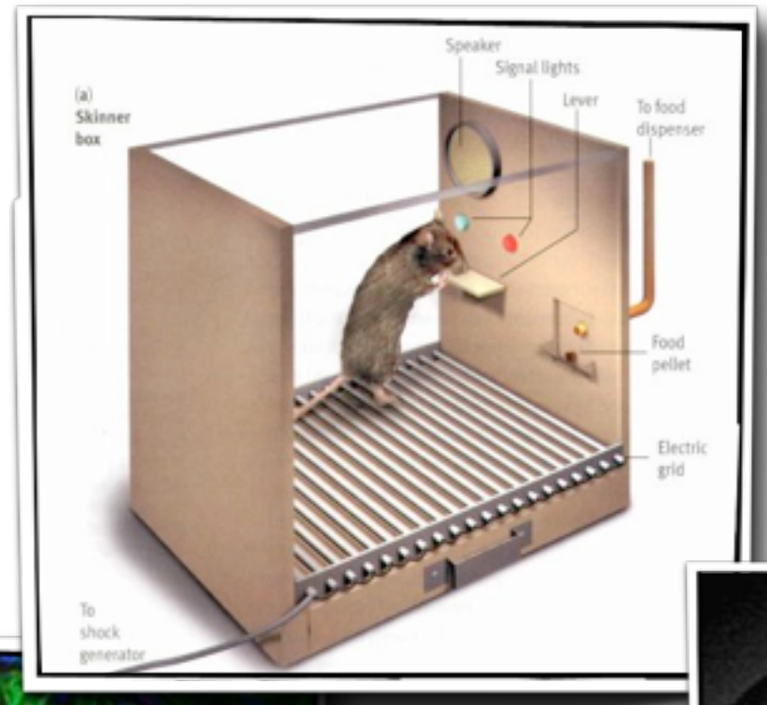
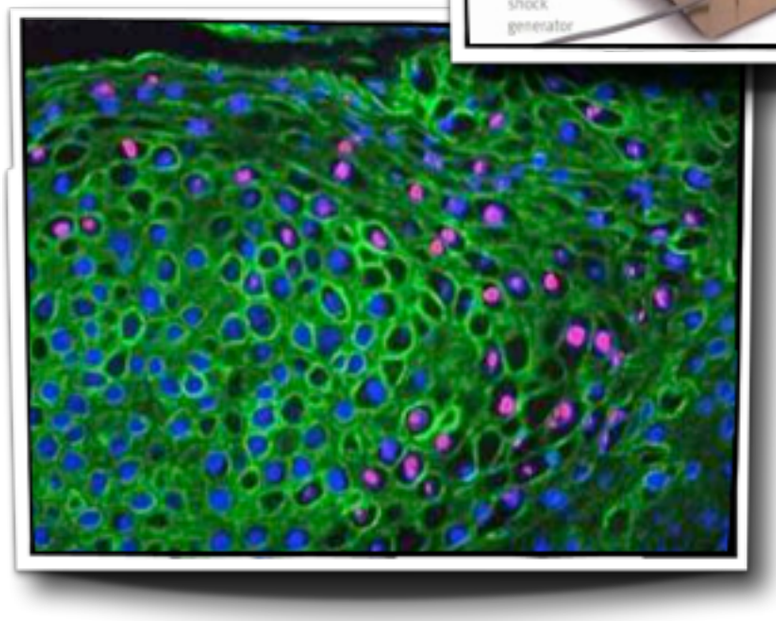
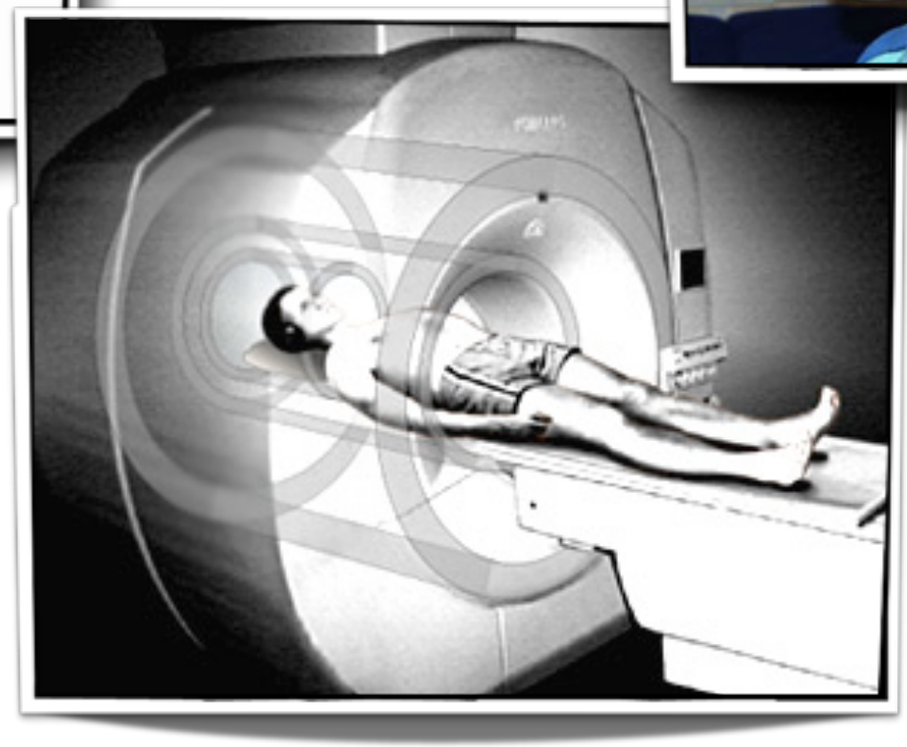
Methods in Behavioural Neurobiology

