

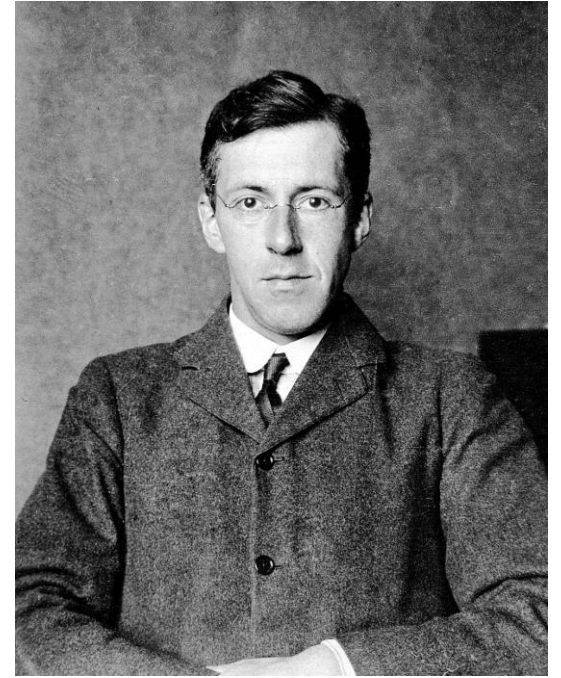
# Oxytocin modulation of neural circuits

Lennart Oettl

2.11.2018

# Oxytocin

- Discovered by Sir Henry H. Dale in 1906



Sir Henry Dale, 1904



Wellcome Physiological Laboratories

# Oxytocin

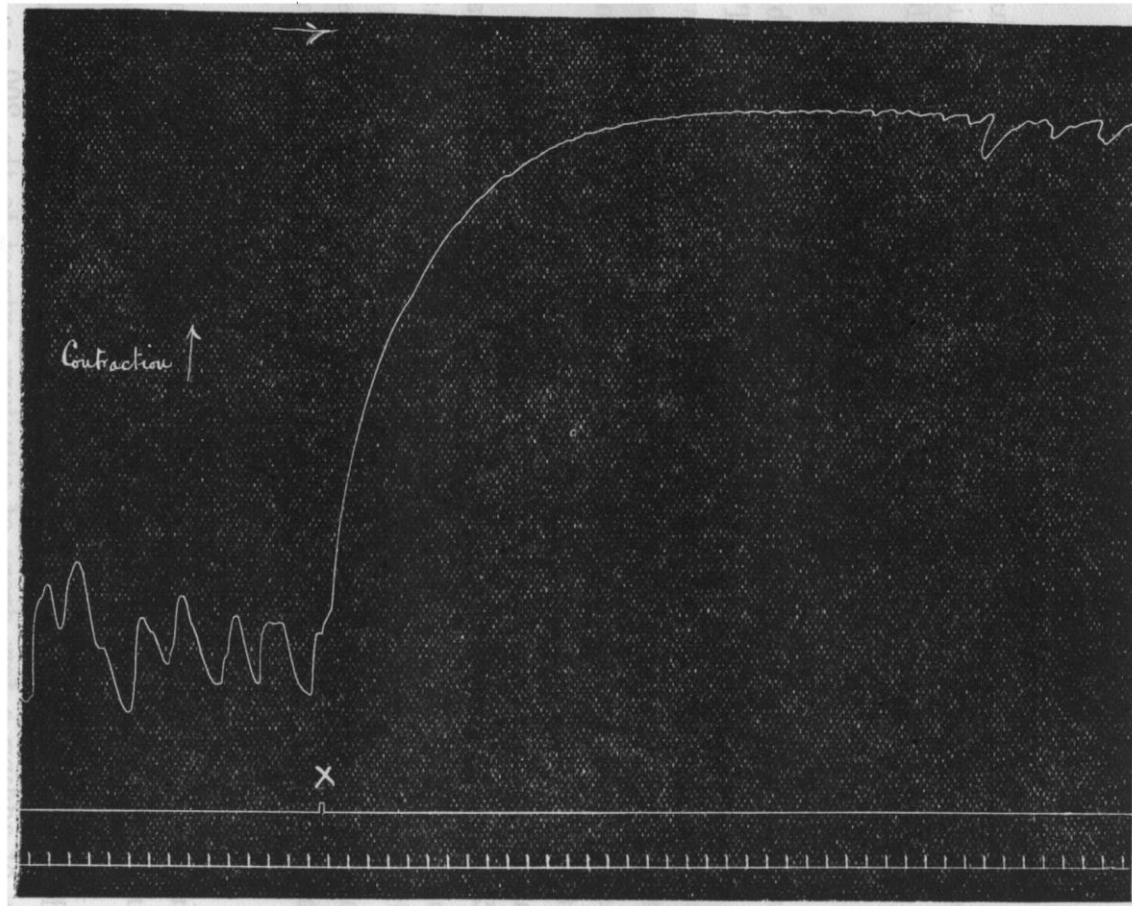
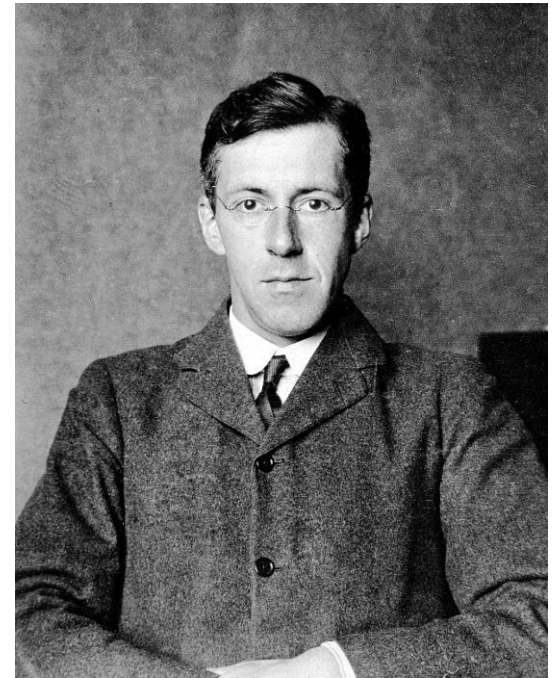


Figure 3.—Contractions of isolated horn of cat's uterus (not pregnant). At  $\times$  3 drops of pituitary extract were added to the 200 c.c. of Ringer's solution in the bath. Time = 10 seconds. Scale,  $\frac{1}{4}$  linear.



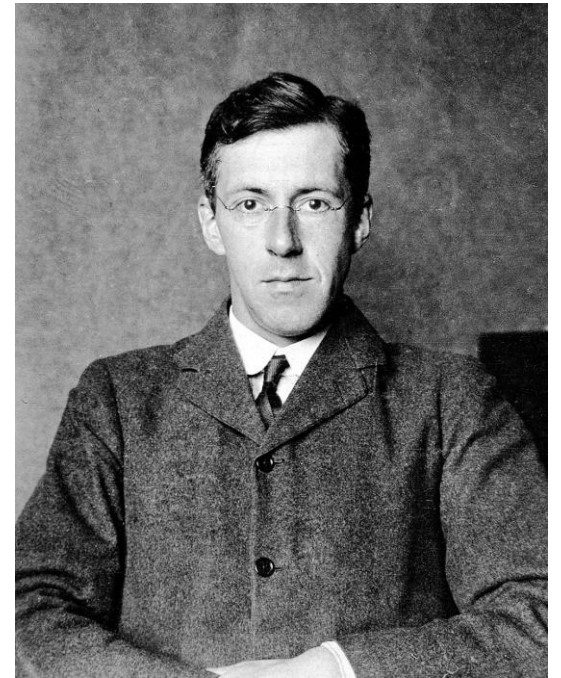
Sir Henry Dale, 1904



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# Oxytocin

- Discovered by Sir Henry H. Dale in 1906
- nine-amino-acid neuropeptide, (sequence elucidated in 1953)
- Greek meaning: “quick birth”
- Mainly known for its physiological roles :  
uterine contractions during parturition  
and milk ejection.



Sir Henry Dale, 1904



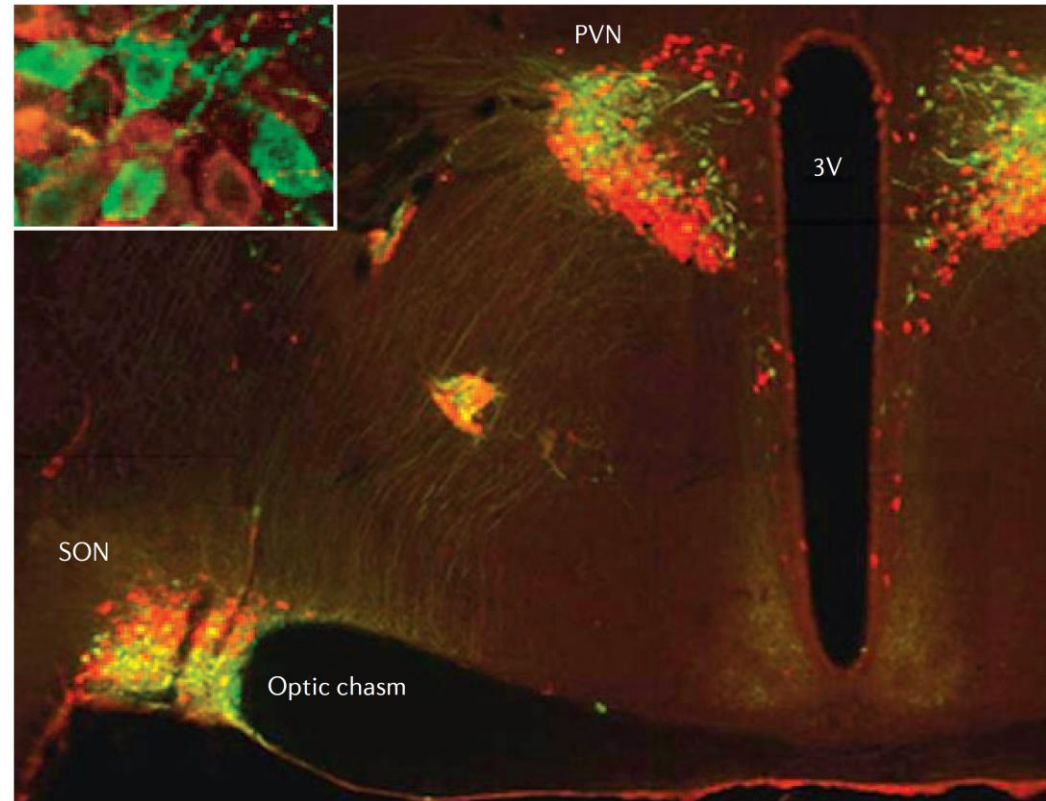
Wellcome Physiological Laboratories

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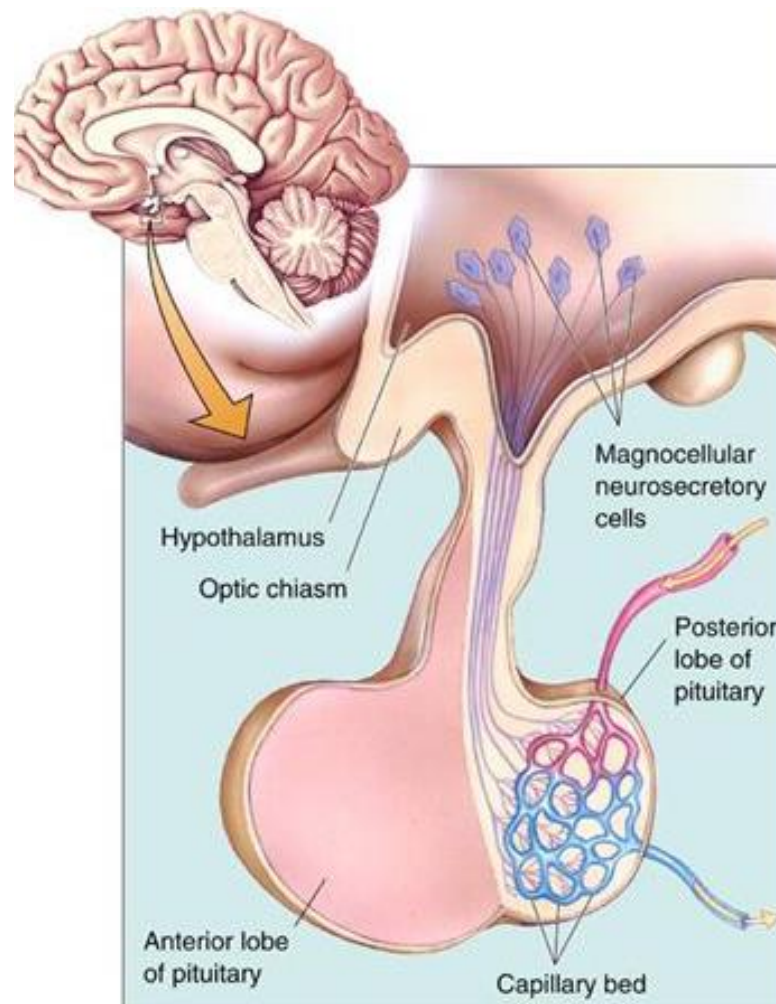


Sir Henry Dale and Otto Loewi



Ludwig & Leng, 2006

- synthesized in the paraventricular (PVN) and supraoptic (SON) nuclei of the hypothalamus
- two types of OT neurons (magnocellular and parvocellular neurons) have been identified (Swanson and Kuypers, 1980)

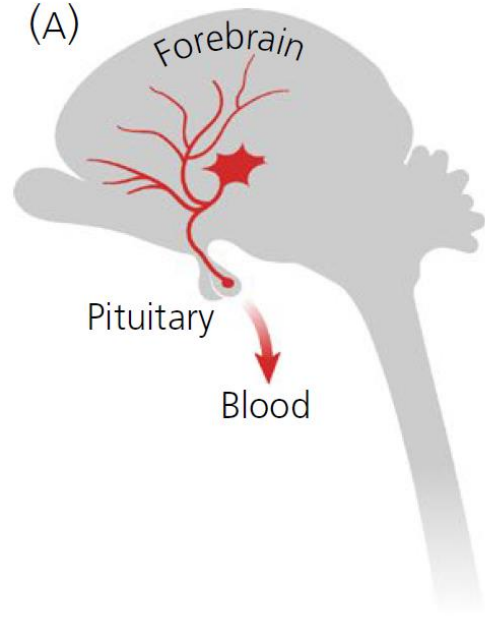


- classical view:

- magnocellular OT neurons -> posterior pituitary (release OT into the blood circulation)
- parvocellular OT neurons -> exclusively to hindbrain areas, where local release of OT modulates vital body functions.

