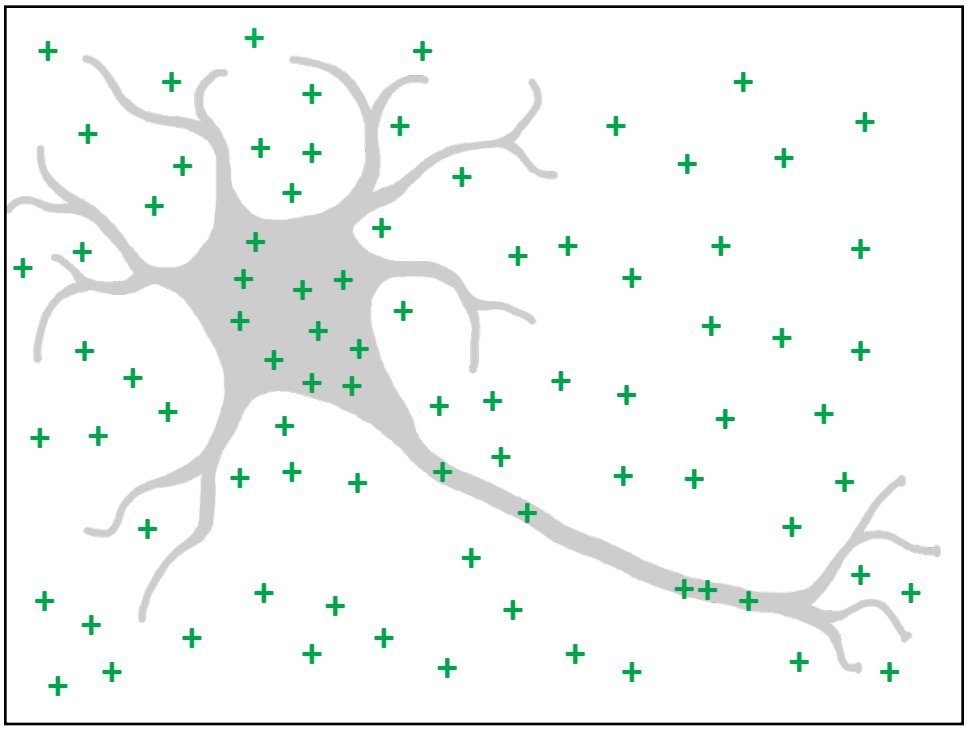
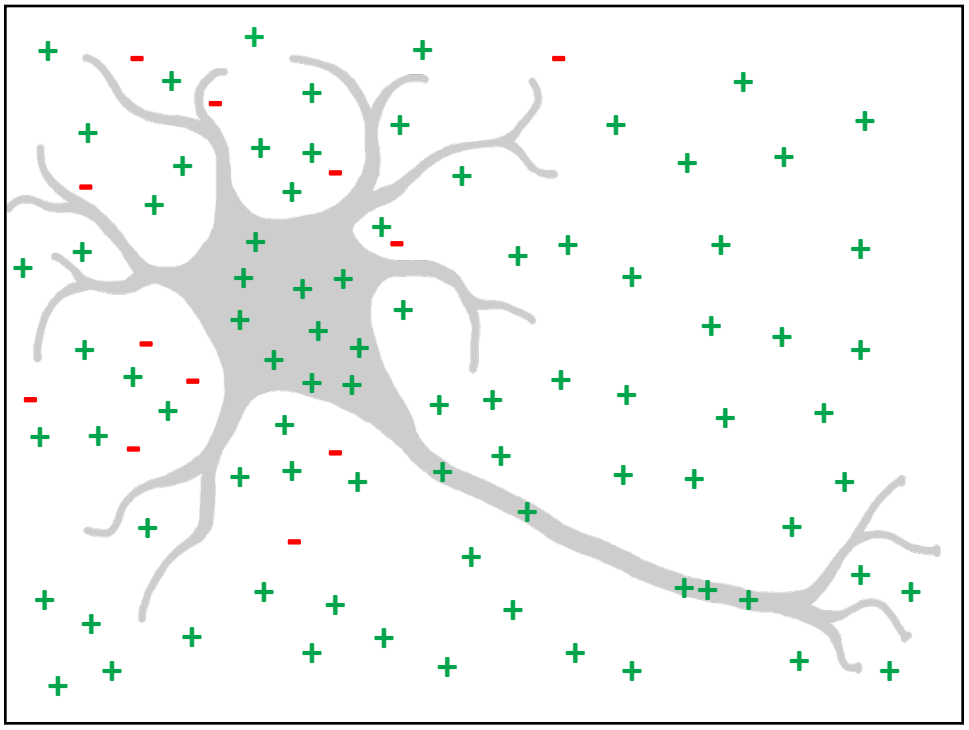
