

***Intracranial Self-Stimulation
To Evaluate Abuse Potential of Drugs***

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to Evaluate Abuse Potential of Drugs***

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Overview

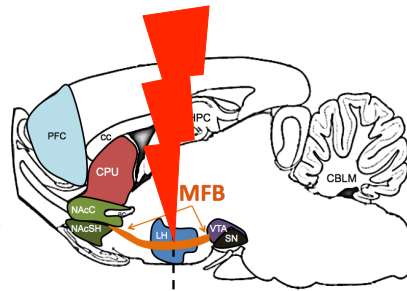
- Methodology
- Comparison of results in ICSS vs. self-administration
- Pros/Cons

Overview

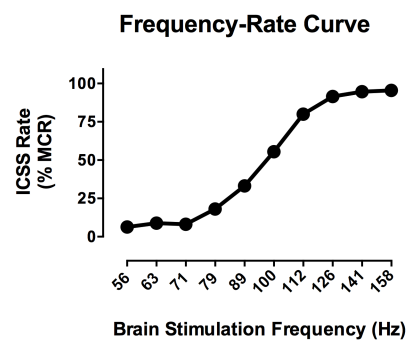
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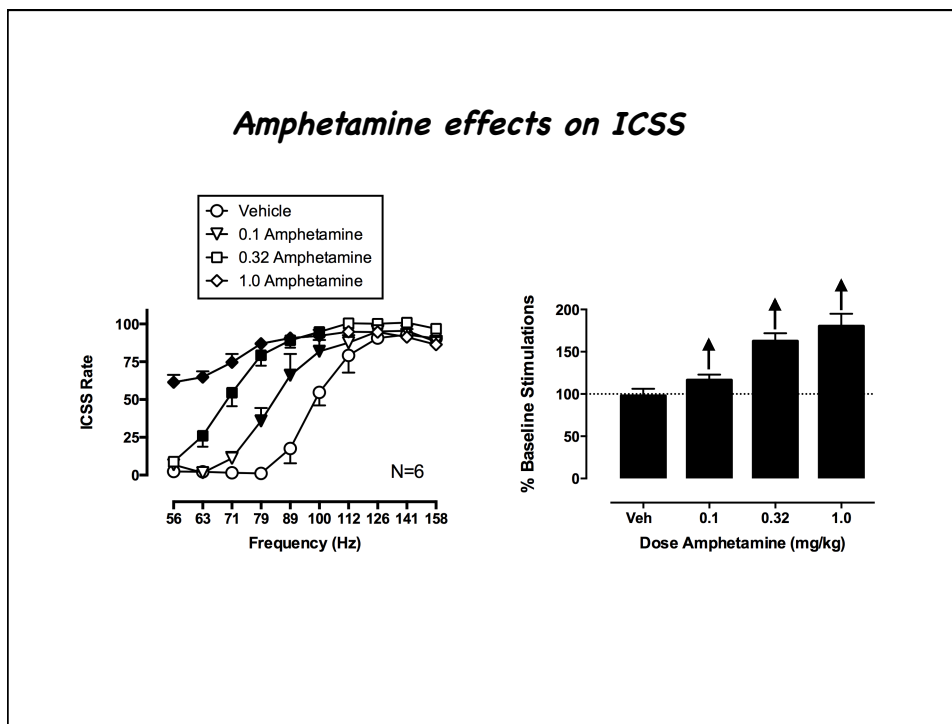
Intracranial Self-Stimulation (ICSS)

Definition: a family of behavioral procedures in which operant responding is maintained by pulses of electrical brain stimulation delivered to brain reward areas