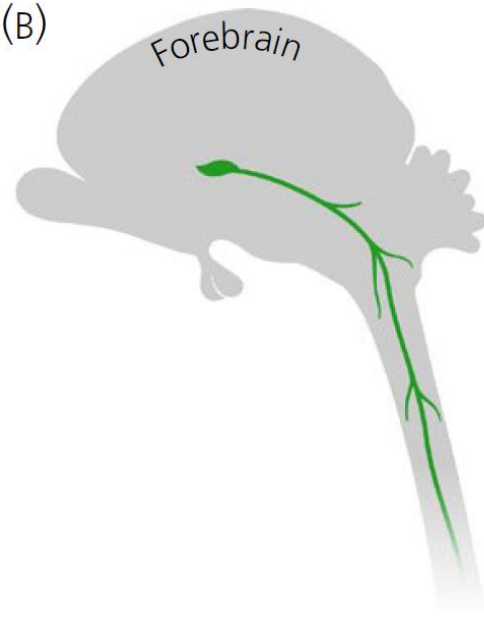
magnocellular

(A)



parvocellular

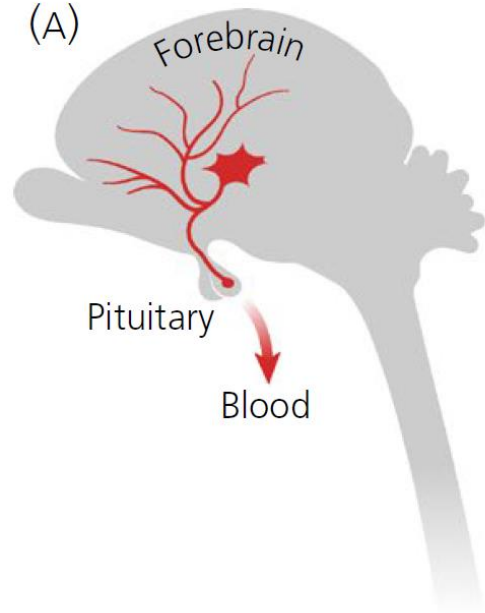
(B)





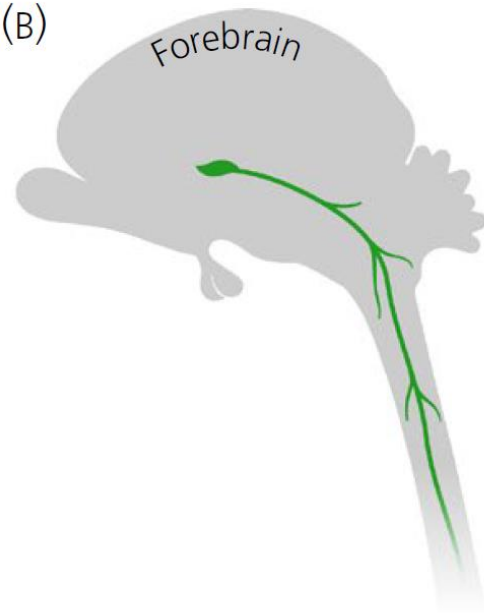
magnocellular

(A)

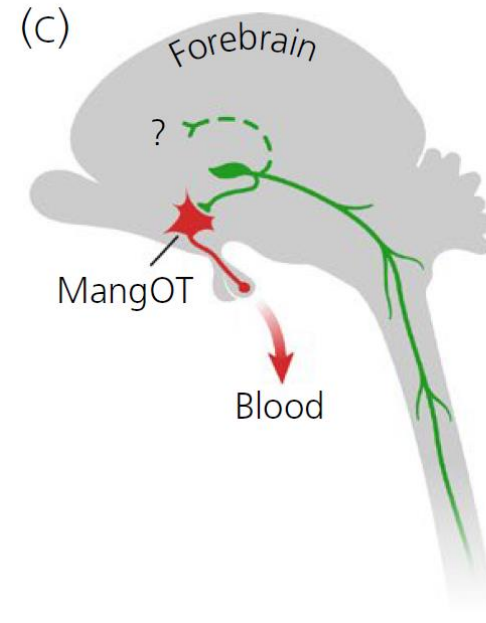


parvocellular

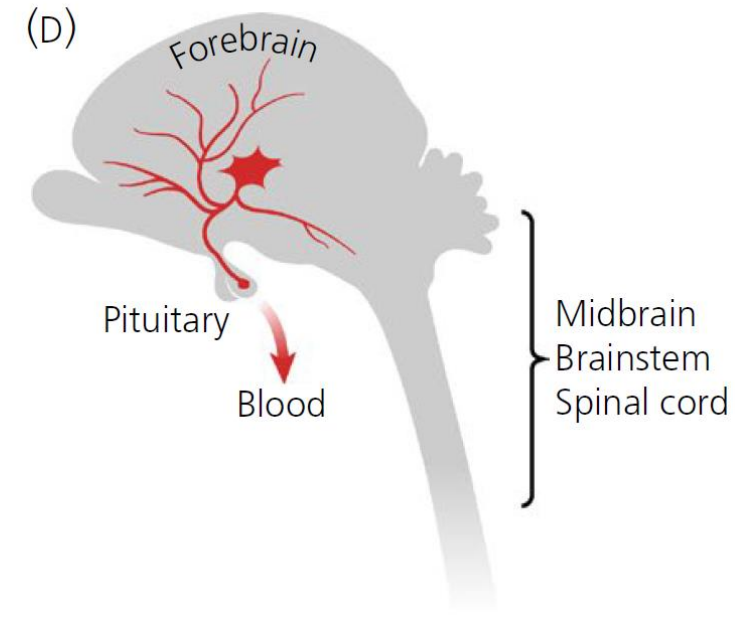
(B)



(C)

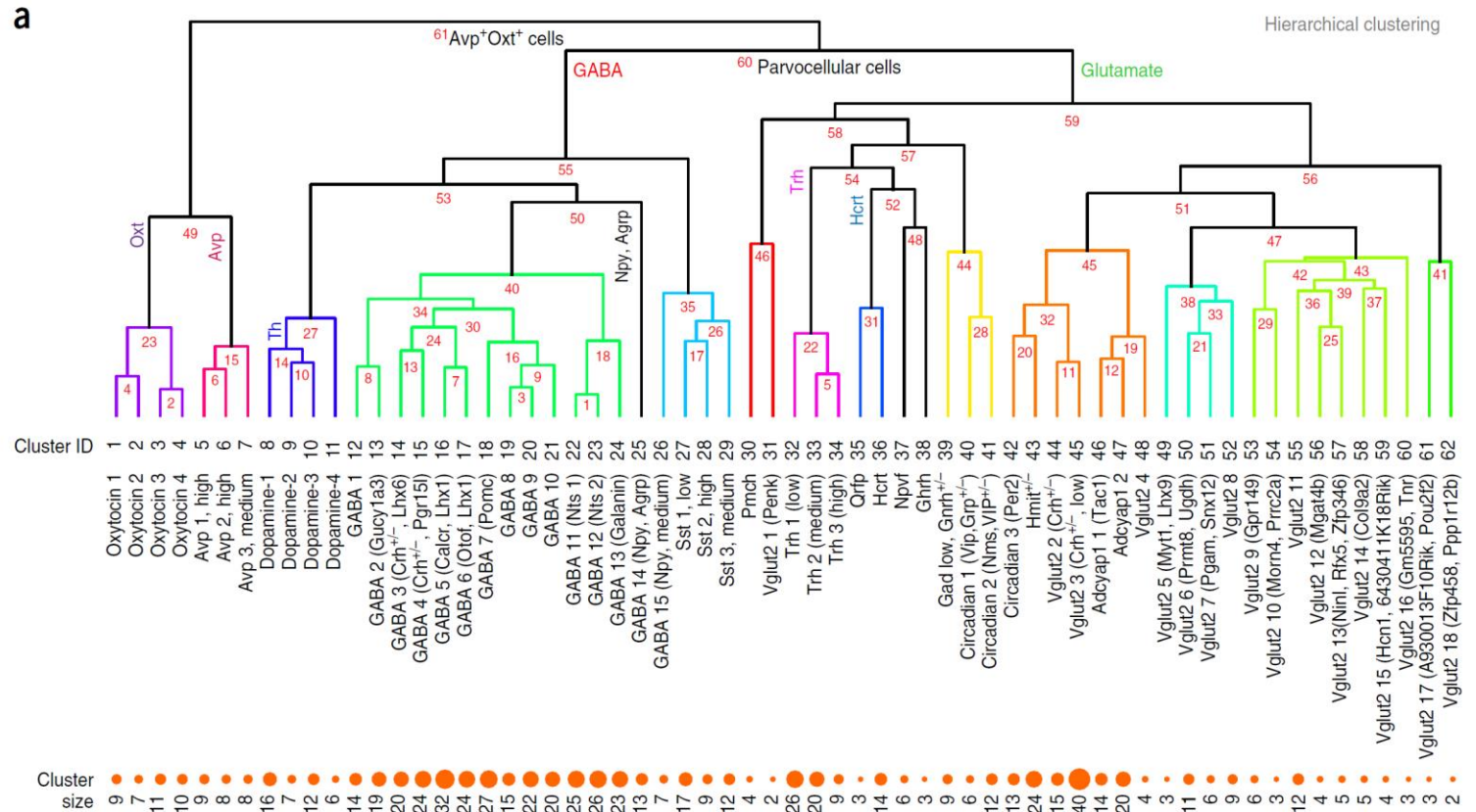


(D)