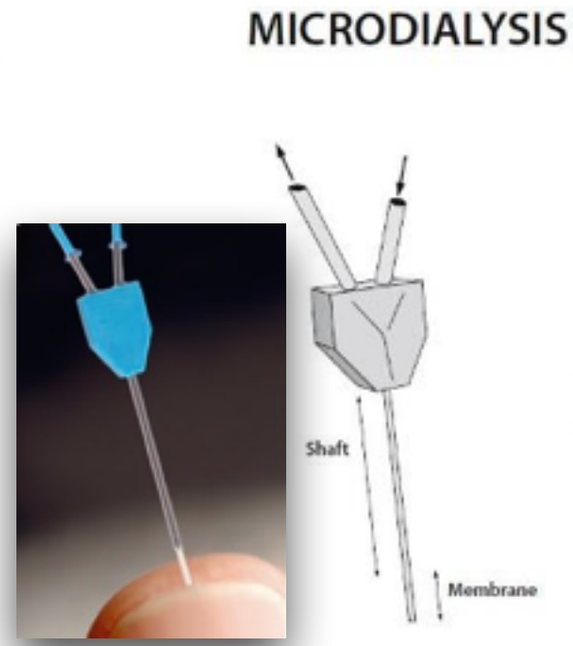


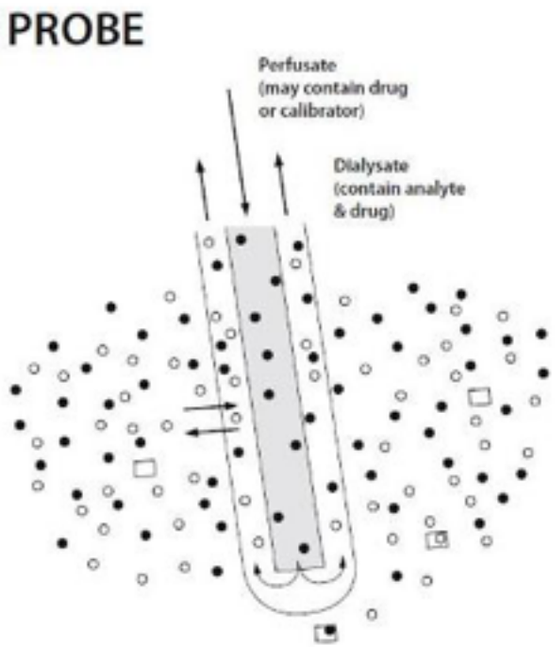


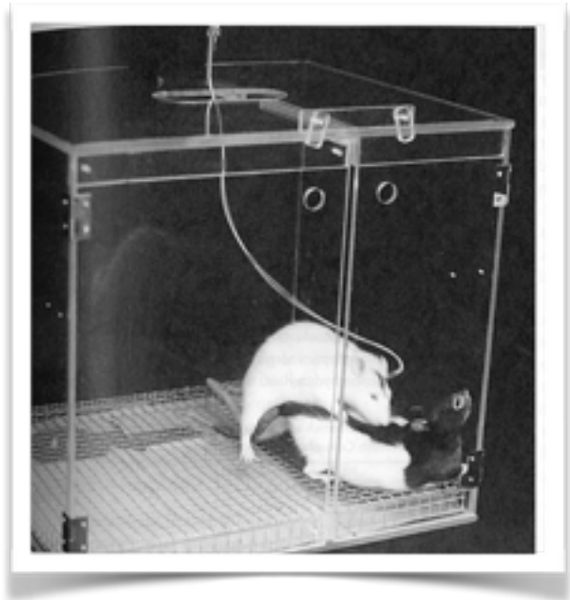


1. Direct measures of Neuronal Activity

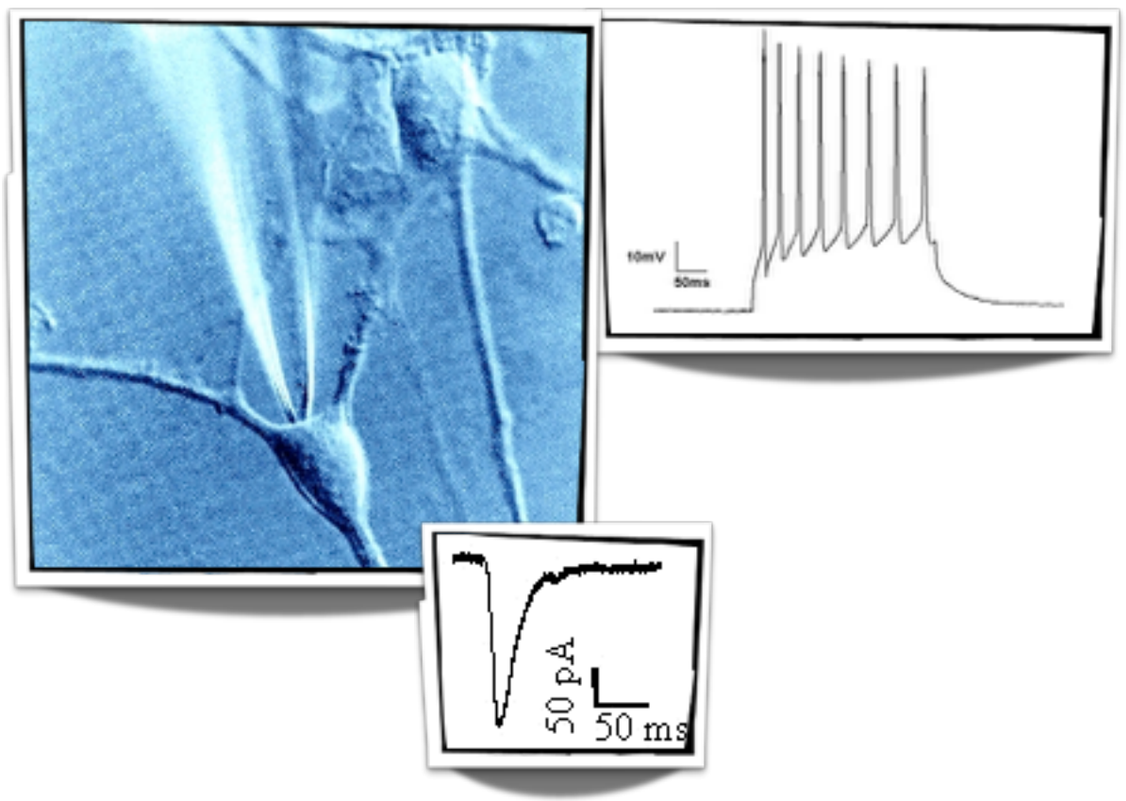
a. Microdialysis

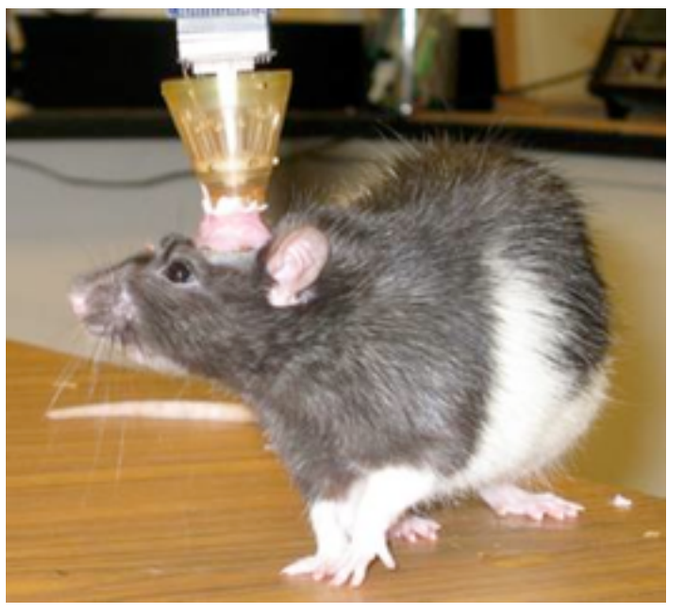


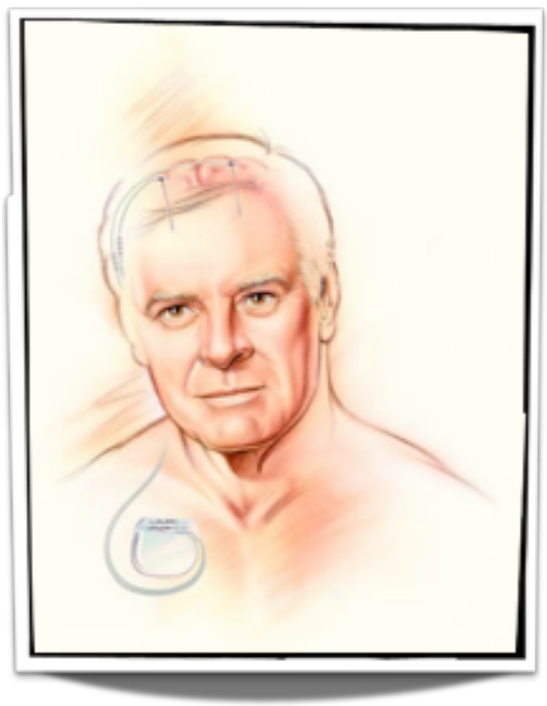




b. Electrophysiological recording (and stimulation)

