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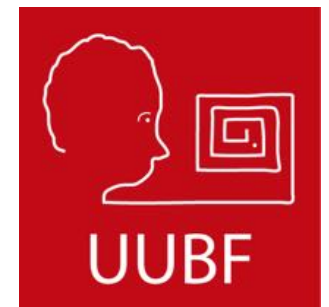
Ålder, kön och konsumtionsmönster ur ett prekliniskt perspektiv

SAD 2018-11-22

Erika Roman

Uppsala University

Erika.Roman@farmbio.uu.se



Medicine & Pharmacy



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- Data from unpublished studies have been removed from this presentation

Homologous behavioral responses

Hedonic Reactions (sweet)

Sweet taste



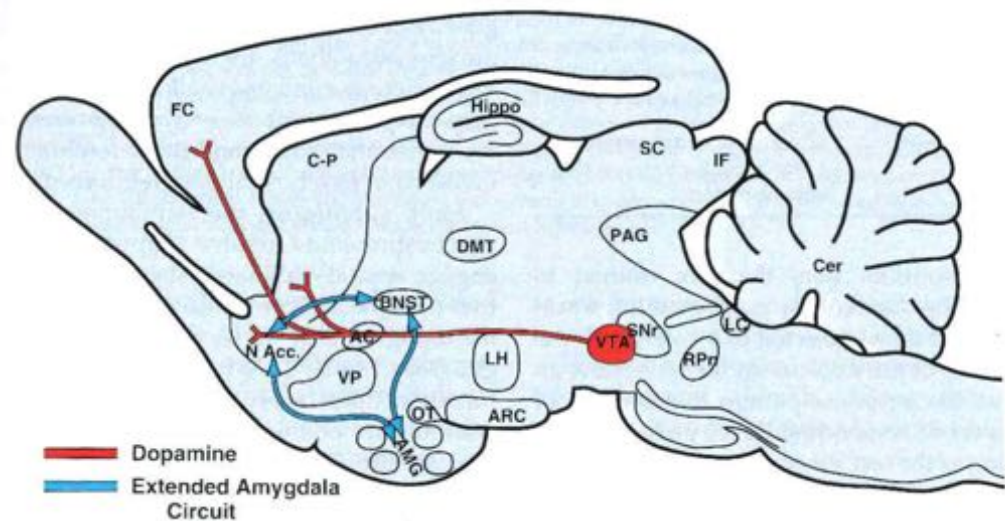
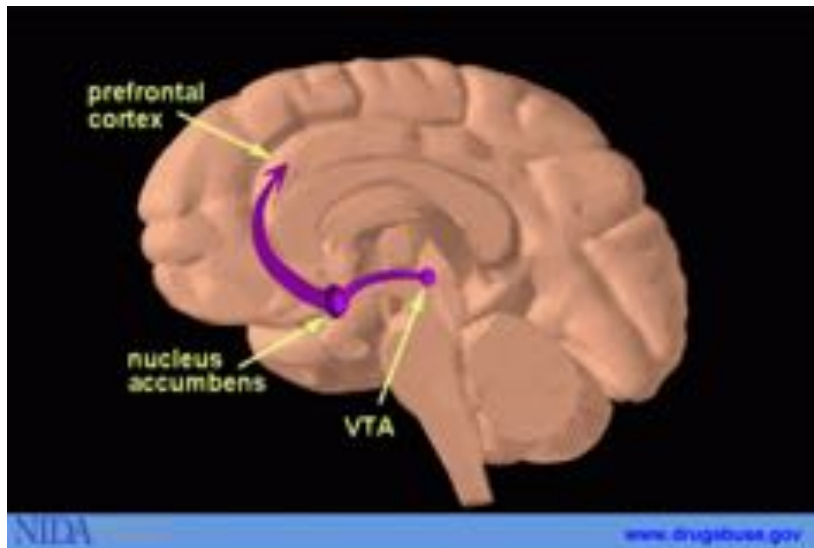
Aversive Reactions (bitter)