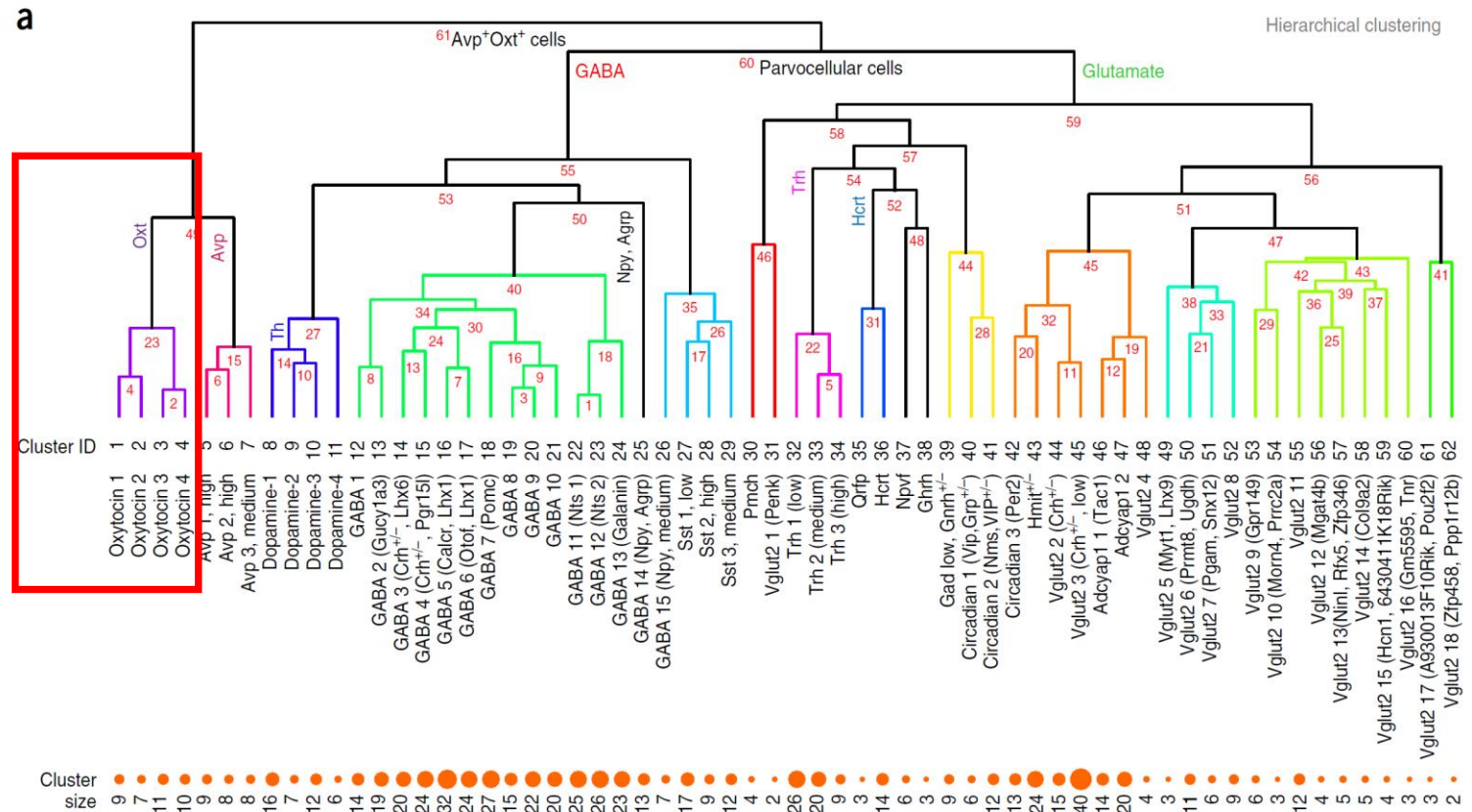


Althammer & Grinevich 2017

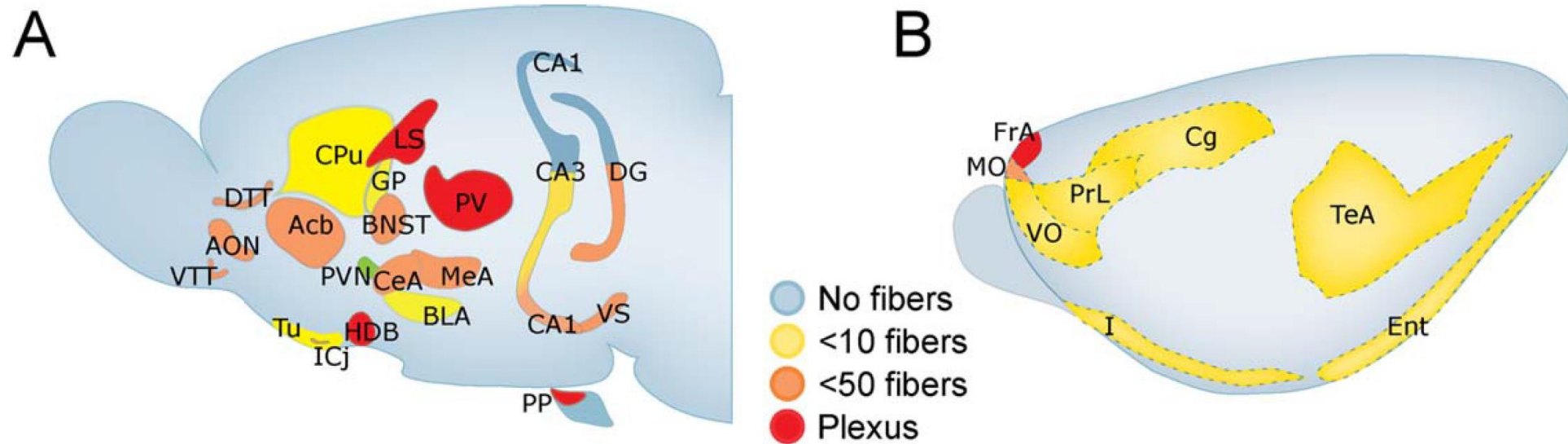
# More than 2 types of Oxytocin neurons?



# More than 2 types of Oxytocin neurons?

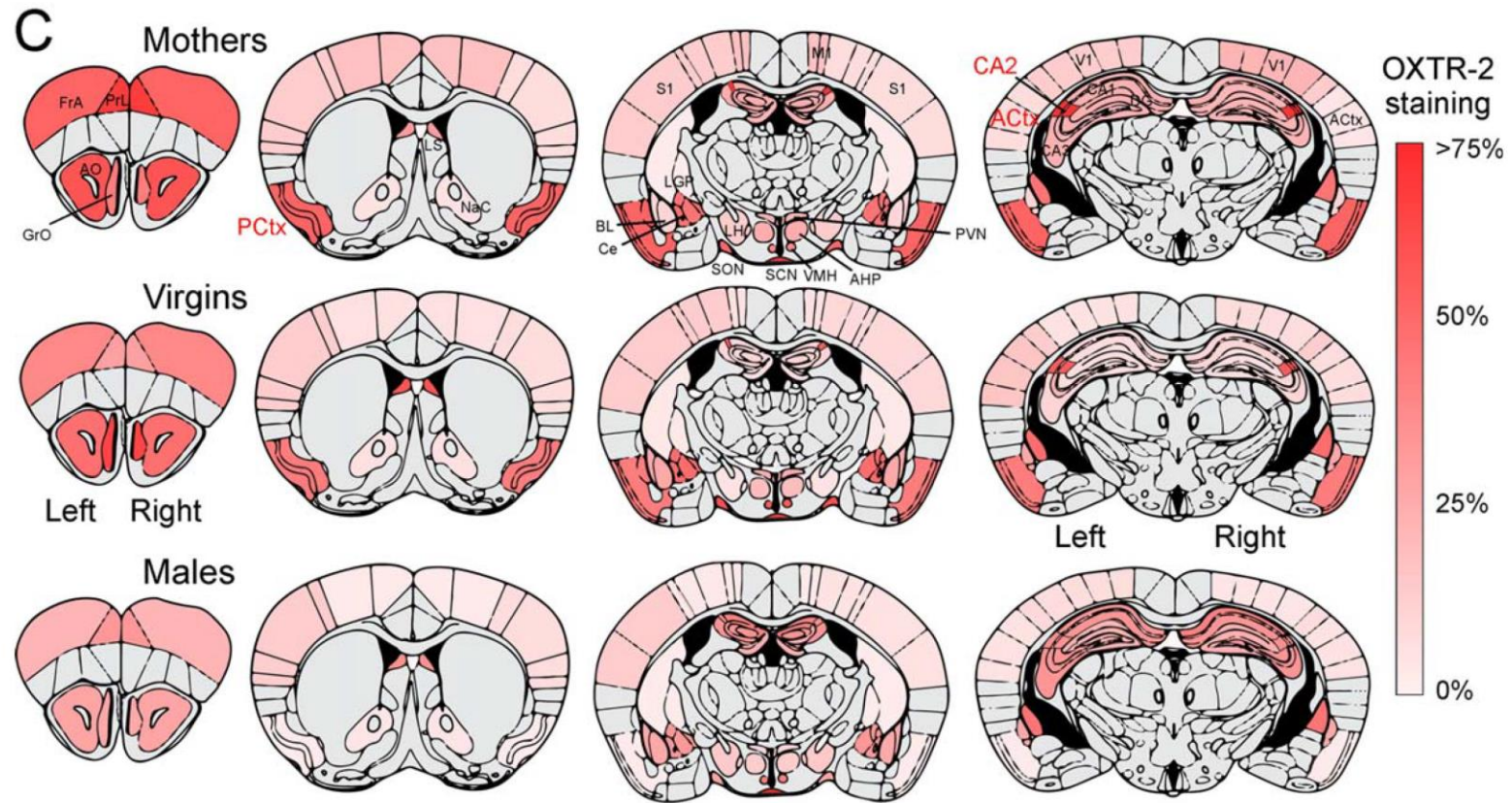


# Distribution of oxytocin fibers in the brain



Knobloch et al 2012

# Distribution of oxytocin receptors in the brain



Mitre et al 2016

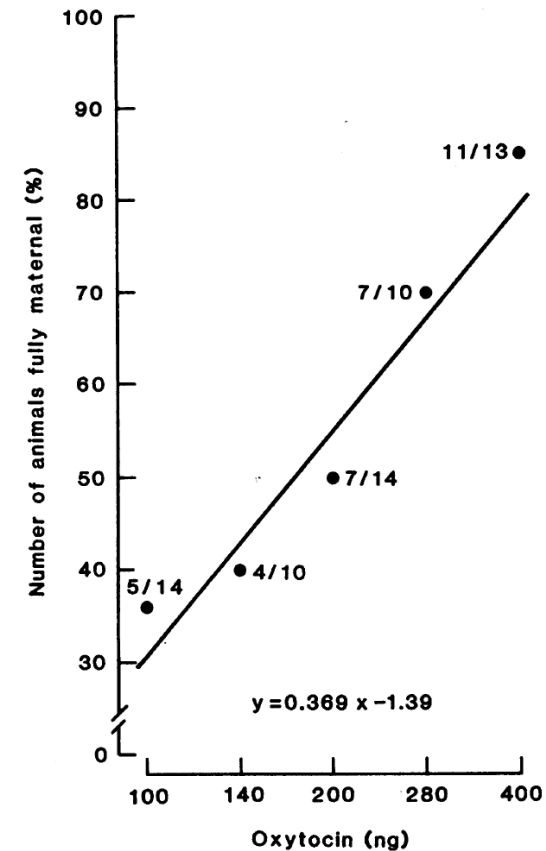
# How does OT reach its targets in the brain?

- volume transmission (release from hypothalamic dendrites followed by diffusion in the extracellular space to other brain areas)
- local axonal release

# Oxytocin Modulation of Behaviour

Substance	N	Percentage of animals fully maternal		
		0 to 60 minutes	60 to 120 minutes	240 to 300 minutes
Oxytocin	107	72*	72*	72* (N = 58)†
Tocinoic acid	24	50‡	50‡	54‡
β-Endorphin	11	27	27	
Luteinizing hormone-releasing hormone	23	26	26	
Thyrotropin-releasing hormone	12	25	25	
Pro-Leu-Gly-NH <sub>2</sub>	12	25	25	
Prolactin	12	25	25	
17β-Estradiol	12	25	25	
Progesterone	12	25	25	
Prostaglandin E <sub>2</sub>	14	21	21	36
Lysine vasopressin	29	21	24	24
Pressinoic acid	15	20	20	20
Bradykinin	10	20	20	
Arginine vasotocin	11	18	27	
Saline	51	18	18	19 (N = 26)†
Prostaglandin F <sub>2α</sub>	19	16	16	21
Arginine vasopressin	31	16	42§	55‡
No ICV injection	20	15	15	15
Substance P	17	12	12	
Neurotensin	11	9	9	

\* $P < .001$ . †N shows the number of animals observed during the third observation period added part way through the experiment. ‡ $P < .01$ . § $P < .05$  compared to the group treated with saline (Fisher's exact probability test).