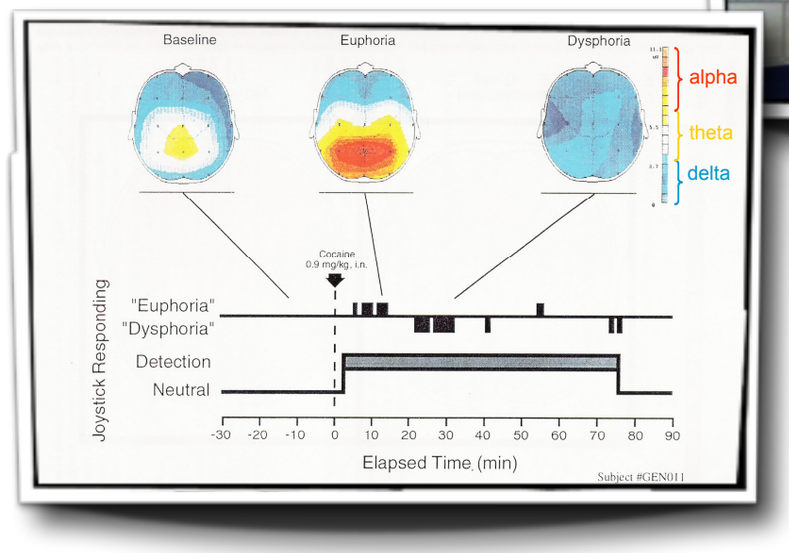




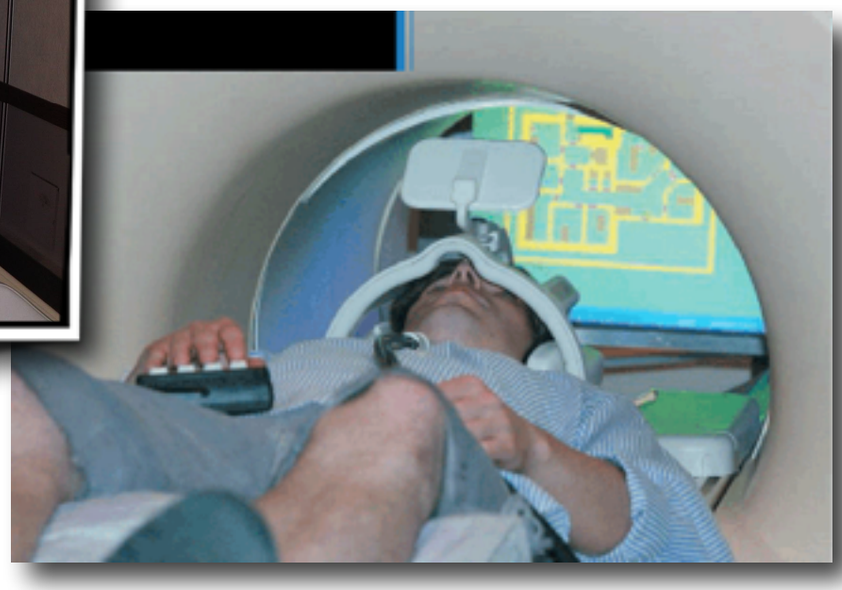


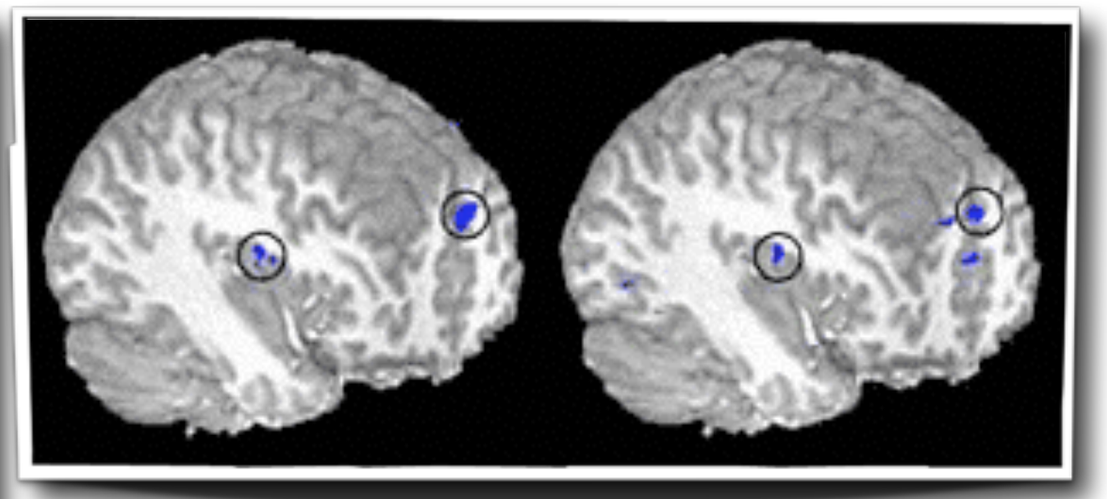
1. Direct measures of Neuronal Activity

c. ElectroEncephaloGraphy (EEG)



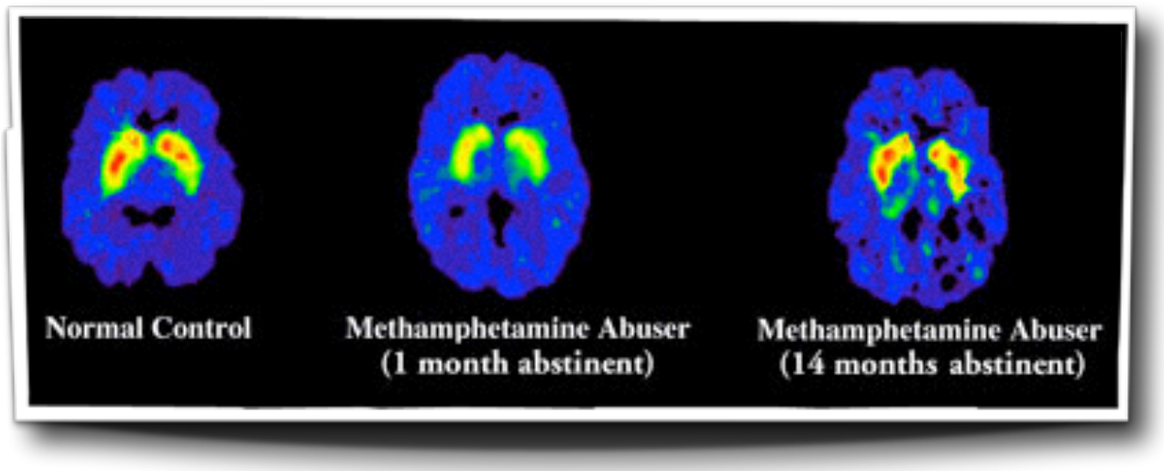
d. functional Magnetic Resonance Imaging (fMRI)



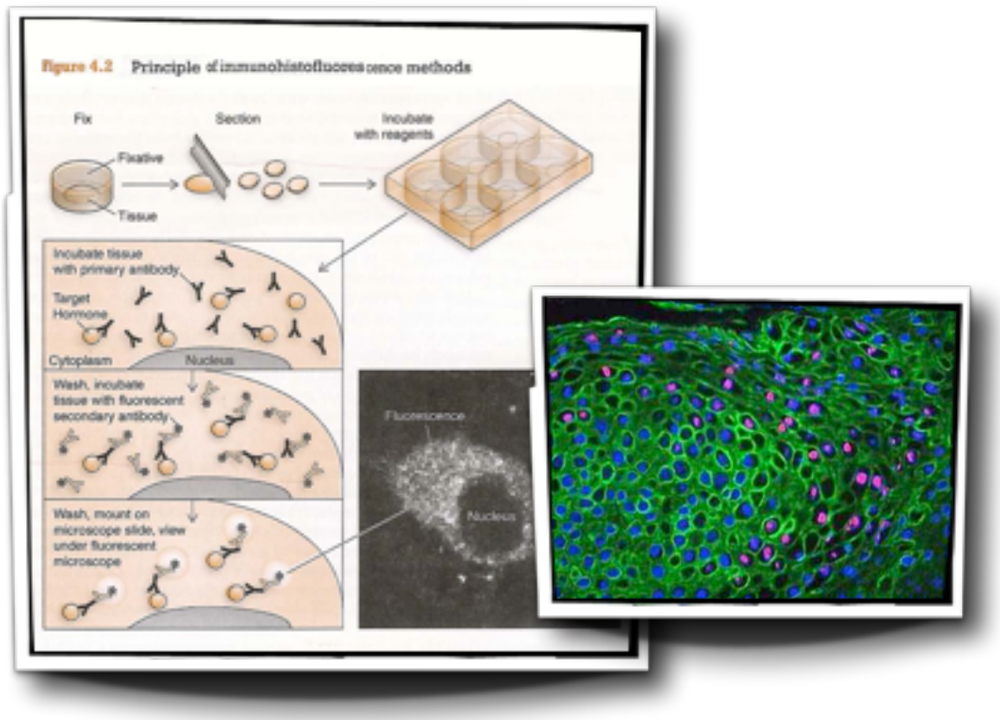


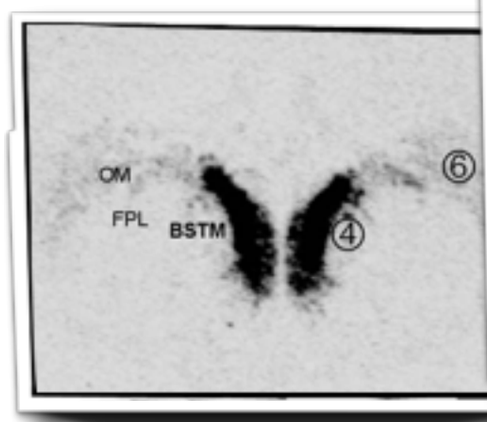
1. Direct measures of Neuronal Activity

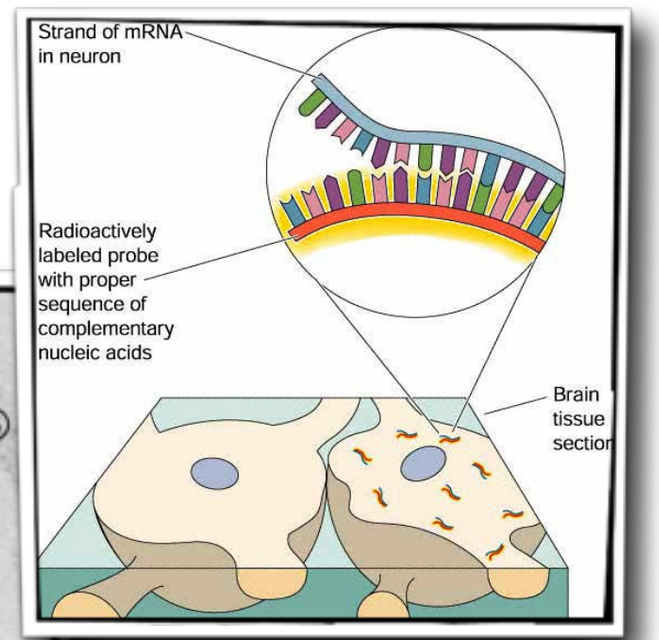
e. Positron Emission Tomography (PET)



