

3/8/04

Quantum* postsynaptic response to one vesicle released

Orbelli effect: presynaptic: sympathetic axons release norepinephrine (makes quantal content go up from motor axons)

postsynaptic: adrenal gland releases epinephrine, plugs up muscle cell leakage channels (increases R so ΔV greater)

pharmacological dissection

- α -adrenergic receptors (presynaptic): agonist = isoproterenol (used for anaphylactic shock)

antagonist = β -propranolol (used for heart patients, stage fright)

agonist = norepinephrine

antagonist = clonidine

- β -adrenergic receptors (postsynaptic): agonist = isoproterenol (used for anaphylactic shock)

antagonist = β -propranolol (used for heart patients, stage fright)

- principle here is synaptic modulation (volume control: modulatory neurotransmitters, eg epinephrine, norepinephrine)

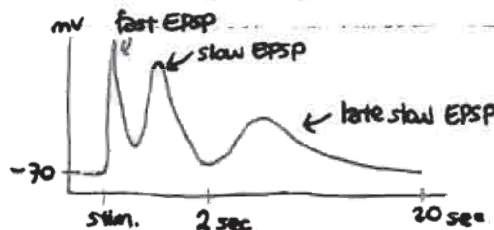
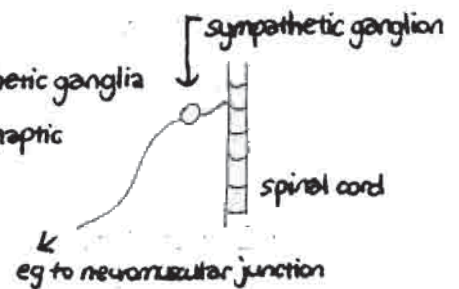
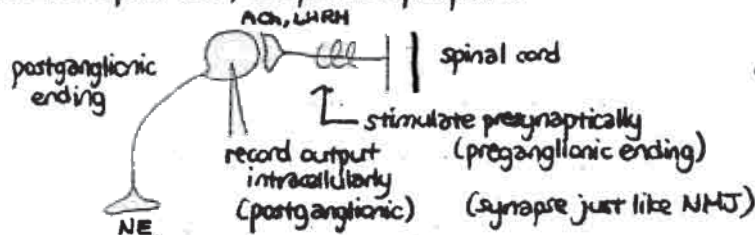
- blurring of function between neurotransmitters + hormones (eg norepinephrine released in vicinity of neuromuscular junction, acts semi-locally, diffuses mms) (epinephrine acts not at all locally)

sympathetic ganglion:

- pioneering work done in bullfrog

- in our sympathetic nervous system, have adrenal gland + sympathetic ganglia

- in spinal cord is lump of nerve cells, some interneurons: presynaptic axon from spinal cord, output norepinephrine



1 stimulation, 3 potentials recorded from 1 cell

- ganglia have lots of ACh: spritzing ACh gives 2 out of 3 (fast + slow EPSPs)



1 kind of neurotransmitter affects 2 different types of receptors (only one blocked by curare: blocks fast but not slow or late slow)

atropine - another cholinergic antagonist

- belladonna used to dilate pupils; atropine is active ingredient (-taking too much is lethal)

↳ (Atropis is Fate w/ scissors, cuts off human life)

- blocker for 2nd class of cholinergic receptors ⌋ ionotropic (ligand-gated channel)

- neuromuscular junction receptor: nicotinic AChR (agonist = nicotine) (antagonist = curare)

- 2nd class of receptors (dominant on heart cells): muscarinic AChR (via metabotropic, 2nd messenger coupled)

↳ like Loewy's vagus nerve heart experiments

(agonist = muscarine) ← from Muscaria mushroom, insecticide

(antagonist = atropine)

- applying curare gets rid of fast EPSP

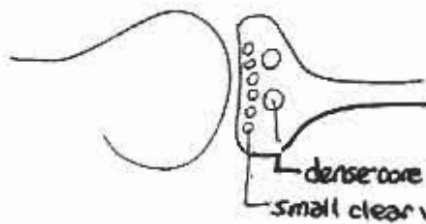
applying atropine gets rid of slow EPSP (no slow EPSP from atropine working on mAChRs)

- mAChR 2nd messenger system: patch clamping shows that stimulation w/ ACh closes H-type

channel (K⁺ channel): closing K⁺ channel is excitatory/

depolarizing, gives you slow EPSP

late slow EPSP:



dense-core vesicles (large): contain lots of things, including peptide neurotransmitters