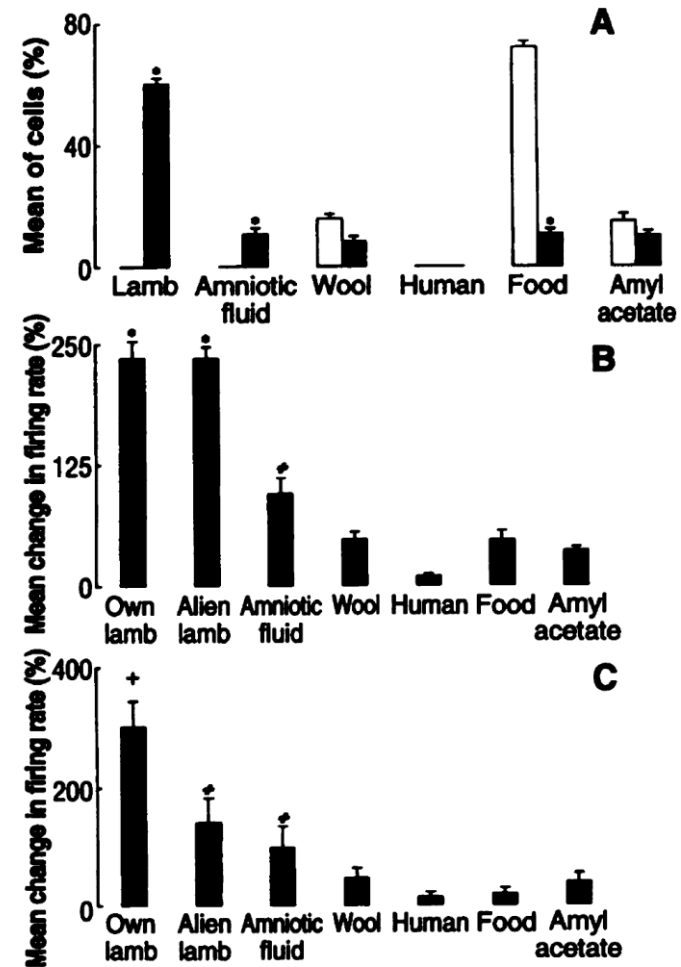


Pedersen et al 1982

# Oxytocin Modulation of Behaviour



Kendrick et al., Science, 1992

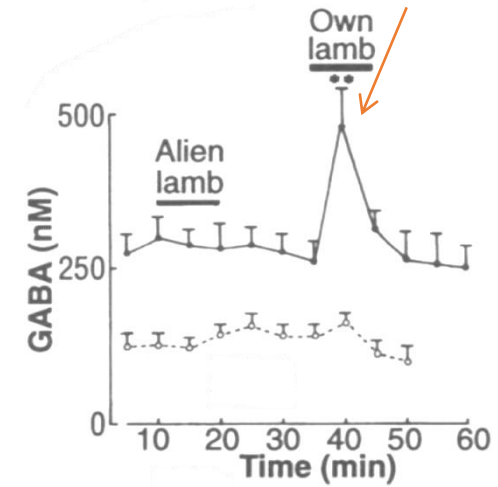
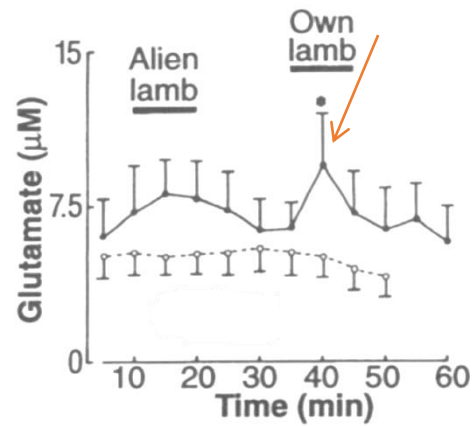
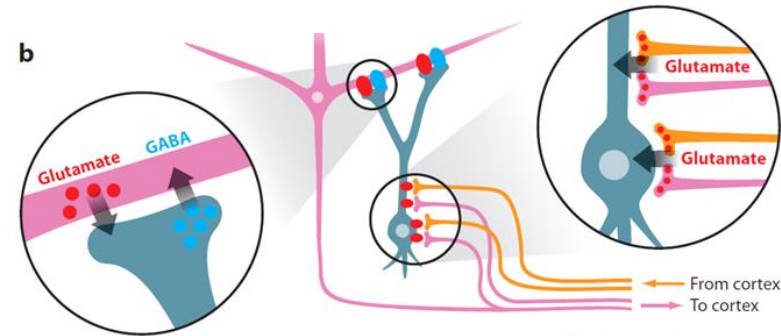




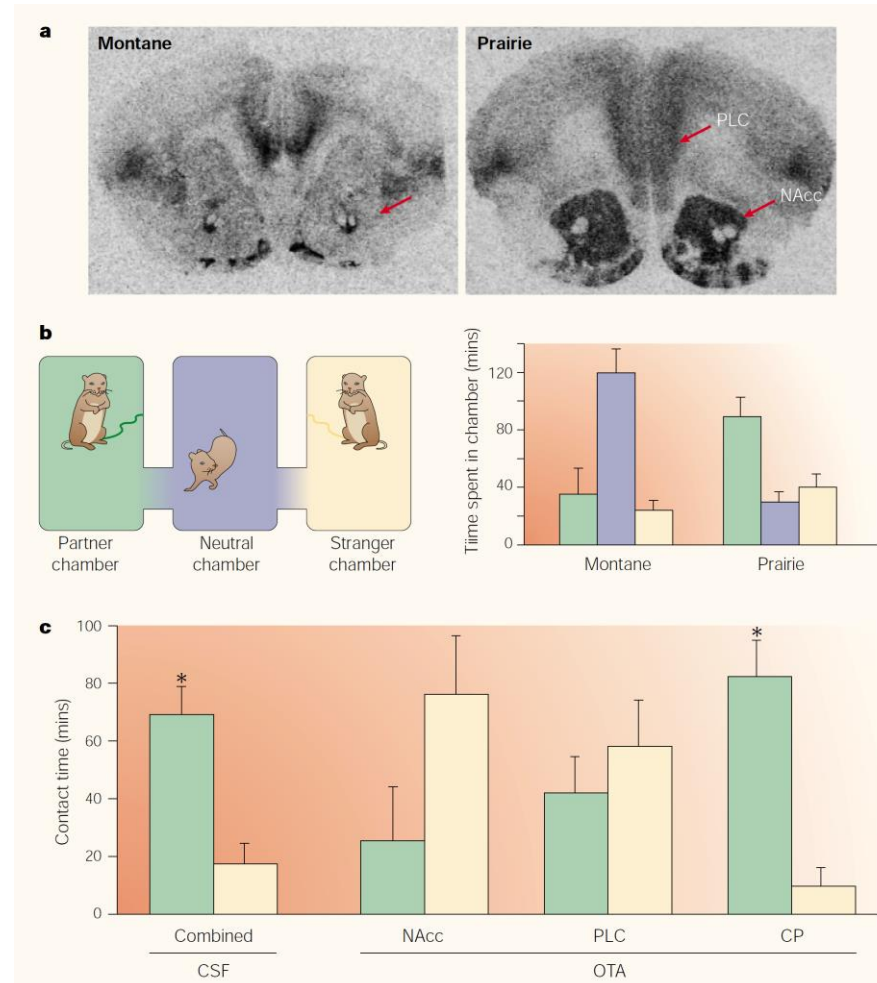
# Oxytocin Modulation of Behaviour



Kendrick et al., Science, 1992



# Oxytocin Modulation of Behaviour



Prairie vole: monogamous  
Montane vole: polygamous

(Prairie vole)

Insel & Young 2001

# Oxytocin Modulation of Human Behaviour

# Oxytocin Modulation of Human Behaviour

Brain peptides, has revealed potential. Acute enhances reciprocity. Recent results, her oxy-

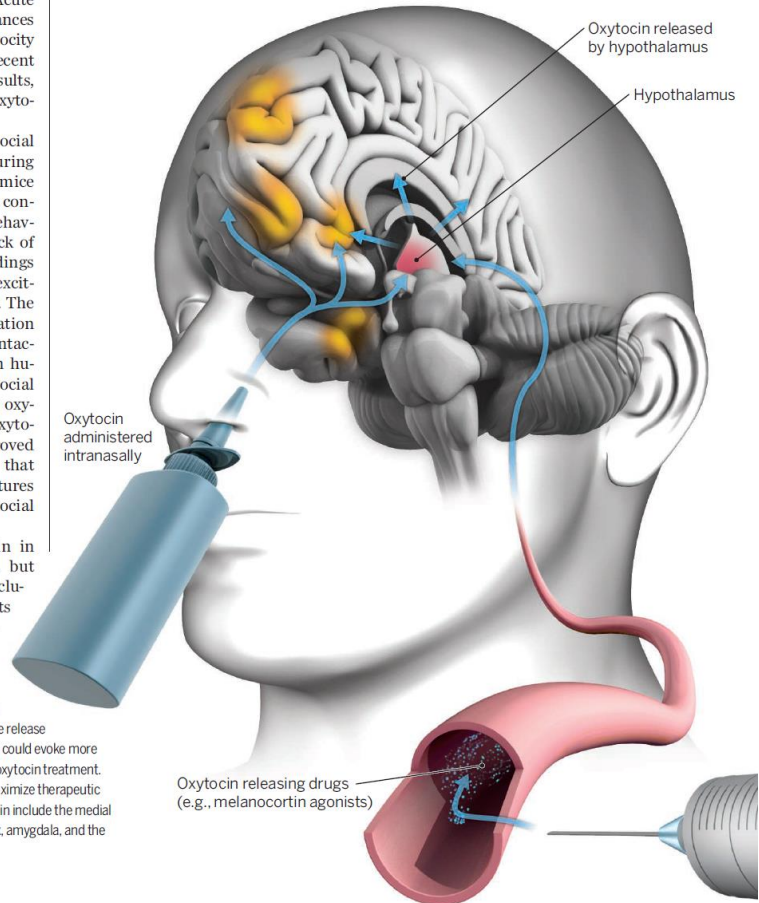
of social nurturing in mice. Lack of findings. ASD. The mutation. Improved that structures cue social

oxytocin in gov), but neonatal adults reverse

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stimuli, oxytocin therapies should be most effective when combined with behavioral therapies.

the developmental switch in the neurotransmitter  $\gamma$ -aminobutyric acid from excitatory to inhibitory neurotransmission at birth in



## Oxytocin increases trust in humans

Michael Kosfeld<sup>1\*</sup>, Markus Heinrichs<sup>2\*</sup>, Paul J. Zak<sup>3</sup>, Urs Fischbacher<sup>1</sup> & Ernst Fehr<sup>1,4</sup>

Published by AAC

Young & Barrett 2014

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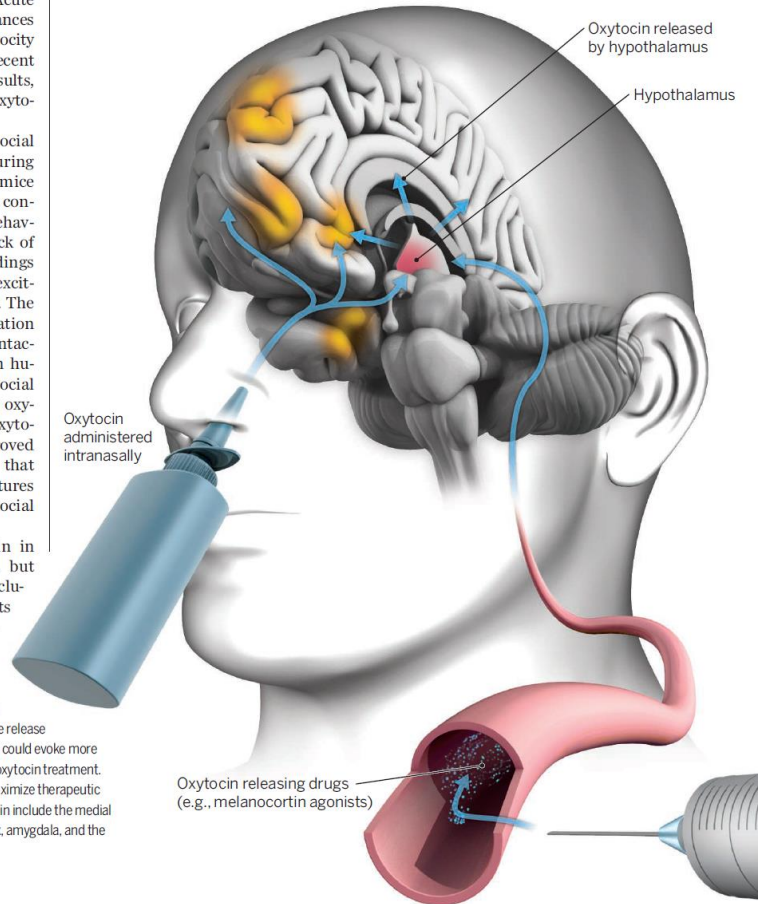
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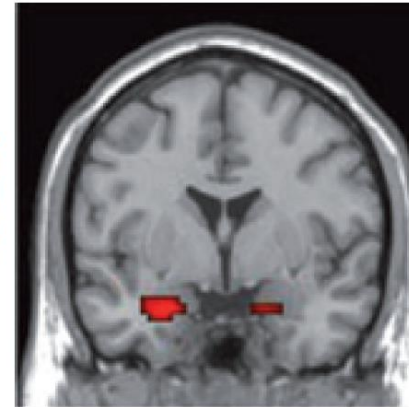
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Young & Barrett 2014

