Exploration of a potential treatment for drug abuse: effects of the cannabinoid antagonist SR141716A on drug induced sub second dopamine release in freely moving rats

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Summer 2004

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Background

- **Fast-scan cyclic voltammetry**
  - Electrochemical technique suited for the detection of sub second neurotransmitter release

- **Dopamine**
  - A molecule found throughout the brain that is involved in many critical functions, such as movement, learning and reward processing
  - Both natural rewards and addictive drugs, including cocaine, promote the release of dopamine in brain reward areas, indicating its importance for the reinforcing properties of abused drugs
  - Transient (sub second) dopamine release is tied to reward and to the pleasurable effects of cocaine

- **Cocaine**
  - A common drug of abuse that acts on the reuptake of dopamine to extend the duration of dopamine’s action

- **SR141716A**
  - A cannabinoid receptor (CB₁) antagonist
  - Reverses the cannabinoid-induced increase in transient dopamine and may affect the modulation of transient dopamine of other drugs of abuse through endogenous cannabinoids

- **Goals:**
  - To characterize the effects of intravenously injected cocaine on transient dopamine release in the nucleus accumbens shell, a pivotal part of the brain reward system
  - To determine the effects of SR141716A on cocaine-induced dopamine transients
Results

• Cocaine Alone
  – Intravenous administration of cocaine (3mg/kg) significantly (p<.05) increased the number of dopamine transients detected from the base-line rate (mean= 2.13; sem=0.76 -- mean= 7.06; sem= 1.57)

• SR141716A on Cocaine
  – SR141716A (3mg/kg) reduced dopamine transients from their cocaine levels at near significant levels (mean= 4.14; sem=0.71)
  – Mean number of transients for the SR epocc is not significantly different from the saline or baseline rates

• Cocaine in the presence of SR141716A
  – An additional injection of cocaine in the presence of SR141716A was not able to produce the same number of transients (p =.054) compared to the initial dose (mean= 4.26; sem=.96) and was not significantly different from the baseline rate of transients
  – In fact, transients from the initial cocaine dose were 65% great in number than transients resulting from the second cocaine dose
Summary

• Drug-seeking behavior, which creates abuse potential, is mediated by sub second dopameric neuronal activity (Phillips 2003)
• Through fast-scan cyclic voltammetry, sub-second release of dopamine was measured
• Cocaine produced a significant increase in sub second dopamine activity which was diminished by the cannabinoid receptor (CB₁) antagonist SR141716A
• This transient dopamine activity is likely a major means by which the neurotransmitter communicates in the nucleus accumbens and reward processing areas of the brain, which may reflect an aspect of cocaine’s reinforcing properties
• These results also show that cocaine’s actions on transient dopamine are at least in part controlled by the endogenous cannabinoid system in reward processing areas of the brain
• Additionally, these physiological data provide preliminary evidence of SR141716A’s potential to reduce transient dopamine and cocaine abuse potential and support previously reported behavioral findings
• Further experiments on this protocol will be conducted to reduce group variance and hopefully increase the statistical strength of the group differences. As well, other drugs of abuse will be explored