Animal Communication – Focus on Vocal Learning

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Language

- A major component of what makes humans unique
- Sensory-motor, conceptual-intentional, recursion (Hauser, Chomsky & Fitch; Science, 2002)
- Preadaptions for subcomponents must exist in other species.
The vocal learning sub-component

- The ability to modify motor programs to make new vocalizations
- Used in mimicry, but can be creative
- Accomplished via hearing others and auditory feedback of self
- Not to be confused as association of innate sounds with objects in the environment
- Not ‘uniquely human’ yet, critical to a sense of well-being
The KE Family Speech Deficit

- videos
  - 'Friends'
  - Timmy w/speech therapist
  - You Tube clip

Need for non-human animal models
How can we prove that a given species is capable of vocal learning?
Animal behaviour: Elephants are capable of vocal learning

Joyce H. Poole, Peter L. Tyack, Angela S. Stoeger-Horwath and Stephanie Watwood

“Two animals coin unexpected sounds as a surprising form of social communication.”
Sonograms of vocalizations

Sonograms are visual depictions of sound

X axis = frequency (pitch), y = time, darkness = amplitude
Evidence for elephant vocal learning

Scatterplot of frequency vs. duration of calls.

Mlaika's imitations (green triangles) resemble truck sounds (light blue triangles) and differ from her normal calls (yellow triangles), which resemble calls of other African elephants (dark blue: stars, adult female; diamonds, adult male; squares, female calf; hexagons, male calf). Calimero makes chirp-like sounds (pink circles) similar to the chirps of the Asian elephants (red circles) who lived with him.
…they look different too!

African elephants    Indian elephant
Songbirds are ideal for the study of vocal learning
Developmental timeline/Critical periods/Auditory dependence
Relative timing of human vs. zebra finch vocal learning

Universal speech perception

Human

0 3 6 9 12 months

Universal speech perception

Sensory acquisition

20 60 100 days

Sensorimotor learning

Finch

Babbling/ language-specific speech perception

First words!

Sensorimotor learning

Crystallization

Hatchling 13days 17days Fledgling Adult
Adult singing: practice vs. performance

Undirected  Directed

adapted from Jarvis et al (1999)
Normal song development

- Sensory Acquisition
- Sensorimotor Learning
- Crystallization

Post-hatch day:
- Sings A
- Sings B > A
Vocal learning depends on hearing

The Eastern phoebe, in contrast to the zebra finch, is not a songbird and doesn’t need to learn its song.

Wilbrecht & Nottebohm, 2003
Kroodsma & Konishi, 1991
Isolation from tutor

- Crystallization
- Sensorimotor Learning
- Sensory Acquisition
- Isolation

Post-hatch day

0 50 100
Isolates learn new notes when controls do not
Two similar birds, but

Memorizes  Does not memorize
Summary of auditory experience

- Females prefer songs of normal > isolate > deaf at 35 > deaf at 20 days

- Isolation can create two birds of the same chronological age, but of different learning states

- Enables identification of molecules unique to the memorizing state

- A similar postponement of sensorimotor learning can be done (Funabiki & Konishi, 2003)
Neural substrate
Zebra finch brains are sexually dimorphic

(courtesy of Eugene Akutagawa)
The avian song circuit

The avian song circuit involves neurons from the HVC and RA projecting to motor neurons controlling the syrinx. The HVC is connected to the RA through a pathway marked with "sing this!". These neural pathways are integrated into the vocal motor pathway and are ultimately regulated by cortical centers.
The avian song circuit

HVC

RA

DLM

LMAN

X

Cortex

Striatum

Thalamus

anterior forebrain pathway

“modify!”
Comparison of avian and human circuitry
Songbird model system

- Vocal learner that captures some of the complexity of human speech
- Socially-learned and influenced
- Parallel phases and neuroanatomy
- Advantage: Identified circuit
The KE family

- Deficits in spoken and written language
- Production and comprehension
- Normal non-verbal IQ but low verbal IQ
- Normal peripheral control of orofacial musculature

Vargha-Khadem et al (1995) PNAS
The basal ganglia is a major site of abnormality

Frontal view striatum

Transverse view striatum
FoxP2 - a molecular entry point to language

- FOX genes are transcription factors, so act by regulating other molecules
- FOX family members act during embryogenesis
- FOXP2 mutations cause orofacial dyspraxia

FoxP2 DNA Binding Domain: R553
Working model for FoxP2 in vocal learning

Formation vs function

Practice vs performance

Sensory acquisition

Sensorimotor learning

Maintenance

FoxP2
Sagittal vs. frontal orientation

HVC

RA

DLM

LMAN

cortex

striatum

thalamus
Detection of 'gene of interest'

Gene: GENE
mRNA: a a g c c t
probe: u u c g g a

bird 4
slide A
Parallel expression of FOXP2 in songbirds and humans

Teramitsu, Kudo, Geschwind, White (2004)
Working model for FoxP2 in vocal learning