Bitter taste



Brain reward networks

The mesocorticolimbic dopamine system



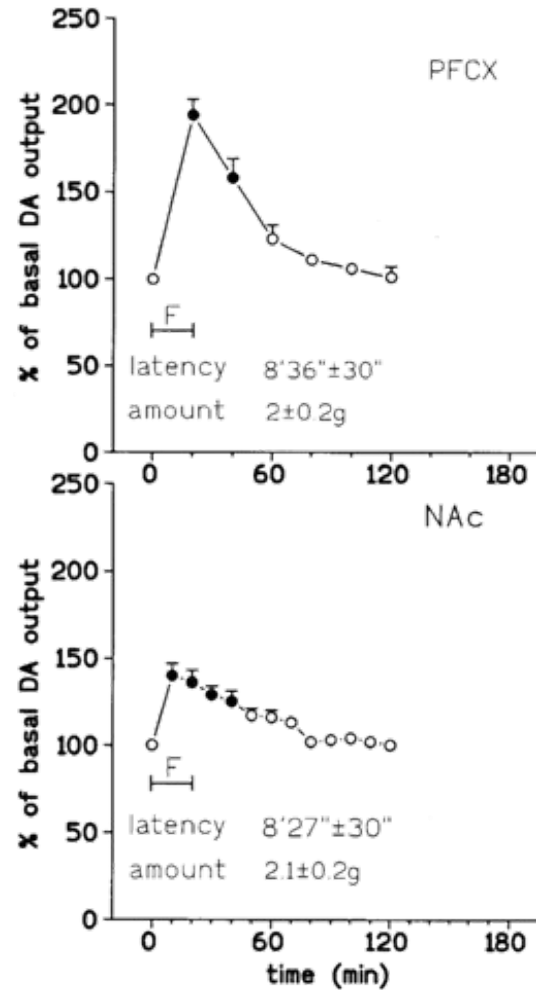
Evolutionary conserved across species

Activation by natural rewards

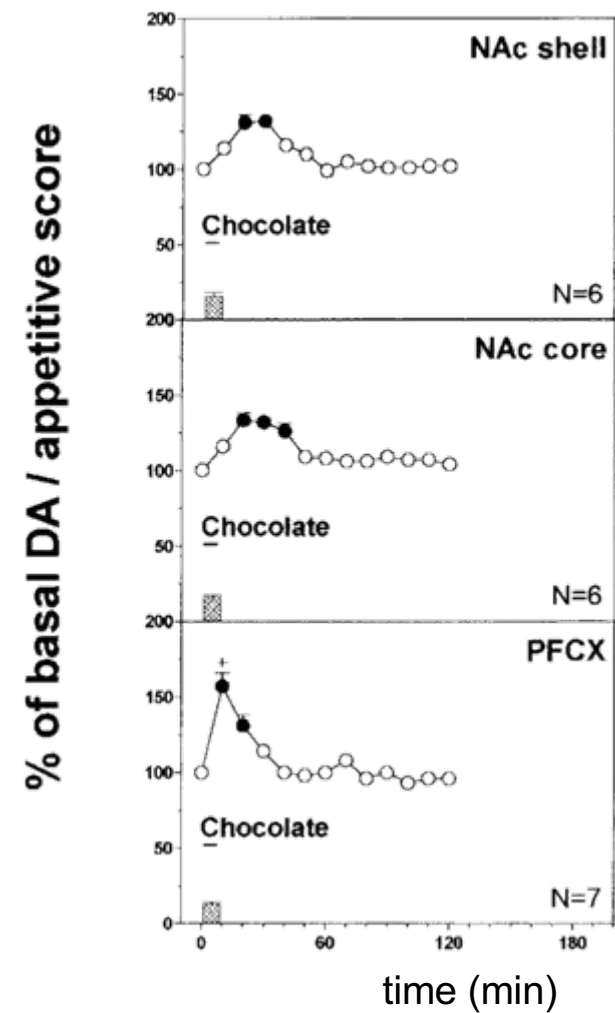


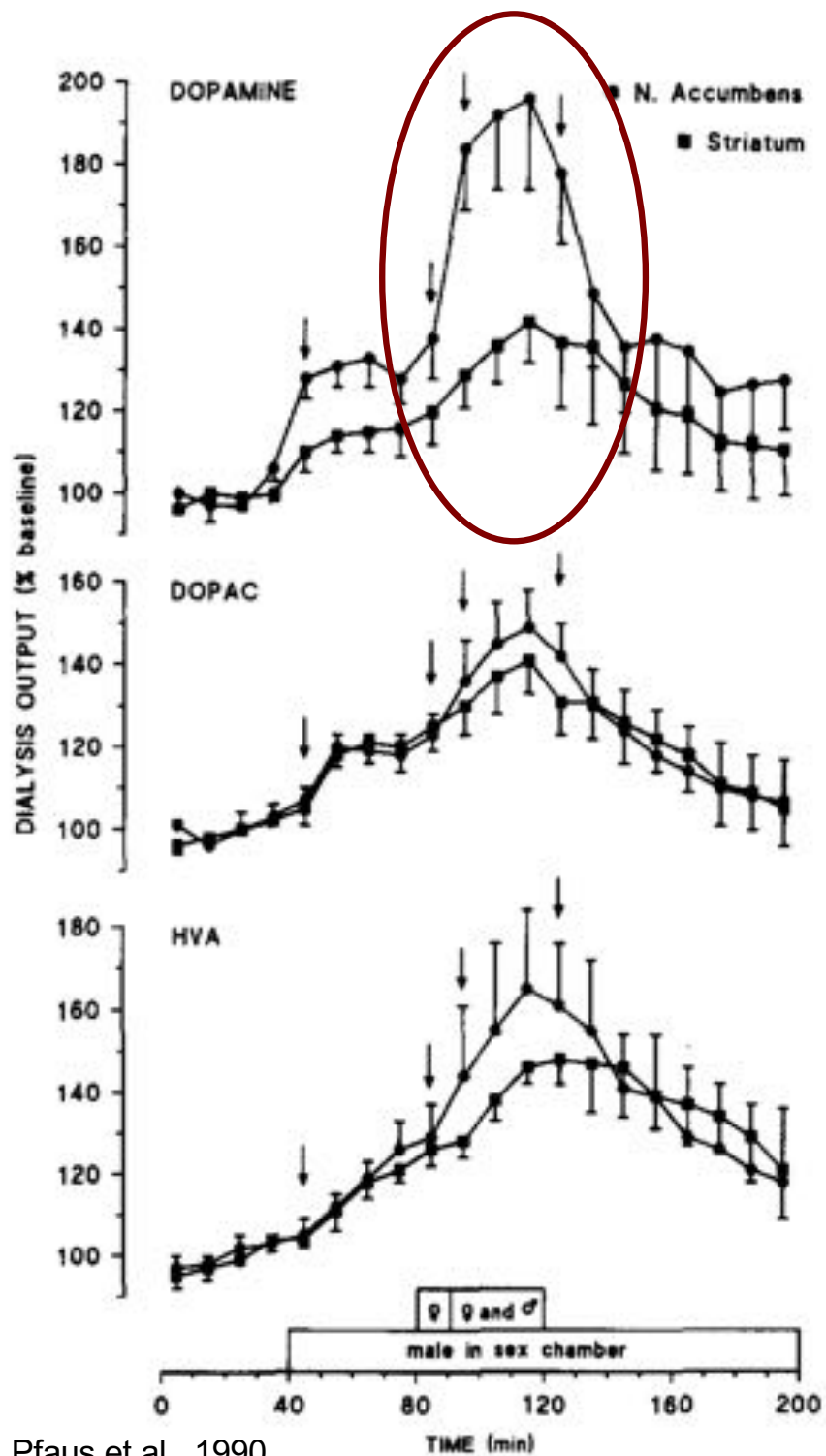
Fonzies

Fonzies-naïve

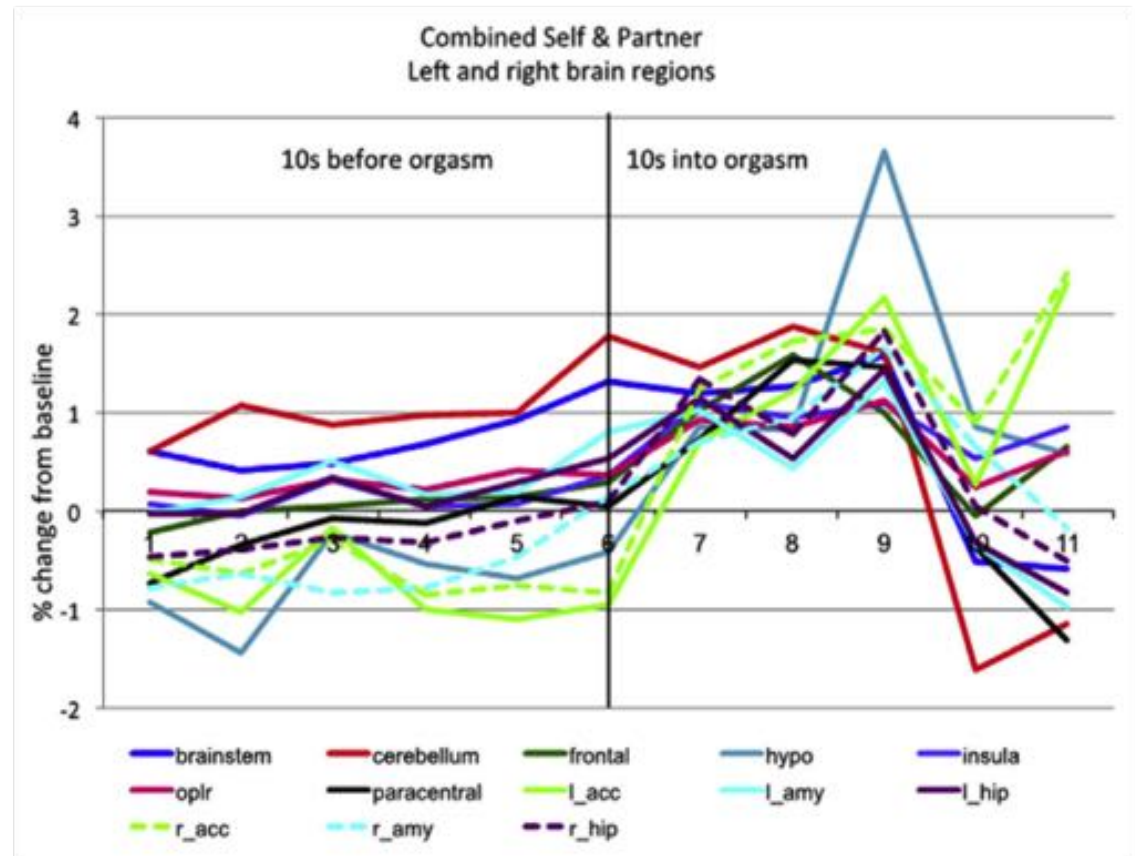


Chocolate naïve





Pfaus et al., 1990



Nucleus accumbens
activation during orgasm in
women

Wise et al., 2017

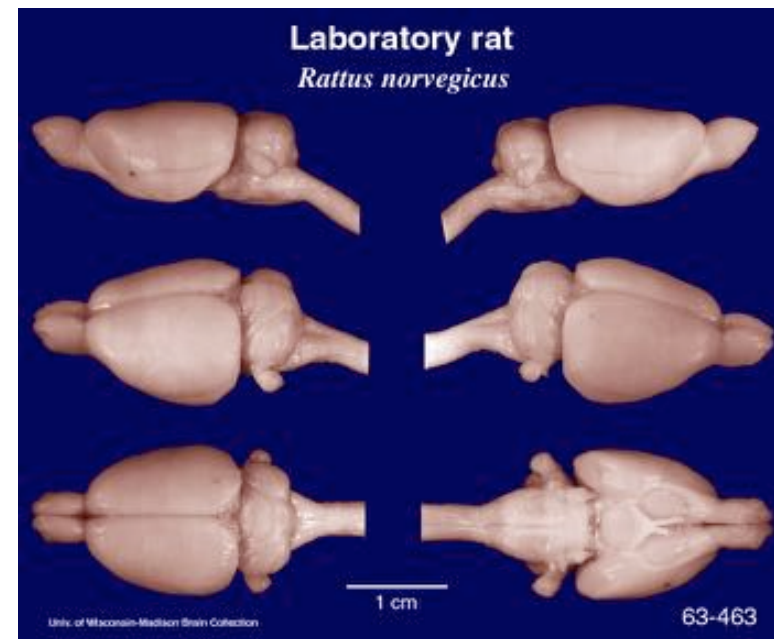
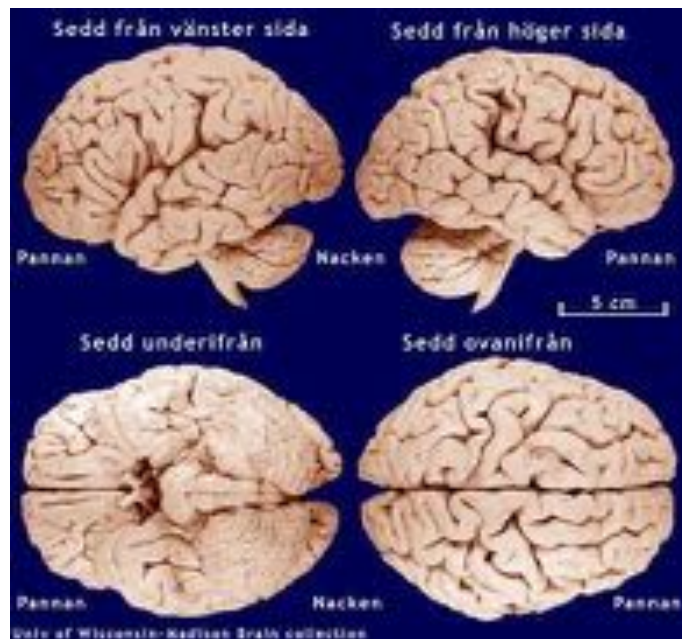
Comparison human versus rat

