Variation in Genes Affecting Dopamine Turnover, Oxytocin, and Serotonin in Inmate and Student Populations

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Disclaimer

- There is no real or apparent conflicts of interest related to the content of this presentation

- Products used:
  - SNaPshot® Multiplex Kit

FSF Emerging Forensic Scientist Award
Paper Presentation

Introduction

Behavioral Genetics Transdisciplinary Group

- Forensic Science
  - Dr. David Gangitano, Department of Forensic Science, Sam Houston State University
- Biosocial Criminology
  - Dr. Todd Armstrong and Dr. Danielle Boisvert, Department of Criminal Justice and Criminology, Sam Houston State University
- Psychiatry
  - Dr. Ramiro Salas, Department of Psychiatry, Baylor College of Medicine

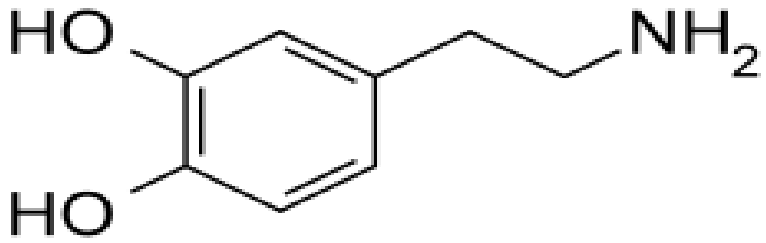
Previous Papers

- **Stress, genes, and generalizability across gender: effects of MAOA and stress sensitivity on crime and delinquency**
  - (Criminology, Wells et al., 2017)
- **Heart rate, serotonin transporter linked polymorphic region (5-HTTLPR) genotype, and violence in an incarcerated sample**
  - (Journal of Criminal Justice, Armstrong et al., 2017)
- **Molecular genetic underpinnings of self-control: 5-HTTLPR and self-control in a sample of inmates**
  - (Journal of Criminal Justice, Wells et al., 2015)
- **Monoamine oxidase A genotype, childhood adversity, and criminal behavior in an incarcerated sample**
  - (Psychiatric Genetics, Armstrong et al., 2014)
- **Serotonin and self-control: A genetically moderated stress sensitization effect**
  - (Journal of Criminal Justice, Boisvert et al., 2017)

Main Neurotransmitters Associated With Behavior

Dopamine

- Strong reinforcing agent
- Important in multiple physiological processes including motor coordination
- Levels of dopamine within the brain can be regulated through synthesis, transportation, and degradation

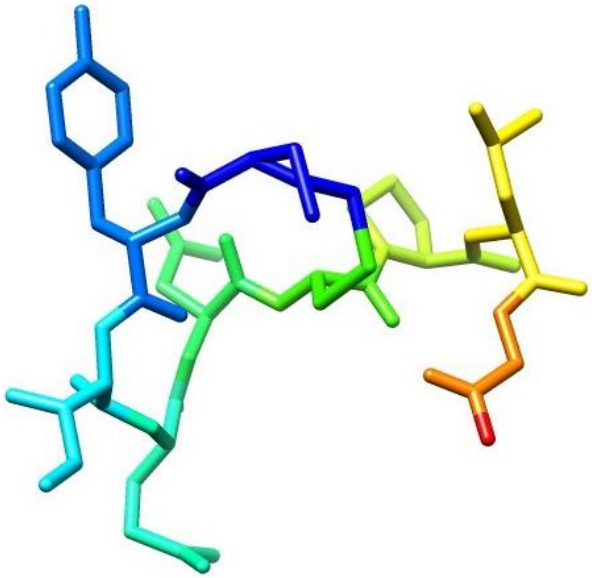


Dopamine Turnover

- Dopamine is synthesized from L-tyrosine and broken down into norepinephrine by dopamine beta-hydroxylase (DβH)
- Dopamine is primarily metabolized by monoamine oxidase (MAO)
  - Two forms that are 73% homologous: monoamine oxidase A (MAOA) and monoamine oxidase B (MAOB)
- Dopamine's metabolite DOPAC is further catabolized by catechol-O-methyl transferase (COMT) into HVA and then excreted by the urine

Oxytocin

- Produced in the hypothalamus
- Function is restricted to the peripheral reproductive tissue and central nervous system
- Equal concentrations in men and women
  - Posterior pituitary
  - Plasma
- Oxytocin receptors (OXTR) are found in many parts of the brain and spinal cord
- OXT is associated with bonding, trust, and empathy



Impact of Aggressive and Antisocial Behavior

- Impact on the criminal justice system
  - United States of America has the highest incarceration rate in the world (over 2,000,000 people currently incarcerated)
  - Over 40% of individuals in prison suffer from mental health problems (Bureau of Justice Statistics)
- Impact on the health field
  - Two of the leading causes of mental health referrals
  - 1 in 5 Americans experience mental illness in their lifetime (National Alliance on Mental Illness)
  - 1 out of 7 children (ages 2-8) have a diagnosed mental, behavioral, or developmental disorder (MBDD) (Center for Disease Control and Prevention)
    - Aggressive behavior is associated with many behavioral problems including Oppositional Defiant Disorder (ODD) and Conduct Disorder (CD)