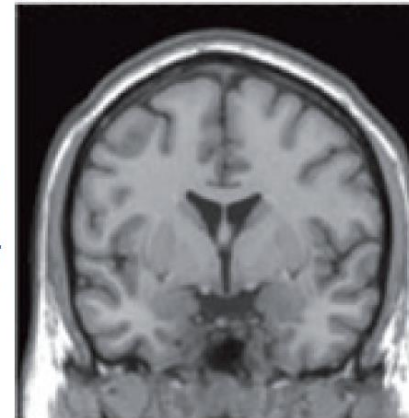
a

OXT

Placebo



Peptide



Kirsch et al 2005

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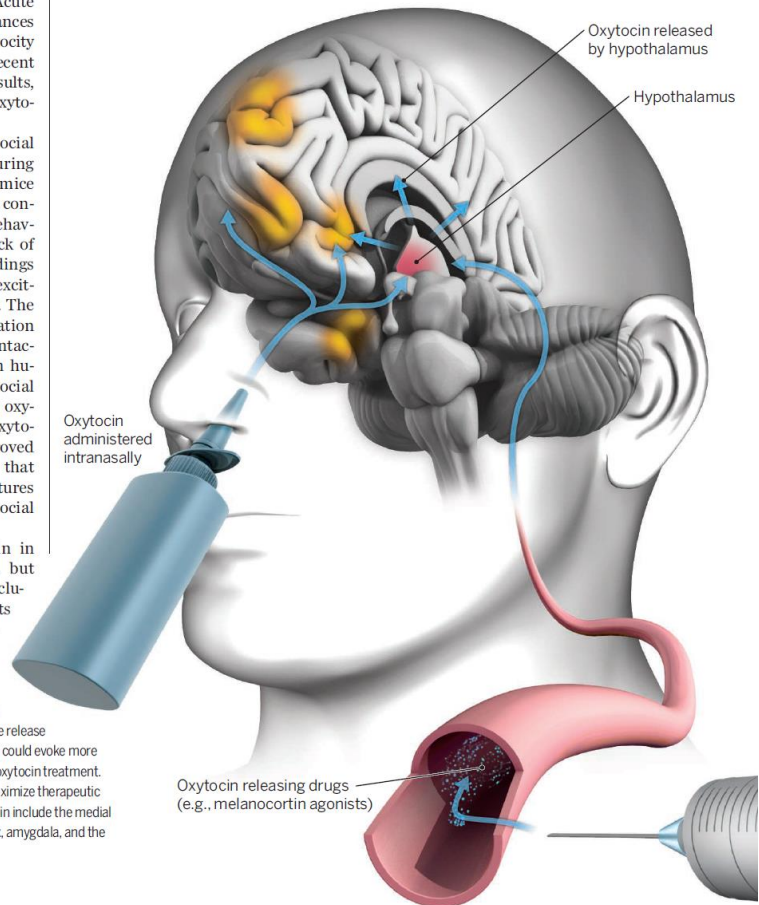
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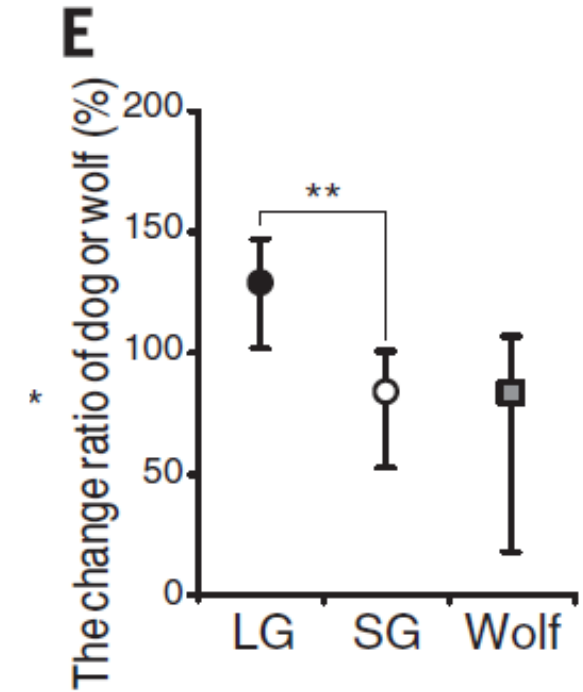
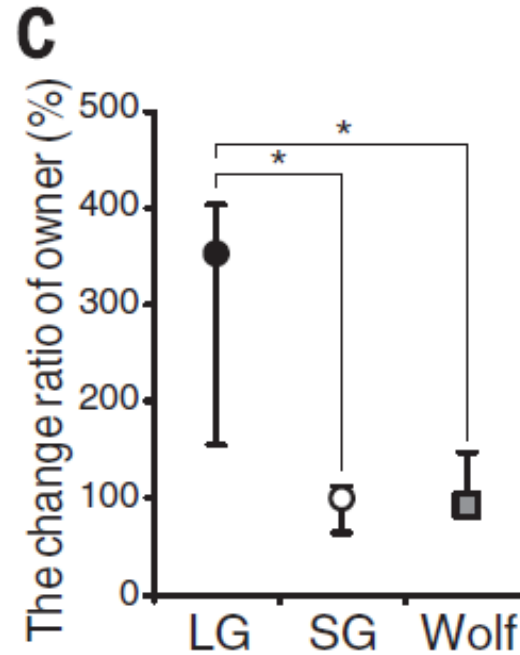
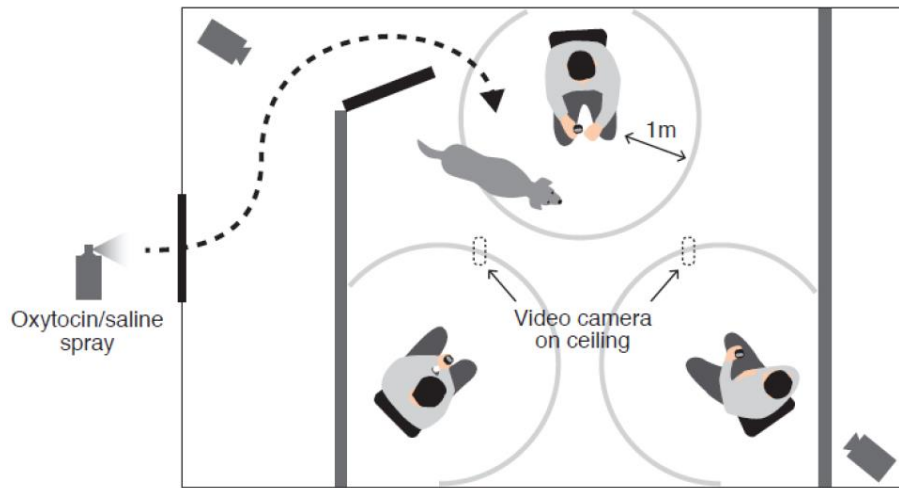
## ORIGINAL ARTICLE

Oxytocin by intranasal and intravenous routes reaches the cerebrospinal fluid in rhesus macaques: determination using a novel oxytocin assay

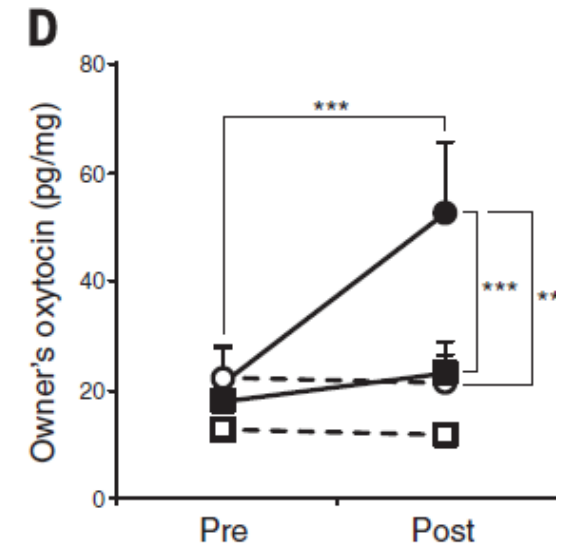
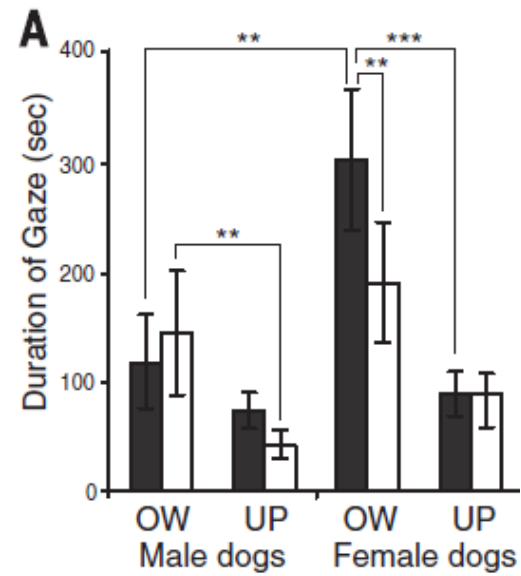
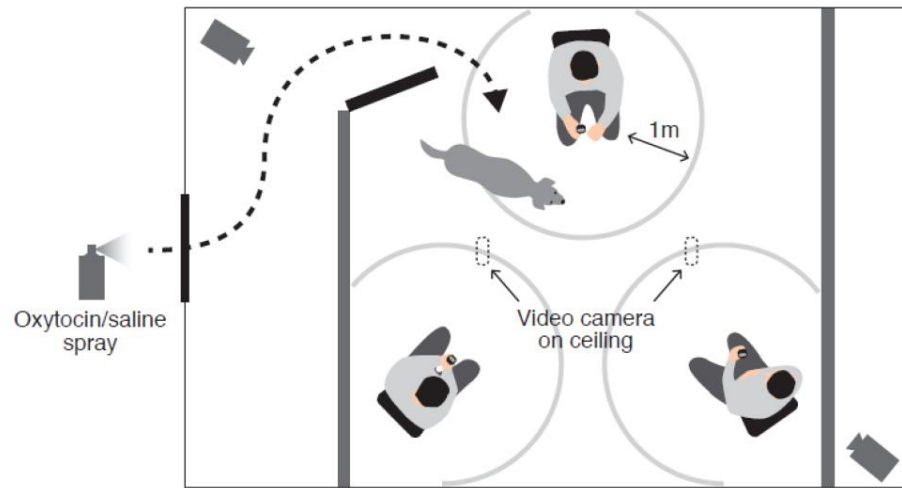
MR Lee<sup>1</sup>, KB Scheidweiler<sup>2</sup>, XX Diao<sup>2</sup>, F Akhlaghi<sup>3</sup>, A Cummins<sup>4</sup>, MA Huestis<sup>2</sup>, L Leggio<sup>1,5,6</sup> and BB Averbeck<sup>4,6</sup>

Young & Barrett 2014

# Oxytocin Modulation of Human Behaviour



# Oxytocin Modulation of Human Behaviour



Nagasawa et al 2015



# Oxytocin Modulation of Human Behaviour

## Experiment 2

Oxytocin or Saline administration and owner-dog interactions.

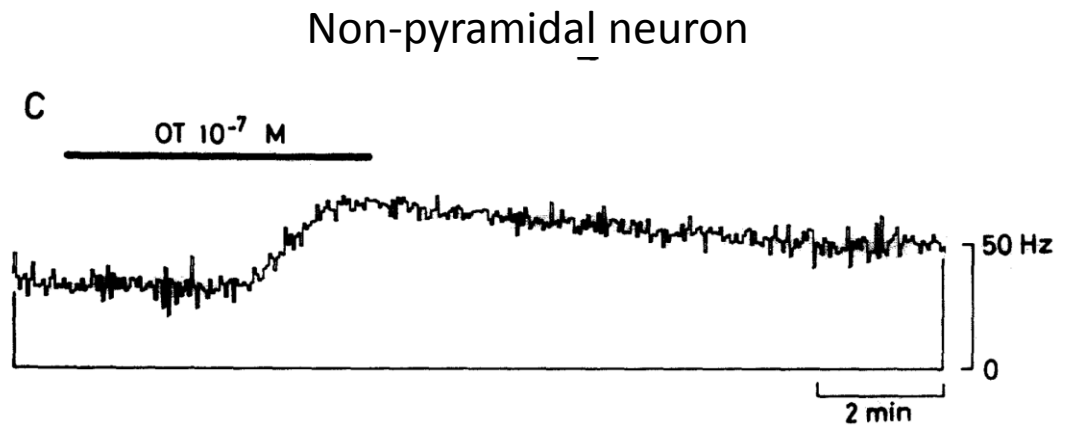
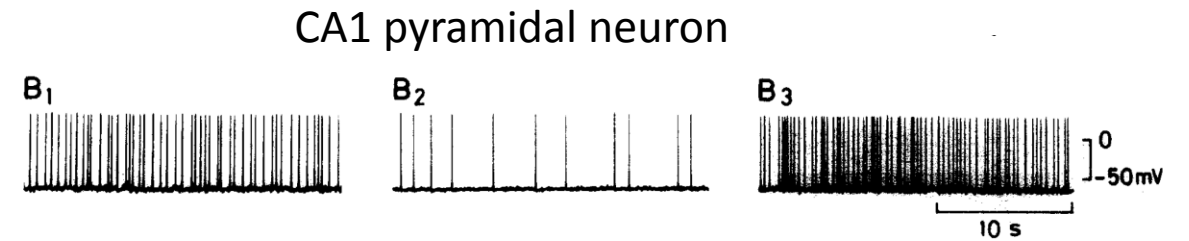
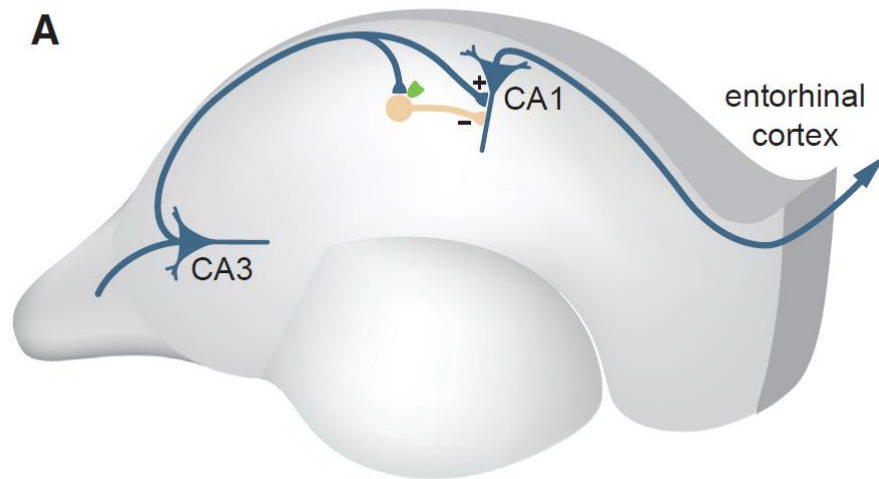
(Left side: Oxytocin administration)

