Sniffing: A master clock for orofacial rhythms?

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Sniffing: A master clock for orofacial rhythms?

- Coordination of orofacial actions during exploration

- Brainstem circuits for control of rapid vibrissa motion

- Circuitry for coordination of all orofacial motor actions
Following Welker’s behavioral study (1964), what orofacial actions are linked to sniffing?

Moore*, Deschenes*, Huber, Smear, Demers & Kleinfeld (Nature 2012)
See also Kepecs, Uchida & Mainen (J Neurophysiology 2007)
Coordination of head bobbing with sniffing
Coordination of nose wiggling with sniffing

Moore, Deschenes & Kleinfeld (unpublished)
Coordination of whisking with sniffing

Moore*, Deschenes*, Furuta, Huber, Smear, Demers & Kleinfeld (Nature 2013)
see also Ranade, Hangya & Kepecs (J Neuroscience 2013)
The cycle of exploratory orofacial actions linked to sniffing
Sniffing: A master clock for orofacial rhythms?

- Coordination of orofacial actions during exploration

- Brainstem circuits for control of rapid vibrissa motion

- Circuitry for coordination of *all* orofacial motor actions
Angular versus phase coordinates for whisking

Vibrissa angle, \( \theta(t) \)

- Maximum protraction
- Maximum retraction
- Midpoint

Phase in whisk cycle, \( \phi(t) \)

- \( \phi = 0 \)
- \( \phi = \pm \pi \)

Decomposition of the whisking signal into phase, amplitude and midpoint

Whisking bout

Hilbert transform

Angle, \( \theta \)

Phase, \( \phi \)

Amplitude, \( \theta_{\text{amp}} \)

Midpoint, \( \theta_{\text{mid}} \)

Time

Data

Reconstruction

Hill, Curtis, Moore & Kleinfeld (Neuron 2011)
Lesson

Whisking is generated by a control signal of the form

\[ \theta(t) = \theta_{\text{amplitude}}(t) \cdot \cos \phi(t) + \theta_{\text{midpoint}}(t) \]

with \( \frac{d\phi(t)}{dt} = 2\pi f_{\text{whisk}} \) for rhythmic whisking

Question

Where, if anywhere, is the locus for generation of the fast signal?
Pharmacological decoupling of the control for whisking amplitude and frequency (Pietr, Knutsen, Shore, Ahissar & Vogel 2010)

![Graphs showing differences between control, Δ⁹-THC, and SR141716A](image)

Suggests selected control of fast versus slow whisking parameters
Signal flow and computing in sensorimotor loops of the vibrissa system

Modified from Kleinfeld & Deschenes (Neuron 2011)
Whisking occurs without sensory feedback

Implies presence of a CPG

Phase resetting of rhythmic **whisking** by **breathing** (sniffing & basal respiration)

Breathing w/o whisking

Sniffing and whisking

Whisking w/o breathing

Ammonia

Intervening whisks

Time

Moore*, Deschenes*, Furuta, Huber, Smear, Demers & Kleinfeld (Nature 2013)
Respiration resets whisking oscillations

Breathing CPG (preBötzinger) → Reset pulse → Whisking CPG → Intrinsic muscles for whisking

Moore*, Deschenes*, Furuta, Huber, Smear, Demers & Kleinfeld (Nature 2013)
Lesson

PreBötzinger respiratory complex is involved in protraction phase of whisking pattern generation
Units in the intermediate reticular formation (IRt) that report inspiration versus protraction

Breathing / Whisking

Pre-Bötzinger

Breathing / Whisking

Vibrissa IRt

- Inspiratory / protraction
- Whisking
Lesson

A newly recognized zone of neurons in the IRt formation code rhythmic motion of the vibrissa

Question

Are these units sufficient to drive rhythmic motion?
Kainic acid activates the vIRt, which drives facial motoneurons.
Lesson

A newly recognized zone of neurons in the IRt formation can drive rhythmic motion of the vibrissa

Question

Are these units necessary to drive rhythmic motion?
Lesion of the vlRt blocks exploratory whisking

- Electrolytic
- Sindbis virus
- Ibotenic acid

Whisking amplitude (°)

Ipsilateral side

Contralateral side

1 s

20

Whisking amplitude (°)

Coronal

Horizontal

Breathing CPG (preBötzinger)  
Whisking CPG (vlRt)

Reset pulse  
Intrinsic muscles for whisking

Moore*, Deschenes*, Furuta, Huber, Smear, Demers & Kleinfeld (Nature 2013)
Lesson

Units in the vIRt are necessary for rhythmic motion of the vibrissae

Question

Can we identify the monosynaptic connections of a minimal breathing and whisking circuit?
PreBötzinger units project to the vibrissa zone of the IRt while facial motoneurons receive premotor input from the vIRt.

