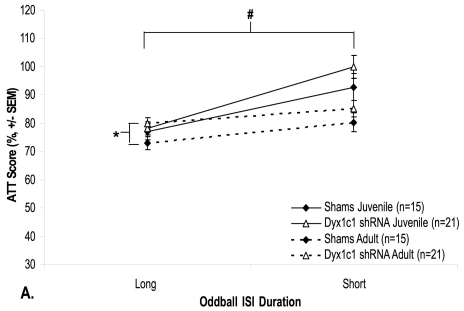
INFANT AUDITORY TEMPORAL PROCESSING AT MEAN AGE 7.5 mths AND LANGUAGE COMPREHENSION AT 24 mths



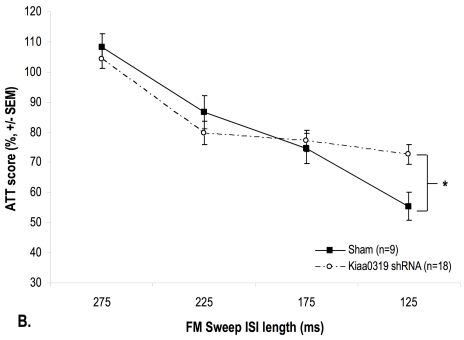
From Benasich et al., Dev Psychobiol, 2002





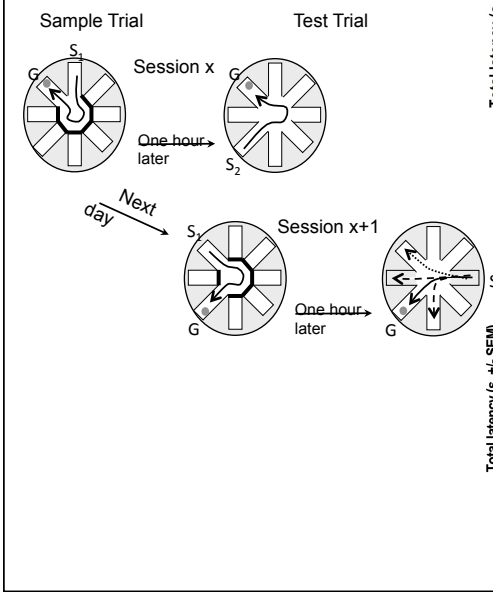


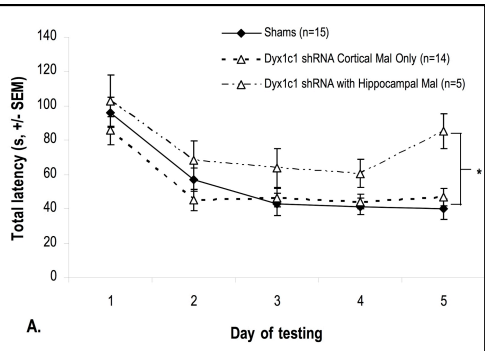
A.

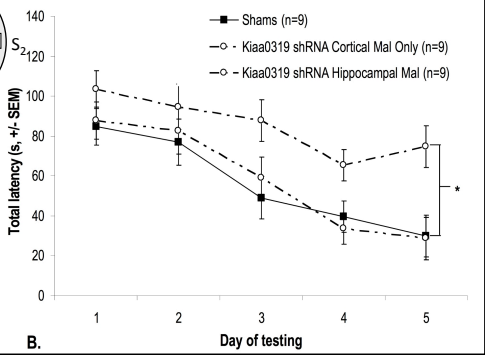


B.