Homo sapiens

Gestation	270 days
Infant	0-24 months
Adolescence	13-18 years
Adulthood	20 years

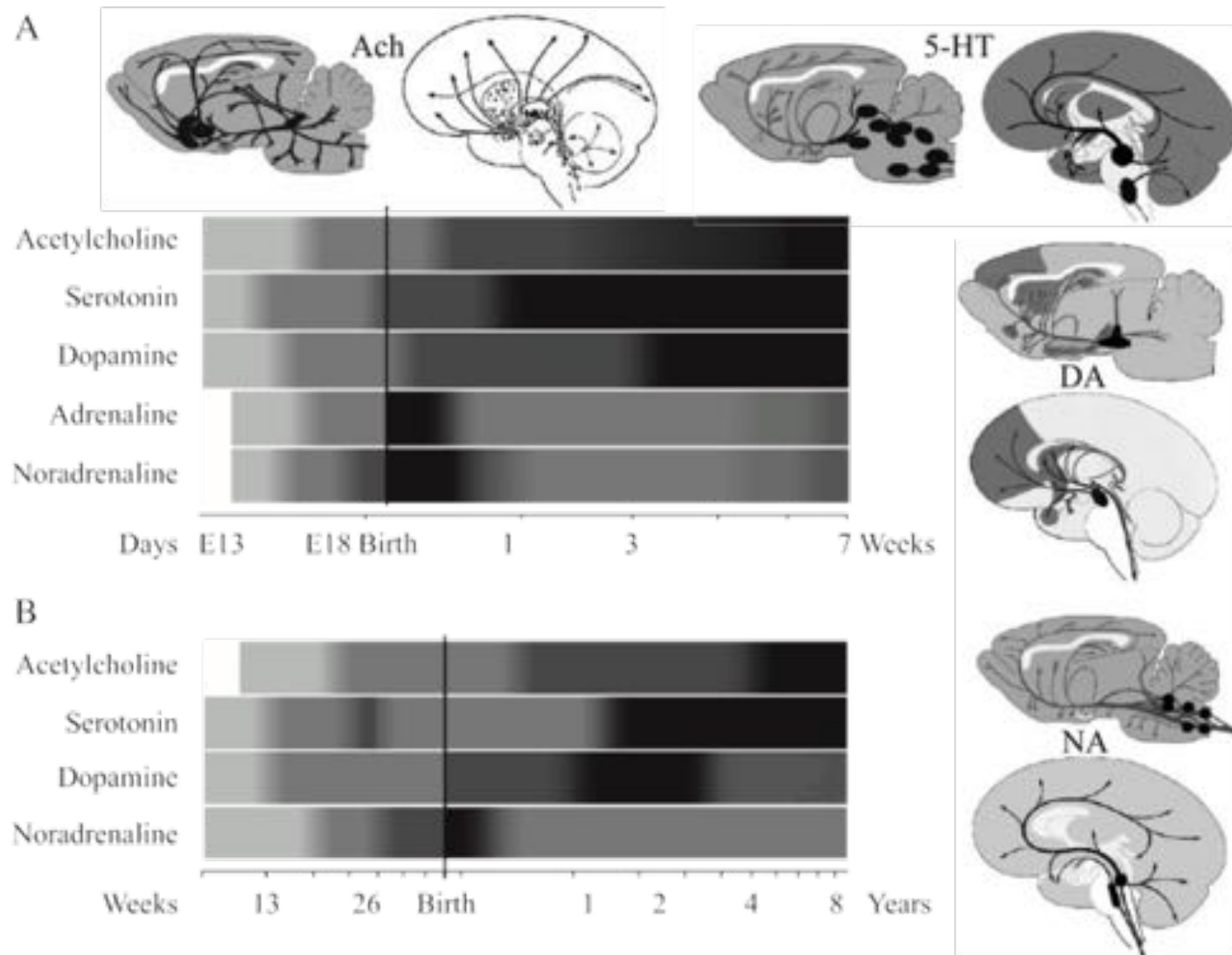
Rattus norvegicus

22 days
0-21 days
4-8 weeks
10 weeks



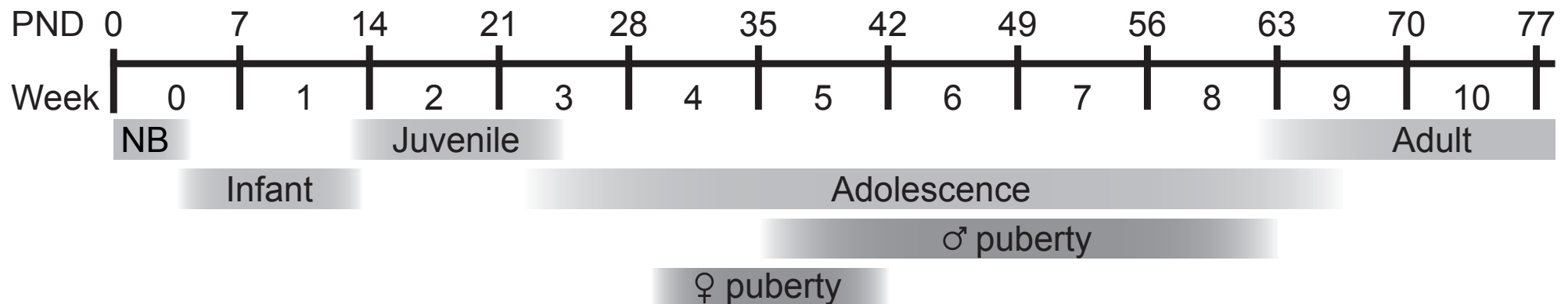
Developmental stages in the rat

Rat



Human

Developmental stages in the rat



Adolescence: 10.5 rat days = 1 human year

Adulthood: 11.8 rat days = 1 human year

Research animal depending on questions

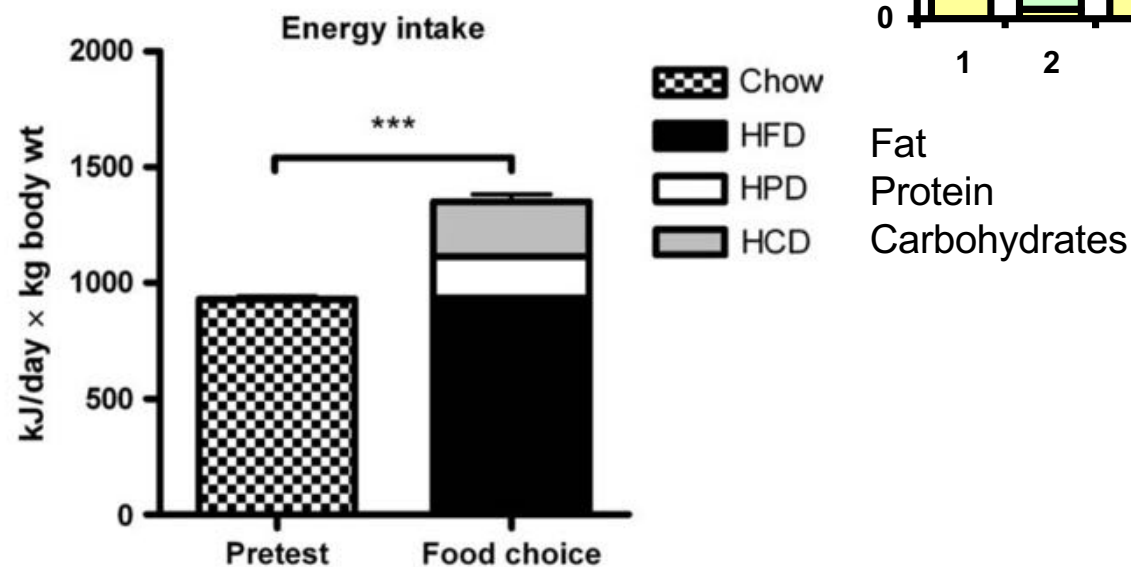
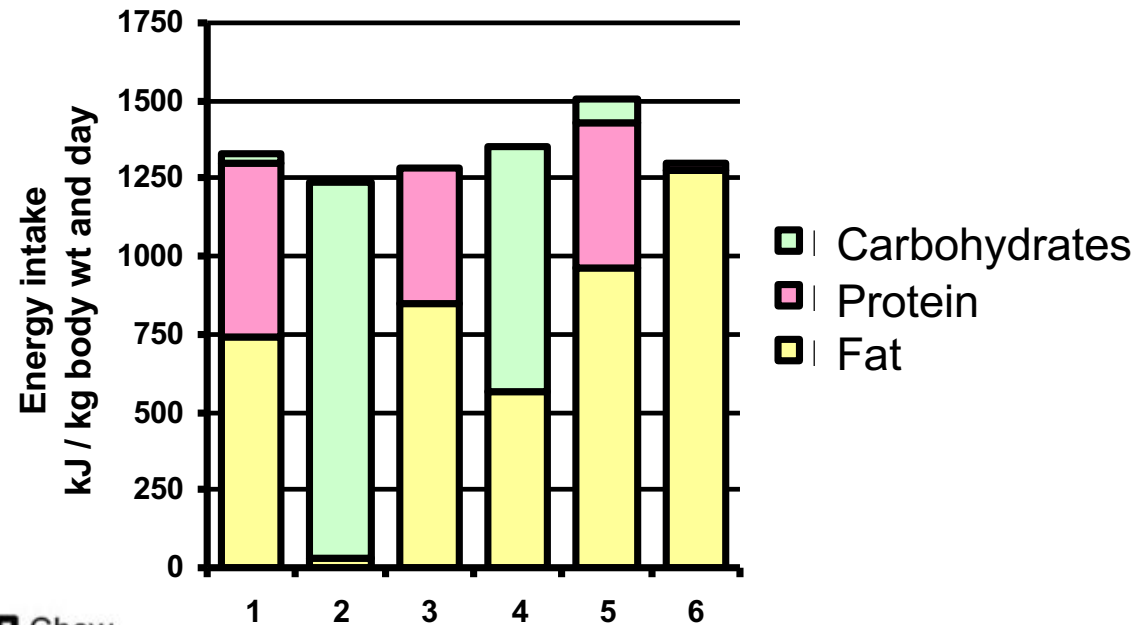
- Outbred stocks
 - Genetic heterogeneity
 - Individual differences
- Inbred strains
 - Brother x sister mating
 - Genetic homogeneity
- Selectively bred lines
 - E.g. alcohol-preferring/alcohol non-preferring