Disynaptic retrograde labeling: ΔG-rabies injected into vibrissa muscles of ChAT-RG mice.

Moore*, Deschenes*, Furuta, Huber, Smear, Demers & Kleinfeld (Nature 2013)
Compendium of evidence for a vibrissa pattern generator region within the intermediate reticular formation (vIRt)

Moore*, Deschenes*, Furuta, Huber, Smear, Demers & Kleinfeld (Nature 2013)

- Premotor to facial nucleus
- Effective whisking lesion
- Rhythmic whisking units
- Kainic acid induced whisking units
Model of the brainstem rhythmic generator for whisking

Intrinsic muscles (vibrissa protraction)
Extrinsic muscles (mystacial pad motion)

Inspiration

Moore*, Deschenes*, Furuta, Huber, Smear, Demers & Kleinfeld (Nature 2013)
Matthews, Deschénes, Furuta, Moore, Wang, Karten* & Kleinfeld* (Journal of Comparative Neurology 2015)
Kainic acid induced whisking is asynchronous

Moore, Deschênes, Kurnikova & Kleinfeld (Nature Protocols 2014)
Respiratory premotor neurons (preBötzingger) in opposite hemispheres are connected by commissural projections (Koizumi, Koshiya, Chia, Cao, Nugent, Zhang & Smith, J Neurosci 2013)
Synchronization of bilateral rhythmic whisking is mediated by the preBötzinger interhemispheric connections

Deschênes, Moore, Demers, Takatoh, Furuta, Kurnikova, Wang & Kleinfeld (manuscript in preparation)
Summary lesson

Breathing coordinates rhythmic whisking
Sniffing: A master clock for orofacial rhythms?

- Coordination of orofacial actions during exploration
- Brainstem circuits for control of rapid vibrissa motion
- Circuitry for coordination of all orofacial motor actions
The cycle of exploratory orofacial actions linked to sniffing
Axon collaterals from the preBötzinger, the inhalation oscillator, span the full extent of the intermediate reticular zone (IRt) (Tan, Pagliardini, Yang, Janczewski & Feldman, J Comp Neurol 2010)
Connections from preBötzinger, the inhalation CPG, to brainstem premotor nuclei involved in orofacial actions.
These data open up questions in both motor control and sensory coding.

What regulates the slowly varying midpoint of whisking, where midpoint plays the role of posture in locomotion?

Does the breathing clock act as a temporal signature to bind separate sensory inputs?
Angular versus phase coordinates for whisking

Vibrissa angle, $\theta(t)$
- Maximum protraction: $180^\circ$
- Midpoint
- Maximum retraction

Phase in whisk cycle, $\phi(t)$
- $\phi = 0$
- $\phi = \pm \pi$

Decomposition of the whisking signal into phase, amplitude and midpoint

Angle, $\theta$

Phase, $\phi$

Amplitude, $\theta_{\text{amp}}$

Midpoint, $\theta_{\text{mid}}$

Time

1 s

Hill, Curtis, Moore & Kleinfeld (Neuron 2011)
Lesion of the whisking oscillator (vLRt) does *not* effect the midpoint: Preliminary evidence for decoupled fast versus slow brainstem control

Intact

Unilateral lesion

Deschenes, Moore & Kleinfeld (unpublished)
Whisking and unit activity in vibrissa primary motor (vM1) cortex

Hill, Curtis, Moore & Kleinfeld (Neuron 2011)
Rodent vM1 cortex reports the slowly varying amplitude and midpoint of whisking

Hill, Curtis, Moore & Kleinfeld (Neuron 2011)
Much previous work showed that stimulation of motor and sensory cortices change vibrissa position and/or activate whisking. 