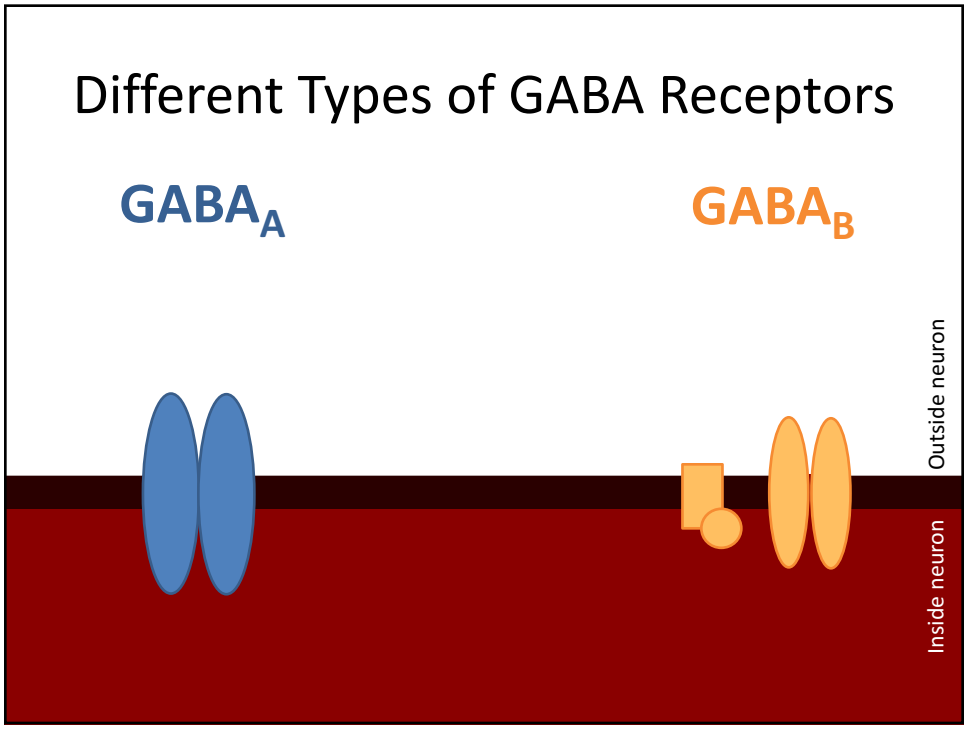
How does GABA inhibit neurons?

