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Animal models of speech and vocal communication deficits associated with psychiatric disorders

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Abstract

Disruptions in speech, language and vocal communication are hallmarks of several neuropsychiatric disorders, most notably autism spectrum disorders. Historically, the use of animal models to dissect molecular pathways and connect them to behavioral endophenotypes in cognitive disorders has proven to be an effective approach for developing and testing disease-relevant therapeutics. The unique aspects of human language when compared to vocal behaviors in other animals make such an approach potentially more challenging. However, the study of vocal learning in species with analogous brain circuits to humans may provide entry points for understanding this human-specific phenotype and diseases. Here, we review animal models of vocal learning and vocal communication, and specifically link phenotypes of psychiatric disorders to relevant model systems. Evolutionary constraints in the organization of neural circuits and synaptic plasticity result in similarities in the brain mechanisms for vocal learning and vocal communication. Comparative approaches and careful consideration of the behavioral limitations among different animal models can provide critical avenues for dissecting the molecular pathways underlying cognitive disorders that disrupt speech, language and vocal communication.

Keywords

language; speech; autism; schizophrenia; animal models; vocal communication

Introduction

Speech and language phenotypes are defining hallmarks of several psychiatric disorders including autism spectrum disorders (ASD) and schizophrenia. The incidence of ASD in the US is currently estimated at 1 in 68 children (1), and approximately 30-50% of these patients with ASD only achieve phrase-level command of language (2). Moreover, the prevalence of schizophrenia is 1% worldwide, and disordered speech is one of three “positive” symptoms of schizophrenia that is diagnostic (3). Specific language impairment

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(SLI) affects approximately 7% of young children (4). This disorder occurs in the absence of other neurodevelopmental symptoms and is limited to general problems with language syntax and/or phonology. Interestingly, SLI has a genetic component and there appears to be some convergence of genes involved in SLI and ASD (5). The prevalence of sustained stuttering worldwide is almost 1% (6), similar to schizophrenia, resulting in approximately 3 million people in the US exhibiting stuttering. Together, these statistics underscore the importance of understanding the basic brain, molecular, and genetic mechanisms underlying speech and language. Besetting this goal is the availability of animal models that have conserved brain circuitry underlying phenotypes akin to speech.

As we rely upon animal models for developing and testing drugs for the treatment of ASD or other psychiatric disorders, it is important to understand the uses and limitations of such models as they pertain to the speech-relevant aspects of these disorders. In this review, we will address the definition of speech and language and how forms of vocal learning in animal models can be appropriated for gaining insights into evolutionarily conserved brain circuits that form the basis for speech learning. We will discuss the use of specific species as well as salient candidate gene models that have provided the most insight into language-related pathways to date. Finally, we will consider which available animal models seem most relevant to specific psychiatric disorders.

Vocal Learning: what is it and who has it?

The use of vocalizations for signaling and social communication is common among vertebrates and the structure, complexity and plasticity associated with vocal behaviors ranges widely among species (7-12). Most forms of vocal communication involve innate emotive vocalizations (10). Although innate, these vocal behaviors are often context dependent and used to signal specific meaning(s) to the receiver (7, 13-15). For example, the purr and hiss of a cat are innate vocalizations produced under different contexts and used to convey very different signals. In contrast to these innate vocalizations, some species learn to produce complex vocalizations through imitation (9, 12, 13, 16). This form of vocal production learning relies on auditory feedback and substantial specialized neural and peripheral motor circuitry that have not evolved in non-vocal learning species (11). Here, we distinguish between three forms of vocal learning (13): production learning, in which animals learn their vocalizations by imitation, usage learning, in which animals learn to use vocalizations in appropriate contexts, and receptive learning, in which receivers learn appropriate behavioral responses to specific vocal signals. Although many species engage in usage and receptive learning, few species have also evolved central and peripheral apparatus for vocal imitation (11). For example, humans are the only primates that learn vocalizations through imitation (8). Indeed, vocal imitation is rare in extant mammals and has only been identified in humans, cetaceans (whales, dolphins and porpoises), elephants, pinnepeds, and bats (11, 12, 16). In addition to these mammals, out of over 36 bird lineages vocal learning has also evolved in three lineages, songbirds, hummingbirds and parrots, which together comprise over 4,800 species (11).

How we define language may have implications for whether language is ultimately a uniquely human trait, but there is little argument that human language is a complex

referential system of signaling that relies upon specialized brain and vocal motor structures that evolved through natural selection. The referential capacity and syntax that define language allow ideas and thoughts to be constructed in an almost infinite number of ways (9, 17, 18). This magnitude of differential output to convey a matched number of exceedingly large associations, inferences, or meanings sets humans apart from other species. As such, human language can convey a wide range of information from the practical to the abstract. The output of human language can be in the form of vocal output (speech) or manual output (i.e. sign language or writing/typing). For relevance to psychiatric disorders, we will strictly focus on vocal output. In addition, while there are the many animals mentioned above that exhibit vocal learning, here, we will focus on those animals that are likely to be studied in the laboratory for the purposes of understanding psychiatric disorders either at the behavioral or neuroanatomical level.

Non-human primates

Investigations into vocal learning in non-human primates have revealed the extensive usage and receptive learning of vocal behaviors, but little evidence of vocal imitation (8, 11, 12, 19-22). The cognitive abilities of non-human primates, including the potential capacity for vocal learning, have fascinated scientists for decades. Extreme examples of this interest have been the integration of baby chimpanzees into human homes and the teaching of sign language to chimpanzees and gorillas. While these animals are able to make associations between signs and objects (symbolic reference) and basic syntax, in none of these cases have the primates achieved a level of complex syntax indicative of language (23). Marmosets exhibit vocal communication that has a strong social component in that they will take turns in calling to one another, reminiscent of the back and forth in conversational speech (24). Indeed, there are some data supporting the idea that marmosets learn this behavior over time, suggesting that usage dependent learning may be involved in these vocal signals (25).