f. Immunohistocemistry/In-situ hybridization







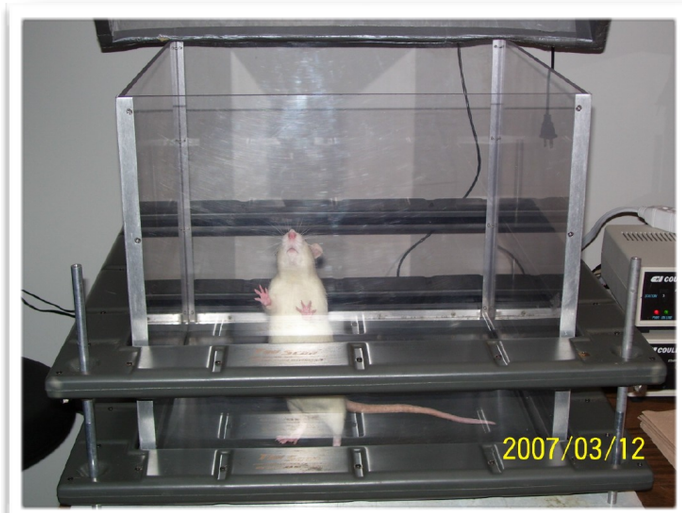
2. Behavioural Evaluation

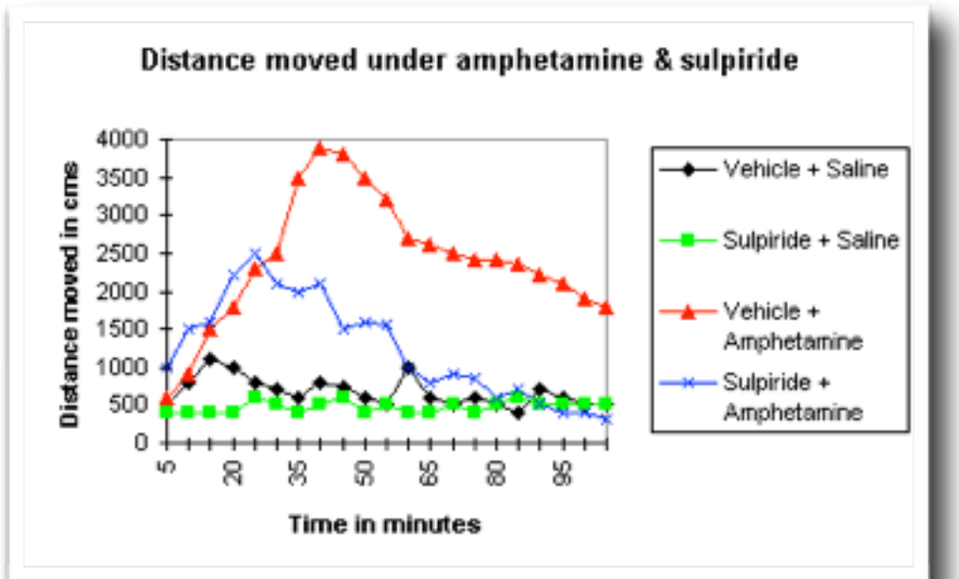
a. Behavioural observations

b. Unconditioned behaviour: non-specific

Catalepsy

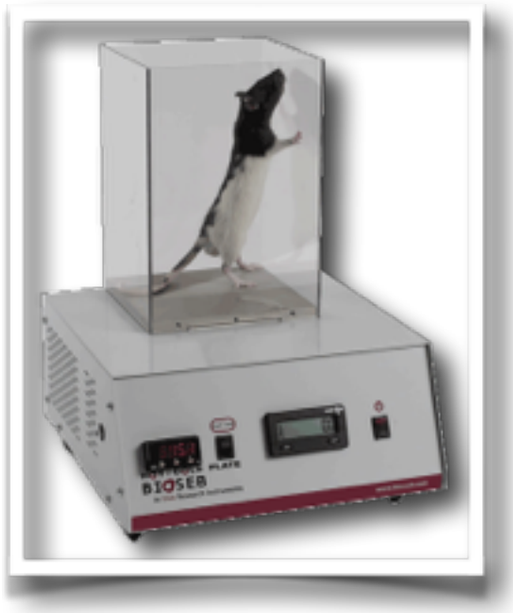
Locomotor activity chamber





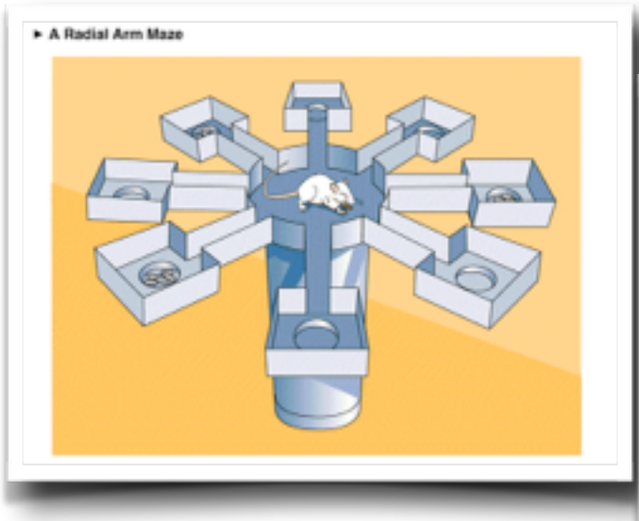
2. Behavioural Evaluation

b. Unconditioned behaviour: specific



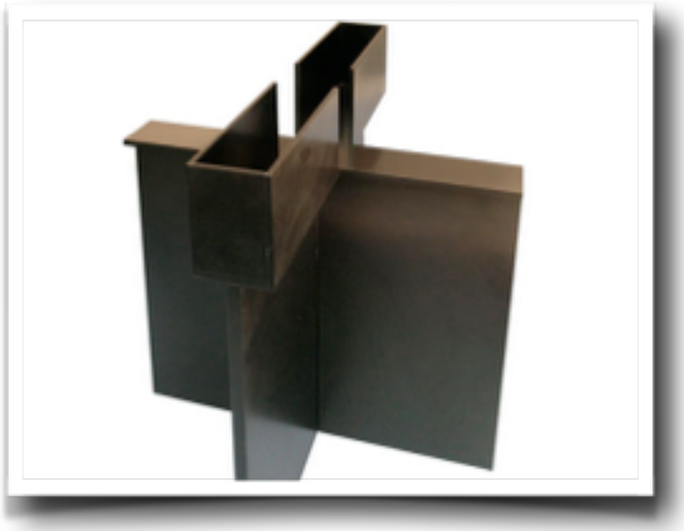
Analgesia: Hot plate

Learning and memory



Morris Water Maze

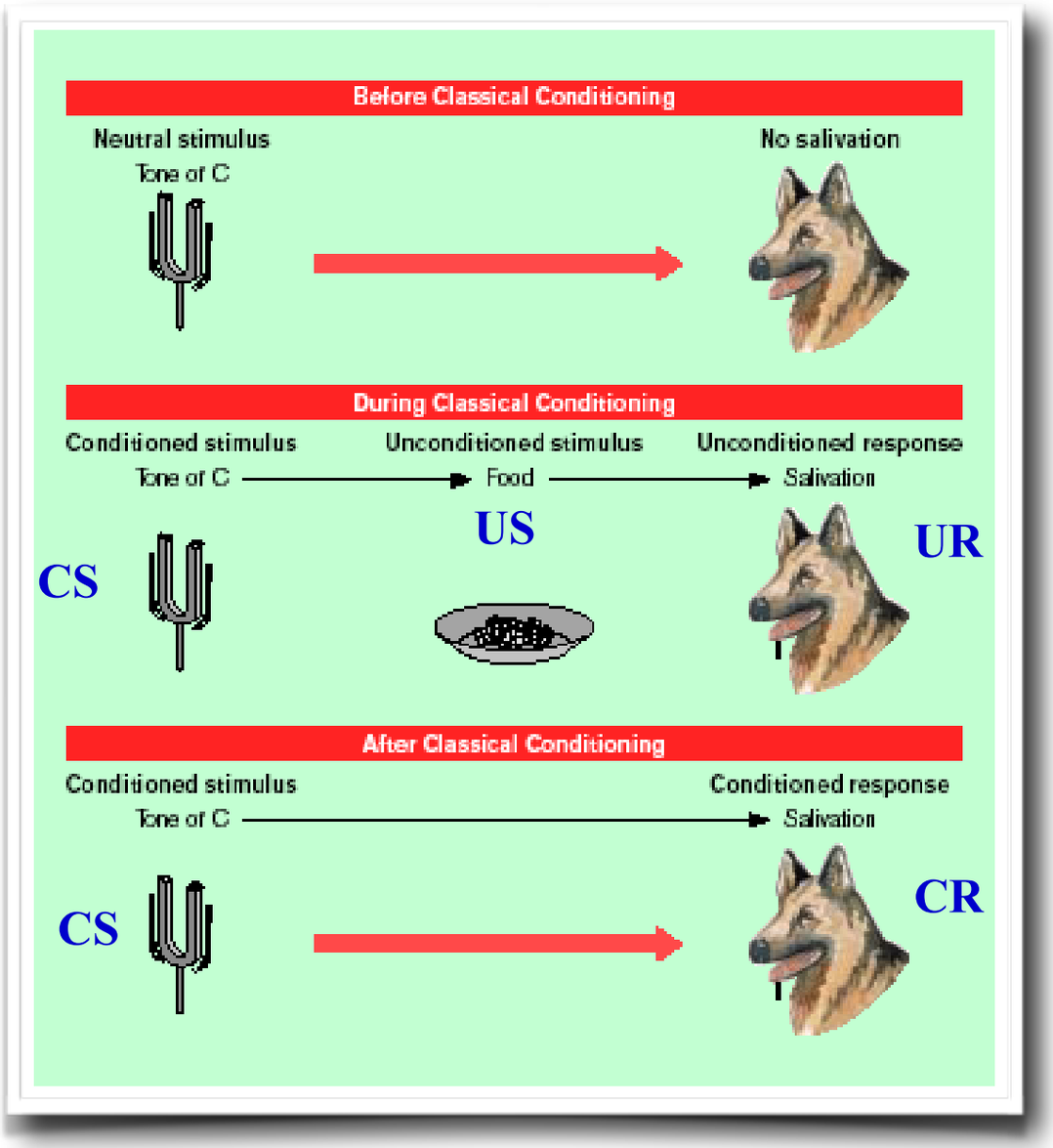
Anxiety: Elevated plus maze



2. Behavioural Evaluation

c. **Conditioned behaviour**

i. Classical (Pavlovian) conditioning (CS-US associations)



2. Behavioural Evaluation

c. **Conditioned behaviour**

ii. Operant (instrumental) conditioning

2. Behavioural Evaluation

c. **Conditioned behaviour**

ii. Operant (instrumental) conditioning

Operant conditioning procedures:

1. Positive reinforcement: the response increases the probability that appetitive stimulus will appear (response rate should increase)
2. Punishment: the response increases the probability that aversive stimulus will appear (response rate should decrease)