The pathways for this control are incompletely understood. Here we consider the spinal trigeminal nuclei as premotor nuclei.

Single neuron stimulation data of Brecht, Schneider, Sakmann & Margrie (Nature 2004)
Modified from Kleinfeld & Deschenes (Neuron 2011)

Signal flow and computing in sensorimotor loops of the vibrissae system

- **Exafference**
  - Peripheral reafference

- **Endbrain**
  - L3 & L4
  - Sensory (vS1) cortex
  - Motor (vM1) cortex

- **Midbrain**
  - VPMdm map
  - Thalamus
  - Zona incerta

- **Periphery**
  - PrV map
  - VPMdm map
  - Trigeminal nuclei
  - Facial motor nuclei
  - Facial nerve

- **Brainstem**
  - PrV
  - SpVo
  - SpVI
  - SpVC
  - nRt

- **Peripheral**
  - Infraorbital branch of trigeminal nerve
  - Mystacial pad (Vibrissa sensorimotor complex)

- **Signal flow and computing**
  - Copy
  - Endbrain
  - Midbrain
  - Periphery
  - Brainstem
  - Peripheral

**Key Terms**
- L3 & L4
- L5b
- L6
- L1 & L5a
- PrV map
- VPMdm map
- Thalamus
- Zona incerta
- Facial motor nucleus
- Facial nerve
- Infraorbital branch of trigeminal nerve
- Mystacial pad (Vibrissa sensorimotor complex)
Five Slides of Unpublished Material Were Removed
These data open up questions in both motor control and sensory coding.

What regulates the slowly varying midpoint of whisking, where midpoint plays the role of posture in locomotion?

Does the breathing clock act as a temporal signature to bind separate sensory inputs?
Paradigm to test if rodents code the azimuthal position of their vibrissae

Behavioral evidence that rodents know the position of their vibrissae

Paradigm to test if rodents code the azimuthal position of their vibrissae

Evidence that vS1 cortex is necessary to report vibrissa position
(O’Connor, Clack, Huber, Komiyama, Myers & Svoboda, Journal of Neuroscience 2010)
Is the vibrissa touch response conditioned solely by phase?

Touch referenced to vibrissa angle, \( \theta(t) \)

Touch referenced to phase in whisk cycle, \( \phi(t) \)

\[ \theta(t) = \theta_{\text{amplitude}}(t) \cdot \cos \phi(t) + \theta_{\text{midpoint}}(t) \]

with \( d\phi(t)/dt = 2\pi f_{\text{whisk}} \) for rhythmic whisking
Vibrissa S1 cortex codes azimuth of vibrissa touch by phase in the whisk (= respiratory) cycle

Sensor

vS1 unit

Video

Contact

Time (ms)

Phase, $\phi(t)$

Angle, $\theta$

$0^\circ$ $125^\circ$

Maximum protraction

Maximum retraction

$180^\circ$

$\theta_{\text{contact}}$

$0^\circ$

Spike rate at contact (Hz)

Angle in whisk cycle at contact

Phase in whisk cycle at contact (radians)

$\phi = \pi$

$\phi = 0, 2\pi$

Curtis & Kleinfeld (Nat Neurosci 2009)
Vibrissa S1 cortex codes azimuth of vibrissa touch, as well as free whisking, by phase in the whisk (= respiratory) cycle.
Olfactory bulb codes odor by phase in respiratory (= whisk) cycle (Shusterman, Smear, Koulakov & Rinberg Nature Neuroscience 2011)
Coordination of sniffing and whisking and their spiking representation in sensory cortices

- Presynaptic from olfactory bulb / smell (Shusterman, Smear, Koulakov & Rinberg, Nat Neuro 2011)
- Olfactory cortex / smell (Miura, Mainen & Uchida, Neuron 2012)
- Vibrissa cortex / touch (Curtis & Kleinfeld, Nat Neuro 2009)

Fraction of respective units

Phase in breathing cycle for maximal cortical response (radians)

Kleinfeld, Deschenes, Wang & Moore (Nature Neuroscience 2014)
Lesson

A common clock for the phase sensitivity of sniffing and whisking

Conjecture

Inhalation as the *master clock* to bind percepts based on orofacial (smell, touch, and taste) inputs
Sniffing: A master clock for orofacial rhythms?

Thank you for your attention!