Formation vs function
- Sensory acquisition
- Sensorimotor learning

Practice vs performance
- Maintenance

FoxP2
- Targets

?
Adult singing: two behaviors in one

adapted from Hessler & Doupe (1999)
FoxP2 expression in Area X is regulated by the social context of song

Non-singing

Undirected

Directed

Kruskal-Wallis, $p < 0.0005$

Teramitsu & White (2006)
Working model for FoxP2 in vocal learning

Formation vs function

Practise vs performance

Sensory acquisition

Sensorimotor learning

Maintenance

FoxP2

Targets
Deafening prior to sensorimotor learning leads to abnormal songs

Tutor

Sham-control son (60d)

Deafened son (60d)
Motor-driven down-regulation of FoxP2

Non-singing vs. singing: $p < 0.02$, both conditions

Teramitsu, Poopatanapong, Torrisi & White (2010)
Hearing links song to FoxP2 levels

Teramitsu, Poopatanapong, Torrisi & White (2010)
Our working model for FoxP2 in vocal learning

Formation vs function  Practice vs performance

Sensory acquisition  Sensorimotor learning  Maintenance

FoxP2 Targets
FoxP1 expression is sexually dimorphic

Teramitsu, Kudo, Geschwind, White (2004)
Assessing the impact of *FOXP1* mutations on developmental verbal dyspraxia Vernes, MacDermot, Monaco and Fisher (2009)

"We conclude that *FOXP1* mutations are unlikely to represent a major cause of DVD"

A 785kb deletion of 3p14.1p13, including the *FOXP1* gene, associated with speech delay, contractures, hypertonia and blepharophimosis Pariani, Spencer, Graham and Rimoin (2009)

"We feel that a deletion of *FOXP1* should be a part of any differential diagnosis when evaluating a patient with speech delay, developmental delay, blepharophimosis, and athrogryposis"

Haploinsufficiency of *foxp1* is associated with Chiari I malformation and speech language disorder Abdul-Rahman, Zimmerman, Justice & Lese-Martin - American Society for Human Genetics meeting, 2008

"Songbird and human fetal brain analysis supports overlapping expression of both *FOXP1* and *FOXP2* in structures important for learned articulation, which may explain the speech/language phenotype in this patient"
These data could NOT have been obtained in humans

- FoxP2 likely has a post-organizational role in learned vocalizations
- FoxP1 may also be critical for language
- Basal ganglia FoxP2 decreases during motor practice, especially during learning
- Hearing links FoxP2 to levels of practice
- Birds may ‘self-regulate’ by how often they practice
Once you're hatched, what's it doing?
FoxP2 as a 'plasticity gate'

Sensorimotor learning   Maintenance

Sound monitoring

Lights on
T=0 for NS-UD

NS or UD
UD analysis

T=2 hours
For NS-UD: NS ends, UD starts
For UD-UD: UD continues if >90 motif criteria was met

First song
T=0 for UD-UD

FoxP2 high or low
Syllables and sequences appear more variable after song practice.

Miller, Hilliard & White (2010)
Sequencing seems more variable after practice

**NS-UD**
(High FoxP2)

**UD-UD**
(Low FoxP2)

Miller, Hilliard & White (2010)
FoxP2 is just the entry point

- FoxP2 targets in humans, songbirds, mice
- Compare gene networks for unique and shared features
FoxP2 is just the entry point

Sound monitoring

NS or UD  UD analysis

Lights on  T=0 hours
T=0 for NS-UD

First song  T=0 for UD-UD

For NS-UD: NS ends, UD starts
For UD-UD: UD continues if >90 motif criteria was met

FoxP2 high or low
WGCNA reveals modules of co-expressed genes

Hilliard, Miller, Horvath & White, submitted
FoxP2 targets in songbird brain: viral transduction
Pilot data suggest altered gene expression in FoxP2+ cultures.
**CNTNAP2** expression is enriched in cortical loops of humans

**Human**

**Rodent**

Abrahams et al. (2007)
**CNTNAP2** punctuates vocal learning circuitry, similar to humans and unlike rodents

**Male**
- Nissl
- Cntnap2

**Female**
- Nissl
- Cntnap2

Panaitof, Abrahams, Dong, Geschwind & White (2010)
Disrupt genes in song nuclei using virus

To motor neurons innervating the syrinx
AAV driven GFP expression in song control region HVC
Our working model for FoxP2 in vocal learning

Formation vs function

Sensory acquisition

Sensorimotor learning

Maintenance

Practice vs performance
Next steps

• Identify zebra finch FoxP2 targets
• Hone in on genes shared with human targets
• Check human data bases for other genes involved in language disorders
• Characterize expression in songbird
• Functional tests on song
• Identify genes related to syllable order
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