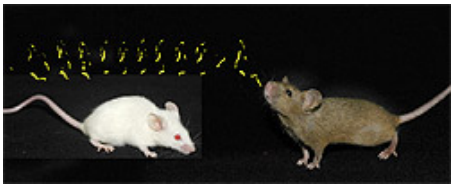
Radial arm delayed match to sample

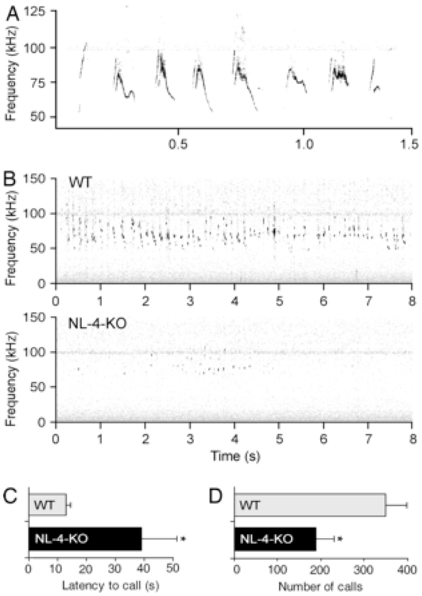


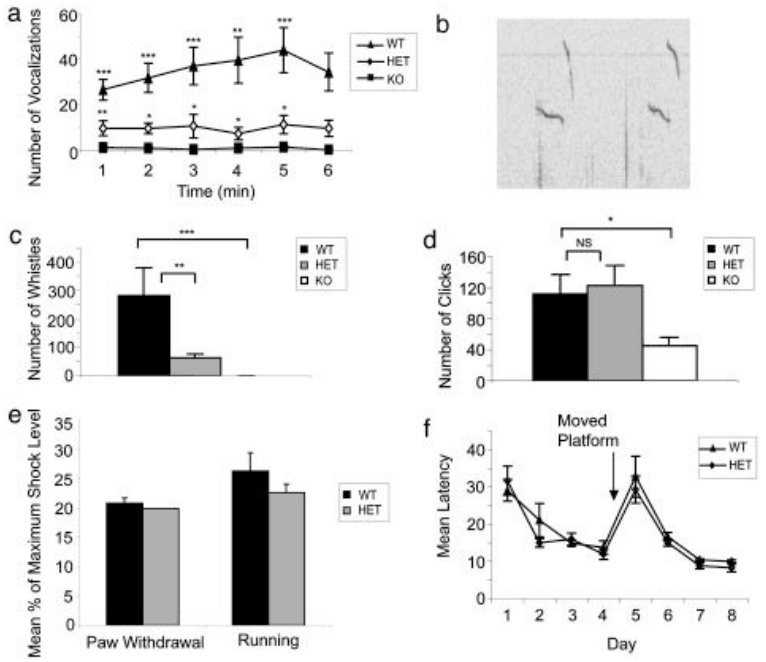




Measures of expressive output (vocalizations)

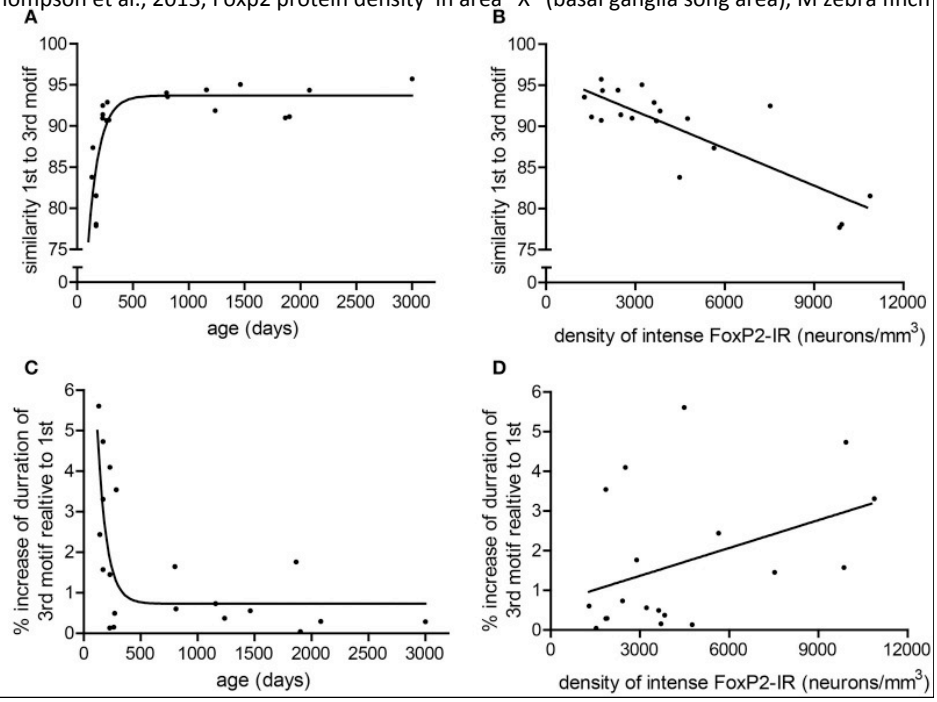






Shu et al., 2005, Vocalizations in Foxp2 KO mice (het and homozygous conditional forebrain