Rodents

There are two major types of rodent vocalizations: pup isolation calls and adult social and mating calls. All of these calls are in the ultrasonic range (hence the term “ultrasonic vocalizations,” or USVs) (26). USVs have been primarily observed in the laboratory setting in either mice or rats. Pup isolation calls are experimentally elicited by isolating the pup from the dam, and although still debatable may be used as a means of social communication between pup and dam (27, 28). It is possible that the structure of the pup call may inform the dam as to the state of the pup and direct her retrieval behavior, however, such a correlation between isolation USV structure and behavior has yet to be directly examined. Adult USVs are frequently used to facilitate mating by males, although same sex USVs also occur in non-aggressive social interactions (29). The structure of USVs change with development from isolation to adult calls, as more complex calls are produced by adult animals than pups (see Figure 1) (30). Again though, the interpretation of what kind of information these complex calls may be conveying compared to simple calls is currently debated (14, 15). Perhaps the most controversial aspect of rodent USVs is whether this form of communication is innate or involves some learning component (14, 31, 32). While the pup USVs are almost certainly innate due to their early postnatal emergence before the ears even open, there is some evidence that adult mouse USVs can be modified by auditory feedback

or social experience suggesting a limited learning component (33). However, studies using genetically engineered deaf mice clearly indicate adult USVs develop normally in the absence of audition, indicating that mice do not learn their vocalizations through imitation (32, 34). Studies of USVs in wild strains of mice have opened up yet another interesting twist to research in rodent vocalizations. Recent work has demonstrated that in a mating paradigm, wild female mice do extensively vocalize unlike what has been observed in laboratory strains (35). Other work has shown that USVs of wild mice exhibit patterns of individuality, which the authors postulate might be due to a genetic or epigenetic signature (36). In general, more work needs to be done across many strains of mice both inbred and wild to assess the behavioral contexts in which rodent USVs might be relevant to psychiatric disorders. Again, with the availability of genome editing it will be possible to manipulate disease-relevant genes in whichever strain(s) prove to exhibit the appropriate behaviors.

Cetaceans & Pinnipeds

There is evidence that whales (*e.g. Orcinus orca* (37)), dolphins and pinnipeds exhibit vocal learning (38, 39). While these individual reports are generally from small numbers of animals and alternative explanations for the observed calls (*e.g.* usage learning) cannot be completely ruled out without further experiments, the aggregate data from these studies indicate that cetaceans and pinnipeds do exhibit vocal learning. Interestingly, recent data suggest that killer whales can alter their vocalizations to match those of dolphins when the two species socialize (40, 41), and dolphin calls do not appear to be “copied” from a tutor like songbird vocal learning, but rather appear to be unique to each animal (40). Even more remarkable is the evidence that cetaceans that spend time with humans can mimic human speech (42). These results attribute a level of complexity to vocal learning in cetaceans and pinnipeds that is lacking in the usage learning of innate sounds found in other mammals such as rodents. Similar to the great apes, experimental studies in cetaceans are both technically and ethically challenging. Although *in vivo* neurobiological manipulations are unlikely to be conducted in cetaceans and pinnipeds, post-mortem neuroanatomical studies could be carried out (43) once specific genomic and molecular pathways are identified in humans and other animal models.

Bats

Bats have documented vocal learning, and are potentially suitable for modeling circuit abnormalities associated with brain disorders. Bats may indeed represent an important future model due to the feasibility of working with bats in the laboratory and the conservation of mammalian brain architecture. Thus far there is very little known about role of social communication calls in bats or about the circuits involved in controlling these calls (44-46). Some species of bats use a form of ultrasonic laryngeal echolocation for finding prey and maneuvering through the environment (47). However, it is unclear whether learning is required for these vocalizations beyond auditory feedback control and whether such calls have a social component. Interestingly, while the *FoxP2* gene (discussed below) has undergone accelerated diversification in bats, there does not appear to be a correlation between changes in *FoxP2* sequence and the evolution of laryngeal echolocation (47, 48). This suggests that unlike the correlation with human FOXP2 amino acid evolution and language (49, 50), the evolution of laryngeal echolocation is not directly correlated with

FoxP2 amino acid composition. Although the laboratory study of bats is not simple, manipulation of gene expression can now be achieved in bats. With the advance of genetic modification techniques it may be possible to employ bats as useful models to study the links between vocal learning and psychiatric disease (51).

Birds

Aside from humans, songbirds and parrots are the two primary terrestrial vertebrates that have been well-studied for vocal learning behavior and brain pathways (9, 16, 52, 53). Oscine songbirds make up a large group of ∼4,000 species of birds that learn their complex songs by imitating other birds, their parents or other sounds that they hear (see (54, 55) and references therein). These vocalizations are primarily used to attract mates and defend nesting sites (53, 56). However, the complexity of song learning and the contexts in which songs are produced is varied across species. In addition, some songbirds are superb mimics and can accurately imitate many sounds, including human speech. Some songbirds can exhibit repertoires of several hundred learned vocalizations, while still other songbird species learn only a single song during their life. In some species of songbird only males learn to sing in order to attract mates, while in other species both male and female birds learn to sing and even learn to sing intricate duets.

Parrots are perhaps the most widely acknowledged vocalists among birds. Parrots also use their vocalization for group affiliation and pair bonding (57, 58). Often, male and female parrots learn their vocalizations and share vocalizations to indicate group identity or pair bonding. Parrots as a group also exhibit tremendous flexibility in their vocal learning ability and are often able to imitate human speech (59-62).

Common behavioral, molecular and neurobiological features make vocal learning in birds an important model for human speech learning and an emerging model for psychiatric disorders that disrupt vocal communication in people (11). Like humans, birds learn their vocalizations during a developmental sensitive period and the details of song and speech development have strong behavioral parallels, including similar transitions through discrete babbling phases and the stepwise acquisition of syllable sequences (63, 64) (see Figure 2). The acquisition and maintenance of song and speech are also dependent on audition and in many songbird species initial learning depends on direct tutoring from adult birds and social interaction (65). Moreover, speech and birdsong are both dependent on analogous interconnected brain structures spanning from the forebrain to the brainstem for accurate vocal learning (11, 12, 21, 66-68) (see Figure 3). In general, the avian brain and the mammalian brain are very similar and there are several reasons to expect that research in birds can reveal general principles about learning, memory and the brain circuits involved in vocal communication in humans (66, 69-74). Although the distinctive nomenclature of the avian brain suggests dissimilarity, organization and structure of the brainstem, midbrain and forebrain.are largely equivalent among birds and mammals, including the input and output cell types of the cortex (71, 72, 75, 76), underscoring the idea that cellular and synaptic plasticity mechanisms for learning and memory are highly conserved. In addition, forebrain regions involved in producing and learning song are analogous to those involved in producing and learning speech (12, 66). Humans and songbird also depend on the expression

of FoxP2, a transcription factor highly expressed in the striatum, for accurate vocal learning. Knockdown of *FoxP2* disrupts song development in a manner that phenocopies disruptions seen in humans, indicating analogous circuit and gene regulatory mechanisms for song and speech development (77-83).

Recent comparative genomic studies have confirmed conserved brain pathways at the molecular level between songbirds and humans (66), thus strengthening the utility of songbird models for understanding human disorders. In particular, data from zebra finch demonstrated robust overlap of genes in two song areas (Area X and RA) with human speech areas (striatum and laryngeal motor cortex). In addition, specific genes were identified that demonstrate convergent expression in the songbird and human brain, opening up possibilities for studying the effects of manipulating these genes in the songbird on vocal learning and song production. These genes also have some links to brain disorders and future disease gene discoveries may uncover additional relevance of these genes to cognitive disorders.