(Right side: Saline administration)

OW: owner

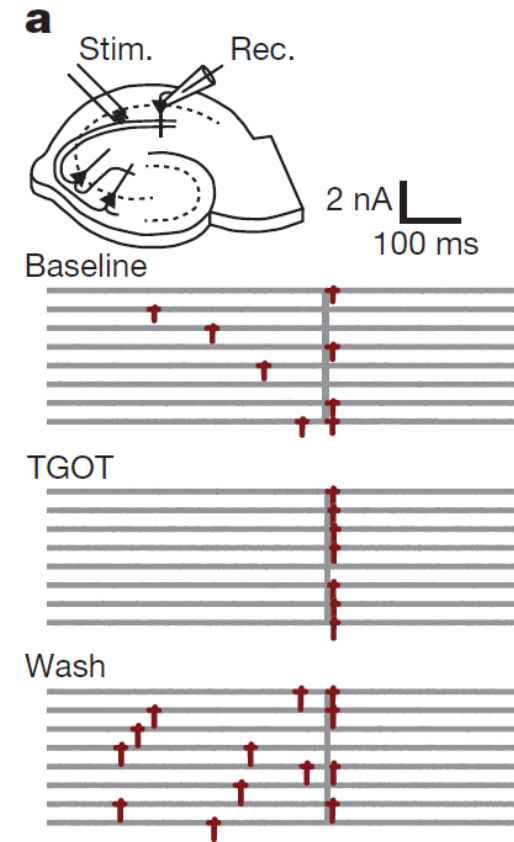
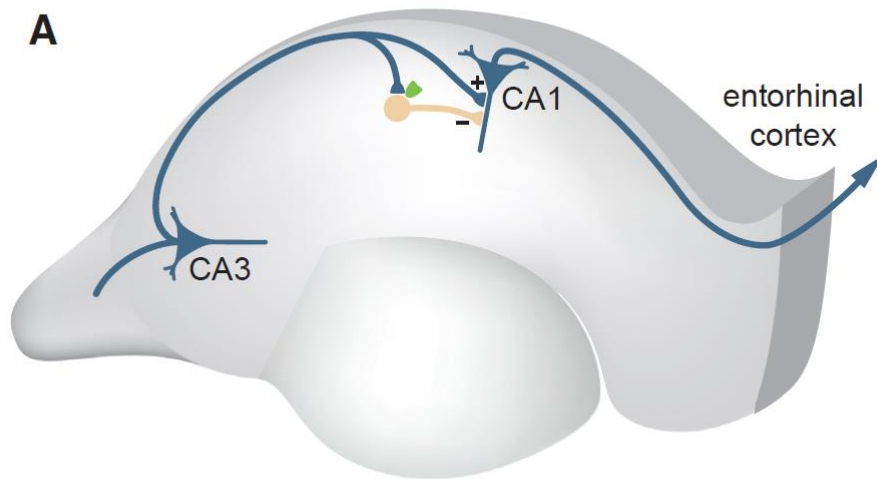
UF: unfamiliar person

# Oxytocin Modulation of Neural Circuits



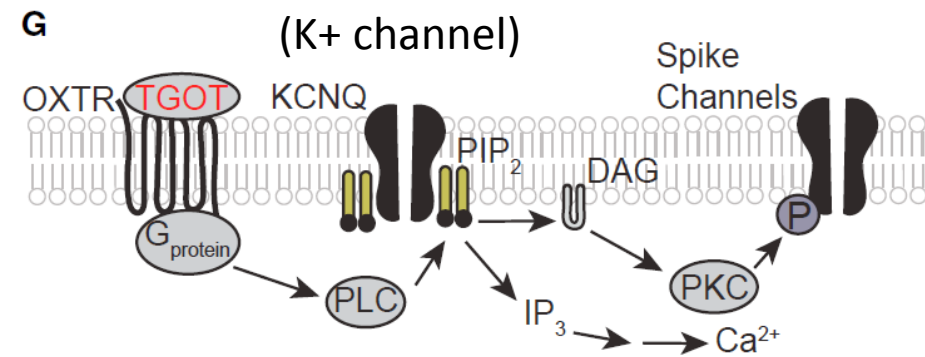
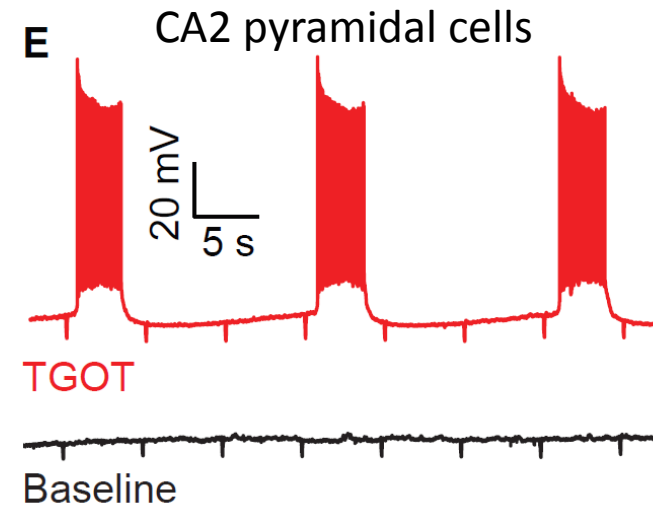
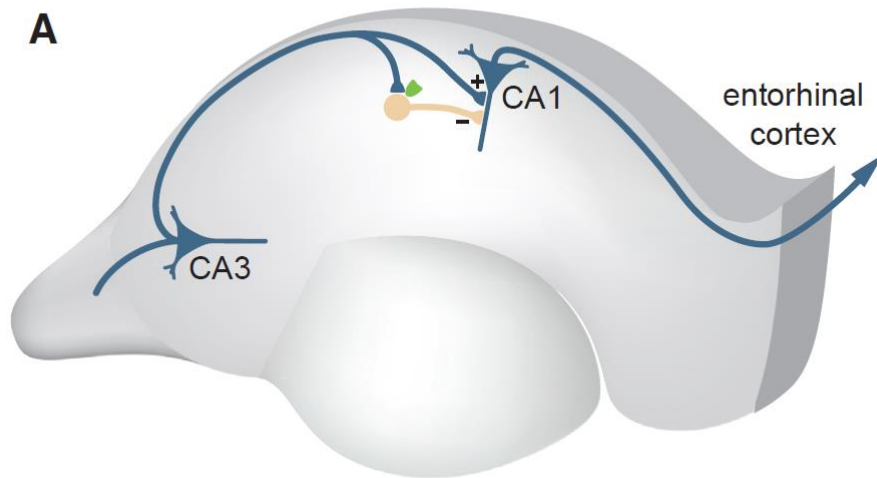
Muhlethaler et al 1984

# Oxytocin Modulation of Neural Circuits



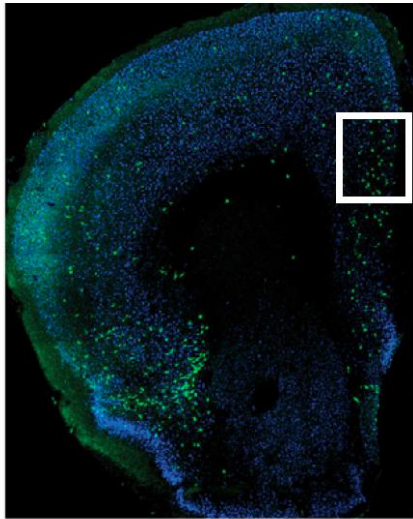
Owen et al 2013

# Oxytocin Modulation of Neural Circuits

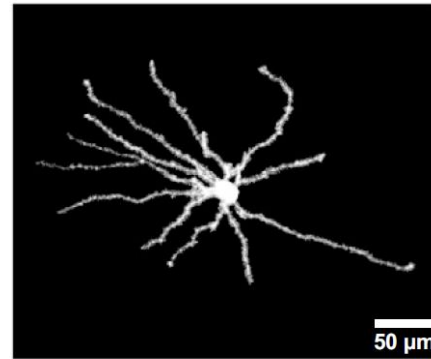
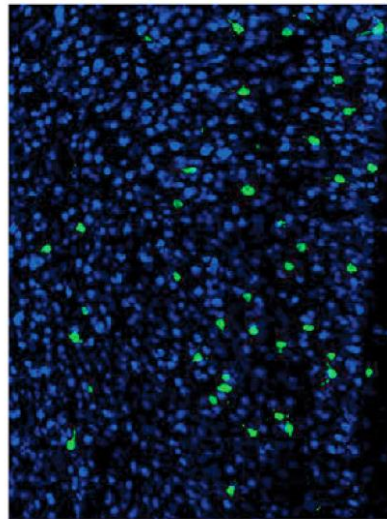


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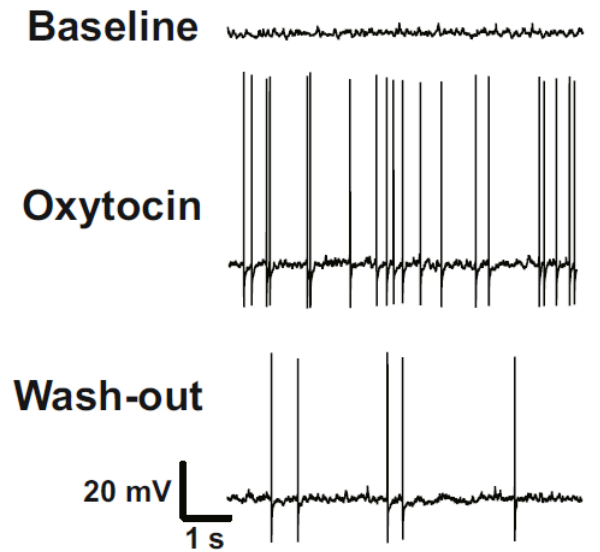
A