Thompson et al., 2013, Foxp2 protein density in area "X" (basal ganglia song area), M zebra finch



- There is considerable overlap among the different forms of autism. The wide variation in symptoms among children with autism, however, has led to the concept of **autism spectrum disorder**, or ASD.

- **ASDs affect one out of every 88 children in the U.S**. They occur more often among boys than girls. While autism appears to be on the rise, it's unclear whether the growing number of diagnoses shows a real increase or comes from improved detection.

- **Signs of ASD:**
- Social interaction
- Communication -- both verbal and non verbal.
- Behaviors and interests

- Each child with an ASD will have his or her own pattern of autism.
- Sometimes, a child's development is delayed from birth. Some children seem to develop normally before they suddenly lose social or language skills. Others show normal development until they have enough language to demonstrate unusual thoughts and preoccupations.
- In some children, a loss of language is the major impairment. In others, unusual behaviors (like spending hours lining up toys) seem to to be the dominant factors.

- Until recently, the types of ASD have been determined by guidelines in the diagnostic manual (DSM - IV) of the American Psychiatric Association. According to the CDC, the three main types of ASD are:
- Asperger's syndrome
- Pervasive developmental disorder, not otherwise specified (PDD-NOS)
- Autistic disorder
- The DSM -IV also included two rare but severe autistic-like conditions -- **Rett syndrome** and **childhood disintegrative disorder (CDD**).

- The new diagnostic manual has made some major changes in this list of disorders. It's unclear, though, how these changes will affect the way health professionals define exactly what is an autistic spectrum disorder.

- **Fragile X Syndrome**
- This disorder is the most common inherited form of mental retardation. It was so named because one part of the X chromosome has a defective piece that appears pinched and fragile under a microscope.
- 5% of people with autism are affected by fragile X, and 10% to 15% of those with fragile X show autistic traits.
- Fragile X syndrome is characterized by moderate intellectual disability in affected males and mild intellectual disability in affected females. Distinctive physical features are sometimes present in affected males including a large head, long face, prominent forehead and chin, protruding ears, loose joints and large testes, but these features develop over time and may not be obvious until puberty. Motor and language delays are usually present but also become more apparent over time. Behavioral abnormalities including autistic behaviors are common.
- Fragile X syndrome is caused by an abnormality (mutation) in the FMR1 gene. Affected individuals have an increased number of copies of a portion of the gene called CGG repeats. The greater the number of copies of CGG, the more likely there will be increased severity of the disorder. Fragile X syndrome occurs more often in males and results in more severe disease in males.

Rett syndrome

ASD that affects girls almost exclusively. It's rare -- about one in 10,000 to 15,000.

In most cases of Rett syndrome, a child develops normally in early life. Between 6 and 18 months of age, changes in the normal patterns of mental and social development begin. Although it's not always detected, a slowing of head growth is one of the first events in Rett syndrome. Loss of muscle tone is also an initial symptom. Soon, the child loses any purposeful use of her hands. Instead, she habitually wrings or rubs her hands together. Around 1 to 4 years of age, social and language skills deteriorate in a girl with Rett syndrome. She stops talking and develops extreme social anxiety and withdrawal or disinterest in other people.

Rett syndrome also causes problems with muscles and coordination. Walking becomes awkward as girls develop a jerky, stiff-legged gait. A girl with Rett syndrome may also have uncoordinated breathing and seizures.

Most children with Rett syndrome have a mutation in a particular gene on the X chromosome. Exactly what this gene does, or how its mutation leads to Rett syndrome, isn't clear.

