J Neurophysiol 94: 33–34, 2005;
doi:10.1152/jn.00247.2005.

Sex Differences in the Brain: Plasticity and Constraints. Focus on "Androgen-Induced Vocal Transformation in Adult Female African Clawed Frogs"

Sabrina S. Burmeister
Department of Biology, University of North Carolina, Chapel Hill, North Carolina

One of the fundamental questions in neuroscience is *How does variation in the nervous system give rise to variation in behavior?* The study of sex differences can be a powerful way to address this question because it enables comparison of divergent neural specializations within a species. The origin of neural and behavioral dimorphisms has been largely attributed to sex steroid hormones. According to the organizational hypothesis, steroid hormones secreted from the gonads during development permanently shape the brain and body of the adult, as though acting on a *tabula rasa*. Although the classic studies described irreversible organization by developmental exposure to androgens, adults of some species retain sensitivity to the organizing power of androgens. These examples provide an important opportunity to dissect the mechanisms by which steroids shape behavior through changes in the nervous system. In this issue of the *Journal of Neurophysiology*, Potter et al. (p. 415–428) demonstrate a remarkable level of androgen-induced vocal plasticity in adult female African clawed frogs (*Xenopus laevis*). The authors' meticulous observation of simultaneous changes in behavior, laryngeal muscle physiology, and motoneuron morphology provide clues to the origins of and constraints on this vocal transformation.

Although both male and female *X. laevis* vocalize, their calls differ acoustically and functionally. The sexual advertisement call of males alternates between fast and slow click rates that are amplitude modulated and functions to solicit matings from females. In contrast, the predominant call of females consists of slow irregular clicks and communicates a lack of sexual receptivity. Since both males and females call, the neural circuit for vocalization is similar in the two sexes (Brahic and Kelley 2003). Many of the acoustic differences between male and female vocalizations can be explained by physiological differences in the vocal organ (larynx) and laryngeal motoneurons in the brain stem which control laryngeal muscular contractions (Kelley 1996). The female larynx is composed only of slow-twitch fibers and is, therefore, incapable of producing male-like click rates. The laryngeal motoneurons, likewise, have specializations that enable accurate temporal encoding of male-like click rates. The dimorphic characteristics of the larynx and the motoneurons controlling them are, in turn, controlled by exposure to androgens during development (Kelley 1996). If juvenile females are implanted with testes early enough during development, they will produce fully masculine calls as adults, as predicted by the organizational hypothesis. Earlier studies had suggested, however, that *X. laevis* does not strictly conform to the organizational hypothesis. That is, some adult females will produce male-like advertisement calls if exposed to testosterone.

Potter et al. set out to map the ontogeny of androgen-induced vocal plasticity in adult females, its origin, and limits. They adopted an intensive behavioral monitoring scheme that allowed them to detect even small changes in vocalizations over time. Motoneuron somas grew to the size of males within 1 week of testosterone administration, and the female's unreceptive calls began to include faster clicks, suggesting changes in the active membrane properties of the motoneurons. Changes in the contractile properties of the laryngeal muscle became fully masculinized by 4 weeks, but male-like advertisement calls appeared only later. By week 13, all females were producing male-like advertisement calls. This lag between behavior and physiology points to additional unidentified androgen-induced changes. One possibility is that the females are *capable* of producing these masculinized calls earlier than they are *motivated* to do so. The motivation to solicit courtship from females may depend on changes in the basal forebrain, such as the androgen-sensitive preoptic area. Motivation clearly matters because androgenized females only produced male-like advertisement calls in the presence of other females.

The pace and extent of vocal transformation were certainly surprising. The importance of these results extends beyond identifying this plasticity, however, and lies, in part, in understanding why the females fall short. Although all females produced male-like sexual advertisement calls, the calls remained acoustically deformed: androgenized females never produced clicks as fast as did males. This is intriguing because Potter et al. conclude that the larynges are capable of producing male-like advertisement calls, and the changes in motoneuron morphology suggest extensive plasticity there as well. The authors suggest that the behavioral gap between androgenized females and males originates in the central nervous system and they focus attention on the neuronal networks with which the motoneurons are integrated—specifically, the androgen-sensitive vocal pattern generator presumed to consist of premotor neurons in the dorsal tegmental area of medulla. Little is known about the vocal pattern generator beyond its neuroanatomical relationship with the laryngeal motor nucleus (Brahic and Kelley 2003). Uncovering functional differences in these circuits between androgenized females and males will extend our understanding of the neural specializations underlying sexually distinct behaviors. In addition, identifying these functional differences will raise important questions about how steroid hormones organize the nervous system. Because juvenile females can be fully masculinized but adult females only partially so, there must be some developmental changes that are permanent and others that remain plastic. Thus *X. laevis*

Address for reprint requests and other correspondence: S. S. Burmeister, Department of Biology, CB# 3280, 403 Coker Hall, South Rd, University of North Carolina, Chapel Hill, NC 27599 (E-mail: sburmeister@unc.edu).

contributes to a more nuanced version of the organizational hypothesis that incorporates variation in steroid-induced neural plasticity.

The *X. laevis* model demonstrates an important principle of steroid-regulation of the nervous system. That is, steroids shape behavior through action on complex networks of interrelated parts. In the case of *X. laevis,* androgens are known to shape the larynx, laryngeal motoneurons, and, in some as yet unidentified way, the vocal pattern generator. Additional brain regions involved in sexual communication, including the auditory midbrain, preoptic area, and ventral striatum, are also androgen sensitive. The challenge in understanding how steroids shape behavior is in uncovering the individual contributions of each part. The androgenized female *X. laevis* model has already demonstrated major potential in this endeavor by focusing attention on the vocal pattern generator and, in doing so, contributed to a broader understanding of how variation in the nervous system generates variation in behavior.

REFERENCES

Brahic CJ and Kelley DB. Vocal circuitry in *Xenopus laevis:* telencephalon to laryngeal motor neurons. *J Comp Neurol* 464: 115–130, 2003.

Kelley DB. Sexual differentiation in *Xenopus laevis.* In: *The Biology of Xenopus,* edited by Tinsely RC and Kobel HR. New York: Oxford University Press, 1996, p. 143–176.

Potter KA, Bose T, and Yamaguchi A. Androgen-induced vocal transformation in adult female African clawed frogs. *J Neurophysiol* 94: 415–428, 2005.