

8 Dec 81

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Leo start and bring us up to date

Receptor purification rat brain
 taking a crack at beef brain
 - more material
 - look at different regions.

affinity column 6-hydroxyethyl nicotine
 150 adsorbent detergent solvent rat brain membranes. (whole brain)
 localized synaptosome preps.

gel filtration hydrophobic Sepharose column
 a few proteins one is MW 60,000 which we suspect is the receptor

binds nicotine with high affinity 200-1000 X
 problem with the protein concentration purification

getting frozen rat brains from pharmaceutical companies (Remuult)

where is receptor - throughout the brain but localized concentrations in some regions.

¹²⁵I-label proteins so they are off affinity column increased sensitivity of detection

What other receptors come at that MW range?
 only one purified is opiate lower MW
 benzodiazepine receptor MW 55-60,000 several groups working on it
 not pure but a major band on PAGE

affinity labeled analog - radioactive -

6-hydroxyethyl nicotine has 1/5 - 1/10 the affinity of nicotine.

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have looked at
6-Me nic.
anabasine

not enough material
to do.

wants to make antibodies to receptor
— monoclonal antibodies — already doing this
with opiate receptor

nicotine receptors on lymphocytes — paper coming out on this
what are they doing there? ???

use antibodies to inactivate nicotine receptor *in vivo*
what is its function in normal animals?
what is the natural (normal) ligand?

Denoble -

Self-administration of nicotine

amount of nicotine in body showing level pressing

give "Free" nicotine to animals self-administering nicotine

total
daily intake of nicotine is constant

can be blocked by mecamylamine but not by hexamethonium

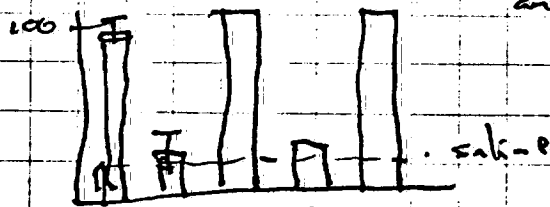
Exp Compound 44 = acetaldehyde

nicotine + acetaldehyde

put out acetaldehyde
and nicotine self-admin. drops way down

2 animals trained on

nic
on acetaldehyde



replicated in
3 animals

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forming 5 units

if animals started at 32

then go to 64 then
they don't go

acetylcholine phenyls
widened and vaso

hydrophilic - depolarizing blockers

osmotic & hydrophilic

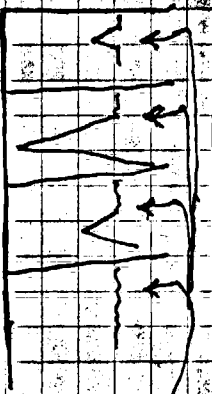


conversion to acetylcholine to

salicylate (epinephrine?)

not to act to cardiac action etc

depolarizing receptors etc



intima - less VLDL

Going to E2 vs LDL? CHD and lot for LDL from liver crossing
hydrophilic in the liver

Going to do all - nicotine soon

Also going to look at minor alkaloids - ephedrine etc

production - paper

don't disappear - inject there → no production

liver needs to discriminate between nicotine and saline completely
administered; goes to stimulate them and administer activity

feedback mechanism

substance interacts with dopaminergic
also interacts with benzodiazepine
receptor