

AVIAN GENOMICS

Convergent transcriptional specializations in the brains of humans and song-learning birds

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INTRODUCTION: Vocal learning, the ability to imitate sounds, is a trait that has undergone convergent evolution in several lineages of birds and mammals, including song-learning birds and humans. This behavior requires cortical and striatal vocal brain regions, which form unique connections in vocal-learning species. These regions have been found to have specialized gene expression within some species, but the patterns of specialization across vocal-learning bird and mammal species have not been systematically explored.

RATIONALE: The sequencing of genomes representing all major vocal-learning and vocal-nonlearning avian lineages has allowed us to develop the genomic tools to

measure anatomical gene expression across species. Here, we asked whether behavioral and anatomical convergence is associated with gene expression convergence in the brains of vocal-learning birds and humans.

RESULTS: We developed a computational approach that discovers homologous and convergent specialized anatomical gene expression profiles. This includes generating hierarchically organized gene expression specialization trees for each species and a dynamic programming algorithm that finds the optimal alignment between species brain trees. We applied this approach to brain region gene expression databases of thousands of samples and genes that we and others generated from multiple species, including

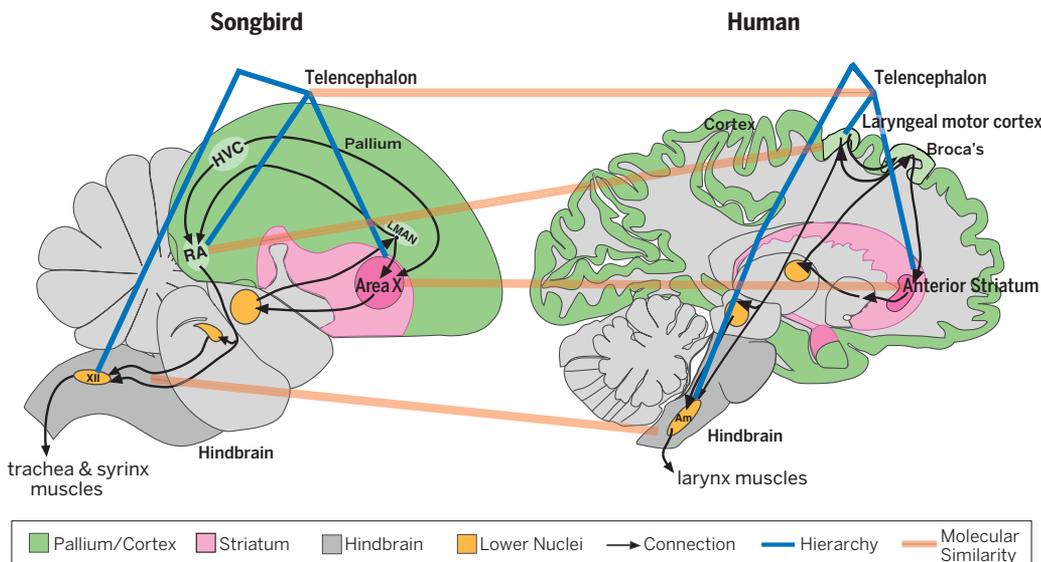
humans and song-learning birds (songbird, parrot, and hummingbird) as well as vocal-nonlearning nonhuman primates (macaque) and birds (dove and quail). Our results confirmed the recently revised understanding of the relationships between avian and mammalian brains. We further found that songbird Area X, a striatal region necessary for vocal learning, was most similar to a part

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of the human striatum activated during speech production. The RA (robust nucleus of the arcopallium) analog of song-learning birds, necessary for song production, was most similar to laryngeal motor cortex regions in humans that control speech production. More than 50 genes contributed to their convergent specialization and were enriched in motor control and neural connectivity functions. These patterns were not found in vocal nonlearners, but songbird RA was similar to layer 5 of primate motor cortex for another set of genes, supporting previous hypotheses about the similarity of these cell types between bird and mammal brains.

CONCLUSION: Our approach can accurately and quantitatively identify functionally and molecularly analogous brain regions between species separated by as much as 310 million years from a common ancestor. We were able to identify analogous brain regions for song and speech between birds and humans, and broader homologous brain regions in which these specialized song and speech regions are located, for tens to hundreds of genes. These genes now serve as candidates involved in developing and maintaining the unique connectivity and functional properties of vocal-learning brain circuits shared across species. The finding that convergent neural circuits for vocal learning are accompanied by convergent molecular changes of multiple genes in species separated by millions of years from a common ancestor indicates that brain circuits for complex traits may have limited ways in which they could have evolved from that ancestor. ■



Identifying molecular brain similarities across species. Brain region gene expression specializations were hierarchically organized into specialization trees of each species (blue lines), including for circuits that control learned vocalizations (highlighted green, purple, and orange regions). A set of comparative genomic algorithms found the most similarly specialized regions between songbird and human (orange lines), some of which are convergently evolved.

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Cite this article as A. R. Pfenning *et al.*, *Science* **346**, 1256846 (2014).
DOI: 10.1126/science.1256846