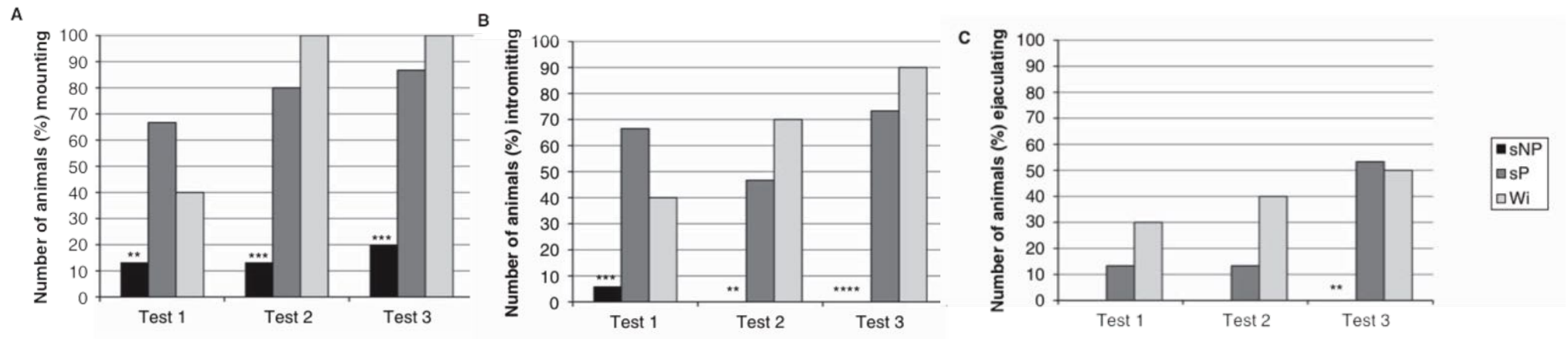
Validity of animal models

- Face validity
 - Similar symptoms and phenomenon's
 - I.e. the degree of descriptive similarity between the behavioral abnormalities seen in the model system and the clinical condition
- Construct validity
 - Similar underlying mechanisms
 - I.e. mechanistic similarities between the model and the clinical condition
- Predictive validity
 - The model allows extrapolation from one species to another, including humans, and from one condition to another
 - Response to pharmacological treatment
- *Problems with validity in many psychiatric disorders BUT good in addiction research*

Dietary preferences in rats



Sexual behavior in selectively bred alcohol-preferring and non-preferring rats



Gambling strategies in rats

- The rat Gambling Task has been established
- Rats with strategic as well as risky gambling strategies can be distinguished



Contents lists available at ScienceDirect

Neuroscience and Biobehavioral Reviews

journal homepage: www.elsevier.com/locate/neubiorev

Review

Female mice liberated for inclusion in neuroscience and biomedical research

Brian J. Prendergast^a, Kenneth G. Onishi^a, Irving Zucker^{b,c,*}^a Department of Psychology and Institute for Mind and Biology, University of Chicago, United States^b Department of Psychology, University of California, Berkeley, United States^c Department of Integrative Biology, University of California, Berkeley, United StatesItoh and Arnold *Biology of Sex Differences* (2015) 6:18
DOI 10.1186/s13293-015-0036-8

RESEARCH

Open Access

Are females more variable than males in gene expression? Meta-analysis of microarray datasets

Yuichiro Itoh and Arthur P. Arnold^{*}Becker et al. *Biology of Sex Differences* (2016) 7:34
DOI 10.1186/s13293-016-0087-5

Biology of Sex Differences

RESEARCH

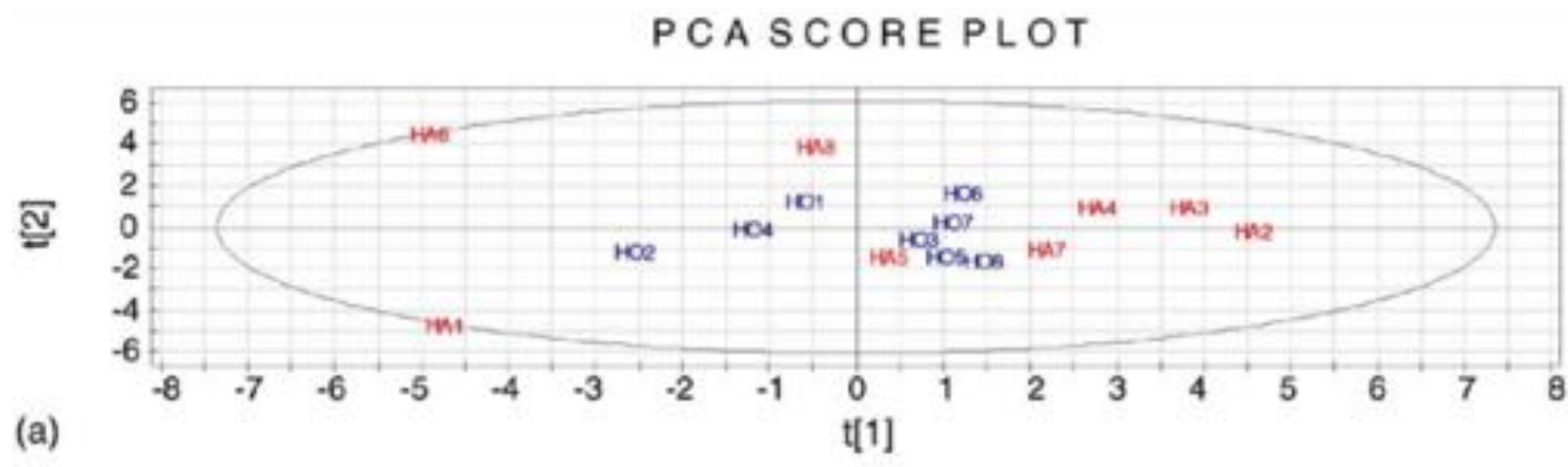
Open Access

Female rats are not more variable than male rats: a meta-analysis of neuroscience studies

Jill B. Becker^{1,2*}, Brian J. Prendergast³ and Jing W. Liang⁴

Adult males and females

No difference in behavioral profiles between adult male and female rats

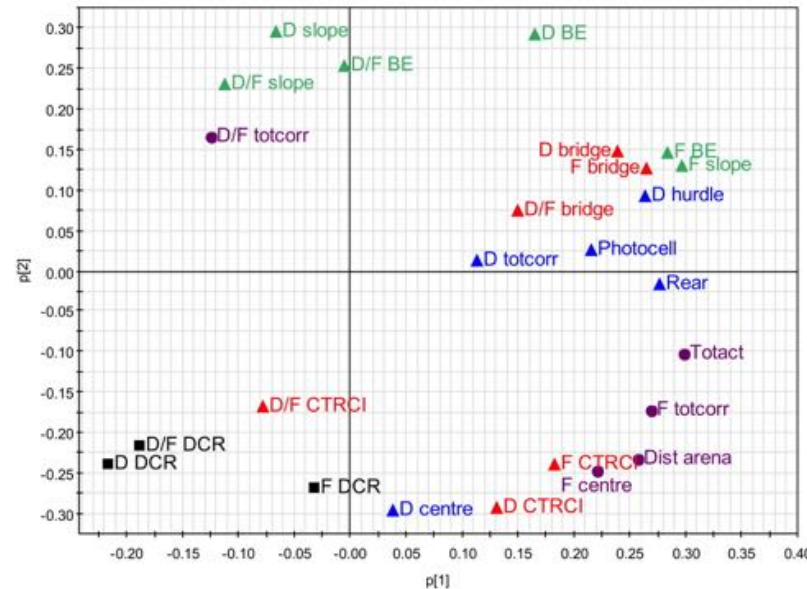


Males

Females

Adult versus adolescent male rats

Adult



Functional categories:

General activity

Exploratory activity

Risk assessment

Risk taking

Shelter seeking

Adolescent rats

- Risk assessment is less pronounced in adolescent rats
- Three behavioral types can be distinguished

