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研究課題名（和文）How attention regulates auditory perception during song learning?

研究課題名（英文）How attention regulates auditory perception during song learning?

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研究者番号：１０８３４９４７

交付決定額（研究期間全体）：（直接経費）　　3,300,000円

研究成果の概要（和文）：コミュニケーションを学ぶには、社会的な交流が不可欠です。社会的音声学習の神経メカニズムはまだ不明です。このプロジェクトは、キンカチョウにおける社会情報と歌の学習を統合するための神経回路を特徴付けることを目的としていました。大人の家庭教師から歌の学習をしている間、私は幼鳥の注意センター LC の神経活動を記録しました。 LC活性は、聴覚記憶領域NCMにおける歌選択的神経反応を調節した。 NCM の LC 末端の光遺伝学的阻害により、生の家庭教師の歌に対するニューロンの反応性が低下し、歌の学習が障害されました。 LC-NCM 神経回路は、社会的相互作用の感覚的証拠を統合して、歌の学習を指示します。

研究成果の学術的意義や社会的意義
These findings suggest a general mechanism for validating social information in brain development.

研究成果の概要（英文）：Social interactions are essential when learning to communicate. However, the neural mechanism of social vocal learning remains unknown. This project aimed to characterize a neural circuit for integration of social information in support of accurate song learning in the zebra finch. I recorded neural activity in the attention control center, the locus coeruleus (LC), of juvenile birds during song learning from a live adult tutor. LC activity increased with social information during learning. During live social song learning, LC activity regulated long-term song-selective neural responsiveness in an auditory memory region, the caudomedial nidopallium NCM). Optogenetic inhibition of LC terminals in the NCM reduced NCM neuronal responsiveness to live tutor singing and impaired song learning. These results demonstrate that the LC-NCM neural circuit integrates sensory evidence of real social interactions, to instruct song learning.

研究分野：Neurobiology

キーワード：song learning　neuronal circuits　Noradrenaline

様　式　Ｃ－１９、Ｆ－１９－１、Ｚ－１９（共通）

１．研究開始当初の背景

In birds and other species with vocal communication, auditory learning is effective when accompanied by social interactions with a live adult parent or tutor. Human infants develop phoneme detection through exposure with real social interactions, while passive auditory exposure is insufficient for successful speech development (Kuhl, Neuron 2010; Kuhl et al., Dev. Sci. 2006). Juvenile songbirds learn to sing successfully through vocal communication with live tutors (Yazaki-Sugiyama, Neurosci Res. 2019) but develop poor songs after passive exposure to recorded playback of tutor song. In juvenile zebra finches, song learning improves when they trigger song playback (Tchernichovski et al., Science 2001), suggesting that attention or motivation enhances learning. The brainstem nucleus for noradrenergic (NE) signaling, the locus coeruleus (LC), modulates attention and arousal. LC neuron activity modulates behavioral processes such as long-term memory, sensory perception, and motivation to facilitate learning and memory (Mather et al., Behav. Brain Sci. 2016; Poe et al., Nat Rev Neurosci. 2020). Exposure of juveniles to a live, singing tutor also drives greater expression of immediate early genes in LC neurons compare to control juveniles passively exposed to the same songs through a speaker (Chen et al., Proc Natl Acad Sci U S A 2016). LC neurons project to avian higher auditory cortex, the caudomedial nidopallium (NCM) (Velho et al., PLoS One 2012), a suggested brain locus for the formation of tutor song memory (Yanagihara and Yazaki-Sugiyama Nat Commun. 2016). Subset of NCM neurons selectively respond to a tutor song, and auditory responses of those neurons increase in the presence of a tutor (Yanagihara and Yazaki-Sugiyama Nat Commun. 2016). Those neurons are suggested to be the place where the first tutor song memories are stored and are referred to in the later text as tutor song-selective broad spiking NCM neurons (TUT-selective BS NCM neurons).

２．研究の目的

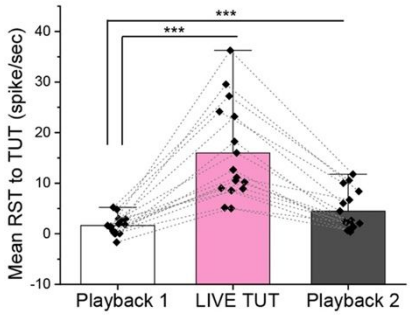
Purpose of this research was to understand whether and how the NCM neural activity can integrate social information from a tutor via the LC. To elucidate this question, it was necessary to record and manipulate neuronal activity in the LC-NCM neural circuit of juvenile zebra finches during song learning from a socially interacting tutor. Later, a quality of song learning from live tutor singing had to be scored in birds whose LC-NCM neuronal circuits were manipulated and compared to the control birds.

