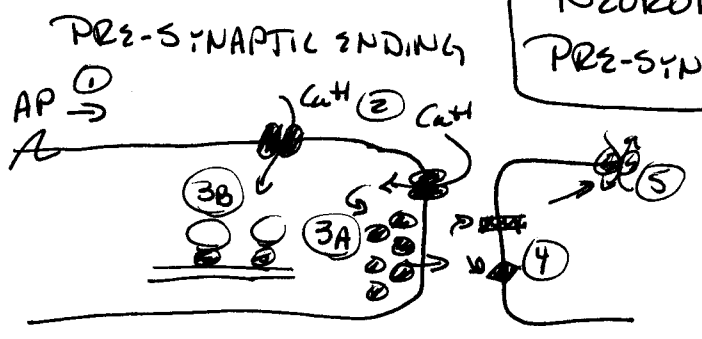
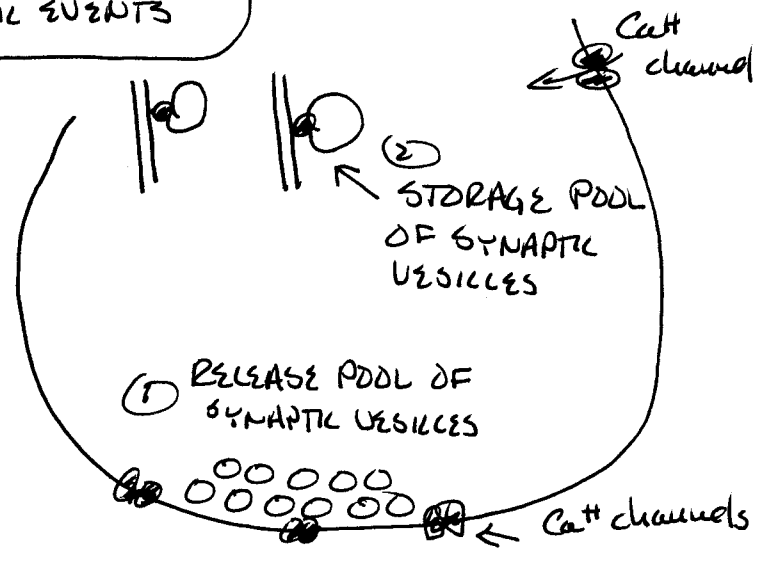


NEUROBIOLOGY 2B
PRE-SYNAPTIC EVENTS



- ① AP → PRE-SYNAPTIC ENDING
- ② VOLTAGE SENSITIVE Ca^{2+} CHANNELS OPEN
- ③ Ca^{2+} → "EXOCYTOSIS" OF VESICLES NT RELEASE
 (A) Ca^{2+} → MOBILIZE "STORAGE" VESICLES TO REPLACE "RELEASE" VESICLES
- ④ RELEASED NT ACTIVATES RECEPTORS
- ⑤ ACTIVATED RECEPTORS INITIATE POST SYNAPTIC CURRENTS (EPSPs, PSPs)
- ⑥* INACTIVATION



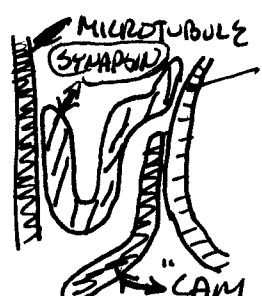
MAJOR ISSUES OF PRE-SYNAPTIC

- ① NT SYNTHESIS
- ② VESICLE CONSTRUCTION
- ③ STORAGE / RELEASE OF VESICLES
- ④ RECYCLING
 - (A) VESICLE MEMBRANES
 - (B) NEUROTRANSMITTERS

EARLY PRE-SYNAPTIC BIOCHEMISTRY
SYNAPSIN / SYNAPTOSOMES | PAUL GREENGARD

1964 - Whillaker et al - SYNAPTOSOMES
PREP. OF PRE-SYNAPTIC ENDINGS
BREAK UP BRAIN (SONICATE)
TINY SUBCELLULAR FRAGMENTS
SEPARATE BY DENSITY CENTRIFUGATION

1973 - UEDA, MAENO & GREENGARD - SYNAPSIN
ID PROTEIN OF SYNAPTOSOME (PRE-SYNAPTIC ENDING)
PHOSPHORYLATED BY PK IN CAMP DEPENDENT MANNER.
= SYNAPSIN (MEMBRANE PROTEIN OF SYNAPTIC VESICLE)