Home cage voluntary alcohol intake



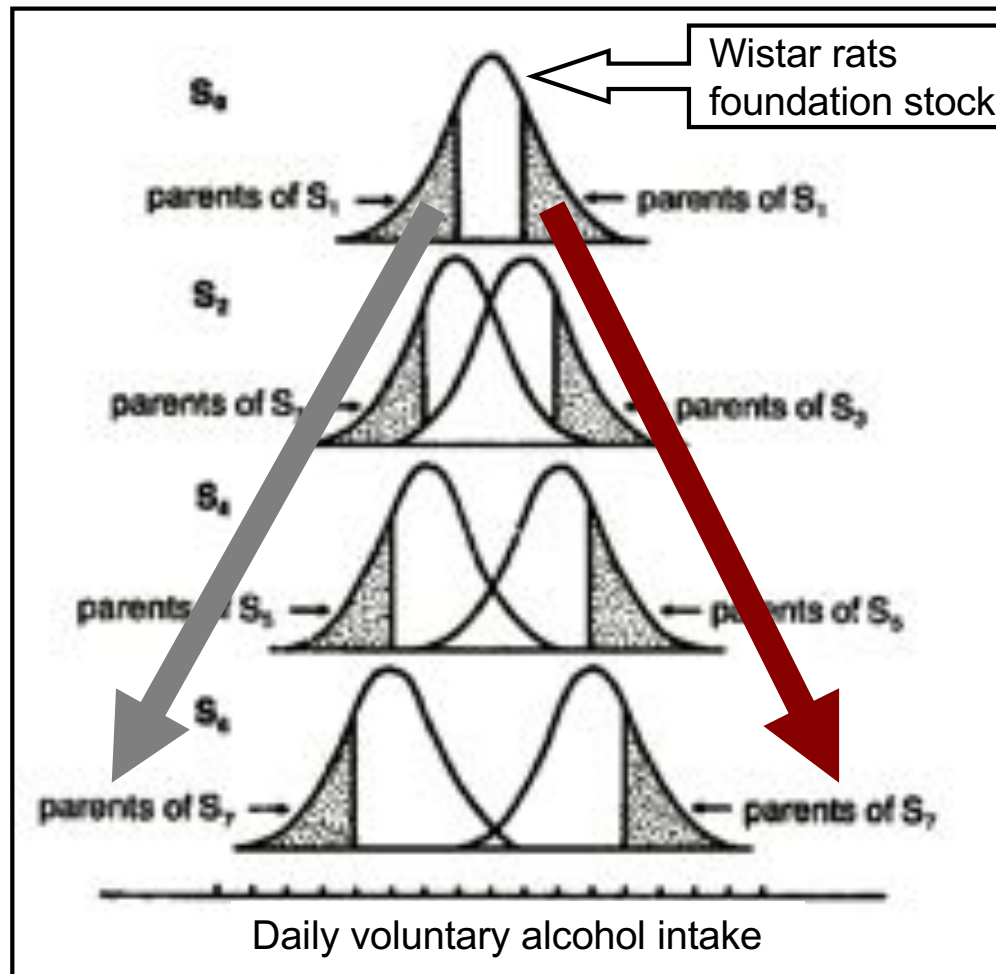
- Voluntary drinking in the home cage
- Free access to ethanol solution, water and food
- 2-bottle free choice (ethanol solution and water)
- Continuous access
- Intermittent access; 24 h, Mo, We, Fri

Research animal depending on questions

- Outbred stocks
 - Genetic heterogeneity
 - Individual differences
- Inbred strains
 - Brother x sister mating
 - Genetic homogeneity
- **Selectively bred lines**
 - **E.g. alcohol-preferring/alcohol non-preferring**



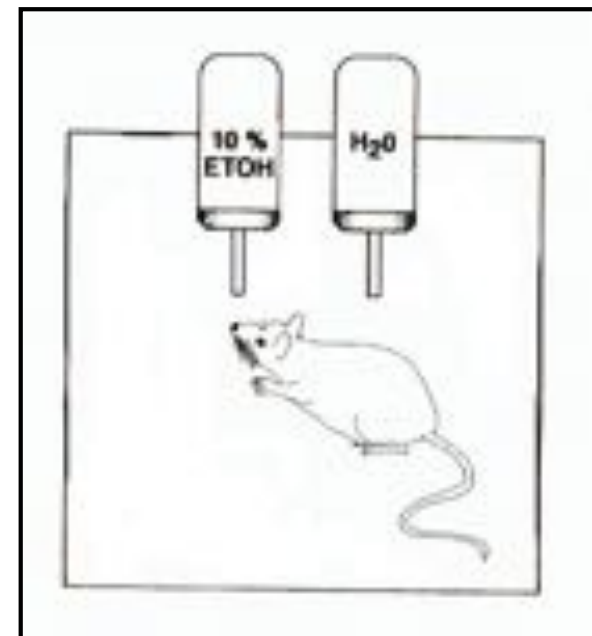
Selective breeding for contrasting alcohol intake



Bidirectional selection for alcohol preference and intake (selected phenotype), in two opposite directions, over successive generations until the selection *plateau* has been reached:

> 5-6 g/kg alcohol/day in preferring rats

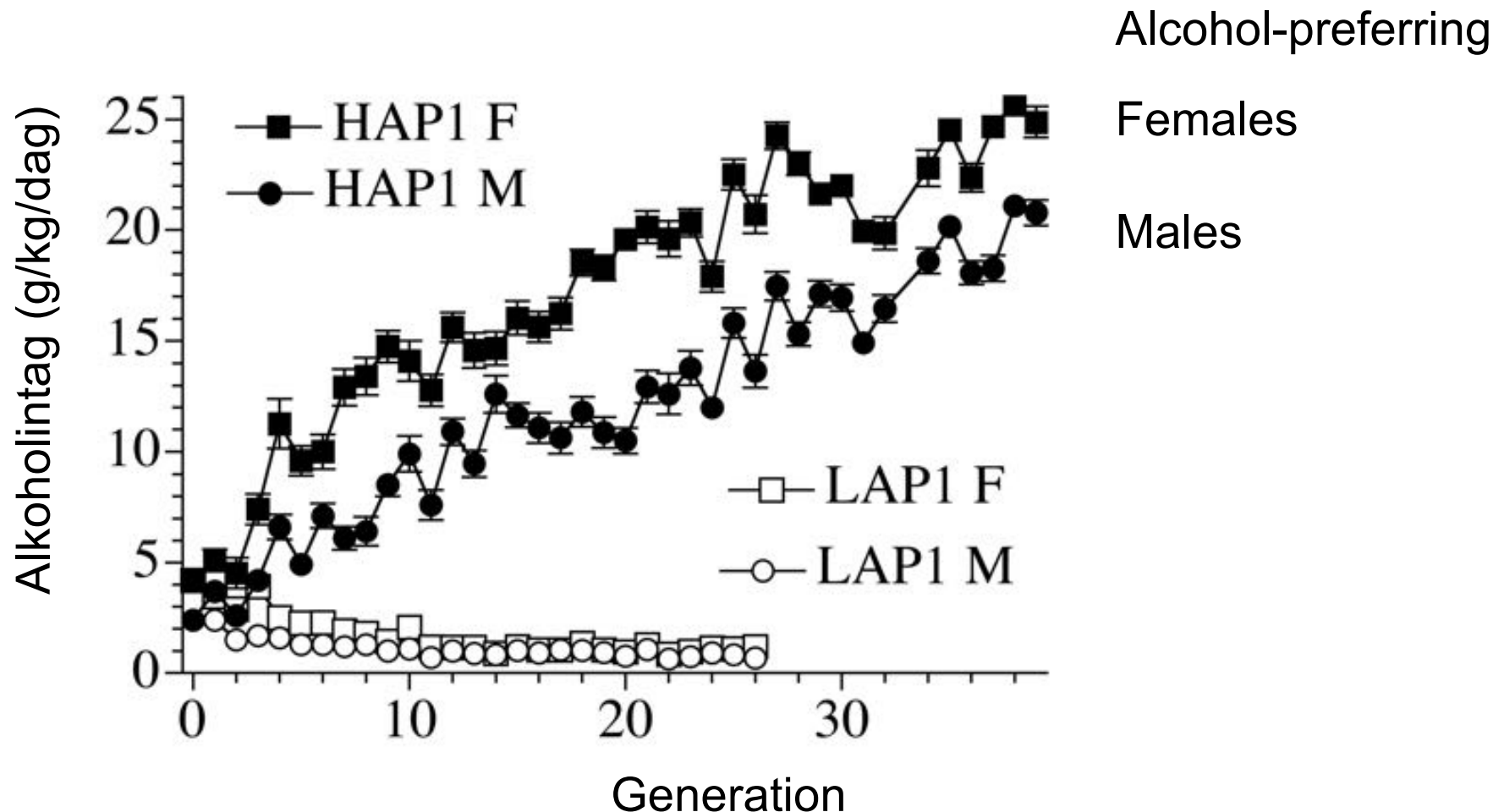
< 0.5 g/kg alcohol/day in non-preferring rats