B

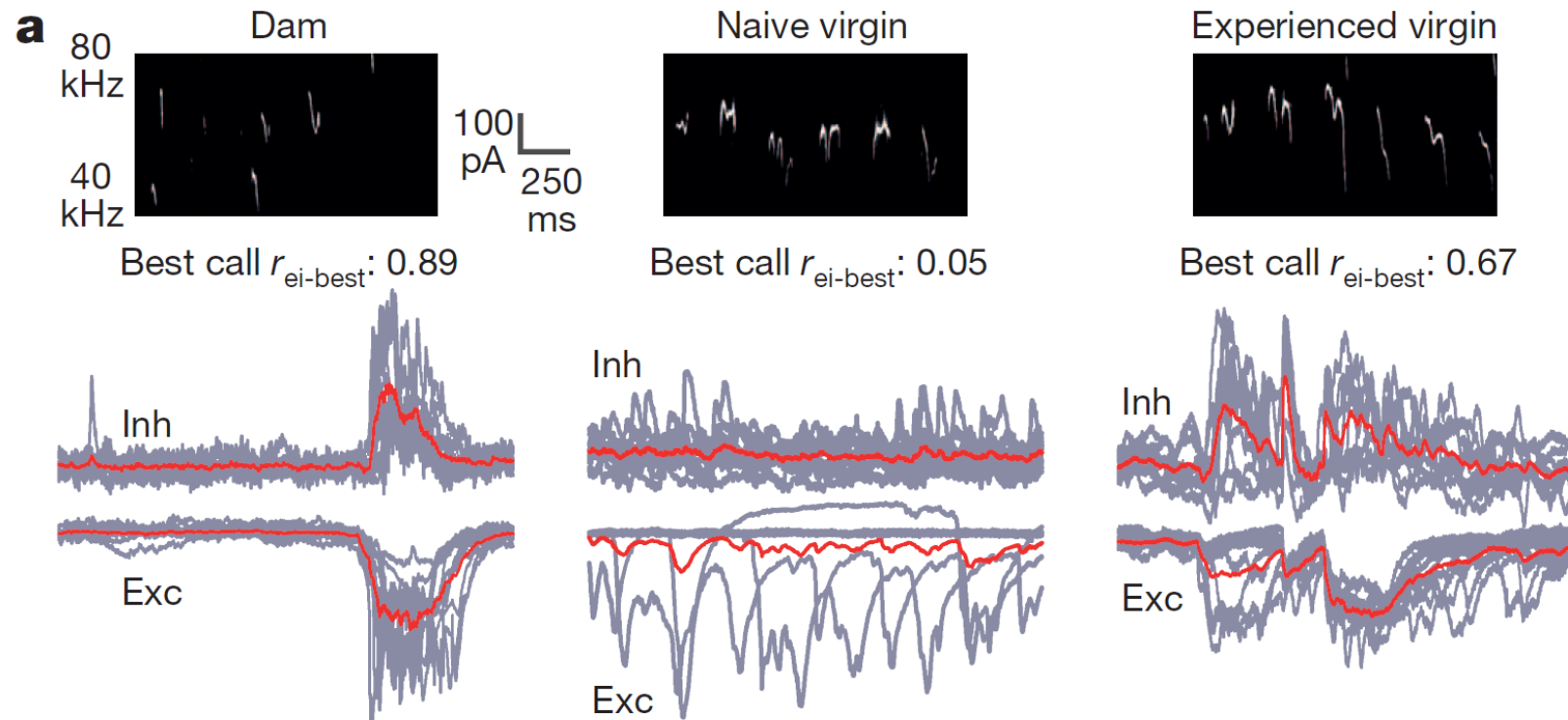


H



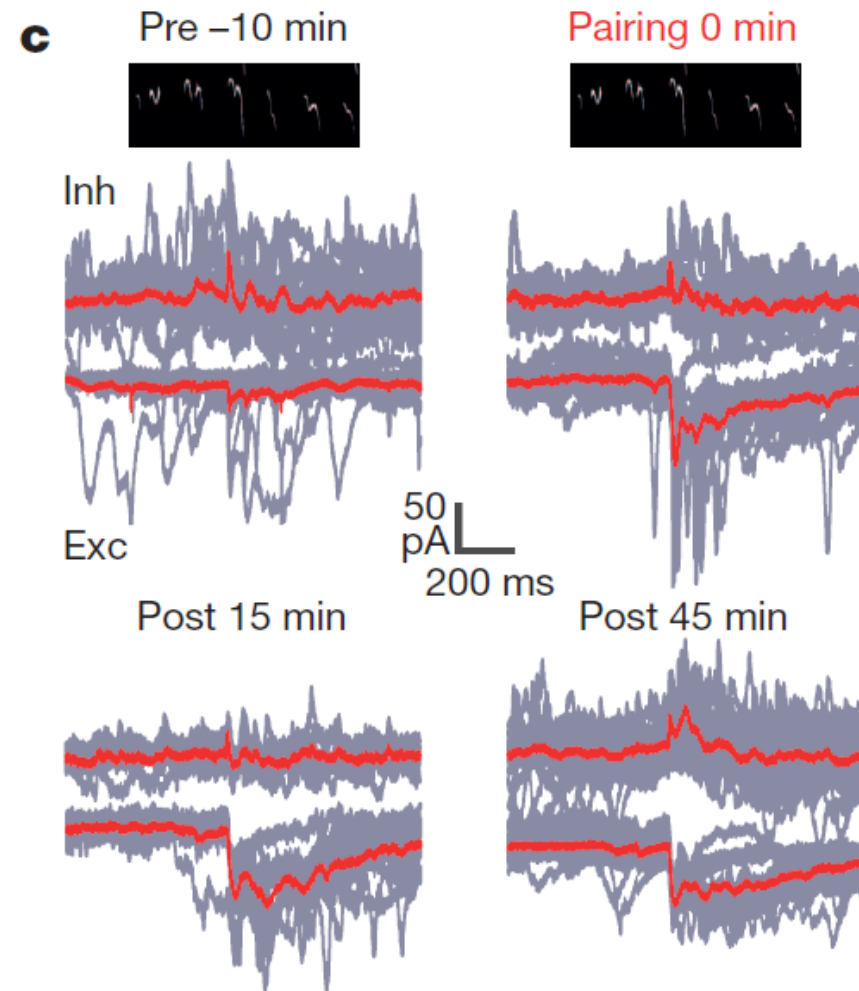
Nakajima et al 2014

# Oxytocin Modulation of Sensory Circuits



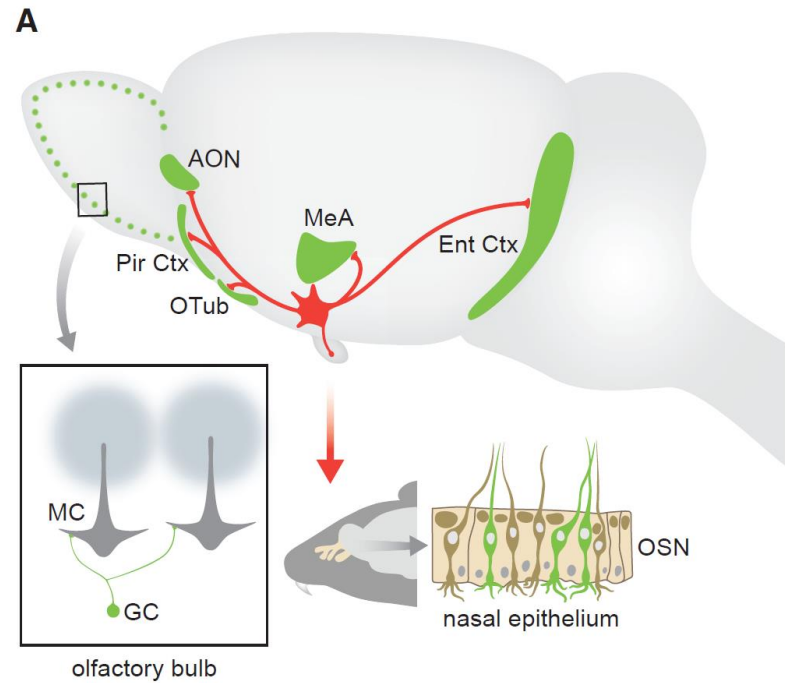
Marlin et al 2015

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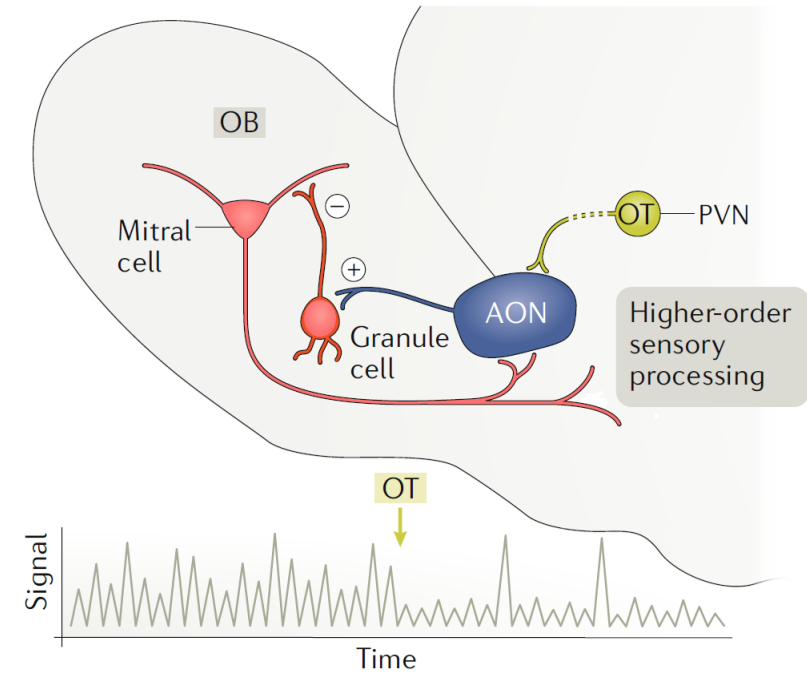
Marlin et al 2015

# Oxytocin Modulation of Sensory Circuits



Grinevich & Stoop 2018

**a** Enhanced signal-to-noise ratio

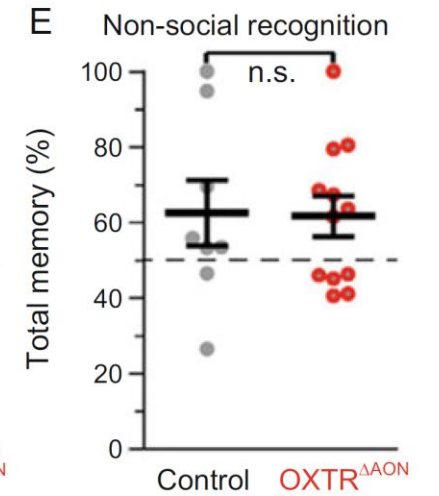
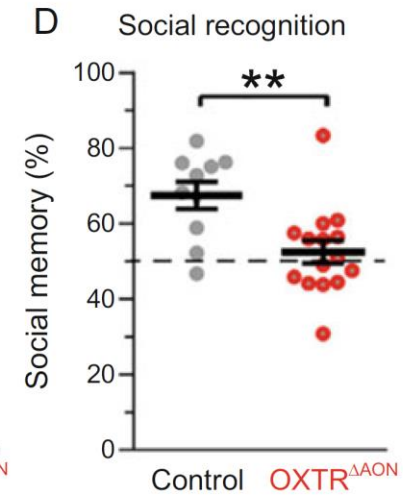
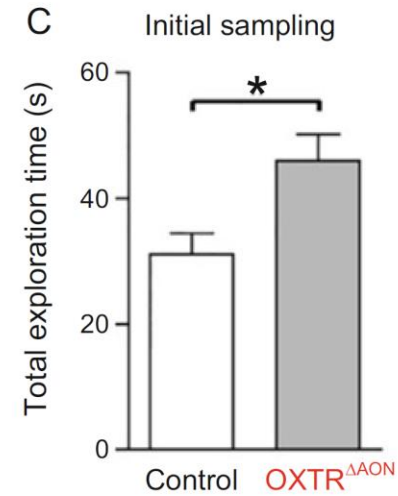
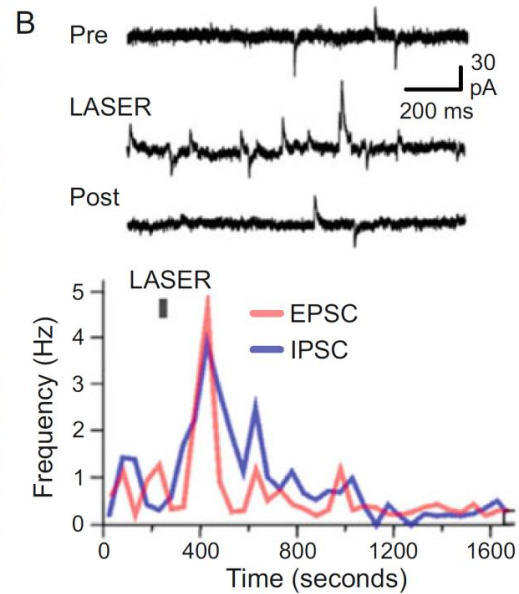
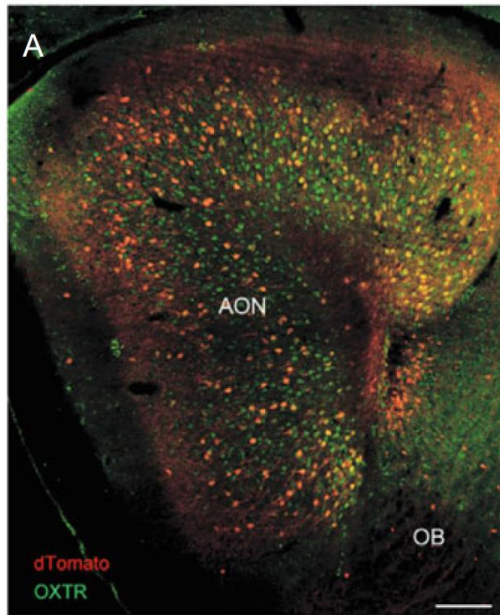


