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Rick Gilmore

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Prelude

Prelude

https://en.wikipedia.org/wiki/Mah_Nà_Mah_Nà

Today's Topics

- Neurotransmitters
- **Quiz 2** on Friday.
- Review Exam 1 on Friday.

The influx of which ion triggers the release of neurotransmitters from the axon terminal?

- Na⁺
- K⁺
- Ca⁺⁺
- Cl⁻

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This type of postsynaptic receptor does NOT contain its own ion channel.

- Ionotropic
- Metabotropic
- Ligand-gated

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Neurotransmitters

Family	Neurotransmitter
Amino acids	Glutamate (Glu) Gamma aminobutyric acid (GABA) Glycine Aspartate

Glutamate

- Primary excitatory NT in CNS
- Role in learning (via NMDA receptor)
- Transporters on neurons and glia (astrocytes and oligodendrocytes)
- Linked to umami (savory) taste sensation, think monosodium glutamate (MSG)
- Dysregulation in schizophrenia? (Javitt 2010)

Glutamate

Type	Receptor	Esp Permeable to
Ionotropic	AMPA	Na+, K+
	Kainate	
	NMDA	Ca++
Metabotropic	mGlu	

GABA

- Primary inhibitory NT in CNS
- Excitatory in developing CNS, $[Cl^-]_{in} \gg [Cl^-]_{out}$
- Binding sites for benzodiazepines (e.g., Valium), barbiturates, ethanol, etc.

Type	Receptor	Esp Permeable to
Ionotropic	GABA-A	Cl-
Metabotropic	GABA-B	K+

GABA

“GABAA-receptor-protein-example” by Chemgirl131 at English Wikipedia - Transferred from en.wikipedia to Commons by Sreejithk2000 using CommonsHelper.. Licensed under Public Domain via Commons.

Acetylcholine (ACh)

- Primary NT of CNS output
- Somatic nervous system (neuromuscular junction)
- Autonomic nervous system
 - Sympathetic branch: preganglionic neuron
 - Parasympathetic branch: pre/postganglionic
- Inactivation by acetylcholinesterase (ACh)

ACh anatomy

<http://myzone.hrvfitltd.netdna-cdn.com/wp-content/uploads/2014/09/Image-1.jpg>

Acetylcholine

Type	Receptor	Esp Permeable to	Blocked by
Ionotropic	Nicotinic (nAChR)	Na ⁺ , K ⁺	e.g., Curare
Metabotropic	Muscarinic (mAChR)	K ⁺	e.g., Atropine

Curare

<http://www.general-anaesthesia.com/images/indian-curare.jpg>

Atropine

- aka, nightshade or belladonna

http://www.aapos.org/client_data/files/2011/_138_dilatingeyedrops2.jpg

How to stop your prey

Substance	Effect
Japanese pufferfish toxin	Blocks voltage-gated Na ⁺ channels
Black widow spider venom	Accelerates presynaptic ACh release
Botulinum toxin	Prevents ACh vesicles from binding presynaptically
Sarin nerve gas	Impedes ACh breakdown by AChE
Pesticides	Impede AChE
Tetanus toxin	Blocks release of GABA, glycine

Monoamine neurotransmitters

Family	Neurotransmitter
Monoamines	Dopamine (DA) Norepinephrine (NE)/Noradrenaline (NAd) Epinephrine (Epi)/Adrenaline (Ad) Serotonin (5-HT) Melatonin Histamine

Monoamine Song

https://en.wikipedia.org/wiki/Mah_Nà_Mah_Nà

Monoamine Song

Monoamines, do-do do do-do Monoamines, do do do-do Monoamines, do do do do-do do do-do do do-do do do do do-do do

Monoamine Song

Monoamines, do-pa-mine is one Monoamines, norepi, too Monoamines, sero-otonin e-pinephrine, dop-a- mine, nor-epinephrine, melatonin, whoo!