Speech deficits in psychiatric diseases and developmental disorders

Communication disorders

The recently released DSM-5 diagnostic criteria places several previously separate communication disorders under one umbrella. These include language disorders (both expressive and receptive), speech sound disorders, childhood-onset fluency disorder (*i.e.* stuttering), and social communication disorder (in the absence of other ASD-relevant symptoms) (84, 85). We will first review recent advances in our understanding of speech disorders that fall under this umbrella, including stuttering and oral facial dyspraxia, and then turn to social communication disorders associated with ASD and schizophrenia.

A few genes have been identified as playing a role in stuttering: *GNPTAB* (N-acetylglucosamine-1-phosphate transferase, alpha and beta subunits), *GNPTG* (N-acetylglucosamine-1-phosphate transferase, gamma subunit), and *NAGPA* (N-acetylglucosamine-1-phosphodiester alpha-N-acetylglucosaminidase) (86). Strikingly, all three of these genes converge on a common biological pathway, as they are enzymes involved in lysosome function. Transgenic mouse models may be able to provide valuable insights into the roles of these pathways in vocal control. Also, further genetic studies to identify additional genes need to be undertaken. Recent work in songbirds have described the emergence of syllable repetitions following lesions of portions of the striatopallidal circuits involved in song learning (87). This work may have relevance to neurogenic stuttering, which has been reported following basal ganglia lesions in humans (88).

Unlike other communication disorders, significant biological insights have been made toward understanding language disorders, specifically orofacial dyspraxia. Orofacial dyspraxia is characterized by ineffective coordination and/or immobility of the face and mouth that results in unintelligible speech (89). Significant insights were made into this isolated speech disorder upon the identification of a causative gene, *FOXP2* (forkhead box P2), in a large family with an inherited form of the disorder (KE family) (82). Interestingly, while the affected KE family members as well as other individuals with *FOXP2* mutations

do not exhibit strong cognitive deficit phenotypes there is evidence for these individuals to have lower than average cognitive performances as well as evidence for FOXP2 regulating genes implicated in ASD and/or schizophrenia (26, 90, 91).

FOXP2 is a transcription factor with brain expression that peaks during embryonic development (92). A number of animal models have been developed to study FoxP2 function. *Foxp2* knockout (KO) mice are neonatal lethal. Within the first postnatal week, these mice exhibit severe motor deficits, with specific reductions in USVs (93, 94). Mice containing a point mutation that mimics that of the KE family (*Foxp2*$^{KE/+}$ mice) also exhibit reduced USVs (95). The reduced number of USVs in the *Foxp2*$^{KE/+}$ heterozygous mice can be rescued by expression of wild type FOXP2 in cerebellar Purkinje neurons (95, 96). In line with this, MRI studies of the KE family have indicated grey matter volumetric deficits in the cerebellum (as well as the caudate nucleus, Broca's area, temporal pole and precentral gyrus) (97). Interestingly, a different line of *Foxp2* mice homozygous for the KE family point mutation, not only exhibit altered USVs but also demonstrate striatal-based motor deficits (98), suggesting a potential link between striatal dysfunction and altered USVs.

Studies in vocal learning songbirds have also found links between FoxP2, striatal circuits and vocal communication (77-80, 99). FoxP2 is highly expressed in the songbird basal ganglia circuit. In particular FoxP2 is prominently expressed in a specialized portion of the striatopallidum, termed Area X, involved in song learning and song production in birds (79, 99). Knockdown of FoxP2 specifically in Area X disrupts song learning in juvenile birds and social context dependent modulation of song variability in adult birds (78, 80). Intriguingly, these FoxP2 associated disruptions in song learning result from noisy production of song syllables, increased levels of vocal variability and repetition or dropping of song syllables. These behavioral disruptions in vocal production parallel disruptions associated with oral facial dyspraxia and are associated with disruptions in dopaminergic sensitivity in striatal circuits (78).

Based on the molecular evolution of FOXP2, “humanized” *Foxp2* mice have been generated containing two human-specific amino acids (100). These mice have changes in the complexity of USVs and also exhibit faster switching between declarative and procedural learning (100, 101). Such changes could be clues to the evolution of language. For instance, the ability to more quickly incorporate procedural learning could have been instrumental for the emergence of language to co-opt existing brain learning circuitry for language. Further detailed analysis of all of these *Foxp2* mutant mice as well as analysis of potential brain region-specific *Foxp2* conditional KO mice (94) should provide additional details about correlations between affected brain regions in rodent models and specific behavioral deficits.

ASD and associated syndromes

Advances in genome editing have allowed for the generation of rat models relevant to ASD. Recently published models include knockout of *Fmr1*, *Nlgn3* (*neuroligin 3*), and *Nrxn1-α* (*Neurexin-1 alpha*) (102-104). While *Fmr1* or *Nlgn3* knockout rats exhibit some altered ASD-relevant behaviors, USVs are not significantly different during juvenile social interactions (104). In contrast, *Fmr1* KO rats exhibit diminished responses to auditory

stimuli in line with altered auditory processing in patients with fragile X syndrome (102). These studies in genetically modified rats are just a beginning for using these animals for the study of ASD and related syndromes. More models are being generated and further work needs to be done to examine vocal behaviors in these animals.

There is significant co-morbidity of ASD with both epilepsy and intellectual disability (105, 106). Mutations in the gene *SRPX2* (sushi-repeat containing protein X-linked 2), which encodes a secreted protein involved in synapse formation, have been linked to a constellation of phenotypes including temporal lobe seizures, oral and speech dyspraxia, and intellectual disability (107, 108). Further work has demonstrated that FOXP2 regulates expression of SRPX2 in cells and a patient-relevant mutation in *FOXP2* could specifically affect FOXP2 regulation of *SRPX2* (109). To directly assess the *in vivo* importance of this signaling pathway, knockdown of SRPX2 in the cortex of rodents was carried out (108). Reduction of SRPX2 leads to decreases in synapse formation and USVs through a Foxp2-dependent mechanism (108). Together, these data suggest that FoxP2 regulation of SRPX2 may be important for both temporal lobe function at risk in epilepsy as well as vocal behavior linked to ASD. Further characterization of SRPX2 function downstream of FoxP2 compared to FoxP2 regulation of other genes should begin to parse out in detail the molecular pathways at risk in ASD.