3. Negative reinforcement: the response increases the probability that aversive stimulus will be removed (response rate should increase)
4. Omission training: the response increases the probability that appetitive stimulus will be removed (response rate should decrease)

2. Behavioural Evaluation

c. **Conditioned behaviour**

ii. Operant (instrumental) conditioning

Schedules of reinforcement

1. Ratio - Fixed (FR-1, FR-10), Variable (VR-2, VR-10)
2. Interval - Fixed (FI-1, FI-5), variable (VI-3, VI-15)

2. Behavioural Evaluation

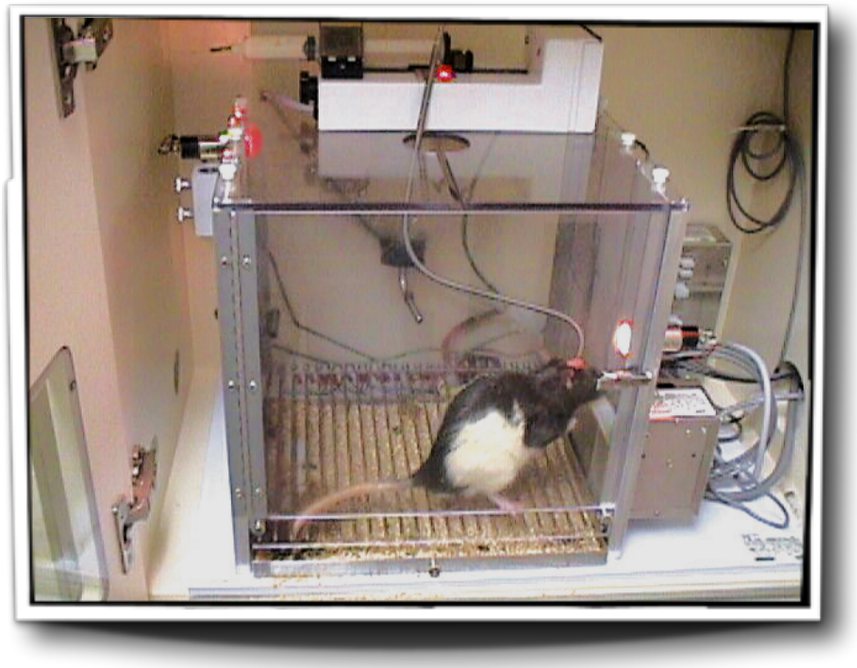
Measurements of drug reward

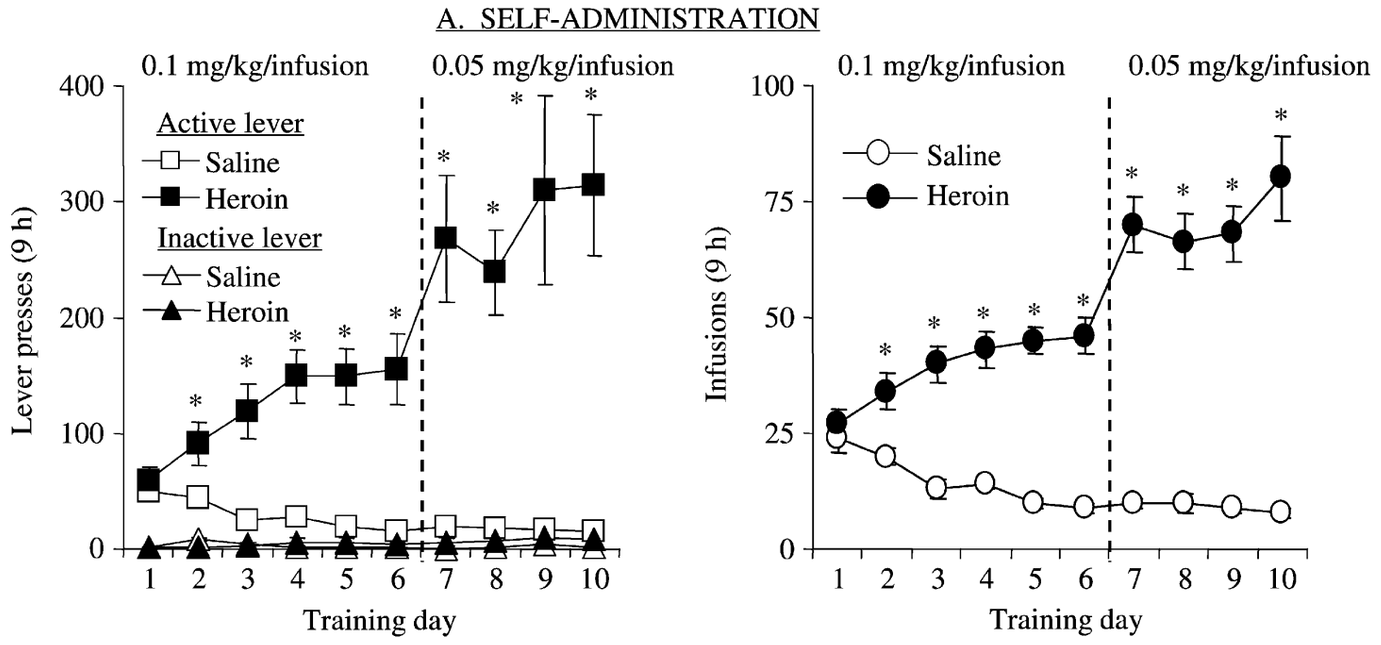
1. Drug self-administration

    i. A steady rate of response

    ii. Response should extinguish when the drug is removed (or much lower response rate on "inactive" option

    iii. Response rate sensitive to drug dose



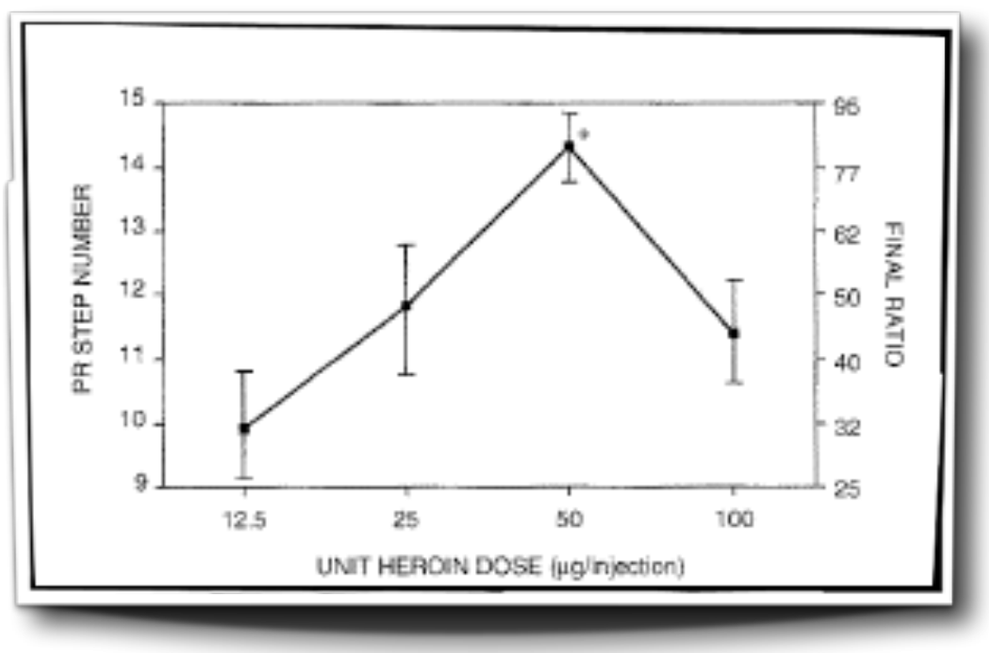


Shalev et al 2003

2. Behavioural Evaluation

Measurements of drug reward

1. Drug self-administration: Schedules of reinforcement
   - usually training initiates with FR-1
   - Can then be increased (FR-5 or higher)
   - To assess motivation to seek drug: Progressive Ratio (PR) - response requirement increases for each successive infusion (1, 2, 4, 6, 9, 12, 15, 20, 25, 32, 40, 50, 62, 77, 95, 118, 145, 178, 219...)

