Intracranial Self-Stimulation
To Evaluate Abuse Potential of Drugs

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Overview

- Methodology
- Comparison of results in ICSS vs. self-administration
- Pros/Cons
**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
Amphetamine effects on ICSS

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Monoamine Releasers

Methamphetamine  MDMA  Fenfluramine

DA  5-HT

• DA>5HT
• High Self-Admin
• High Abuse Liability

• DA<5HT
• Low Self-Admin
• Low Abuse Liability

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

![Graph showing correlation between ICSS in rats and self-administration by rh. monkeys.](image)

**ICSS vs. Self-Administration**

<table>
<thead>
<tr>
<th>Self-Admin</th>
<th>ICSS</th>
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<td>Yes</td>
<td>DA Releasers/Uls</td>
<td>D2/3 DA Agonists</td>
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<td>Mu Opioid Agonists</td>
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<td>Delta Opioids</td>
</tr>
</tbody>
</table>
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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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