Dr. Amanda Freeman



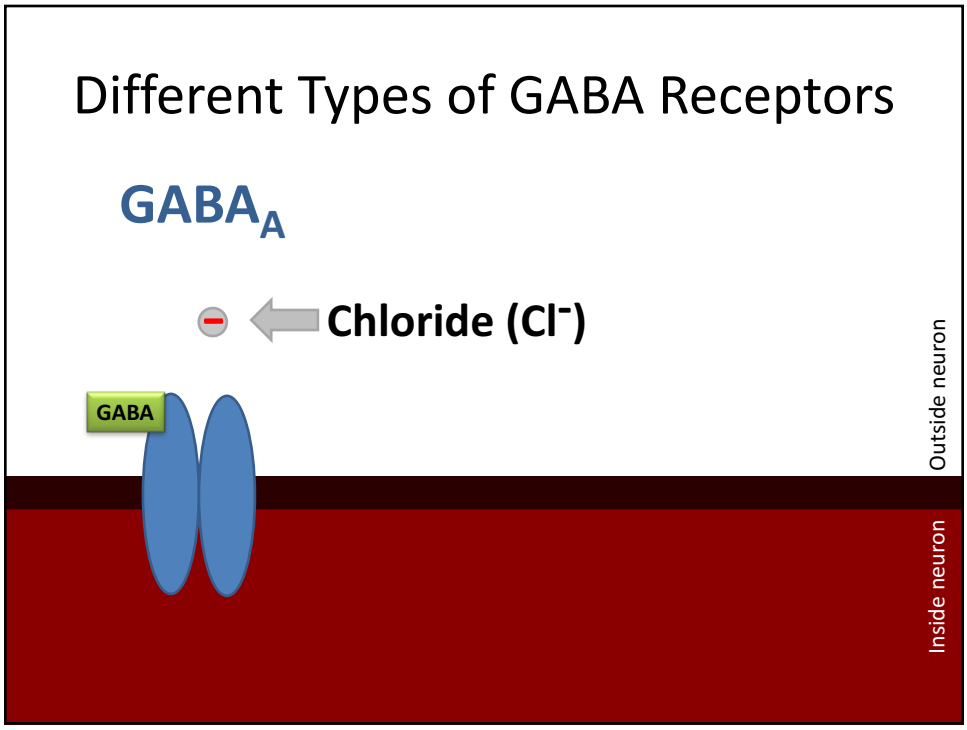


Different Types of GABA Receptors



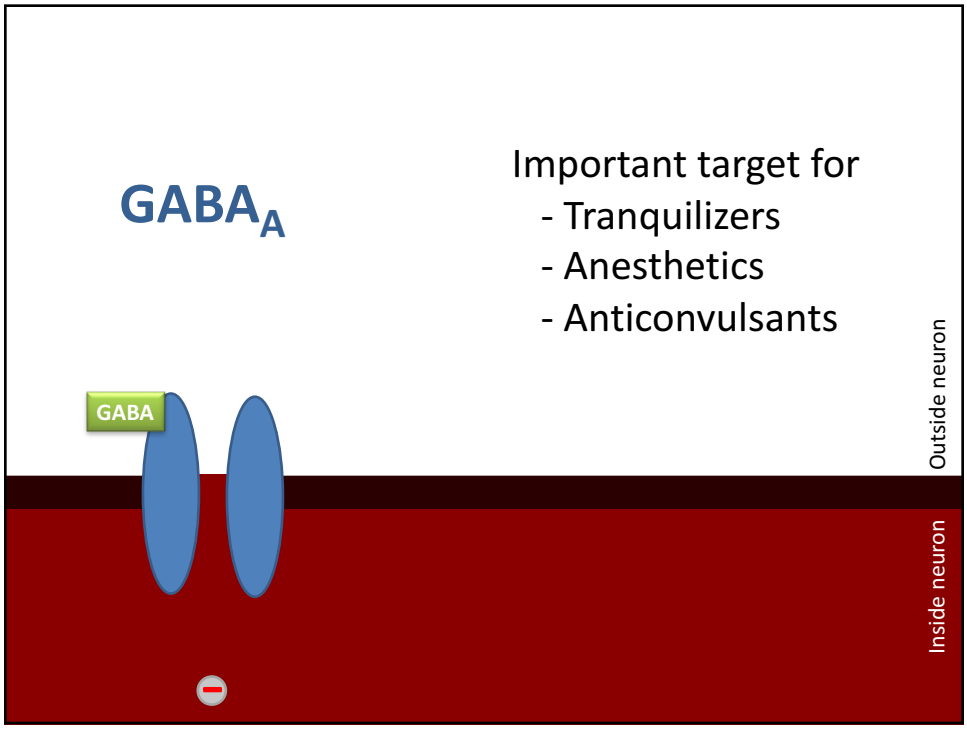
Different Types of GABA Receptors