Many mouse models of ASD demonstrate altered USVs, however, a clear pattern has not emerged in terms of consistent changes in either pup or adult USVs with ASD-relevant models (110). Recent MRI data of 26 ASD mouse models uncovered at least 3 groups of mice that could be clustered based on neuroanatomical changes (111), and some of these models have been tested for USV deficits (110). Further studies correlating anatomical and vocal abnormalities in ASD mouse models are needed, but this recent work hints that with further research more general patterns may emerge. Mouse models of syndromic forms of ASD (i.e. Rett's syndrome and Fragile X syndrome) illustrate this as both *Mecp2* and *Fmr1* mouse models have decreased USVs and striatal volumes (110, 111).

Schizophrenia

While disordered language is a clinically defining aspect of schizophrenia, this symptom is debated as either a specific deficit in language functions such as impairment in syntactic comprehension accuracy that cannot be accounted for by global cognitive deficits (112, 113), or as an indication of disordered thought in general, rather than a specific deficit in speech or language (114). With the exception of a few genes, the field of schizophrenia has suffered from a lack of genetic models for studying the biology and brain circuitry involved in this disorder. However, a recent large-scale genome-wide association study has identified 108 robust loci in schizophrenia corresponding to association with roughly 90 genes (115). This may represent a manageable number of genes to model in animals across the entire research community. A few pharmacological models that induce schizophrenia-like symptoms in rats have been used in the investigation of effects on vocalizations. Administration of methylazoxymethanol acetate (MAM), which methylates DNA, leads to an increased stress response including more USVs in an acute foot shock paradigm (116). Similar effects were also found in a maternal immune activation model using prenatal

exposure to polyinosinic:polycytidylic acid (poly I:C) in that rats had increased USVs in a fear conditioning paradigm (117). Thus, these results suggest that USVs in rodents can be altered together with other behavioral and neuroanatomical deficits reminiscent of schizophrenia. It will be very informative to initiate future studies that utilize alterations of novel schizophrenia related genes to determine whether specific aspects of vocalizations are affected in this disorder.

Conclusions and future directions

There is no perfect animal model for human speech and language disorders. However, comparative approaches can be used to provide insights into how genetic disorders disrupt conserved brain processing for complex communicative behaviors and by implication inform us as to how humans learn speech and language. As greater insights are made into the genes and molecular pathways at risk in human psychiatric disorders, such information can be used to more directly model these mechanisms in animal models and ultimately develop targeted therapies.

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References

1. Developmental Disabilities Monitoring Network Surveillance Year Principal I, Centers for Disease C, Prevention. Prevalence of autism spectrum disorder among children aged 8 years - autism and developmental disabilities monitoring network, 11 sites, United States, 2010. MMWR Surveill Summ. 2014; 63:1–21.
2. Wodka EL, Mathy P, Kalb L. Predictors of phrase and fluent speech in children with autism and severe language delay. Pediatrics. 2013; 131:e1128–1134. [PubMed: 23460690]
3. Tandon R, Gaebel W, Barch DM, Bustillo J, Gur RE, Heckers S, et al. Definition and description of schizophrenia in the DSM-5. Schizophr Res. 2013; 150:3–10. [PubMed: 23800613]
4. Tomblin JB, Records NL, Buckwalter P, Zhang X, Smith E, O'Brien M. Prevalence of specific language impairment in kindergarten children. J Speech Lang Hear Res. 1997; 40:1245–1260. [PubMed: 9430746]
5. Vernes SC, Newbury DF, Abrahams BS, Winchester L, Nicod J, Groszer M, et al. A functional genetic link between distinct developmental language disorders. N Engl J Med. 2008; 359:2337–2345. [PubMed: 18987363]
6. Yairi E, Ambrose N. Epidemiology of stuttering: 21st century advances. Journal of fluency disorders. 2013; 38:66–87. [PubMed: 23773662]
7. Hauser, MD. The evolution of communication. Cambridge, Massachusetts: MIT Press; 1996.
8. Egnor SE, Hauser MD. A paradox in the evolution of primate vocal learning. Trends Neurosci. 2004; 27:649–654. [PubMed: 15474164]
9. Doupe AJ, Kuhl PK. Birdsong and human speech: common themes and mechanisms. Annu Rev Neurosci. 1999; 22:567–631. [PubMed: 10202549]
10. Janik VM, Slater PJB. Vocal learning in mammals. Adv Study Behav. 1997; 26:59–99.
11. Petkov CI, Jarvis ED. Birds, primates, and spoken language origins: behavioral phenotypes and neurobiological substrates. Front Evol Neurosci. 2012; 4:12. [PubMed: 22912615]

12. Jarvis ED. Learned birdsong and the neurobiology of human language. Ann N Y Acad Sci. 2004; 1016:749–777. [PubMed: 15313804]
13. Janik VM, Slater PJ. The different roles of social learning in vocal communication. Anim Behav. 2000; 60:1–11. [PubMed: 10924198]
14. Portfors CV, Perkel DJ. The role of ultrasonic vocalizations in mouse communication. Curr Opin Neurobiol. 2014; 28C:115–120. [PubMed: 25062471]
15. Fischer J, Hammerschmidt K. Ultrasonic vocalizations in mouse models for speech and socio-cognitive disorders: insights into the evolution of vocal communication. Genes Brain Behav. 2011; 10:17–27. [PubMed: 20579107]
16. Nowicki S, Searcy WA. The evolution of vocal learning. Curr Opin Neurobiol. 2014; 28:48–53. [PubMed: 25033109]
17. Hauser MD, Chomsky N, Fitch WT. The faculty of language: what is it, who has it, and how did it evolve? Science. 2002; 298:1569–1579. [PubMed: 12446899]
18. Kuhl PK. Brain mechanisms in early language acquisition. Neuron. 2010; 67:713–727. [PubMed: 20826304]
19. Call J, Tomasello M. Does the chimpanzee have a theory of mind? 30 years later. Trends Cogn Sci. 2008; 12:187–192. [PubMed: 18424224]
20. Hopkins WD, Taglialatela J, Leavens DA. Chimpanzees Differentially Produce Novel Vocalizations to Capture the Attention of a Human. Anim Behav. 2007; 73:281–286. [PubMed: 17389908]
21. Miller, DJ.; Konopka, G. Evolution and Development of Language. In: Streelman, JT., editor. Advances in Evolutionary Developmental Biology. Hoboken, N.J.: John Wiley & Sons, Inc.; 2013. p. 173-201.
22. Miller CT, Wren Thomas A. Individual recognition during bouts of antiphonal calling in common marmosets. J Comp Physiol A Neuroethol Sens Neural Behav Physiol. 2012; 198:337–346. [PubMed: 22277952]
23. Savage-Rumbaugh S, Sevcik RA, Hopkins WD. Symbolic cross-modal transfer in two species of chimpanzees. Child Dev. 1988; 59:617–625. [PubMed: 2454784]
24. Takahashi DY, Narayanan DZ, Ghazanfar AA. Coupled oscillator dynamics of vocal turn-taking in monkeys. Curr Biol. 2013; 23:2162–2168. [PubMed: 24139740]
25. Snowdon CT. Affiliative processes and vocal development. Ann N Y Acad Sci. 1997; 807:340–351. [PubMed: 9071362]
26. Lepp S, Anderson A, Konopka G. Connecting signaling pathways underlying communication to ASD vulnerability. Int Rev Neurobiol. 2013; 113:97–133. [PubMed: 24290384]
27. Curry T, Egeto P, Wang H, Podnos A, Wasserman D, Yeomans J. Dopamine receptor D2 deficiency reduces mouse pup ultrasonic vocalizations and maternal responsiveness. Genes Brain Behav. 2013; 12:397–404. [PubMed: 23521753]
28. Ehret G. Infant rodent ultrasounds -- a gate to the understanding of sound communication. Behav Genet. 2005; 35:19–29. [PubMed: 15674530]
29. Holy TE, Guo Z. Ultrasonic songs of male mice. PLoS Biol. 2005:3–e386.
30. Grimsley JM, Monaghan JJ, Wenstrup JJ. Development of social vocalizations in mice. PLoS One. 2011:6–e17460.
31. Arriaga G, Jarvis ED. Mouse vocal communication system: are ultrasounds learned or innate? Brain Lang. 2013; 124:96–116. [PubMed: 23295209]
32. Mahrt EJ, Perkel DJ, Tong L, Rubel EW, Portfors CV. Engineered deafness reveals that mouse courtship vocalizations do not require auditory experience. J Neurosci. 2013; 33:5573–5583. [PubMed: 23536072]
33. Arriaga G, Zhou EP, Jarvis ED. Of mice, birds, and men: the mouse ultrasonic song system has some features similar to humans and song-learning birds. PLoS One. 2012; 7:e46610. [PubMed: 23071596]
34. Hammerschmidt K, Reisinger E, Westekemper K, Ehrenreich L, Strenzke N, Fischer J. Mice do not require auditory input for the normal development of their ultrasonic vocalizations. BMC neuroscience. 2012; 13:40. [PubMed: 22533376]