Ca^{2+} BINDS TO CAM KINASE II WHICH PHOSPHORYLATES SYNAPSIN WHICH RELEASES FROM MT FREEING VESICLE - REPLACE "CAM KINASE II" RELEASED VESICLES

I. NT SYNTHESIS

4 CLASSES OF NT

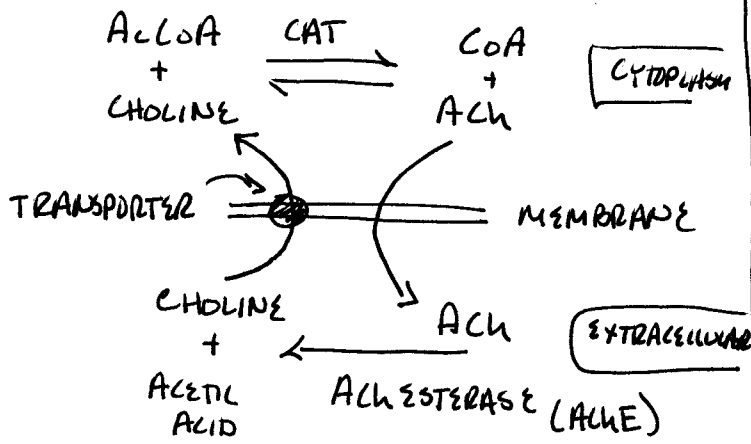
① ACh	② AMINO ACIDS Glu Gly GABA	③ BIOGENIC AMINES (CATACHOLAMINES) 5HT DOPAMINE EPINEPHRINE NDR-EP HISTAMINE	④ PEPTIDES 50-100
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SYNTHESIZED IN PRE-SYNAPTIC ENDINGS

SYNTH IN CELL BODY (GENE EXP) TRANSPORTED TO PRE-SYNAP.

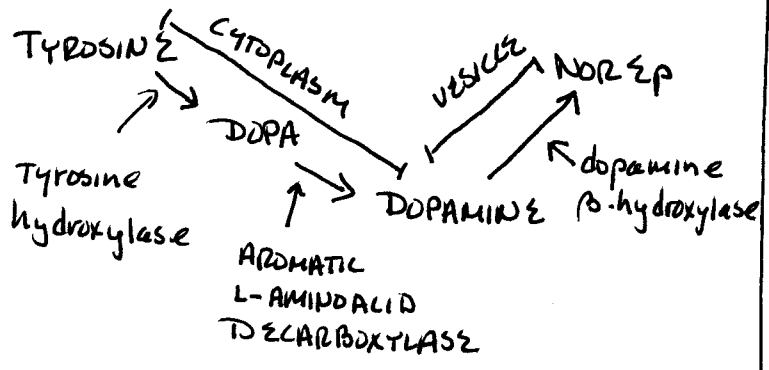
SEE FIG 7 ALKOFIGHT ET AL CELL 100/NEURON 25, 2000

ACETYLCHOLINE (ACh)

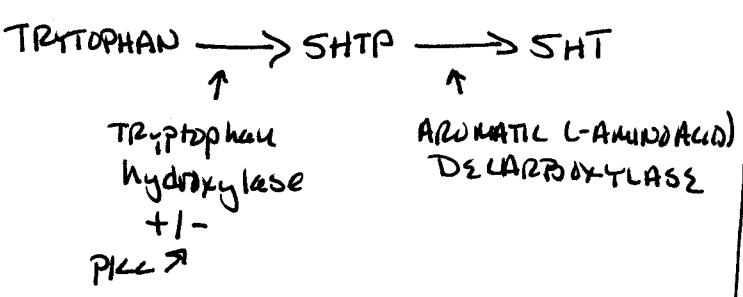


(CAT = CHOLINE ACETYLTRANSFERASE)

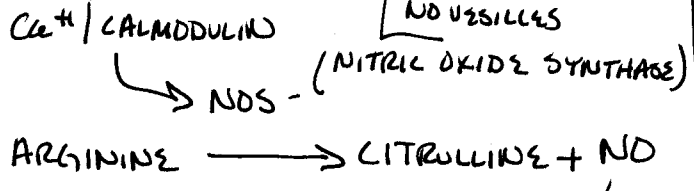
DOPAMINE, NOR EPINEPHRINE



5-HT (SEROTONIN) (5-hydroxytryptamine)