$GABA_A$

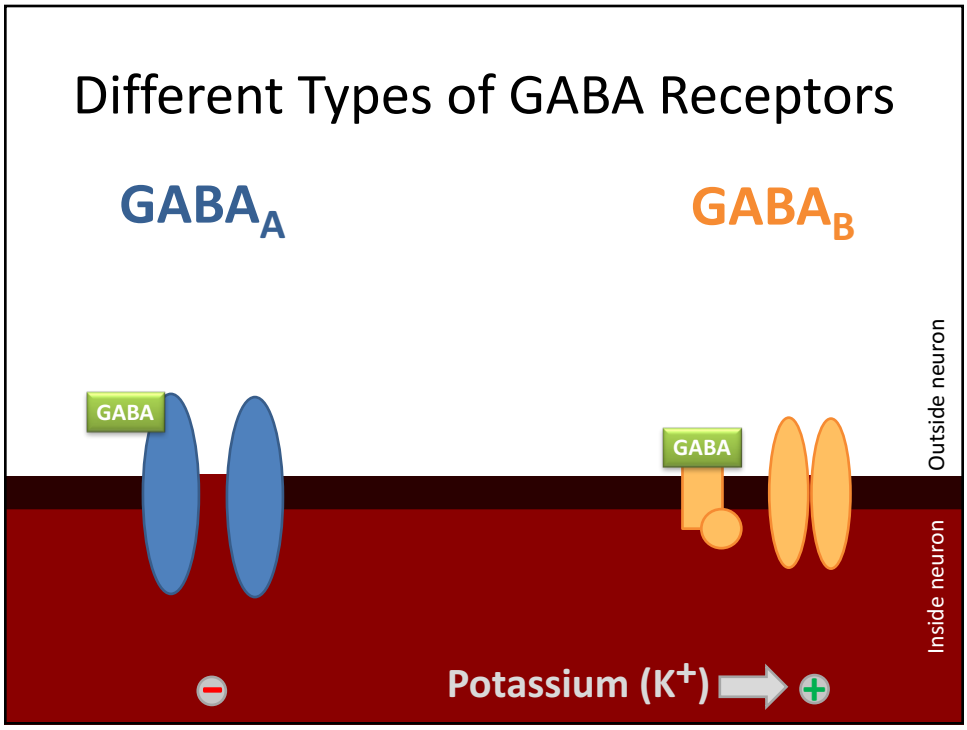


$GABA_A$

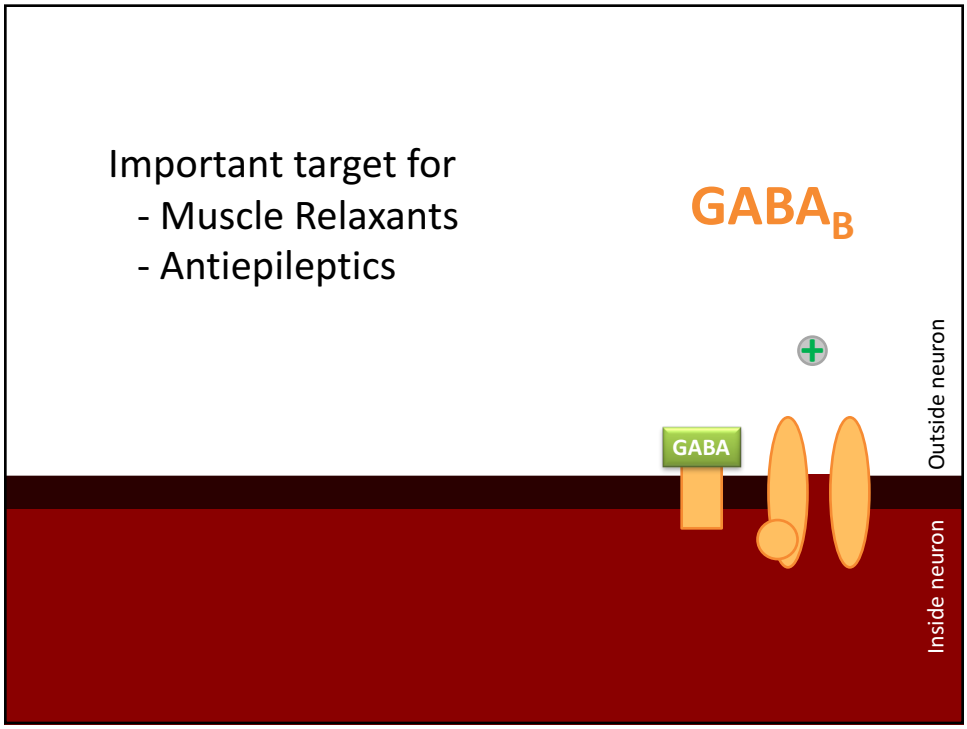
Important target for
- Tranquilizers
- Anesthetics
- Anticonvulsants