Walum & Young 2018

Oettl et al 2016

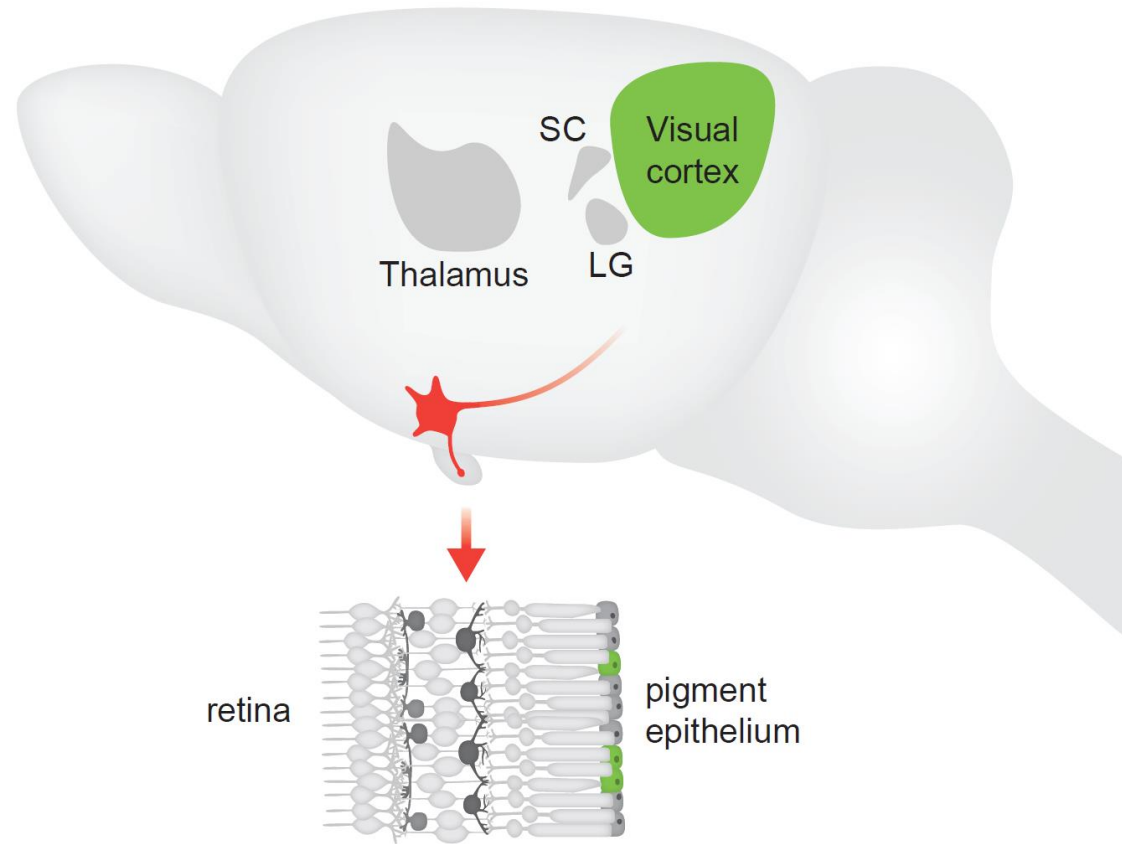


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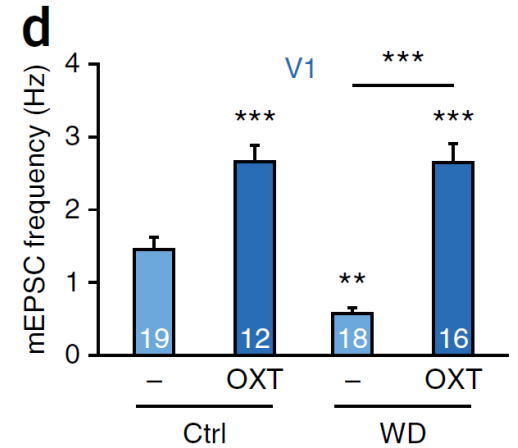
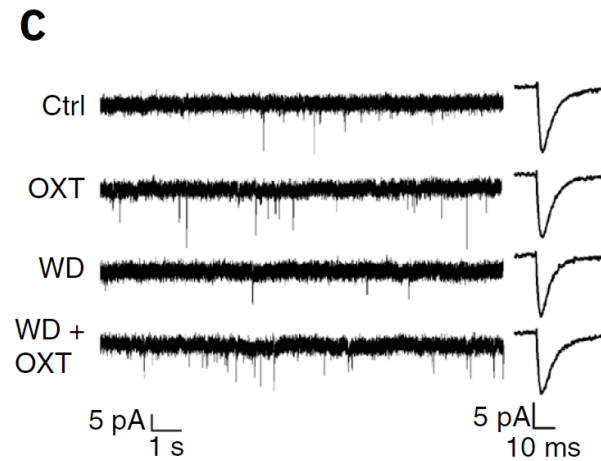
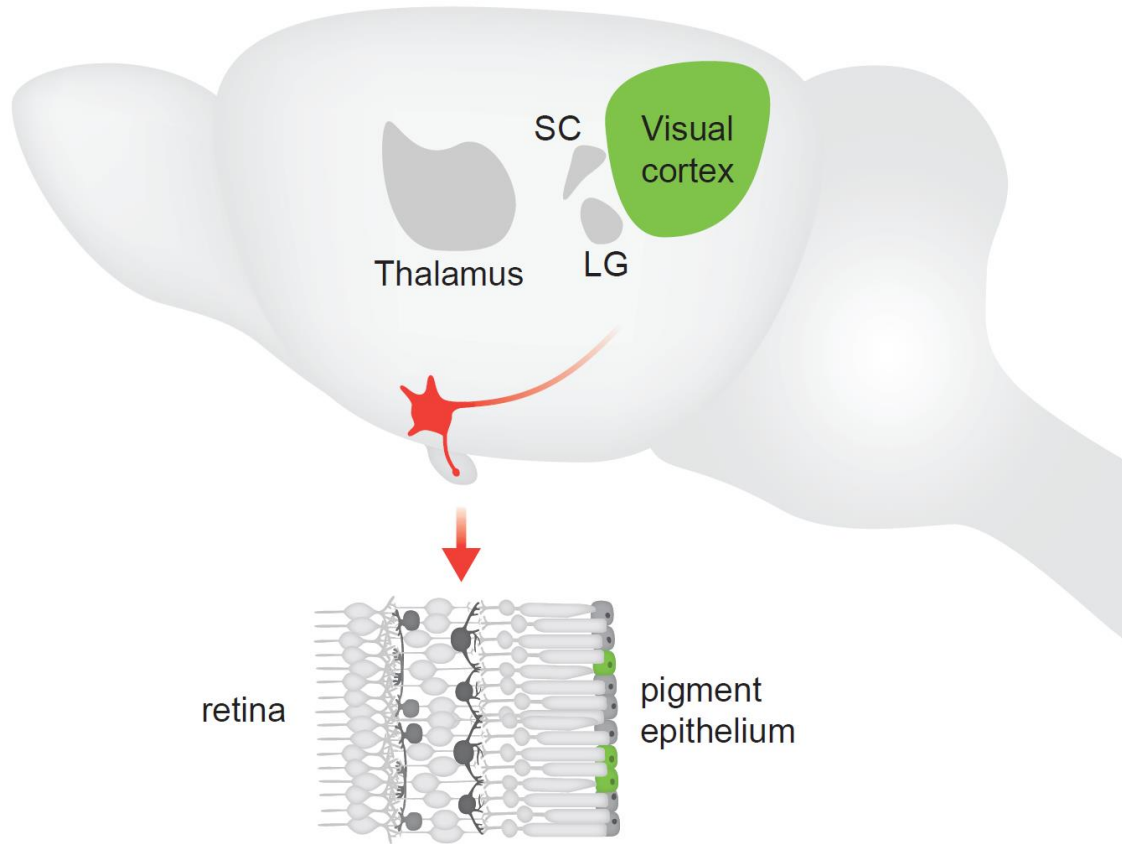


Oettl et al 2016

# Oxytocin Modulation of Sensory Circuits



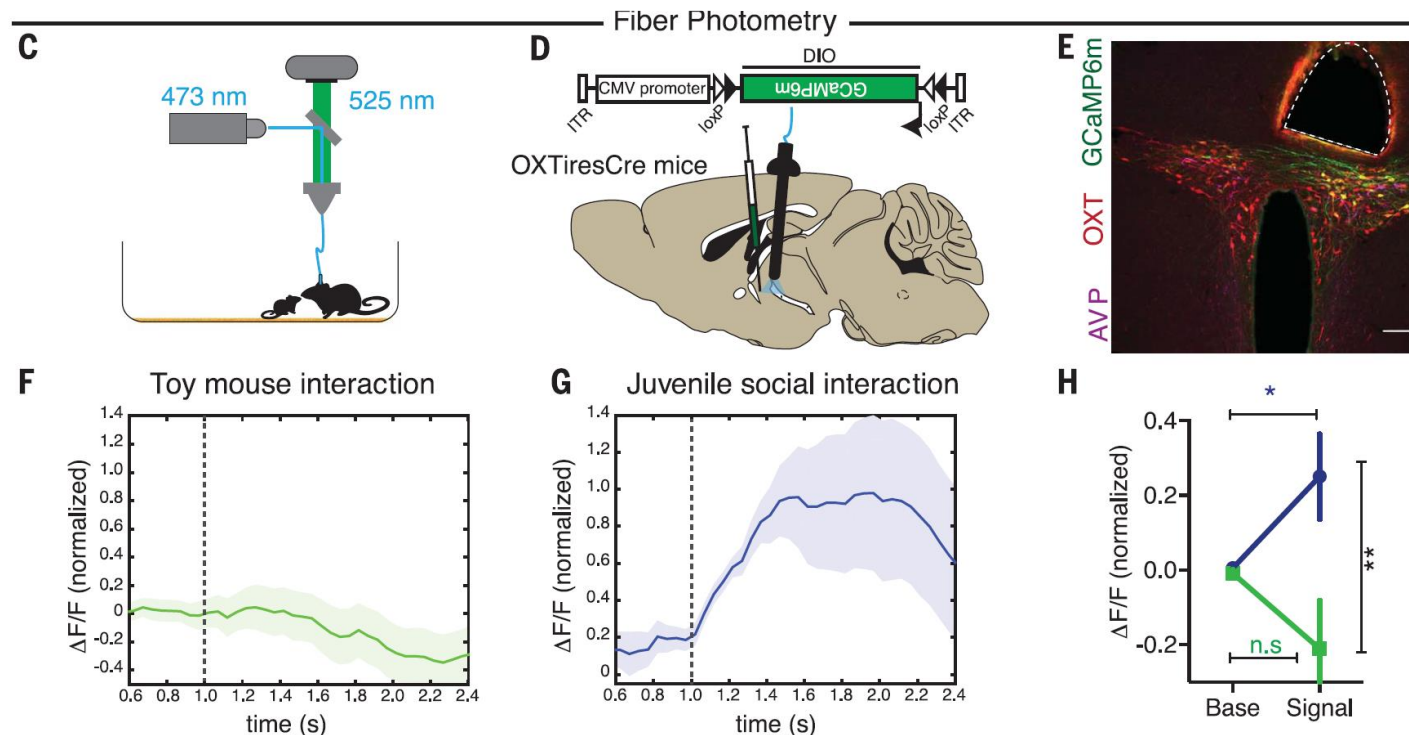
# Oxytocin Modulation of Sensory Circuits



Zheng et al 2014

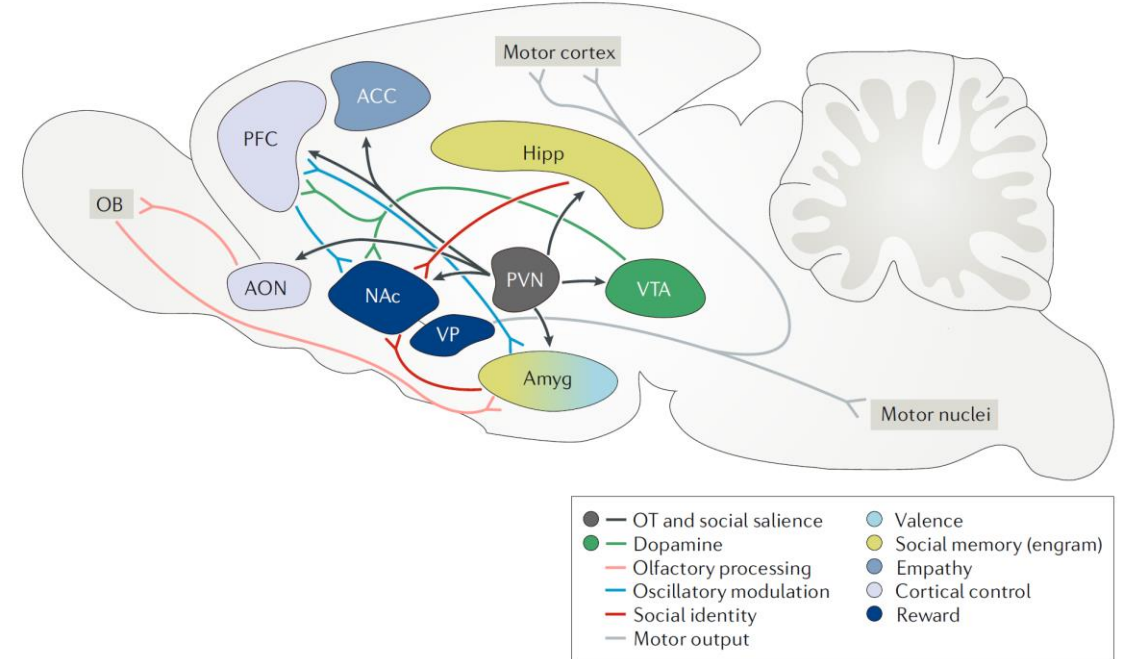
# Outstanding questions

- Not much is known about the natural release of oxytocin in response to natural stimuli



Hung et al 2017

# Conclusion



Walum & Young 2018

- Oxytocin might play a general role in facilitating the flow of social information across multiple brain regions
- (E-I balance, SNR)