35. von Merten S, Hoier S, Pfeifle C, Tautz D. A role for ultrasonic vocalisation in social communication and divergence of natural populations of the house mouse (Mus musculus domesticus). PLoS One. 2014; 9:e97244. [PubMed: 24816836]
36. Hoffmann F, Musolf K, Penn DJ. Spectrographic analyses reveal signals of individuality and kinship in the ultrasonic courtship vocalizations of wild house mice. Physiol Behav. 2012; 105:766–771. [PubMed: 22037196]
37. Foote AD, Griffin RM, Howitt D, Larsson L, Miller PJ, Hoelzel AR. Killer whales are capable of vocal learning. Biol Lett. 2006; 2:509–512. [PubMed: 17148275]
38. Janik VM. Cetacean vocal learning and communication. Curr Opin Neurobiol. 2014; 28C:60–65. [PubMed: 25057816]
39. Reichmuth C, Casey C. Vocal learning in seals, sea lions, and walruses. Curr Opin Neurobiol. 2014; 28:66–71. [PubMed: 25042930]
40. King SL, Janik VM. Bottlenose dolphins can use learned vocal labels to address each other. Proc Natl Acad Sci U S A. 2013; 110:13216–13221. [PubMed: 23878217]
41. Musser WB, Bowles AE, Grebner DM, Crance JL. Differences in acoustic features of vocalizations produced by killer whales cross-socialized with bottlenose dolphins. The Journal of the Acoustical Society of America. 2014; 136:1990. [PubMed: 25324098]
42. Ridgway S, Carder D, Jeffries M, Todd M. Spontaneous human speech mimicry by a cetacean. Curr Biol. 2012; 22:R860–861. [PubMed: 23098588]
43. Butti C, Raghanti MA, Sherwood CC, Hof PR. The neocortex of cetaceans: cytoarchitecture and comparison with other aquatic and terrestrial species. Ann N Y Acad Sci. 2011; 1225:47–58. [PubMed: 21534992]
44. Knornschild M, Nagy M, Metz M, Mayer F, von Helversen O. Complex vocal imitation during ontogeny in a bat. Biology letters. 2010; 6:156–159. [PubMed: 19812069]
45. Esser KH. Audio-vocal learning in a non-human mammal: the lesser spear-nosed bat Phyllostomus discolor. Neuroreport. 1994; 5:1718–1720. [PubMed: 7827315]
46. Boughman JW. Vocal learning by greater spear-nosed bats. Proc Biol Sci. 1998; 265:227–233. [PubMed: 9493408]
47. Jones G, Teeling EC, Rossiter SJ. From the ultrasonic to the infrared: molecular evolution and the sensory biology of bats. Frontiers in physiology. 2013; 4:117. [PubMed: 23755015]
48. Yin, J.; Ma, J.; Zhang, S.; Metzner, W. Society for Neuroscience. Washington, D.C: 2008. FoxP2 expression in the brain of echolocating and non-echolocating bats and its possible role in vocalization.
49. Enard W, Przeworski M, Fisher SE, Lai CS, Wiebe V, Kitano T, et al. Molecular evolution of FOXP2, a gene involved in speech and language. Nature. 2002; 418:869–872. [PubMed: 12192408]
50. Konopka G, Bomar JM, Winden K, Coppola G, Jonsson ZO, Gao F, et al. Human-specific transcriptional regulation of CNS development genes by FOXP2. Nature. 2009; 462:213–217. [PubMed: 19907493]
51. Chen Q, Zhu T, Jones G, Zhang J, Sun Y. First knockdown gene expression in bat (Hipposideros armiger) brain mediated by lentivirus. Mol Biotechnol. 2013; 54:564–571. [PubMed: 22965420]
52. Brainard MS, Doupe AJ. What songbirds teach us about learning. Nature. 2002; 417:351–358. [PubMed: 12015616]
53. Mooney, R.; Prather, JF.; Roberts, TF. Birdsong, a neurethological approach to learning and memory. In: Byrne, JH., editor. Learning and memory: a comprehensive reference (memory systems volume). Elsevier; 2008.
54. Catchpole, CK.; Slater, PJ. Bird Song: Biological Themes and Variations. 2nd. Cambridge, UK: Cambridge University Press; 2008.
55. Marler, P.; Slabbekoorn, H. Nature's Music, The Science of Birdsong. 1st. San Diego, California: Elsevier Academic Press; 2004.
56. Marler P. Song learning: the interface between behaviour and neuroethology. Philosophical Transactions of the Royal Society of London - Series B: Biological Sciences. 1990; 329:109–114. [PubMed: 1978357]