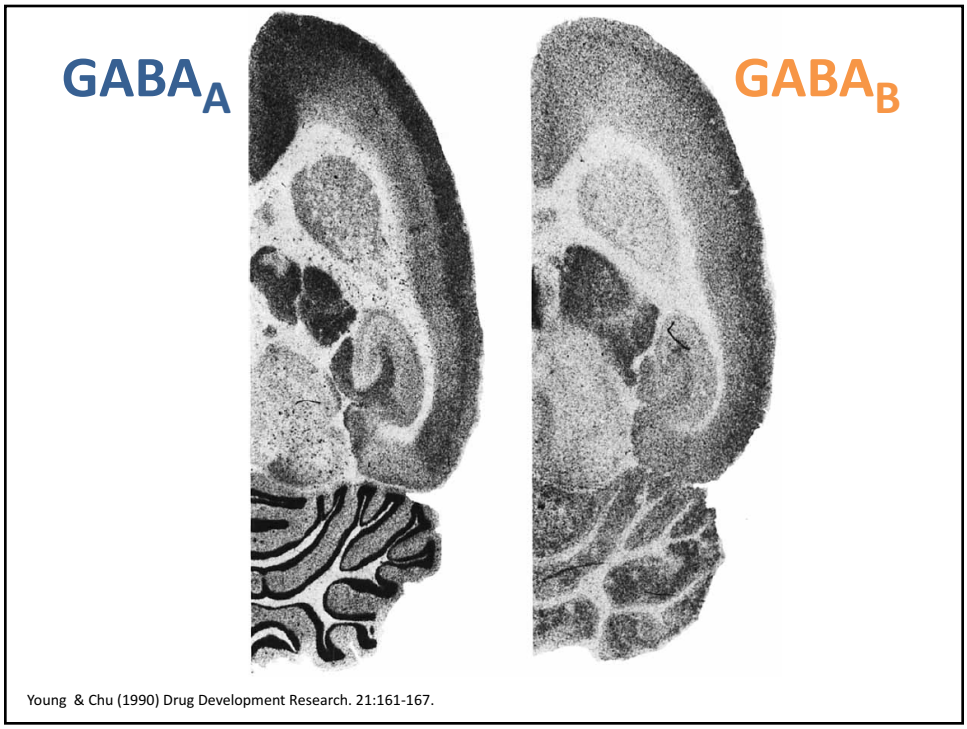


Different Types of GABA Receptors



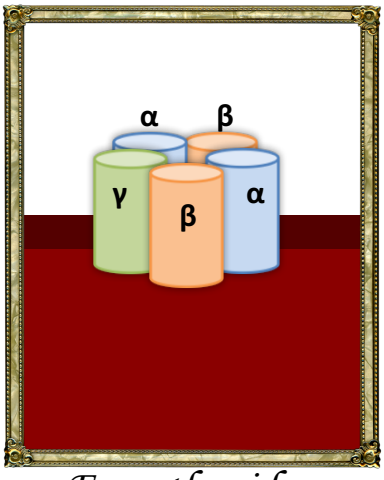
Important target for
- Muscle Relaxants
- Antiepileptics



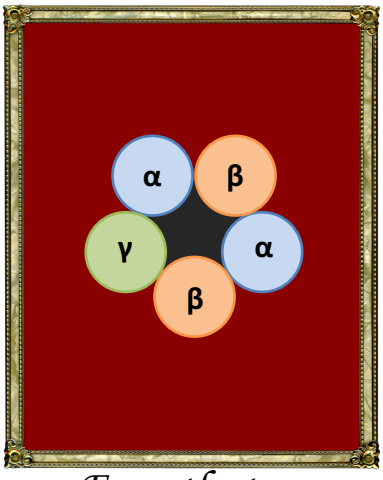


Young & Chu (1990) Drug Development Research. 21:161-167.