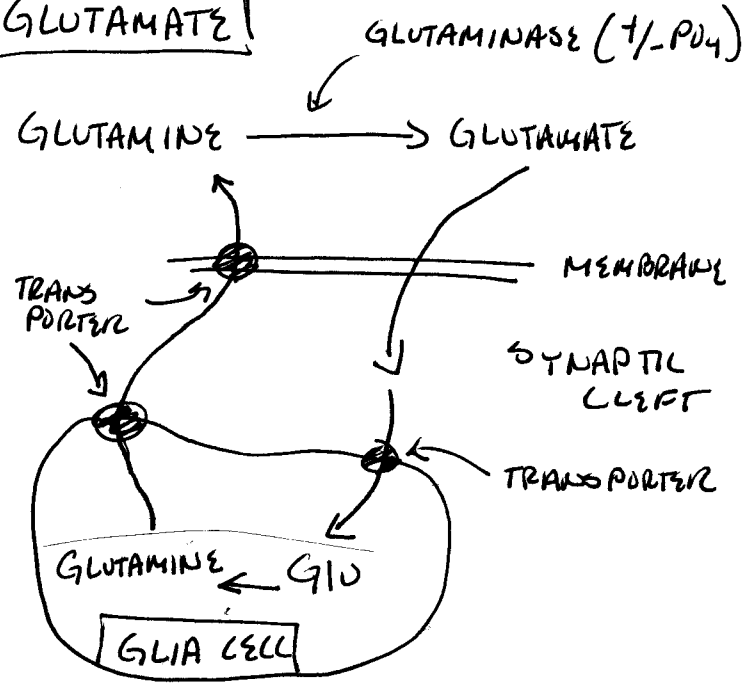


NO (NITRIC OXIDE)

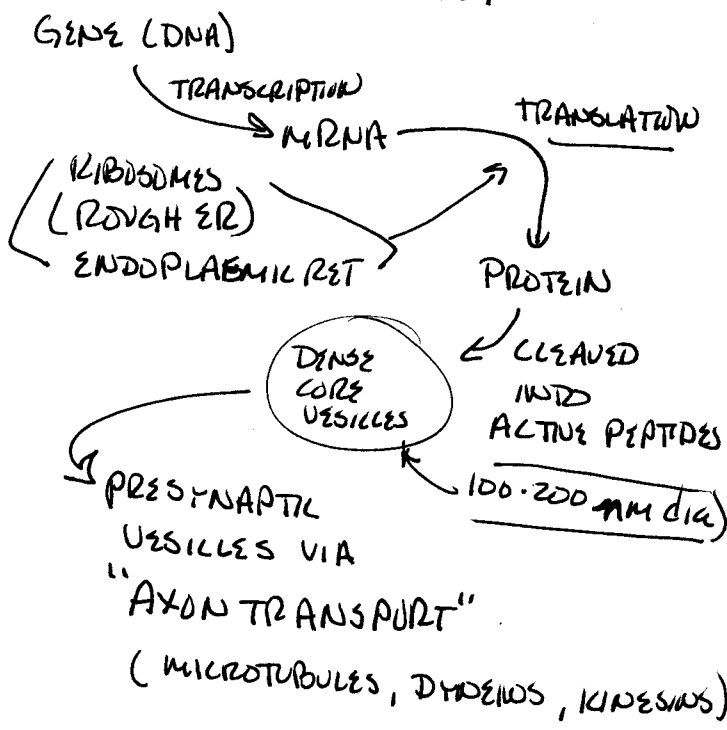


CGMP ← ACTIVATES cytosolic GUANYLATE cyclase

GLUTAMATE



PEPTIDES - SYNTHESIZED IN CELL BODY

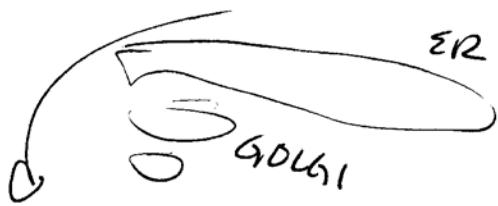


PACKAGING PEPTIDES → VESICLES
 BASIC CELL BIOLOGY RE ER/GOLGI

NOTE: DIFF AXONS MAY HAVE DIFF PEPTIDES - ISSUES OF SORTING PEPTIDE VESICLES DOWN DIFF AXONS OR AXON BRANCHES - SORTING !!