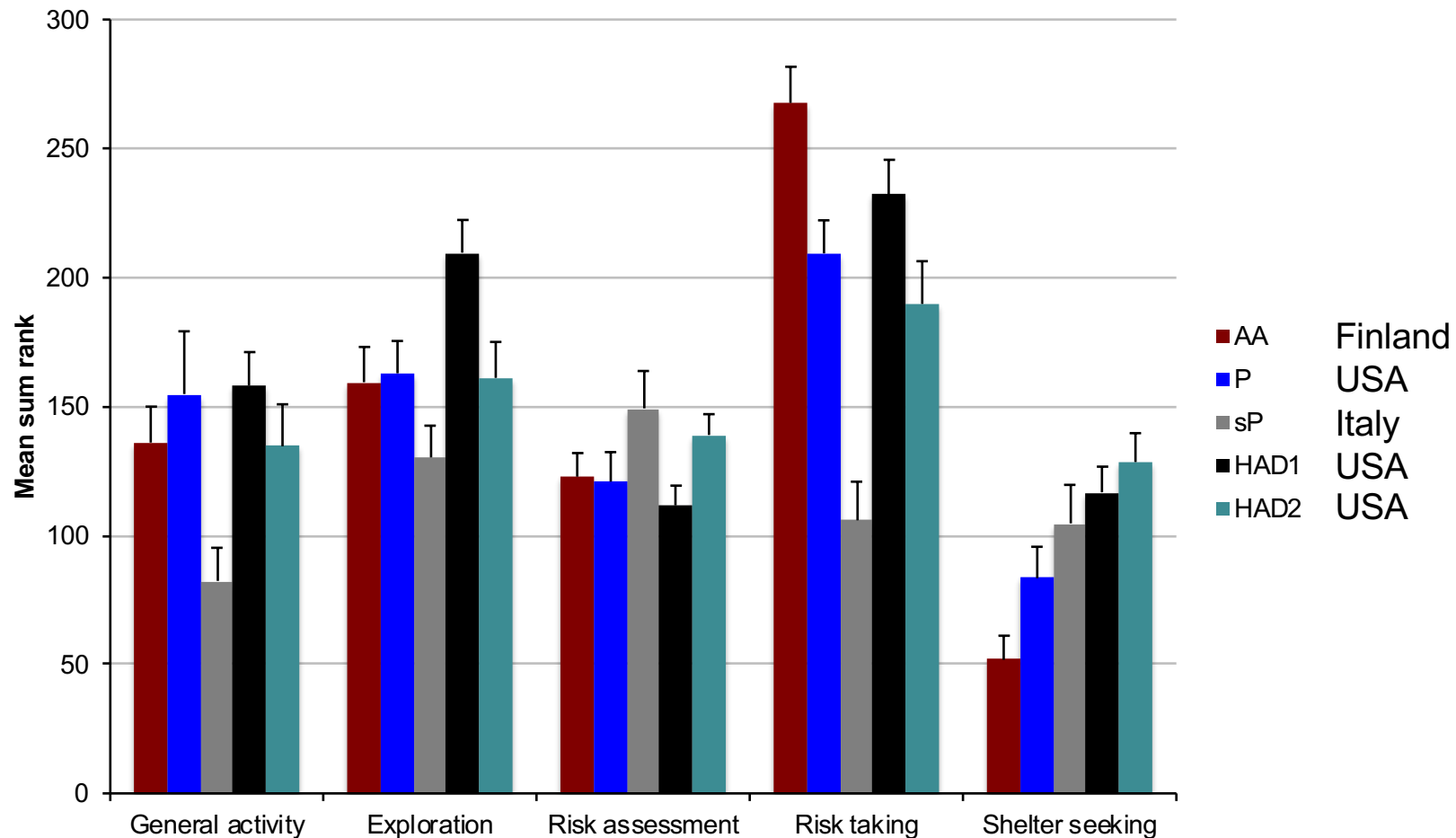
Alcohol-preferring rats

Alcohol non-preferring rats

Selective breeding for contrasting alcohol intake

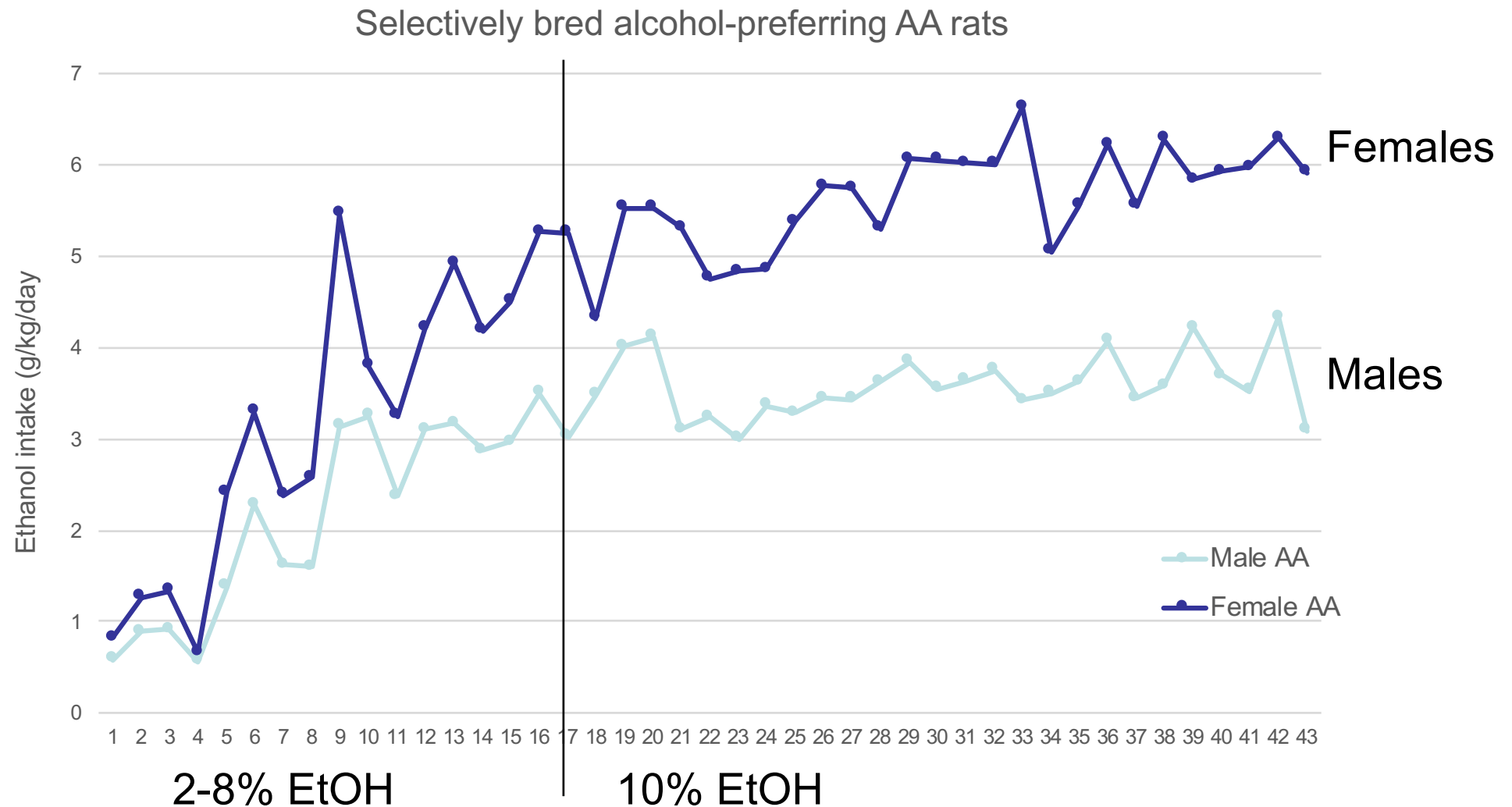


Behavioral profiling of multiple pairs of selectively bred alcohol-preferring male rats



- No common behavioral profile associated with high alcohol intake and preference