GABA$_A$ Receptor



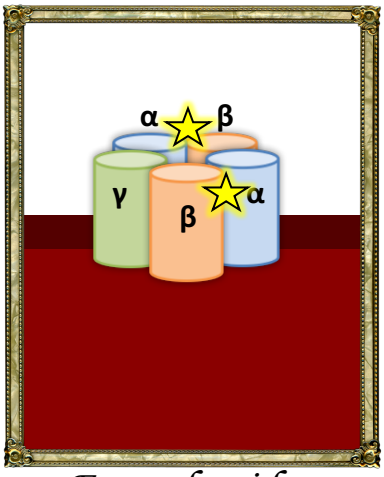
From the side



From the top

$GABA_A$ Receptor

☆ *GABA binding sites*



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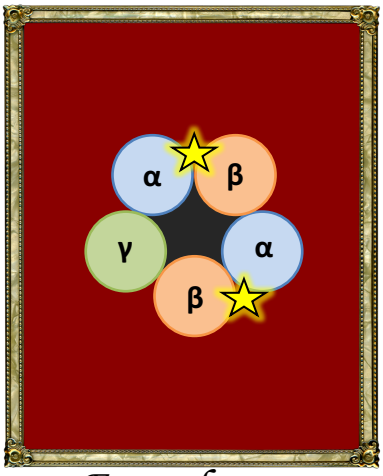
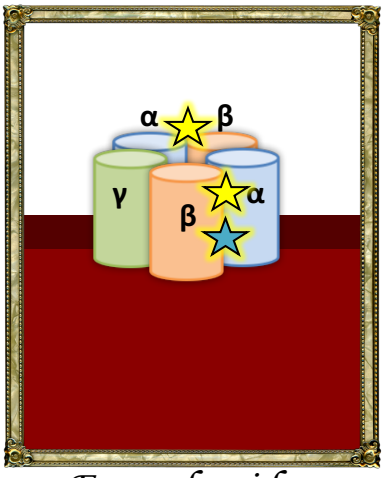


From the top

$GABA_A$ Receptor

☆ *Ethanol and volatile anesthetic binding sites*



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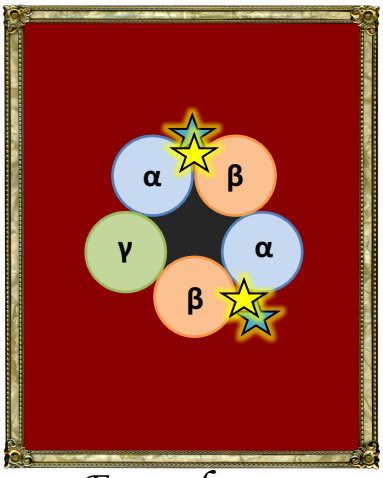
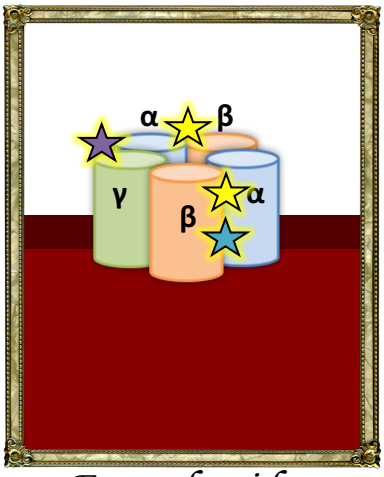


From the top

$GABA_A$ Receptor

★ *Benzodiazepine binding site*



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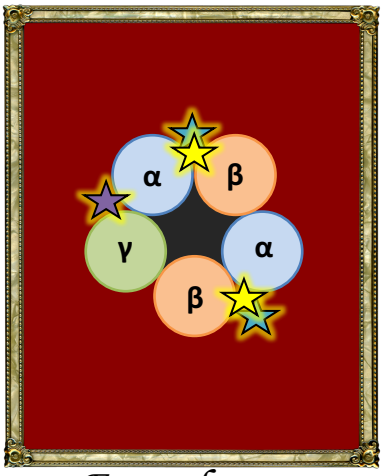