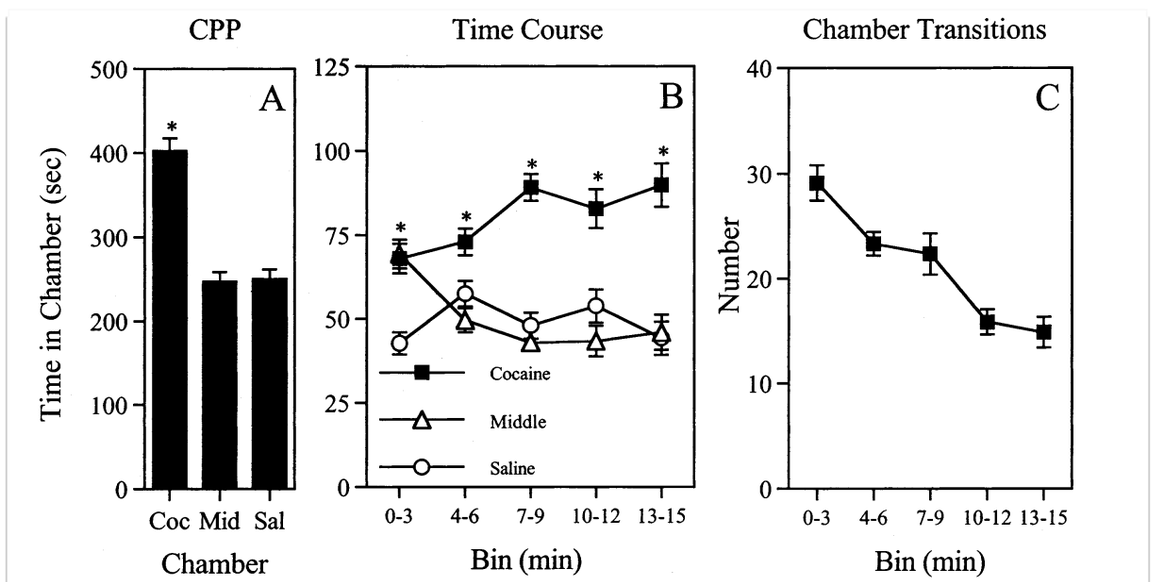


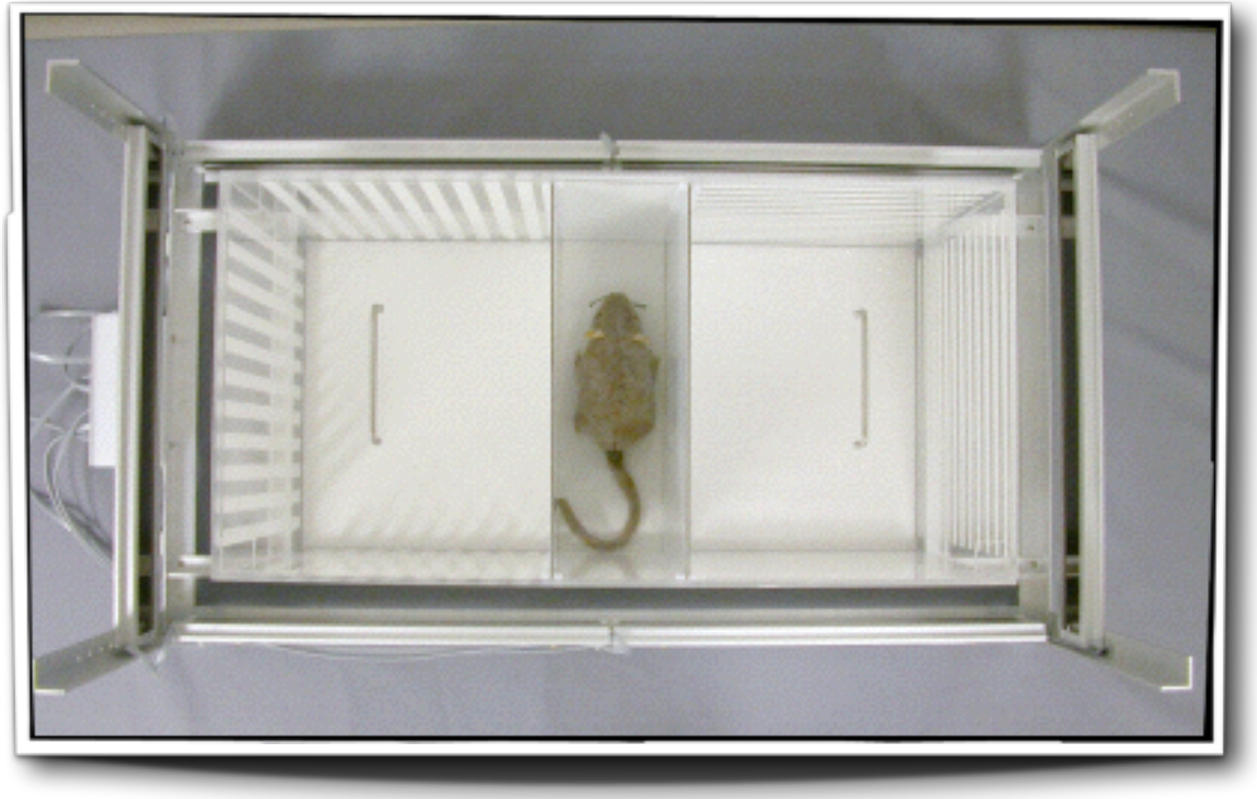
2. Behavioural Evaluation

Measurements of drug reward

2. Conditioned Place Preference (CPP)

- A classical conditioning procedure
- The subjects spend more time in the "drug environment"





3. Direct neuronal activation/inhibition

a. Deep-brain stimulation

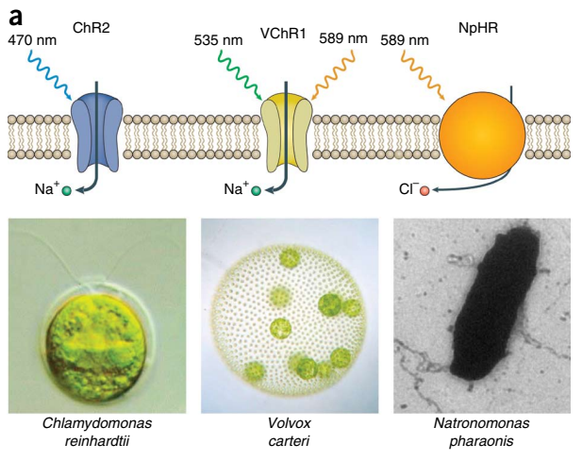
b. TMS

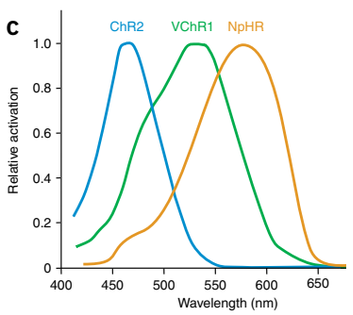
} Mentioned earlier...