Although Rett syndrome seems to be genetic, the faulty gene is almost never inherited from the parents. Rather, it's a chance mutation that happens in the girl's own DNA. No Rett syndrome risk factors have been identified, other than being female. There is no known method for preventing Rett syndrome.

When boys develop the Rett syndrome mutation, they die shortly after birth. Because boys have only one X chromosome (instead of the two girls have), the disease is more serious, and quickly fatal.

Table 2 Known and putative autism genes (organized by pathogenesis)

Protein name (function)	Gene symbol/locus	Test availability
Neuronal cell adhesion and/or synapse function		
Neuroligin 3 (synapse formation and function)	*NLGN3X* Xq28	Clinical
Neuroligin 4 (synapse formation and function)	*NLGN4X* Xp22.33	Clinical
Neurexin 1 (transsynaptic binding partner for neuroligins)	*NRXN1* 2p16.3	Research
SH3 and multiple ankyrin repeat domains (organizes post synaptic density and binds neuroligins)	*SHANK3* 22q13	Research
Contactin-associated protein-like 2 (synaptic binding partner for contactin molecules involved in neuronal migration)	*CNTNAP2* 7q36	Research
Contactin 4 and Contactin 3 (neuronally expressed adhesion molecules)	*CNTN4* and *CNTN3* 6p26-p25	Research
Protocadherin 10 (a cadherin-related neuronal receptor: may play a role in the establishment and function of specific cell-cell connections; essential for normal forebrain axon outgrowth)	*PCDH10* 4q28	Research
Neuronal cell adhesion molecule	*NRCAM* 7q31	Research
Neuronal activity regulation		
Methyl CpG-binding protein 1 (CAN methylation-dependent transcriptional repressor)	*MECP2* Xq28	Clinical
Ubiquitin protein ligase E3A	*UBE3A* 15q11-q13	Clinical
Deleted in autism	*DIA1* (c3orf58) 3q	Research
Ataxin 2-binding protein 1	*A2BP1* 16p13	Research
Neurodevelopmental genes		
Engrailed 2 (homeobox gene involved in midbrain and cerebellum development)	*EN2* 7q36	Research
Homeobox A1 (involved in hindbrain development)	*HOXA1* 17p15.3	Clinical
Homeobox B1 (involved in hindbrain development)	*HOXB1* 17q21-q22	Research
Reelin (signaling protein involved in neuron migration)	*RELN* 7q22	Research
WENT2 (signaling proteins involved in embryonic patterning, cell proliferation, and cell determination)	*WNT2* 7q31	Research
FOXP2 (transcription factor involved in embryogenesis and neural functioning)	*FOXP2* 7q31	Research
ARX homeobox gene	*ARX* Xp22.13	Clinical
Patched domain containing 1 gene	*PTCHD1* Xp22.11	Research
Sodium channel		
Sodium channel, voltage-gated, type VII	*SCN7A* 2q	Research
Na+/H+ exchanger isoform 9	*SLC9A9* (*NHE9*) 3q24	Research
Calcium channel		
Calcium channel, voltage-dependent, L type, alpha 1C subunit (Timothy syndrome)	*CACNA1C* 12p13.3	Clinical
Calcium channel, voltage-dependent, alpha 1H subunit	*CACNA1H* 16p13.3	Research
Calcium channel, voltage-dependent, L type, alpha 1F subunit	*CACNA1F* Xp11.23	Clinical
Neurotransmitter genes		
GABA receptor subunits (major inhibitory transmitter receptors in the brain)	*GABRB3, GABRA5, GABRG3* 15q11.2-q12	Research
Serotonin transporter	*SLC6A4* 17q11.1-q12	Clinical
Mitochondrial		
Mitochondrial aspartate/glutamate transporter (mitochondrial function and maintaining ATP levels)	*SLC25A12* 2q24	Research
Other genes		
Oxytocin receptor	*OXTR* 3p26.2	Research
Laminin beta 1	*LAMB1* 7q31.1	Research
RING finger protein 8 (ubiquitin ligase and transcriptional coactivator)	*RNF8* 6p21.3	Research

Adapted from GeneReviews, http://www.genetest.org. Copyright, University of Washington, Seattle 1997–2010.