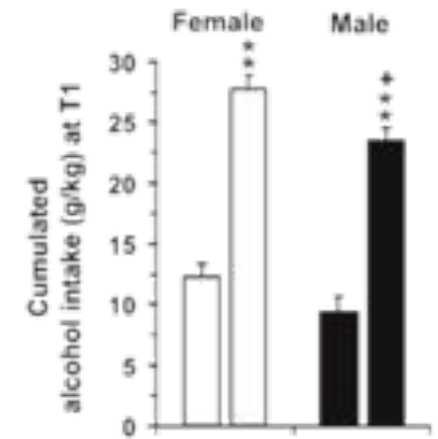
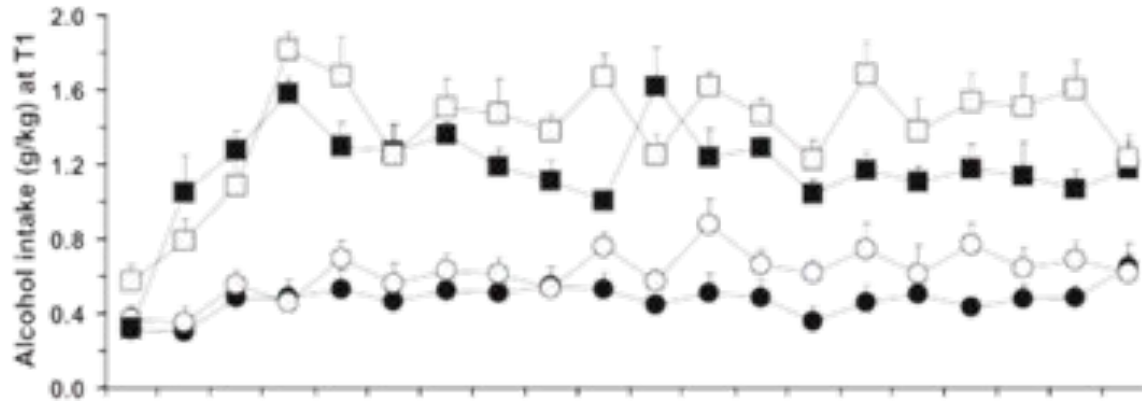
Adult selectively bred alcohol-preferring rats



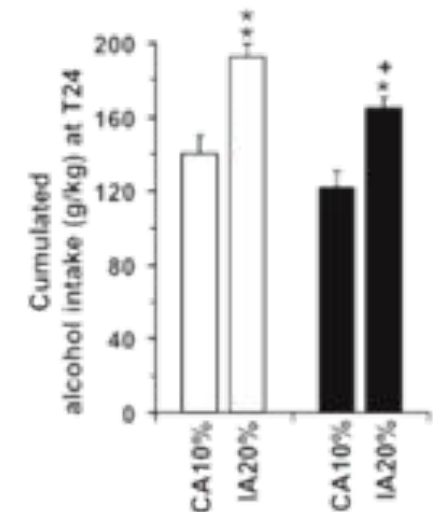
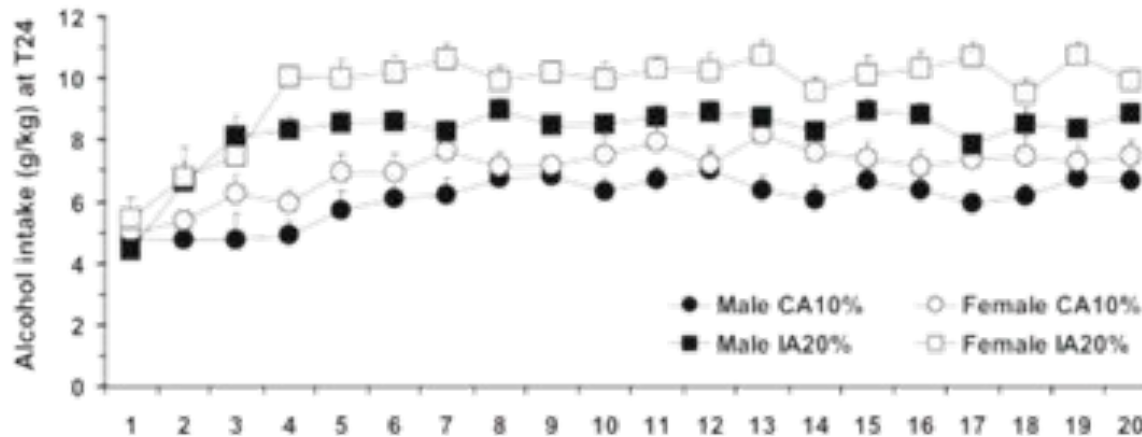
Adult selectively bred alcohol-preferring rats

Selectively bred alcohol-preferring sP rats

First hour



24 h

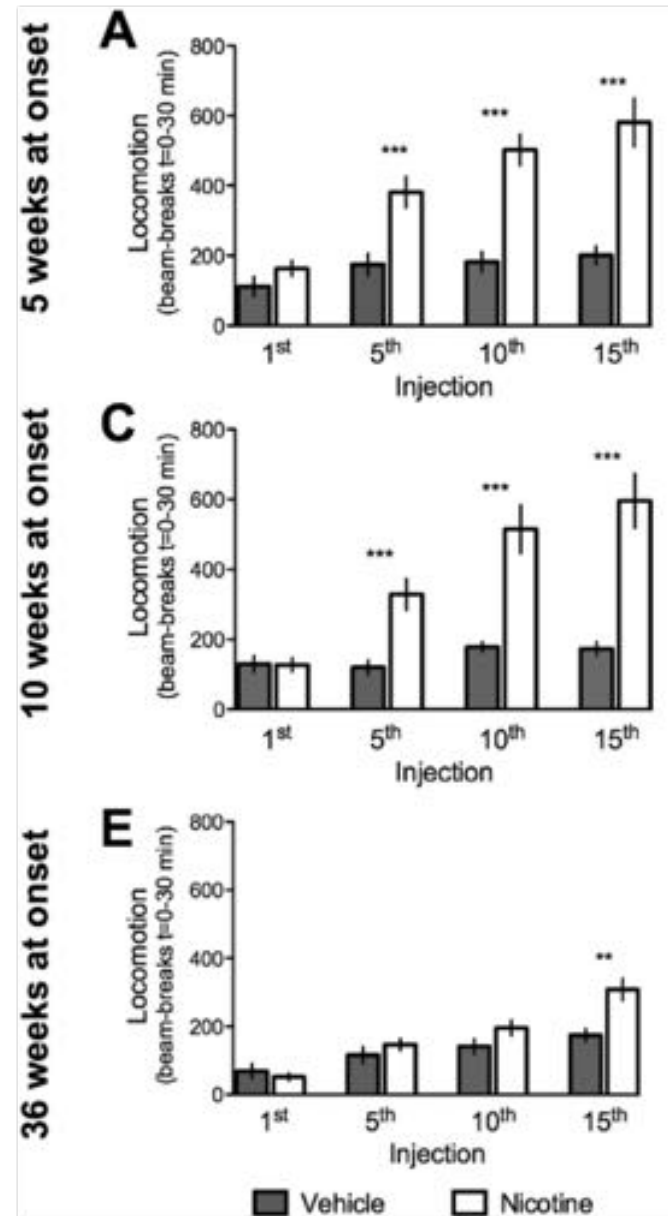


Research animal depending on questions

- **Outbred stocks**
 - Genetic heterogeneity
 - Individual differences
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 - E.g. alcohol-preferring/alcohol non-preferring



