RNA interference of gonadotropin-inhibitory hormone gene induces arousal in songbirds

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Gonadotropin-inhibitory hormone (GnIH) was originally identified as a hypothalamic neuropeptide inhibitor of pituitary gonadotropin synthesis and release. However, GnIH neuronal fibers do not only terminate in the median eminence to control pituitary function but also terminate widely in the brain. Wide distribution of GnIH neuronal fibers in the brain suggests its multiple roles in the regulation of behaviors. To identify the role of GnIH neurons in the regulation of behaviors, we investigated the effect of RNA interference (RNAi) of GnIH gene on the behaviors of white-crowned sparrows, highly social songbird species. Administration of small interfering RNA against GnIH precursor mRNA into the third ventricle of male and female birds reduced resting time, spontaneous productions of complex vocalizations, and stimulated brief agonistic vocalizations. GnIH RNAi further enhanced song production in male birds and copulation solicitation in female birds when they were challenged by playbacks of novel male songs. These behaviors resembled the behaviors of breeding birds during territorial defense and courtship. The overall results suggest that GnIH gene silencing induces general and sexual arousal. Analyses of GnIH neuronal fiber distributions in the brain further suggested the importance of GnIH neuronal fibers interacting with gonadotropin-releasing hormone neurons in the regulation of arousal.