- got Abx to these peptides, eg

LHRH

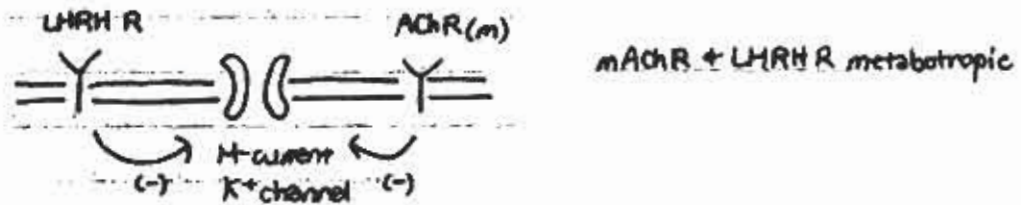
↳ from rat estrus cycle, makes

lutinizing hormone in pituitary

- system of tiny hormones in rat pituitary tells it to release other hormones (or something)

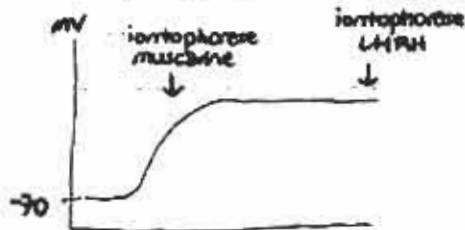
spritzing LHRH on sympathetic ganglia give you late slow EPSP

- can have 2 synaptic messengers released from same sympathetic ending



- occlusion experiments:

- record from postganglionic cell



no additional response: muscarine occludes effect of LHRH

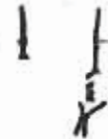
- downstream pathways converge, so saturating w/ one input (all K⁺ channels closed) means other input will have no effect

- not order-dependent

- used to test for convergent downstream effector (eg same or different 2nd messenger systems, but converge eventually)

- in sympathetic ganglion, B & C cells

↳ big



spritzing LHRH on C give no effect
spritzing on B gives late slow EPSP

- LHRH effect only seen on B cells (only B cells have late slow EPSP)

- paradox is: immunoreactivity (LHRH vesicles) only seen on presynaptic endings to C cells

- ACh released conventionally across synaptic cleft for both B & C cells

- LHRH diffuses from synaptic cleft of C cells to that of B cells, late slow EPSP

(blurring of transmitters/hormones, localization of action) ↳ (partly b/c of diffusion)

- this is interesting b/c shows you electron microscopy not infallible: must confirm w/ electrophysiology

Aplysia californica californica: "sea hare" (but is basically sea slug): lives in tide pool, eats kelp

(will eat kimwipe)

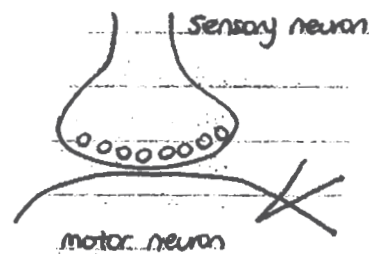


squirt terrible-smelling purple ink

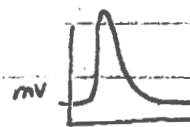
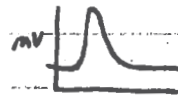
- have 7 ganglia, 20,000 cells (very large)

- reproducible arrangements of cells, eg all abdominal ganglia same

- Eric Kandel did circuit tracing in *Aplysia* for gill-withdrawal reflex (poking in gill causes gill to withdraw)
- can get contraction that can be measured in muscle: eventually, will get habituation (waning in strength of reflexive response)
- give strong tail shock: this sensitizes
- sensory neurons make monosynaptic connections on motor neurons that contract gill
 - all cells in abdominal ganglia: tail shock gives you greater reaction, after many days will get permanently larger reaction (sensitization is opposite of habituation)



record intracellularly for EPSP



sensitization
(more efficient synaptic transmission:
synaptic facilitation)



habituation

this reflex comes w/ memory,
can be related to synaptic events
(can only be done in this system)

- what causes these changes? (sensitizing us: release epinephrine & norepinephrine)
- biogenic amines: 5-HT, epinephrine, dopamine, ACh, norepinephrine, etc in us
5-HT, dopamine, octopamine in animals (epinephrine w/o HO)
- sensitized bunch of animals, found out 5-HT ↑ (measured neurotransmitter levels in abdominal ganglia)
dopamine ↑
octopamine ↑
- spritzed these, found that only 5-HT gave change (synaptic facilitation)
- long responses require 2nd messenger systems coupled to metabotropic receptors
(at this time, only cAMP 2nd messenger system understood: spritzing 5-HT → cAMP ↑)
- synaptic facilitation presynaptic or postsynaptic? lower $[Ca^{2+}]_i$, do quantal analysis, found increased probability of failure (so presynaptic): cAMP activates kinase, blocking kinase blocks effect decreased

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