３．研究の方法

- Recording the single neuron activity in the LC and the NCM , especially TUT-selective BS NCM neurons, of freely moving juvenile zebra finches when they were alone versus interacting with a live singing tutor to determine if the LC or NCM neurons encode information from social interactions with a tutor. Extracellular recording of neuronal activities was done in free-moving juvenile birds when the birds were subjected to playbacks of multiple songs, including the tutor song (TUT), as well as while the juveniles were subjected to the live tutor singing from a present tutor (LIVE TUT).
- Recording the single neuron activity of the NCM of freely moving juveniles while manipulating the LC-NCM circuit activity using optogenetics. A viral vector mix carrying either inhibitory opsin Arch-GFP (Opto-inhibition group) or only GFP (Control group) was injected into the LC of isolated juvenile birds. Three weeks later, all birds got opto-electrode implanted into the NCM: NCM neuronal activity was measured while the LC terminals were inhibited with light. NCM neuronal activity was measured when the birds were subjected to playbacks of multiple songs, including the tutor song (TUT), as well as while the juveniles were subjected to the live tutor singing from a present tutor (LIVE TUT). LC terminal activity in the NCM was only inhibited with light when the juveniles were subjected to the live tutor singing from a present tutor (LIVE TUT). The effect LC terminal inhibition has on the NCM neuronal response, especially on the TUT-selective BS NCM neurons, was measured and compared between the Opto-inhibition and Control groups.
- Similarity score to the tutor song (TUT) and other song playbacks was measured and compared between Opto-inhibition and Control groups to assess the effectiveness of TUT song learning and to evaluate if the LC-NCM circuit is involved in successful song learning and song copying.
- Inhibition of ADRB2 noradrenergic receptor that is abundantly expressed in the juvenile NCM while the juvenile is subjected to the live tutor singing from a present tutor (LIVE TUT) to access if noradrenaline secreted in from the LC in the NCM plays an important role during song learning. Isolated juveniles were injected with the ADRB2 noradrenergic receptor antagonist propranolol and subjected to the LIVE TUT. Their song learning was measured using a similarity score to the tutor song (TUT) in the sibling group injected with propranolol and those injected with the same volume of saline.

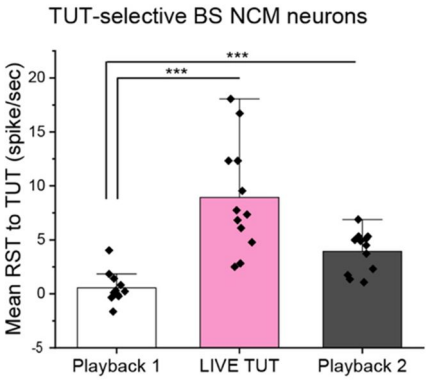
４．研究成果

- LC neurons increased their activities to live tutor singing and sustained them



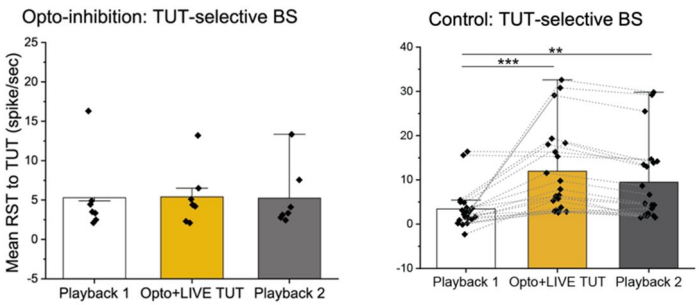
Mean response strength (RST) of LC neurons to tutor song playback (Playback 1 and 2), tutor singing (LIVE TUT) before (Playback 1) and after (Playback 2) hearing LIVE TUT. Number of LC neurons = 16, number of birds = 8. mean ± s.e.m., *p < 0.05, ***p < 0.001.

- Tutor singing has a long-term effect on TUT selectivity of NCM neurons



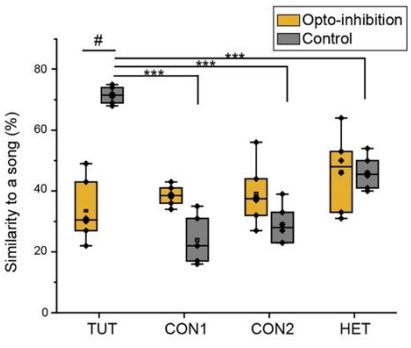
Mean response strength (RST) of TUT-selective BS NCM neurons to tutor song playback (Playback 1 and 2), tutor singing (LIVE TUT) before (Playback 1) and after (Playback 2) hearing LIVE TUT. Number of TUT-selective BS NCM neurons = 12, number of birds = 5. mean ± s.e.m., ***p < 0.001.