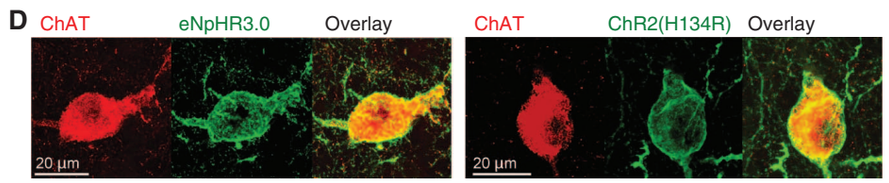
C. Optogenetics

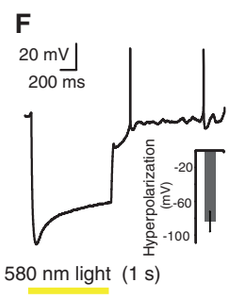
Karl Deisseroth

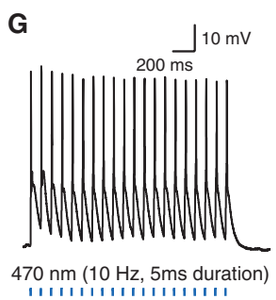
Activation & inhibition of Ach neurons in the NAc

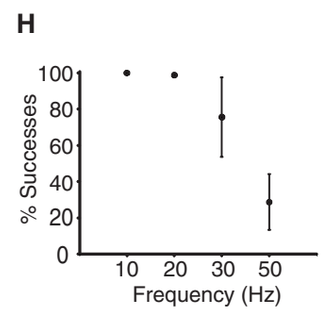


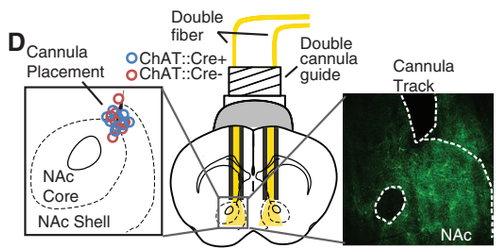


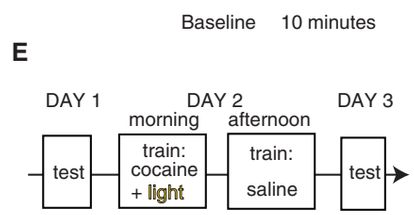


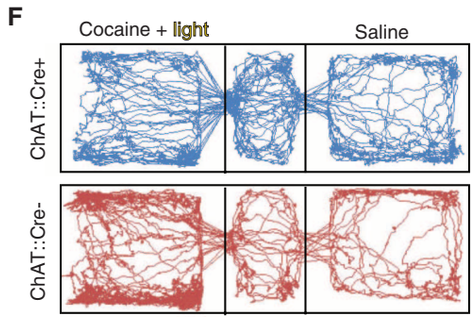


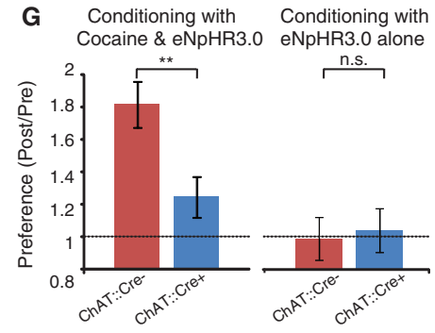












(Witten et al 2010)

3. Direct neuronal activation/inhibition

d. DREADD (Designer Receptor Exclusively Activated by Designer Drug)

- Mutant ACh muscarinic receptors: activated only be clozapine N-oxide (CNO; pharmacologically inert lignad).

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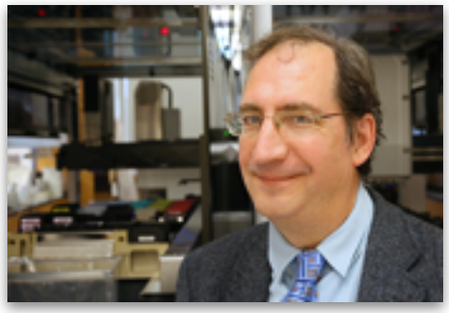
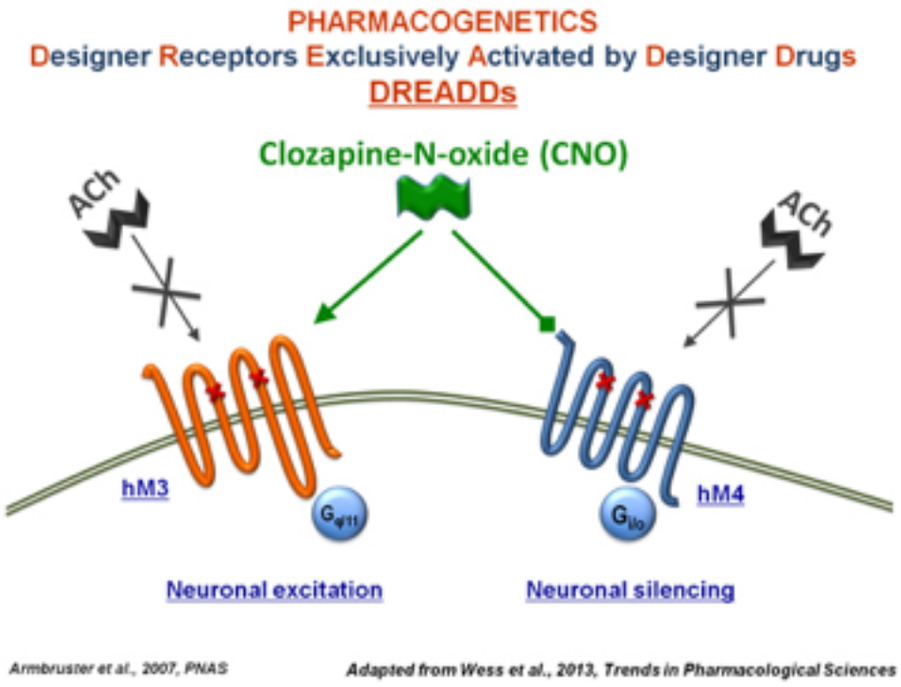
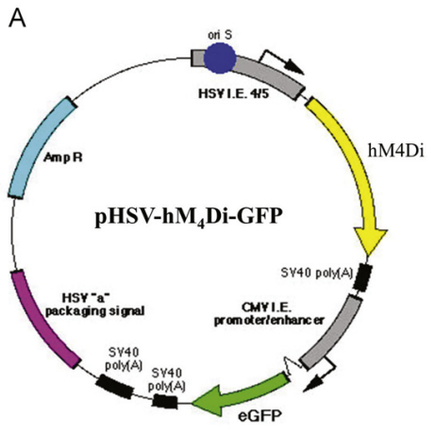
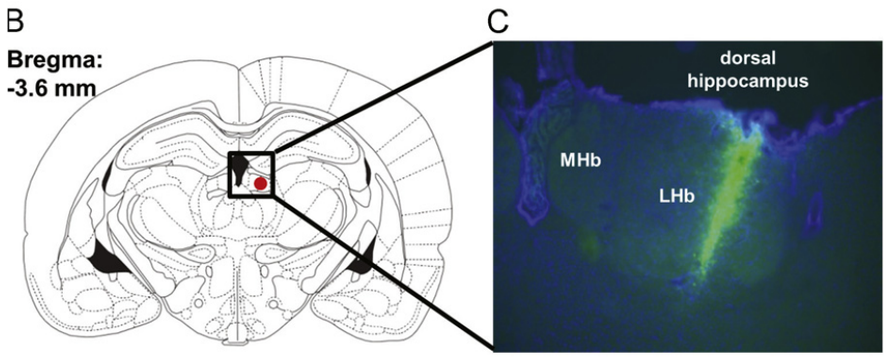