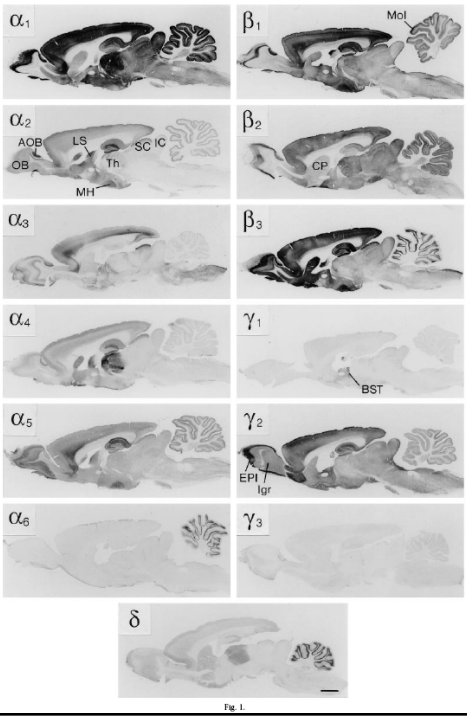
From the top

$GABA_A$ receptor subtype	Percentage of all $GABA_A$ receptors	Function
α_1 ($\alpha_1\beta_2\gamma_2$)	60%	Anesthetics Sedation* Amnesia* Anticonvulsant*
α_2	15-20%	Anxiolytic*
α_3	10-15%	Muscle relaxation* Anxiolytic*
α_5	<5%	Learning and Memory

** Effects of Benzodiazepines*

Based upon Nutt (2006) Journal of Clinical Sleep Medicine, 2(2):S7-S11.

$GABA_A$ receptor subunits

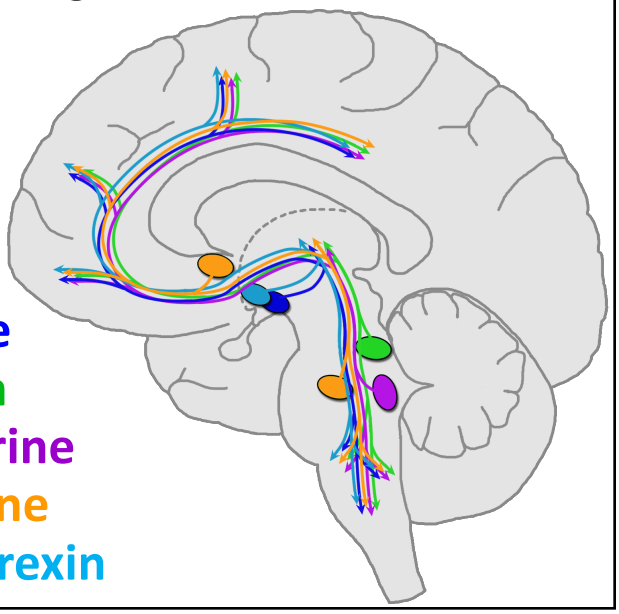


Pirker et al. (2000) Neuroscience . 101(4):815-850.

Fig. 1.

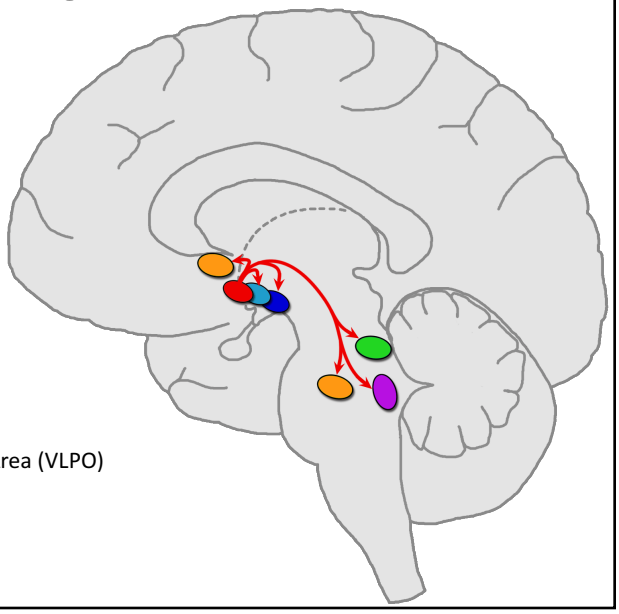
What does GABA have to do with sleep?

Wake Promoting



Histamine
Serotonin
Norepinephrine
Acetylcholine
Hypocretin/Orexin

Sleep Promoting



GABA
From Ventrolateral Preoptic Area (VLPO)

SLEEP

Modulation of Vigilance in the Primary Hypersomnias by Endogenous Enhancement of $GABA_A$ Receptors

David B. Rye,[1]* Donald L. Bliwise,[1] Kathy Parker,[2] Lynn Marie Trotti,[1] Prabhjyot Saini,[1] Jacqueline Fairley,[1] Amanda Freeman,[1] Paul S. Garcia,[3,4] Michael J. Owens,[5] James C. Ritchie,[6] Andrew Jenkins[3,7]

(2012) Science Translational Medicine 4(161):161ra151