- Inhibition of LC inputs impaired development of TUT selectivity in NCM



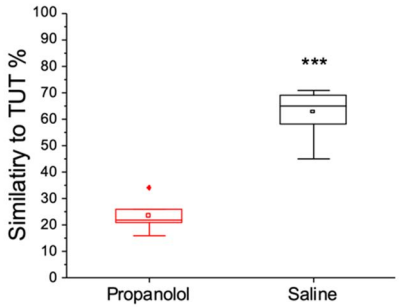
Mean response strength (RST) of TUT-selective BS NCM neurons to tutor song playback (Playback 1 and 2), tutor singing (LIVE TUT) before (Playback 1) and after (Playback 2) hearing LIVE TUT paired with light inhibition (Opto+LIVE TUT). Number of TUT-selective BS NCM neurons = 7 (Opto-inhibition) or 19 (Control), number of birds = 6 for each group. mean ± s.e.m., *p < 0.01, ***p < 0.001.

- Inhibition of LC inputs in NCM degrades tutor song learning



Mean song similarity score of adults to each song stimuli in birds whose LC inputs were optogenetically inhibited (Opto-inhibition) or in birds whose NCM neurons received laser stimulation (Control) during tutor singing. The boxes show the 25-75%, the center lines are defined by the median and open squares by the mean. The whiskers include all data points within 1.5 IQR (Interquartile range). TUT: tutor song, CON1: conspecific song 1, CON2: conspecific song, HET: heterospecific song, number of birds = 6 for each group, "***" indicates differences within the same group, "#" indicates differences between two groups of animals, mean ± s.e.m., #$p < 0.001$, ***$p = 0.001$, Two-sided Student T-test.

- Adrenergic beta 2 receptor antagonist impaired song learning



Mean song similarity score of adults to the tutor song (TUT) stimuli in siblings where 300ul of 0.4 ug/ul ADRB antagonist Propranolol (Propranolol) or same volume of saline (Saline) was injected in the NCM 30 minutes before during tutor singing. The boxes show the 25-75%, the center lines are defined by the median and open squares by the mean. The whiskers include all data points within 1.5 IQR (Interquartile range). Number of birds = 2 for each group, mean ± s.e.m., #$p < 0.001$, ***$p = 0.001$, Two-sided Student T-test.

- From those results, it is conclusive that the intact LC-NCM circuit in juvenile birds is necessary for successful song learning. The LC likely modifies NCM activity by releasing noradrenaline that binds to its receptors ADRB2 in the NCM, although further experiments are required to corroborate those preliminary data.

５．主な発表論文等

〔雑誌論文〕　計1件（うち査読付論文　1件／うち国際共著　1件／うちオープンアクセス　1件）

１．著者名 Jelena Katic, Yuichi Morohashi, Yoko Yazaki-Sugiyama	４．巻 13(1):4442
２．論文標題 Neural circuit for social authentication in song learning	５．発行年 2022年
３．雑誌名 Nature Communications	６．最初と最後の頁 1-12
掲載論文のDOI（デジタルオブジェクト識別子） 10.1038/s41467-022-32207-1.	査読の有無 有
オープンアクセス オープンアクセスとしている（また、その予定である）	国際共著 該当する

〔学会発表〕　計4件（うち招待講演　0件／うち国際学会　4件）

１．発表者名 Jelena Katic
２．発表標題 Social interaction shapes selective memory in the higher auditory area through the neuronal activities of Locus Coeruleus
３．学会等名 Neuroscience 2021, SfN 50th annual meeting（国際学会）
４．発表年 2021年

１．発表者名 Jelena Katic and Yoko Yazaki-Sugiyama
２．発表標題 HOW ATTENTION SHAPES SONG PERCEPTION IN JUVENILE ZEBRA FINCHES DURING SONG LEARNING
３．学会等名 FENS Regional Meeting 2019（国際学会）
４．発表年 2019年

１．発表者名 Jelena Katic and Yoko Yazaki-Sugiyama
２．発表標題 How attention shapes song perception in juvenile zebra finches during song learning
３．学会等名 Japanese neuroscience meeting 2019（国際学会）
４．発表年 2019年

１．発表者名 Jelena Katic and Yoko Yazaki-Sugiyama
２．発表標題 How social interactions affect attention and song perception in juvenile zebra finches during song learning
３．学会等名 Neuroscience 2019 - Society for Neuroscience（国際学会）
４．発表年 2019年

〔図書〕　計0件

〔産業財産権〕

〔その他〕

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６．研究組織

	氏名 （ローマ字氏名） （研究者番号）	所属研究機関・部局・職 （機関番号）	備考

７．科研費を使用して開催した国際研究集会

〔国際研究集会〕　計0件

８．本研究に関連して実施した国際共同研究の実施状況

共同研究相手国	相手方研究機関