II. VESICLE CONSTRUCTION

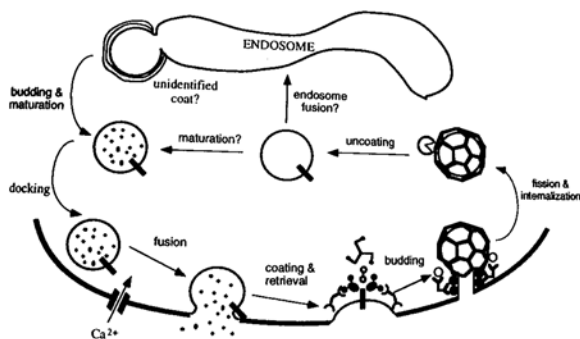
CELL BIOLOGY



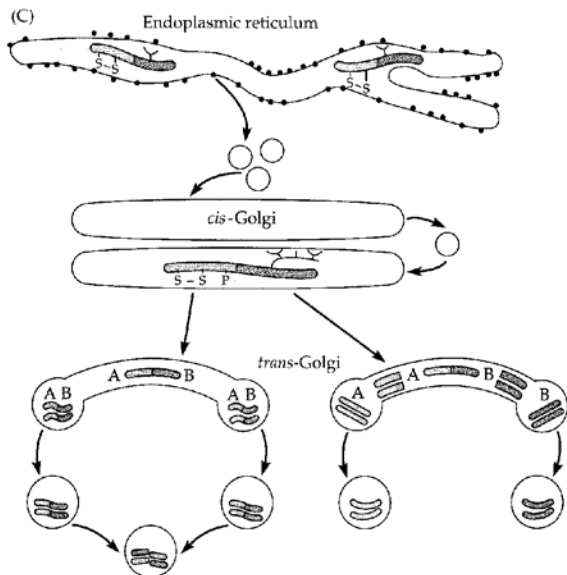
PROCESS IS CONSISTENT W/
"NORMAL" CELL BIOLOGY OF ER/GOLGI

MEMBRANE & EXTRACELLULAR PROTEINS
ARE PROCESSED THROUGH SUCH PATHWAYS

DO NOT REMARKABLE TO HAVE VESICLES
W/ MEMBRANE PROTEINS AND
INSIDE CONTENTS



Note: Pre-synaptic endings may contain multiple NTs, but there is only one NT per vesicle.
Therefore: the ending has multiple "types" of vesicles, each type requiring an independent production pathway:



III. VESICLE STORAGE & RELEASE

RELEASE - Ca²⁺ DEPENDENT & INDEPENDENT

VESICLE PROTEINS / PLASMA MEMB. PROTEINS

VESICLE MOVES TO MEMBRANE
"SNARE" COMPLEX FORMS

VESICLE PROT: SYNAPTOSOMIN
PLASMA MEMB PROT: SNAP-25 & SYNTAXIN

THESE PROTEINS FORM A
HELICAL COMPLEX

VERY UNSTABLE - 3 PROTEINS ALONE
CAN CAUSE
VESICLE FUSION &
NT RELEASE



2ND VESICLE PROTEIN
BINDS Ca²⁺
SYNAPTOTAGMIN

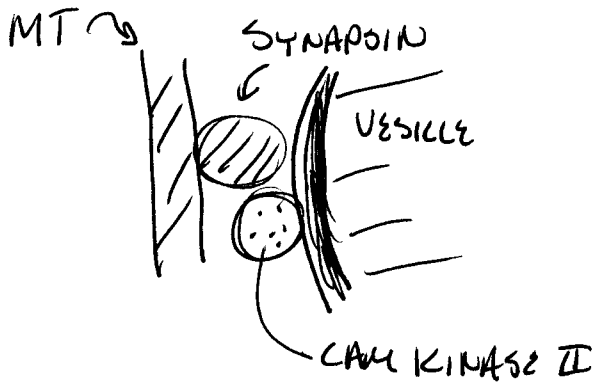
Ca²⁺ / SYNAPTOTAGMIN INTERACTS
W/ SNARE TO GREATLY
DESTABILIZE COMPLEX
& ↑ PROB OF FUSION