57. Salinas-Melgoza A, Wright TF. Evidence for vocal learning and limited dispersal as dual mechanisms for dialect maintenance in a parrot. PloS one. 2012; 7:e48667. [PubMed: 23139809]
58. Pepperberg IM, Sandefer RM, Noel DA, Ellsworth CP. Vocal learning in the Grey parrot (Psittacus erithacus): effects of species identity and number of trainers. J Comp Psychol. 2000; 114:371–380. [PubMed: 11149541]
59. Lavenex PB. Lesions in the budgerigar vocal control nucleus NLc affect production, but not memory, of english words and natural vocalizations. J Comp Neurol. 2000; 421:437–460. [PubMed: 10842208]
60. Pepperberg IM. Proficient performance of a conjunctive, recursive task by an African gray parrot (Psittacus erithacus). J Comp Psychol. 1992; 106:295–305. [PubMed: 1395498]
61. Pepperberg IM, Brezinsky MV. Acquisition of a relative class concept by an African gray parrot (Psittacus erithacus): discriminations based on relative size. J Comp Psychol. 1991; 105:286–294. [PubMed: 1935007]
62. Pepperberg IM. Comprehension of “absence” by an African Grey parrot: Learning with respect to questions of same/different. Journal of the experimental analysis of behavior. 1988; 50:553–564. [PubMed: 16812572]
63. Lipkind D, Marcus GF, Bemis DK, Sasahara K, Jacoby N, Takahasi M, et al. Stepwise acquisition of vocal combinatorial capacity in songbirds and human infants. Nature. 2013; 498:104–108. [PubMed: 23719373]
64. Tchernichovski O, Mitra PP, Lints T, Nottebohm F. Dynamics of the vocal imitation process: how a zebra finch learns its song. Science. 2001; 291:2564–2569. [PubMed: 11283361]
65. Deregnaucourt S, Poirier C, Kant AV, Linden AV, Gahr M. Comparisons of different methods to train a young zebra finch (Taeniopygia guttata) to learn a song. Journal of physiology, Paris. 2013; 107:210–218.
66. Pfenning AR, Hara E, Whitney O, Rivas MV, Wang R, Roulhac PL, et al. Convergent transcriptional specializations in the brains of humans and song-learning birds. Science. 2014; 346:1256846. [PubMed: 25504733]
67. Brainard MS, Doupe AJ. Translating birdsong: songbirds as a model for basic and applied medical research. Annu Rev Neurosci. 2013; 36:489–517. [PubMed: 23750515]
68. Bolhuis JJ, Okanoya K, Scharff C. Twitter evolution: converging mechanisms in birdsong and human speech. Nat Rev Neurosci. 2010; 11:747–759. [PubMed: 20959859]
69. Chen CC, Winkler CM, Pfenning AR, Jarvis ED. Molecular profiling of the developing avian telencephalon: regional timing and brain subdivision continuities. J Comp Neurol. 2013; 521:3666–3701. [PubMed: 23818174]
70. Jarvis ED, Yu J, Rivas MV, Horita H, Feenders G, Whitney O, et al. Global view of the functional molecular organization of the avian cerebrum: mirror images and functional columns. J Comp Neurol. 2013; 521:3614–3665. [PubMed: 23818122]
71. Reiner A, Perkel DJ, Mello CV, Jarvis ED. Songbirds and the revised avian brain nomenclature. Ann N Y Acad Sci. 2004; 1016:77–108. [PubMed: 15313771]
72. Dugas-Ford J, Rowell JJ, Ragsdale CW. Cell-type homologies and the origins of the neocortex. Proc Natl Acad Sci U S A. 2012; 109:16974–16979. [PubMed: 23027930]
73. Butler, AB.; Hodos, W. Comparative Vertebrate Neuroanatomy: Evolution and Adaptation. 2nd. New York: Wiley; 2005.
74. Striedter, GF. Principles of Brain Evolution. Sunderland, MA: Sinauer; 2005.
75. Reiner A, Perkel DJ, Bruce LL, Butler AB, Csillag A, Kuenzel W, et al. Revised nomenclature for avian telencephalon and some related brainstem nuclei. J Comp Neurol. 2004; 473:377–414. [PubMed: 15116397]
76. Jarvis ED, Gunturkun O, Bruce L, Csillag A, Karten H, Kuenzel W, et al. Avian brains and a new understanding of vertebrate brain evolution. Nat Rev Neurosci. 2005; 6:151–159. [PubMed: 15685220]
77. White SA, Fisher SE, Geschwind DH, Scharff C, Holy TE. Singing mice, songbirds, and more: models for FOXP2 function and dysfunction in human speech and language. J Neurosci. 2006; 26:10376–10379. [PubMed: 17035521]