Monoamine Song

Monoamines, mod-u-late neurons Monoamines, throughout the brain Monoamines, keep people happy, brains snappy, not sleepy, not sappy, do-do do-do do-do do

Monoamine neurotransmitters

Family	Neurotransmitter
Monoamines	Dopamine (DA) Norepinephrine (NE)/Noradrenaline (NAd) Epinephrine (Epi)/Adrenaline (Ad) Serotonin (5-HT) Melatonin Histamine

Dopamine

- Released by two pathways
 - Substantia nigra -> striatum, *meso-striatal projection*
 - Ventral tegmental area (VTA) -> nucleus accumbens, ventral striatum, hippocampus, amygdala, cortex; *meso-limbo-cortical projection*

DA pathways

DA Disruption linked to

- Parkinson's Disease (mesostriatal)
 - DA agonists treat (agonists facilitate/increase transmission)
- ADHD (mesolimbocortical)
- Schizophrenia (mesolimbocortical)
 - DA antagonists treat
- Addiction (mesolimbocortical)

DA Inactivated by

- Dopamine transporter (DAT) and chemical breakdown

http://www.scholarpedia.org/article/Dopamine_anatomy#Dopamine_receptors

Dopamine receptors

Type	Receptor	Comments
Metabotropic	<i>D1-like (D1 and D5)</i>	more prevalent
	<i>D2-like (D2, D3, D4)</i>	target of many antipsychotics

Norepinephrine

- Released by
 - *locus coeruleus* in pons
 - postganglionic sympathetic neurons onto target tissues
- Role in arousal, mood, eating, sexual behavior

NE and Monoamine oxidase inhibitors (MAOIs)

- inactivate monoamines in neurons, astrocytes
- MAOIs increase NE, DA
- Treatment for depression, but have side effects

NE Anatomy

NE receptors

Type	Receptor	Comments
Metabotropic	α (1,2)	antagonists treat anxiety, panic
	β (1,2,3)	'beta blockers' in cardiac disease

Serotonin (5-HT)

- Released by *raphe nuclei* in brainstem
- Role in mood, sleep, eating, pain, nausea, cognition, memory
- Modulates release of other NTs
- Most of body's 5-HT regulates digestion

5-HT anatomy

5-HT receptors

- Seven families (5-HT 1-7) with 14 types
- All but one metabotropic

5-HT clinical significance

- Ecstasy (MDMA) disturbs serotonin
- So does LSD
- Fluoxetine (Prozac)
 - *Selective Serotonin Reuptake Inhibitor (SSRI)*

- Inhibits reuptake -> increases extracellular concentration
- Treats depression, panic, eating disorders, others
- 5-HT₃ receptor antagonists are anti-mimetics used in treating nausea

Melatonin

- Released by pineal gland into bloodstream

Pineal gland

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Histamine

- In brain, released by hypothalamus, projects to whole brain
 - Metabotropic receptors
 - Role in arousal/sleep regulation
- In body, part of immune response

Other NTs

- Gases
 - *Nitric Oxide (NO)*, *carbon monoxide (CO)*
- Neuropeptides
 - *Substance P* and *endorphins* (endogenous morphine-like compounds) have role in pain
 - *Orexin/hypocretin*, project from lateral hypothalamus across brain, regulate appetite, arousal

Other NTs

- Neuropeptides (continued)
 - *Cholecystokinin (CCK)* stimulates digestion
 - *Oxytocin* and *vasopressin* released by posterior hypothalamus onto posterior pituitary, regulate social behavior

Non-chemical communication between neurons

- Gap junctions
- Electrical coupling
- Connect cytoplasm directly
- Fast, but fixed, hard to modulate
- Examples, retina, cardiac muscle

Gap junctions

Ways to think about synaptic communication

- Specificity: point-to-point vs. broadcast

- Direct vs. modulatory
- Agonists vs. antagonists

Agonists vs. Antagonists

- *Agonists*
 - bind to receptor
 - mimic action of endogenous chemical
- *Antagonists*
 - bind to receptor
 - block/impede action of endogenous chemical

Valium is a GABA-A receptor agonist. This means:

1. It decreases inhibition
2. It activates a metabotropic Cl⁻ channel
3. It facilitates/increases inhibition
4. It blocks an ionotropic channel

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Next time...

- Hormones

References

Javitt, Daniel C. 2010. "Glutamatergic Theories of Schizophrenia." *Israel Journal of Psychiatry and Related Sciences* 47 (1): 4.