Behavioral sensitization to nicotine

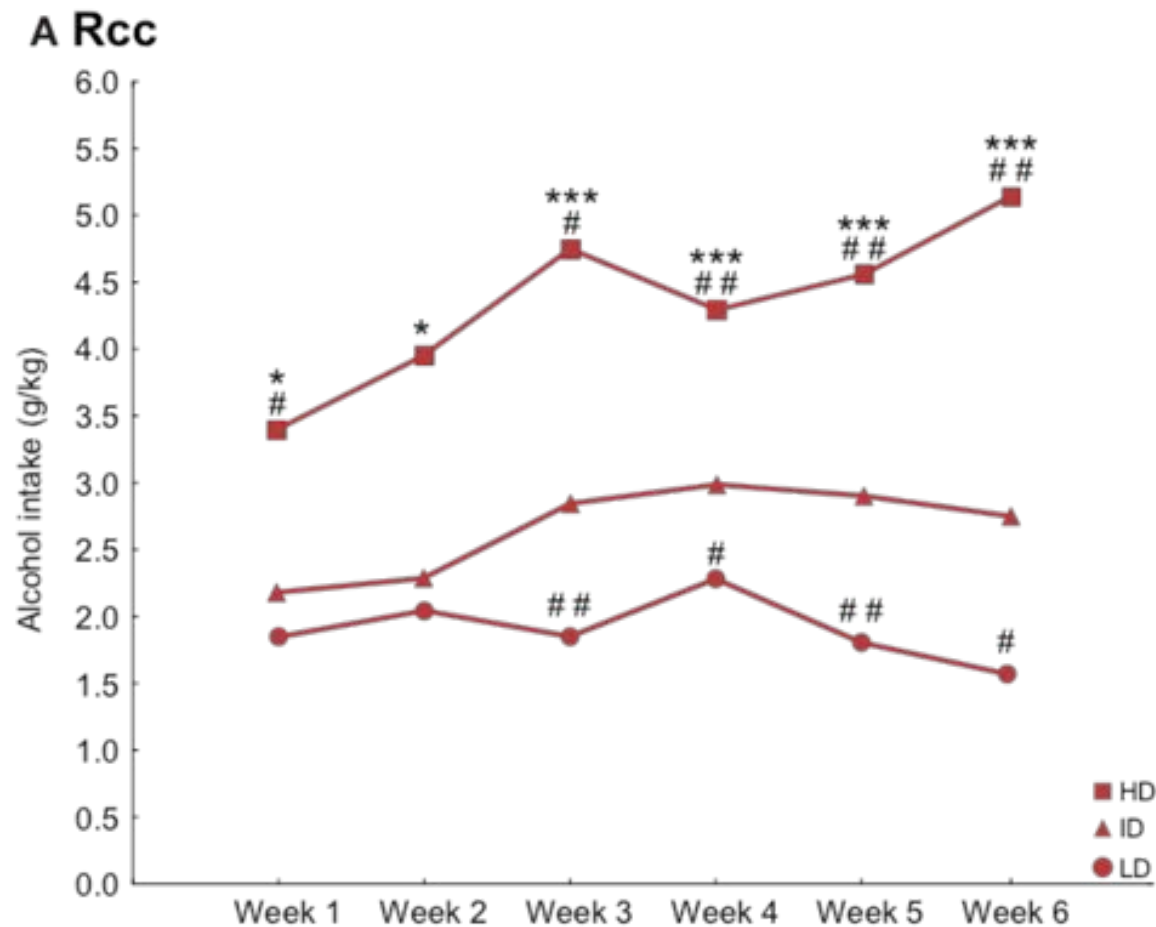


5 weeks of age

10 weeks of age

36 weeks of age

Importance of studying subgroups



Intermittent access
20% EtOH and water
Six weeks

Momeni S et al. 2015

Alcohol intake in adult males and females

Refinement of housing conditions in studies of voluntary alcohol intake

Higher voluntary alcohol intake in females than in males

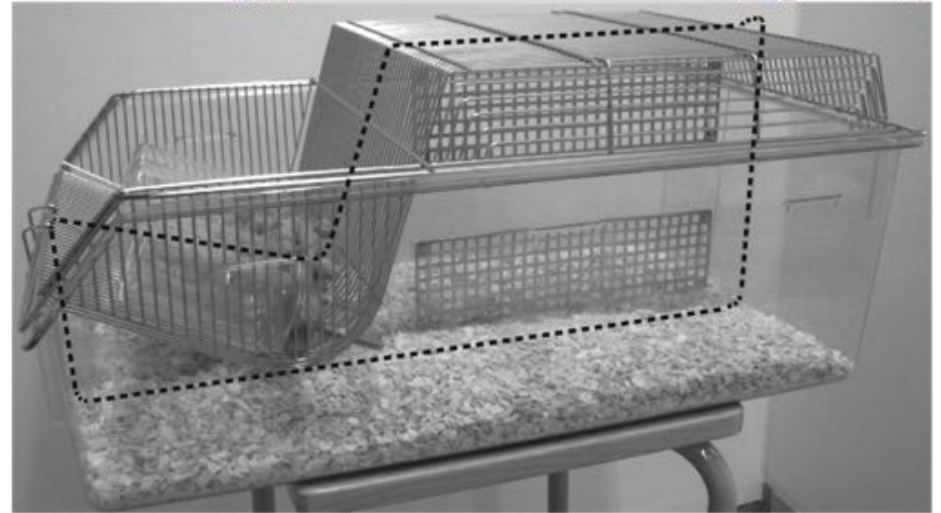
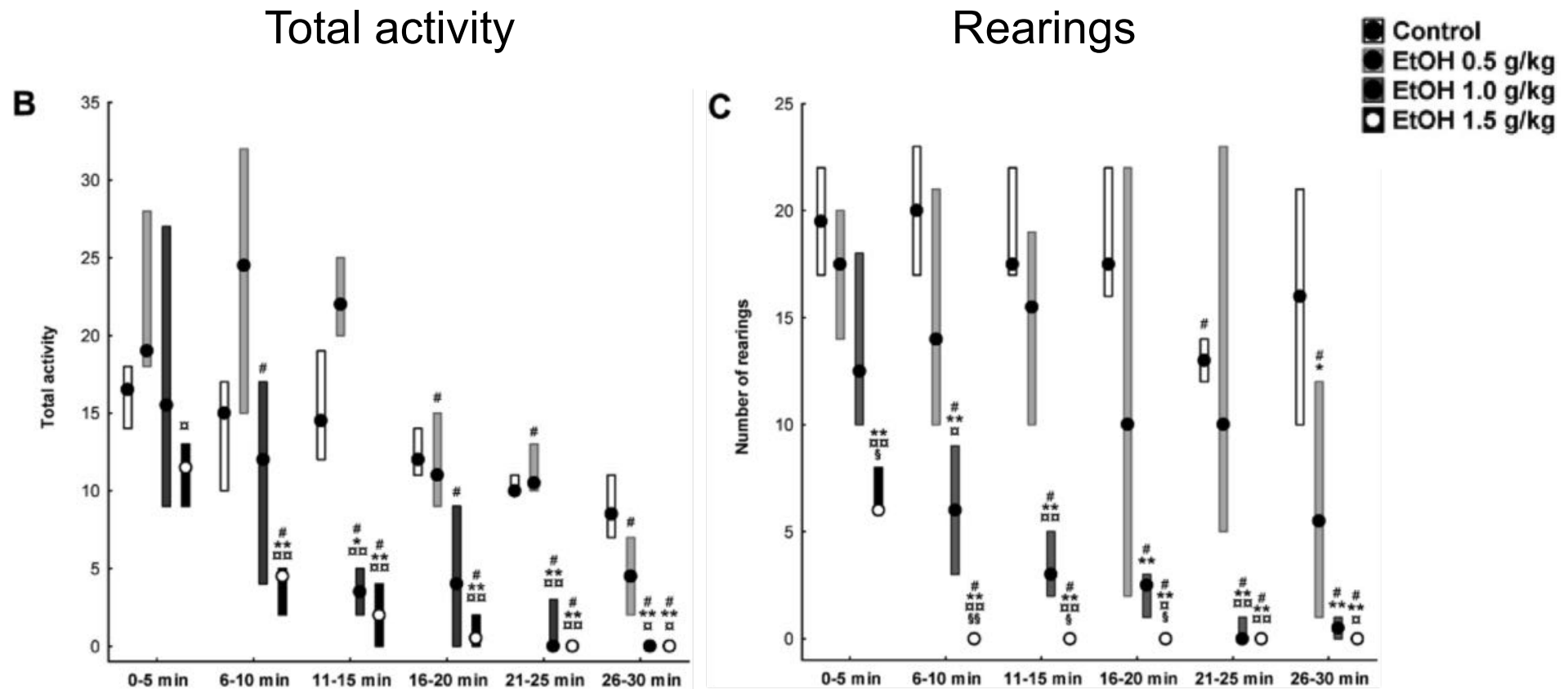


Photo: Sara Palm

Alcohol-induced effects on behavior in adult males





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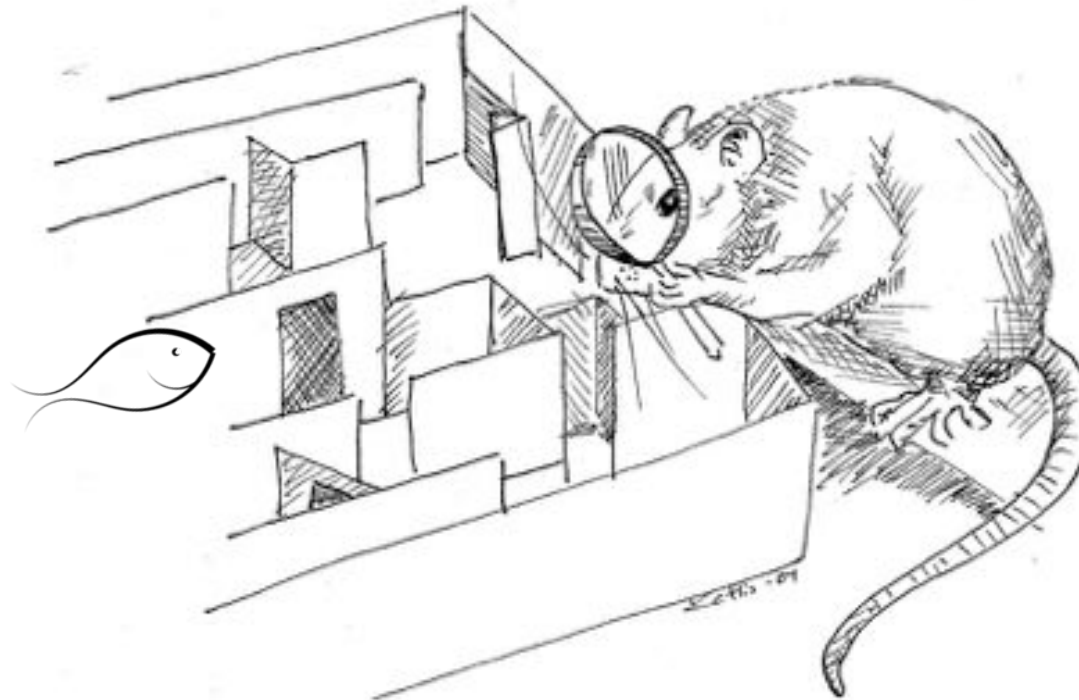
Summary

- Larger focus on females, especially female subgroups
- Differences between adolescents and adults
- Adolescence is short in rats
- Much remains to be studied in
 - females
 - adolescents



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Thank you for your attention!



VR-MH, ERAB, SRA, Svenska Spel Research Council, Facias Foundation
Bertil Göransson scholarship

Medicine & Pharmacy