Effects of Ethanol on Neurons and Neuronal Structures

Psychology 472: Pharmacology of Psychoactive Drugs

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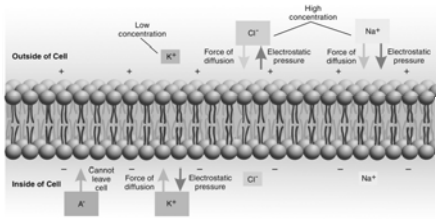
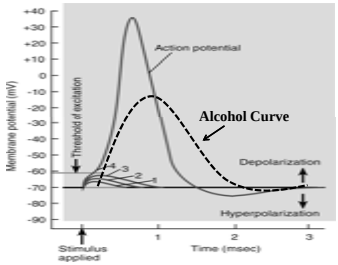
Bi-Phasic Effects

- **At low doses, (<1 drink)**
  - **Get some stimulation in neurons**
- **Higher doses (>1 drink)**
  - **Alters neuronal membrane (Lipid Bilayer)**
- **Results**
  - **Decreased amounts of Na that enters the axon**
  - **Decreased height of the action potential**
  - **Other consequences**

Alters the Lipid Bilayer



The Action Potential



Result

- **Alters Ca influx**
  - **Decreases the amount of NT that is released**
- **Decreases transmission speed of all neurons**
  - **Slows down stimulatory neurons**

Behavioral Bi-Phasic Effects

- At low levels (<.05 BAC)
- Alcohol causes you to feel good, makes you euphoric, loosens inhibitions etc.
  - Usually occurs on the ascending portion of the BAC curve
- Higher levels (>.05 BAC)
  - Euphoric feelings go away
  - Feel depressed
  - Descending portion of the BAC curve

Reason for the Changes

- Lower levels
  - Get increased levels of Dopamine in MFB
- Higher levels
  - Begin to sedate the brain, levels of dopamine decrease. Etc.

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Effects on Receptors

- GABA
- NDMA
- Glutamate
- Opiate

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GABA A Receptor

- Is an Axoaxonic receptor
  - Binds on presynaptic elements of stimulatory neurons
  - Designed to shut down stimulatory neurons
- Normally needs lots of GABA to work
  - High Affinity State

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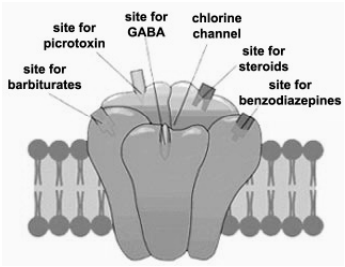
GABA Receptor



Has Many Binding Sites

- GABA site
  - Site for GABA to bind
- BZ site
  - Site where BZ (α1,α2,α3,α5) and Alcohol (α4,α6) binds
  - Many types (some more sedative, others more anxiolytic)
- Barbiturate site
  - Site where Barbiturates bind
- Picrotoxin
  - Blocks effects of Barbiturates
- Neuroactive steroid site

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Alcohol

Alters GABA Receptors

- Binds on the BZ site (α4,α6)
- Changes affinity for GABA from High to Low
- Increases the amount of Cl influx into most stimulatory neurons
- Further decreases the amount of Ca influx
- Decreases the amount of NT

NDMA Receptor
N-methyl *D*-aspartate)

- Is a specific type of Ionotropic glutamate receptor
- Is important for synaptic plasticity and memory
- Requires both glutamate or aspartate and glycine
- When activated, lets Ca into the cell

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Alcohol and NDMA Receptors

- Acts as an antagonist
- Inhibits the function of NDMA receptors
- Decreases the responsiveness of NDMA receptors to glutamate

- Have enhanced stimulation when the person withdrawals from alcohol
  - Can get agitation, have elieptform seizures, etc

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Opiate Receptors

- Alcohol triggers release of endogenous opiates (β-endorphin)
  - Causes a release of dopamine in MFB
  - Makes you feel good

  - Use antagonists to reduce craving
    - *Naltrexone*

Serotonin Receptors

- Serotonin receptors
  - Alcohol use increases serotoninergic activity.
  - Increases secretion of dopamine from nucleus accumbens.
  - Makes you feel good
- SSRI's
  - Are effective in reducing drinking in lower-risk alcohol males.

Cannabinoid Receptors

- Chronic alcohol use stimulates formation of endogenous cannabinoid transmitter *anandamide* (an-an′dă-mīd_.
  - Leads to down regulation of cannabinoid receptors, disinhibiting nucleus accumbens.

- Cessation of drinking
  - Get hyperactive endocannabinoid reaction
  - Results in alcohol craving

Summary

- Affects the entire neuron
  - Alcohol decreases transmission speed
  - Alcohol decreases NT release
  - Alcohol increases Cl in post synaptic elements
- Shuts down structures that inhibit neurons of medial forebrain bundle
  - Get more firing in MFB
  - Feel good

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Withdrawal Management

- Benzodiazepines
  - e.g., Chlordiazepoxide (Librium), Diazepam (Valium)
  - Increase GABA activity.
  - Decreases withdrawal symptoms; prevent seizures and DTs.
  - Long-acting, prevent withdrawal symptoms (either maintained or slowly withdrawn), allowing person to function.
  - Drawbacks: sedation, psychomotor deficits, additive interactions with alcohol, abuse and dependence liabilities.

Anticonvulsant Mood Stabilizers

- Fewer limitations than benzodiazepines
- Older anticonvulsants effective, but have side effects (e.g., liver and pancreatic problems).
  - e.g., Carbamazepine (Tegretol), Valproic Acid (Depakote)
- Newer anticonvulsants are less toxic and have significant potential.
  - e.g., Gabapentin (Neurontin), Oxcarbazepine (Trileptal)

Acamprosate

- Acamprosate (Campral)
  - First pharmacological agent designed to maintain abstinence in alcoholics after detoxification.
  - Both GABA-agonistic and NMDA-inhibitory, similar to ethanol.
  - Comparably effective to Naltrexone; combination of both drugs may be additively effective.

Dopaminergic Drugs

- Bupropion (Wellbutrin)
  - Works on both positive reward and withdrawal
  - Seems to involve dopaminergic reward system.

Conclusions

- Alcohol has many impacts on Neurons
- Creates lots of problems
- Has lots of implications for pharmacologic interventions

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