Bryan Roth



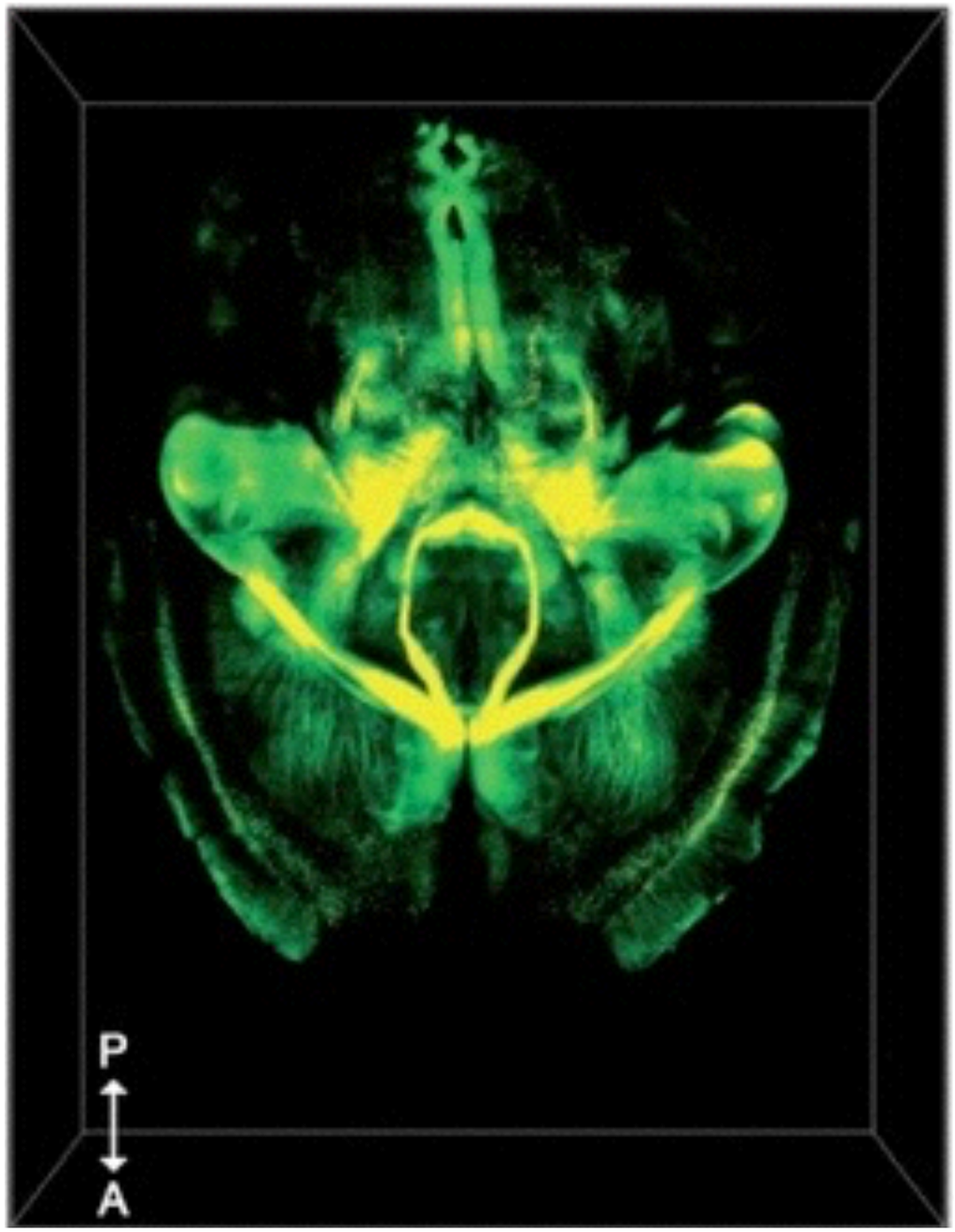
Viral-mediated gene transfer



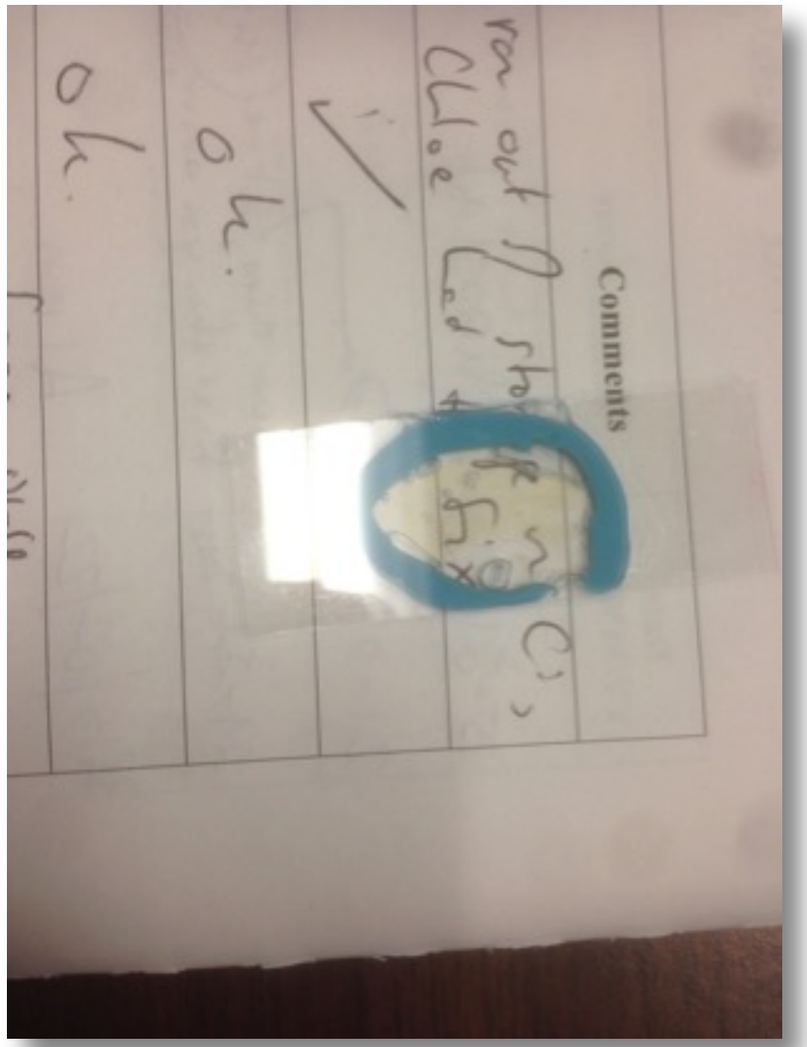
eGFP expression 4 days after viral infection



The transparent brain

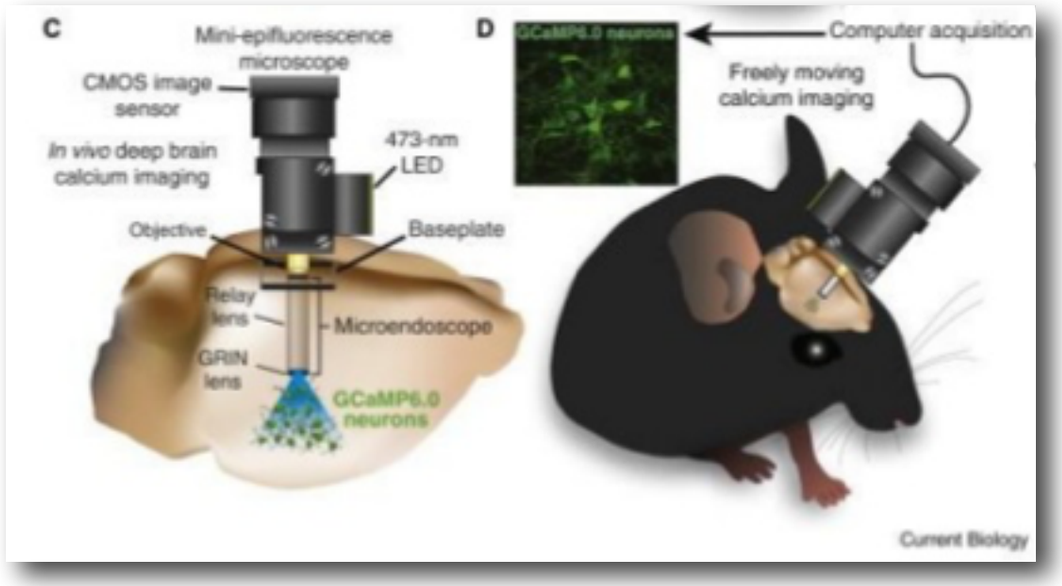


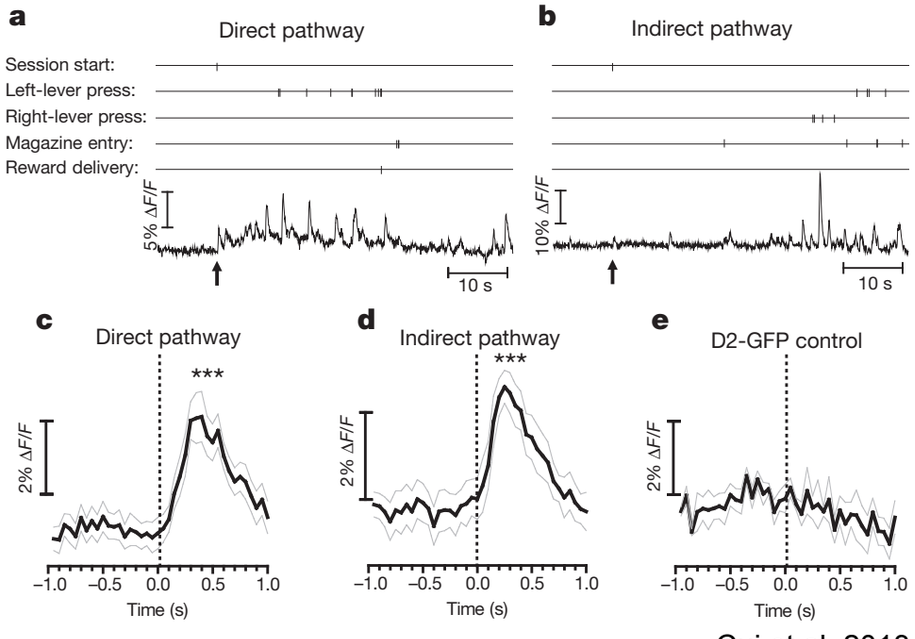
https://www.youtube.com/watch?v=c-NMfp13Uug



Fiber photometry

- GCaMP (Ca indicator) expressed in specific neutrons (through viral infection)





Cui et al. 2013

- Mice trained to press a lever for reward
- GCaMP was expressed selectively in striatal cells expressing DA D1 direct pathway) or D2 receptors (indirect pathway)