78. Murugan M, Harward S, Scharff C, Mooney R. Diminished FoxP2 Levels Affect Dopaminergic Modulation of Corticostriatal Signaling Important to Song Variability. Neuron. 2013; 80:1464–1476. [PubMed: 24268418]
79. Haesler S, Wada K, Nshdejan A, Morrisey EE, Lints T, Jarvis ED, et al. FoxP2 expression in avian vocal learners and non-learners. J Neurosci. 2004; 24:3164–3175. [PubMed: 15056696]
80. Haesler S, Rochefort C, Georgi B, Licznerski P, Osten P, Scharff C. Incomplete and inaccurate vocal imitation after knockdown of FoxP2 in songbird basal ganglia nucleus Area X. PLoS Biol. 2007; 5:e321. [PubMed: 18052609]
81. Fisher SE, Scharff C. FOXP2 as a molecular window into speech and language. Trends Genet. 2009; 25:166–177. [PubMed: 19304338]
82. Lai CS, Fisher SE, Hurst JA, Vargha-Khadem F, Monaco AP. A forkhead-domain gene is mutated in a severe speech and language disorder. Nature. 2001; 413:519–523. [PubMed: 11586359]
83. MacDermot KD, Bonora E, Sykes N, Coupe AM, Lai CS, Vernes SC, et al. Identification of FOXP2 truncation as a novel cause of developmental speech and language deficits. Am J Hum Genet. 2005; 76:1074–1080. [PubMed: 15877281]
84. Gibson J, Adams C, Lockton E, Green J. Social communication disorder outside autism? A diagnostic classification approach to delineating pragmatic language impairment, high functioning autism and specific language impairment. J Child Psychol Psychiatry. 2013; 54:1186–1197. [PubMed: 23639107]
85. Association AP. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). Washington, DC: American Psychiatric Association; 2013.
86. Kang C, Riazuddin S, Mundorff J, Krasnewich D, Friedman P, Mullikin JC, et al. Mutations in the lysosomal enzyme-targeting pathway and persistent stuttering. N Engl J Med. 2010; 362:677–685. [PubMed: 20147709]
87. Kubikova L, Bosikova E, Cvikova M, Lukacova K, Scharff C, Jarvis ED. Basal ganglia function, stuttering, sequencing, and repair in adult songbirds. Sci Rep. 2014; 4:6590. [PubMed: 25307086]
88. Alm PA. Stuttering and the basal ganglia circuits: a critical review of possible relations. J Commun Disord. 2004; 37:325–369. [PubMed: 15159193]
89. Vargha-Khadem F, Watkins KE, Price CJ, Ashburner J, Alcock KJ, Connelly A, et al. Neural basis of an inherited speech and language disorder. Proc Natl Acad Sci U S A. 1998; 95:12695–12700. [PubMed: 9770548]
90. Spiteri E, Konopka G, Coppola G, Bomar J, Oldham M, Ou J, et al. Identification of the transcriptional targets of FOXP2, a gene linked to speech and language, in developing human brain. Am J Hum Genet. 2007; 81:1144–1157. [PubMed: 17999357]
91. Vargha-Khadem F, Watkins K, Alcock K, Fletcher P, Passingham R. Praxic and nonverbal cognitive deficits in a large family with a genetically transmitted speech and language disorder. Proc Natl Acad Sci U S A. 1995; 92:930–933. [PubMed: 7846081]
92. Usui N, Co M, Konopka G. Decoding the molecular evolution of human cognition using comparative genomics. Brain Behav Evol. 2014; 84:103–116. [PubMed: 25247723]
93. Shu W, Cho JY, Jiang Y, Zhang M, Weisz D, Elder GA, et al. Altered ultrasonic vocalization in mice with a disruption in the Foxp2 gene. Proc Natl Acad Sci U S A. 2005; 102:9643–9648. [PubMed: 15983371]
94. French CA, Groszer M, Preece C, Coupe AM, Rajewsky K, Fisher SE. Generation of mice with a conditional Foxp2 null allele. Genesis. 2007; 45:440–446. [PubMed: 17619227]
95. Fujita E, Tanabe Y, Shiota A, Ueda M, Suwa K, Momoi MY, et al. Ultrasonic vocalization impairment of Foxp2 (R552H) knockin mice related to speech-language disorder and abnormality of Purkinje cells. Proc Natl Acad Sci U S A. 2008; 105:3117–3122. [PubMed: 18287060]
96. Fujita-Jimbo E, Momoi T. Specific expression of FOXP2 in cerebellum improves ultrasonic vocalization in heterozygous but not in homozygous Foxp2 (R552H) knock-in pups. Neurosci Lett. 2014; 566:162–166. [PubMed: 24607928]
97. Belton E, Salmond CH, Watkins KE, Vargha-Khadem F, Gadian DG. Bilateral brain abnormalities associated with dominantly inherited verbal and orofacial dyspraxia. Hum Brain Mapp. 2003; 18:194–200. [PubMed: 12599277]

98. Groszer M, Keays DA, Deacon RM, de Bono JP, Prasad-Mulcare S, Gaub S, et al. Impaired synaptic plasticity and motor learning in mice with a point mutation implicated in human speech deficits. Curr Biol. 2008; 18:354–362. [PubMed: 18328704]

99. Teramitsu I, Kudo LC, London SE, Geschwind DH, White SA. Parallel FoxP1 and FoxP2 expression in songbird and human brain predicts functional interaction. J Neurosci. 2004; 24:3152–3163. [PubMed: 15056695]

100. Enard W, Gehre S, Hammerschmidt K, Holter SM, Blass T, Somel M, et al. A humanized version of Foxp2 affects cortico-basal ganglia circuits in mice. Cell. 2009; 137:961–971. [PubMed: 19490899]

101. Schreiweis C, Bornschein U, Burguiere E, Kerimoglu C, Schreiter S, Dannemann M, et al. Humanized Foxp2 accelerates learning by enhancing transitions from declarative to procedural performance. Proc Natl Acad Sci U S A. 2014

102. Engineer CT, Centanni TM, Im KW, Rahebi KC, Buell EP, Kilgard MP. Degraded speech sound processing in a rat model of fragile X syndrome. Brain Res. 2014; 1564:72–84. [PubMed: 24713347]

103. Esclassan F, Francois J, Phillips KG, Loomis S, Gilmour G. Phenotypic characterization of nonsocial behavioral impairment in neurexin 1alpha knockout rats. Behavioral neuroscience. 2015; 129:74–85. [PubMed: 25420124]

104. Hamilton SM, Green JR, Veeraragavan S, Yuva L, McCoy A, Wu Y, et al. Fmr1 and Nlgn3 knockout rats: novel tools for investigating autism spectrum disorders. Behavioral neuroscience. 2014; 128:103–109. [PubMed: 24773431]

105. Brooks-Kayal A. Epilepsy and autism spectrum disorders: are there common developmental mechanisms? Brain Dev. 2010; 32:731–738. [PubMed: 20570072]

106. Matson JL, Williams LW. The making of a field: the development of comorbid psychopathology research for persons with intellectual disabilities and autism. Res Dev Disabil. 2014; 35:234–238. [PubMed: 24269230]

107. Roll P, Rudolf G, Pereira S, Royer B, Scheffer IE, Massacrier A, et al. SRPX2 mutations in disorders of language cortex and cognition. Hum Mol Genet. 2006; 15:1195–1207. [PubMed: 16497722]

108. Sia GM, Clem RL, Huganir RL. The human language-associated gene SRPX2 regulates synapse formation and vocalization in mice. Science. 2013; 342:987–991. [PubMed: 24179158]

109. Roll P, Vernes SC, Bruneau N, Cillario J, Ponsole-Lenfant M, Massacrier A, et al. Molecular networks implicated in speech-related disorders: FOXP2 regulates the SRPX2/uPAR complex. Hum Mol Genet. 2010; 19:4848–4860. [PubMed: 20858596]

110. Michetti C, Ricceri L, Scattoni ML. Modeling social communication deficits in mouse models of autism. Autism. 2012; S1

111. Ellegood J, Anagnostou E, Babineau BA, Crawley JN, Lin L, Genestine M, et al. Clustering autism: using neuroanatomical differences in 26 mouse models to gain insight into the heterogeneity. Mol Psychiatry. 2014

112. Condray R, Steinhauer SR, van Kammen DP, Kasparek A. The language system in schizophrenia: effects of capacity and linguistic structure. Schizophr Bull. 2002; 28:475–490. [PubMed: 12645679]

113. Paulsen JS, Romero R, Chan A, Davis AV, Heaton RK, Jeste DV. Impairment of the semantic network in schizophrenia. Psychiatry Res. 1996; 63:109–121. [PubMed: 8878307]