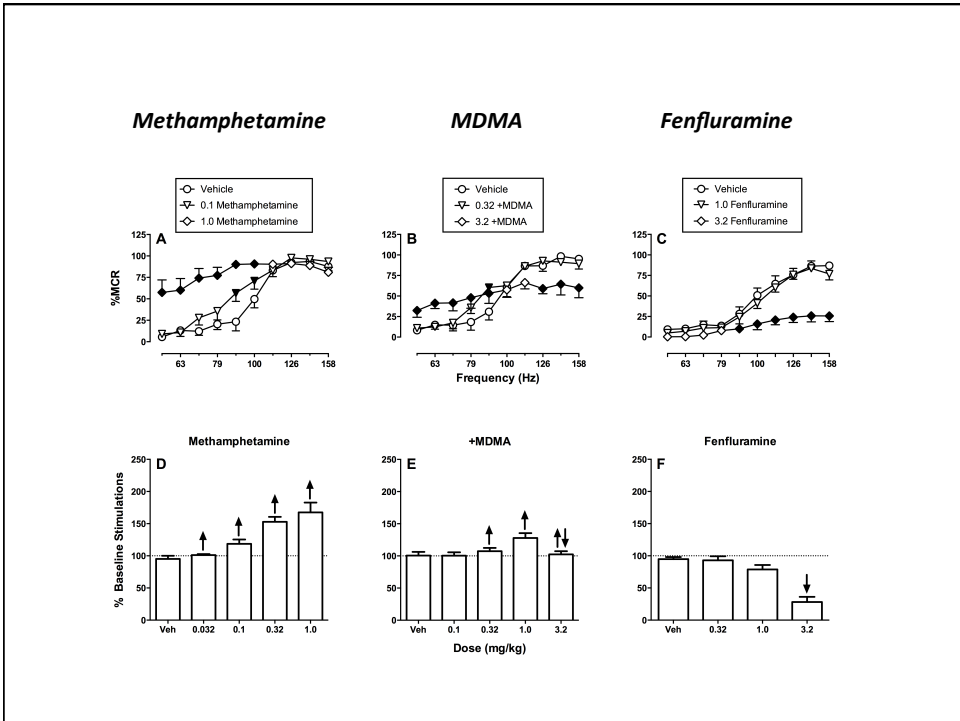
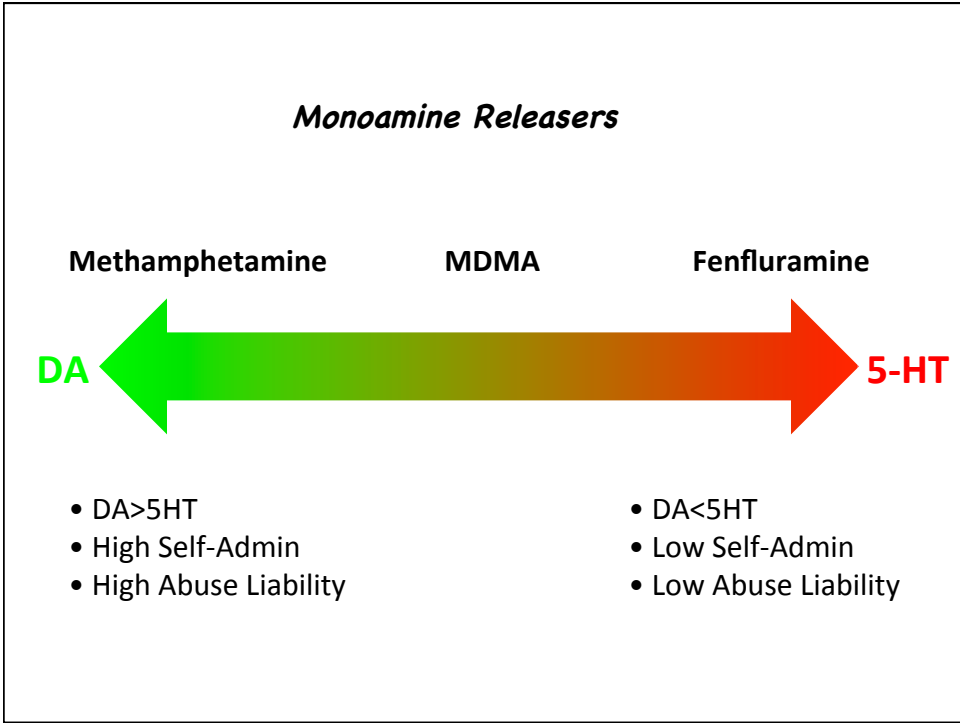
Intracranial Self-Stimulation (ICSS)



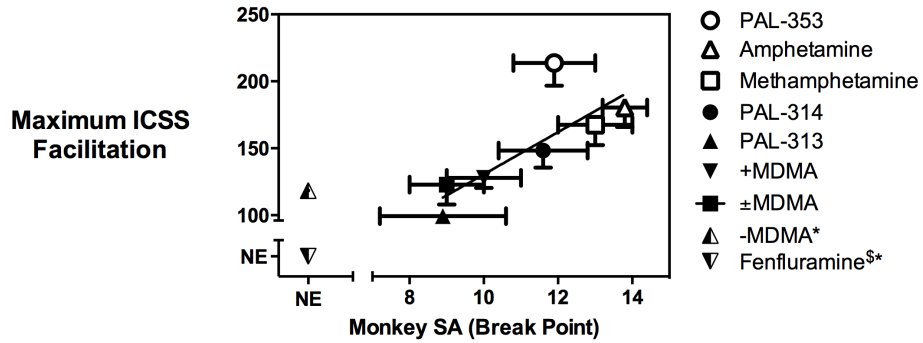


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**Correlation between ICSS in Rats
& Progressive Ratio Self-Administration by Rh. Monkeys**



ICSS vs. Self-Administration

		ICSS	
		Yes	No
Self-Admin	Yes	DA Releasers/UIs Mu Opioid Agonists Benzodiazepines Barbiturates Nicotine	D2/3 DA Agonists Clonidine Zolpidem Baclofen Ketamine
	No	Caffeine	5HT Releasers/UIs 5HT2A Agonists NE UIs NSAIDs DA Antagonists Kappa Opioids Delta Opioids

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Similarities between ICSS and Drug Self-Administration

- Both are operant procedures with similar technical requirements for surgery and equipment
- Both are more stable in rats than in mice
- They share similar predictive validity

Advantages of ICSS vs. Drug Self-Administration

- Fewer false positives
- Permits stratification of abuse potential similar to that provided by progressive-ratio self-administration
- Can be used with any route of drug administration
- Can be used in drug-naïve or drug experienced animals
- Can be used to track changes in abuse liability as a function of drug experience or other state changes (e.g. pain, stress)
- Can be easily used to assess drug time course
- Experimental design not dependent on drug time course
- Large and growing data base

Disadvantages of ICSS vs. Drug Self-Administration

- Lacks face validity of drug SA
- Several variants exist for both procedure and data analysis
- Lack of consensus on details of methodology, experimental design, and data analysis for regulatory purposes

Standardization is next step

**Specific recommendations are offered
in Negus and Miller review article.**

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