SYNAPTOTAGMIN HAS 2 Ca²⁺ BINDING
DOMAINS



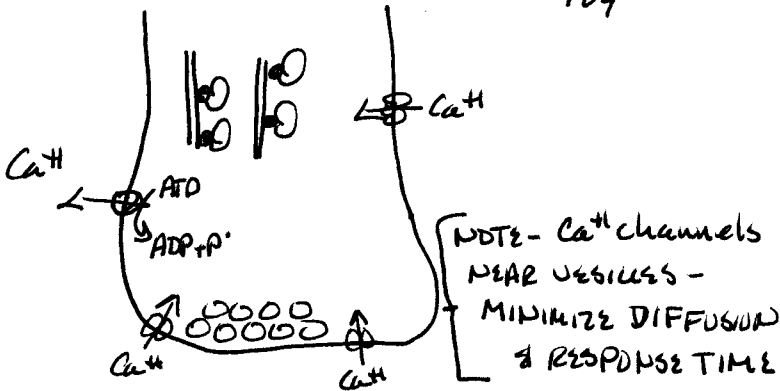
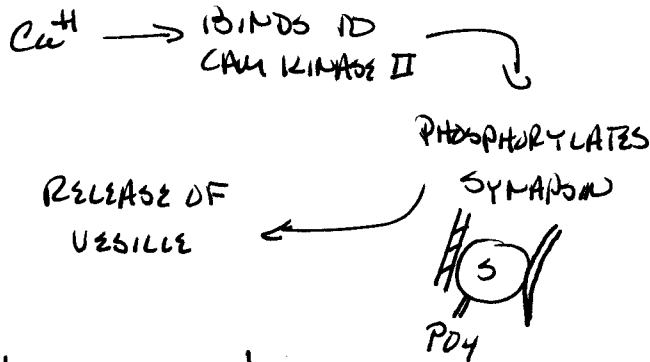
III cont.

STORAGE POOL - VESICLES



VESICLES ANCHORED TO MICROTUBULES (MT)

VIA SYNAPSOIN { MEMBRANE BOUND VESICLE PROTEIN



AP OPENS Ca²⁺ CHANNELS

Ca²⁺ TRIGGERS RELEASE OF "RELEASE POOL"

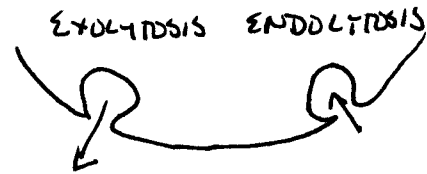
Ca²⁺ TRIGGERS MOBILIZATION OF "STORAGE POOL"

Ca²⁺ PUMP (ATPase) WORKS IN BACK GROUND TO REMOVE Ca²⁺

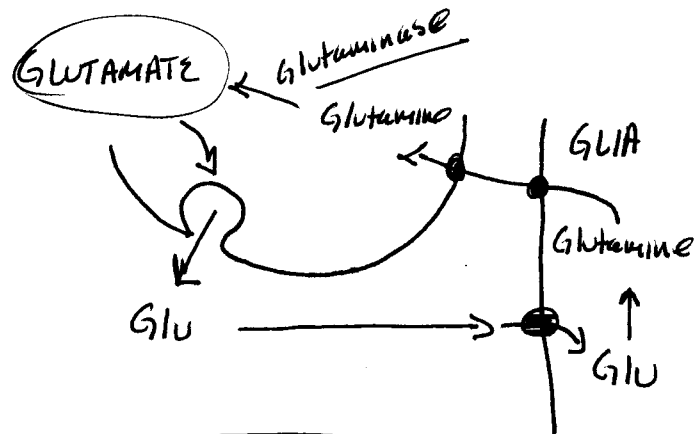
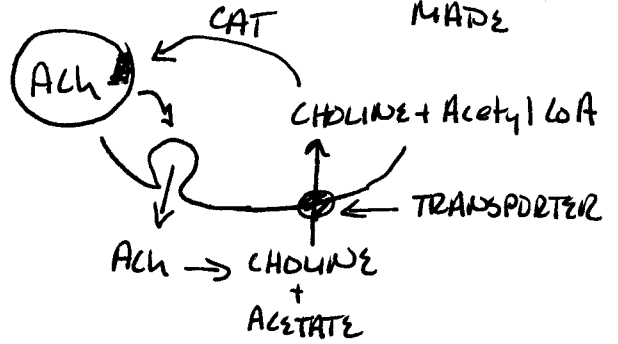
IV RECYCLE

MEMBRANE - ISSUE

VESICLE FUSION ADDS MEMBRANE TO PRE-SYAPTIC MEMBRANE - NEED TO REMOVE THIS MATERIAL TO MAINTAIN BALANCE



NEUROTRANSMITTER - REUSE WHAT ENERGY HAS MADE



RELEASED NT MOLECULES ARE CAPTURED BY GLIAL CELLS OR BY PRE-SYAPTIC ENDING - SPECIFIC TRANSPORT PROTEINS