114. Harrow M, O'Connell EM, Herbener ES, Altman AM, Kaplan KJ, Jobe TH. Disordered verbalizations in schizophrenia: a speech disturbance or thought disorder? Comprehensive psychiatry. 2003; 44:353–359. [PubMed: 14505295]

115. Schizophrenia Working Group of the Psychiatric Genomics C. Biological insights from 108 schizophrenia-associated genetic loci. Nature. 2014; 511:421–427. [PubMed: 25056061]

116. Zimmerman EC, Bellaire M, Ewing SG, Grace AA. Abnormal stress responsivity in a rodent developmental disruption model of schizophrenia. Neuropsychopharmacology. 2013; 38:2131–2139. [PubMed: 23652286]

117. Yee N, Schwarting RK, Fuchs E, Wohr M. Increased affective ultrasonic communication during fear learning in adult male rats exposed to maternal immune activation. Journal of psychiatric research. 2012; 46:1199–1205. [PubMed: 22687817]

118. Roberts TF, Gobes SM, Murugan M, Olveczky BP, Mooney R. Motor circuits are required to encode a sensory model for imitative learning. Nat Neurosci. 2012; 15:1454–1459. [PubMed: 22983208]

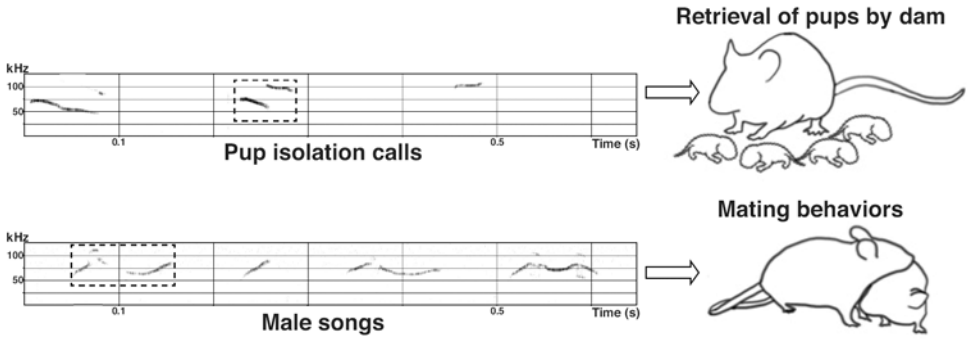

Figure 1. Rodent ultrasonic vocalizations

Top panel: rodents exhibit USVs as pups when isolated from the dam, and these calls assist in retrieval of the pups. Bottom panel: adult male rodents emit USVs when attracting a female for mating. Not shown are instances when males or females emit USVs in the presence of a rodent of the same sex. Example sonograms are depicted for each type of behavior. A representative complex call containing a frequency “jump” is boxed in each example. Adult USVs or songs typically have greater numbers of complex calls than seen in pup isolation calls.

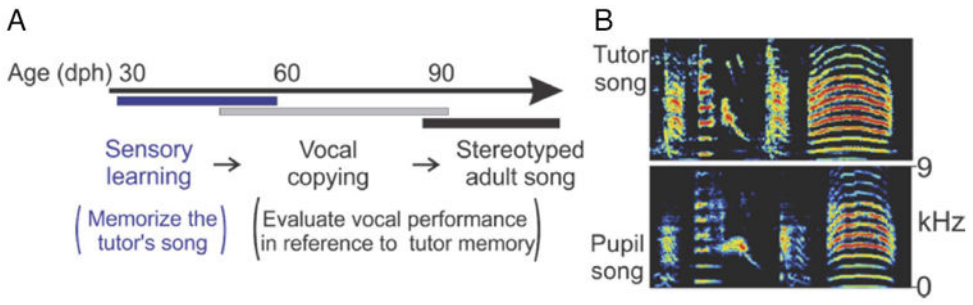

Figure 2. Vocal imitation in songbirds

Left panel (a): Developmental timeline for zebra finch song learning. Zebra finches are a commonly studied species of songbird that learn a single song during a developmental critical period that extends from 30 to 90 days post-hatching. This critical period is composed of three phases. During the first phase young birds memorize the song of an adult model. During the second phase young birds use auditory feedback to evaluate their song imitation and slowly learn to produce a nearly perfect copy of the memorized song. During this period young birds may practice their song as much as 3,000 times a day. After 90 days of age birds begin to crystallize this adult song, leading to a highly stereotyped adult song pattern. Right panel (b): These panels show sonograms (frequency versus time plots) of an adult bird's song and imitation of the song by another bird. The song contains 4 syllables, indicated by the four separate acoustic elements and is 600 milliseconds long. Comparison of the timing and acoustic features of the songs shows clear patterns of vocal imitation. Figure modified from Roberts et al., 2012 (Fig 1a and Fig 2e) (118).

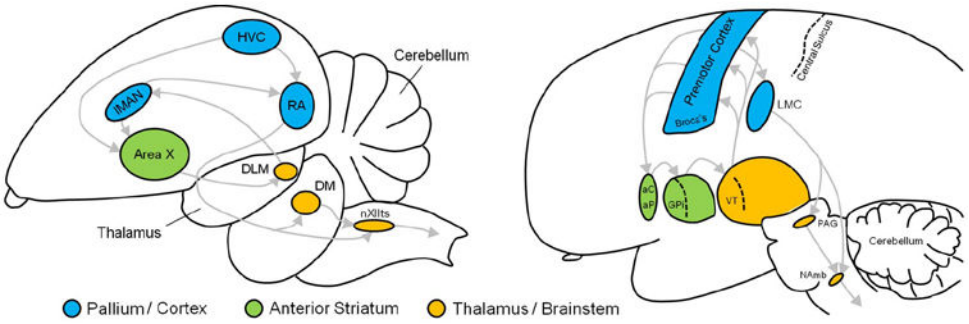

Figure 3. Conserved brain pathways between songbird and human

Left panel: schematic of songbird brain. Right panel: schematic of human brain. Abbreviations: Area X, area X of the striatum; DLM, medial nucleus of the dorsolateral thalamus; DM, dorsal medial nucleus of the midbrain; HVC, nidopallial vocal nucleus; lMAN, lateral magnocellular nucleus of anterior nidopallium; nXIIts, tracheosyringeal subdivision of the hypoglossal nucleus; RA, arcopallial vocal nucleus; aC, anterior caudate nucleus; aP, anterior putamen; FMC, facial motor cortex; GPi, inferior globus pallidus; NAmb, nucleus ambiguous; PAG, periaqueductal gray matter; VT, ventral thalamus. Figure modified from Miller and Konopka, 2013 and based on Pfenning et al., 2014 (21, 66).