Understanding Behavior

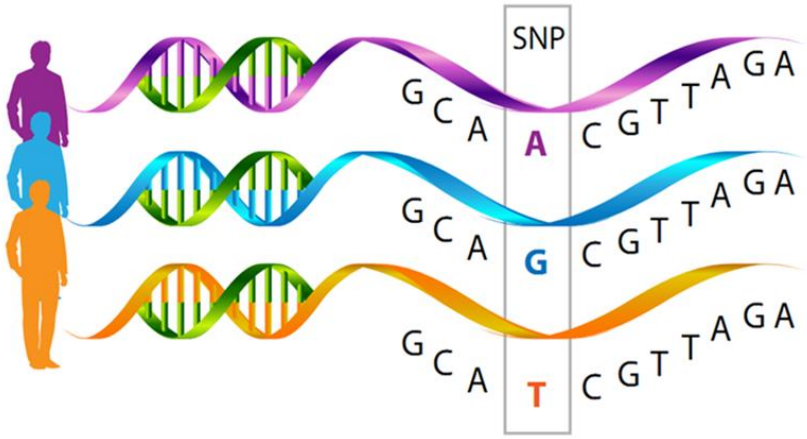
1. Genetic studies

2. Behavioral tests

3. Measurements of neurotransmitters and metabolites

Single Nucleotide Polymorphisms (SNPs)

- Single base variations located at a specific location on the genome
- Most abundant type of polymorphism
- Previous studies have linked polymorphisms associated with these neurotransmitters to behavior



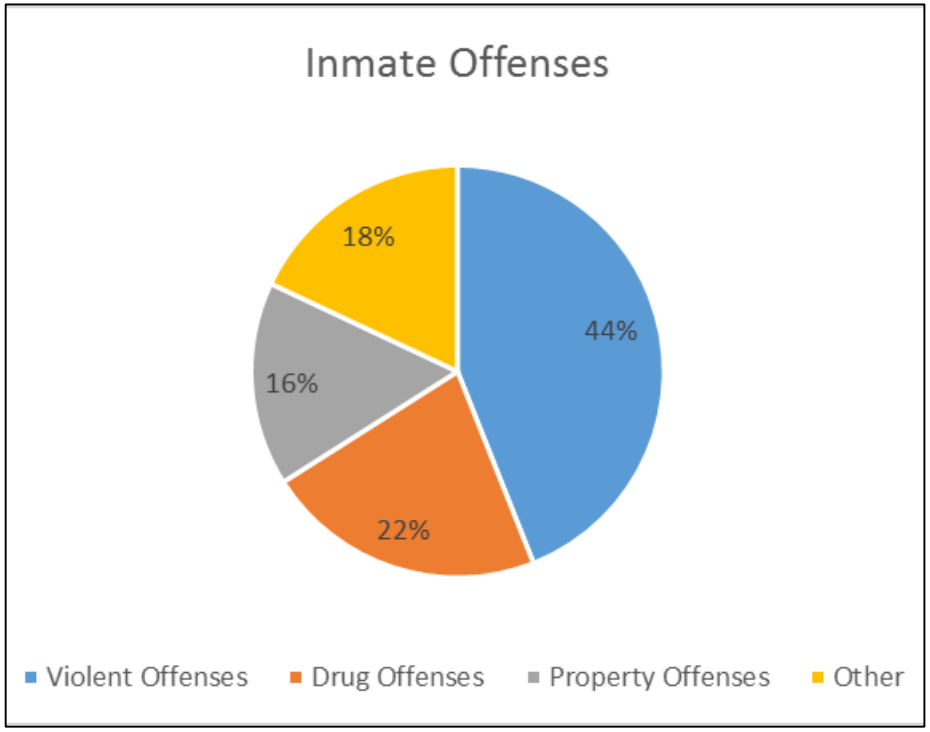
Methods/Materials

Samples

- Control - buccal swabs from Sam Houston State University students (N=100)
- Inmate swabs (N=100)
- Approved by Institutional Review Board
- Each individual participated in a survey designed to access multiple behaviors including psychopathy, empathy, and aggression

Sample Breakdown

	Control	Inmate
African American	58	58
Hispanic	25	25
Caucasian	12	12
Other	4	4



SNPs

Dopamine Turnover

- rs2283729 (MAOB)
- rs1799836 (MAOB)
- rs3788862 (MAOA)
- rs909525 (MAOA)
- rs979605 (MAOA)
- rs740603 (COMT)
- rs161115 (DβH)
- rs165599 (COMT)
- rs4680 (COMT)
- rs129882 (DβH)

Serotonin

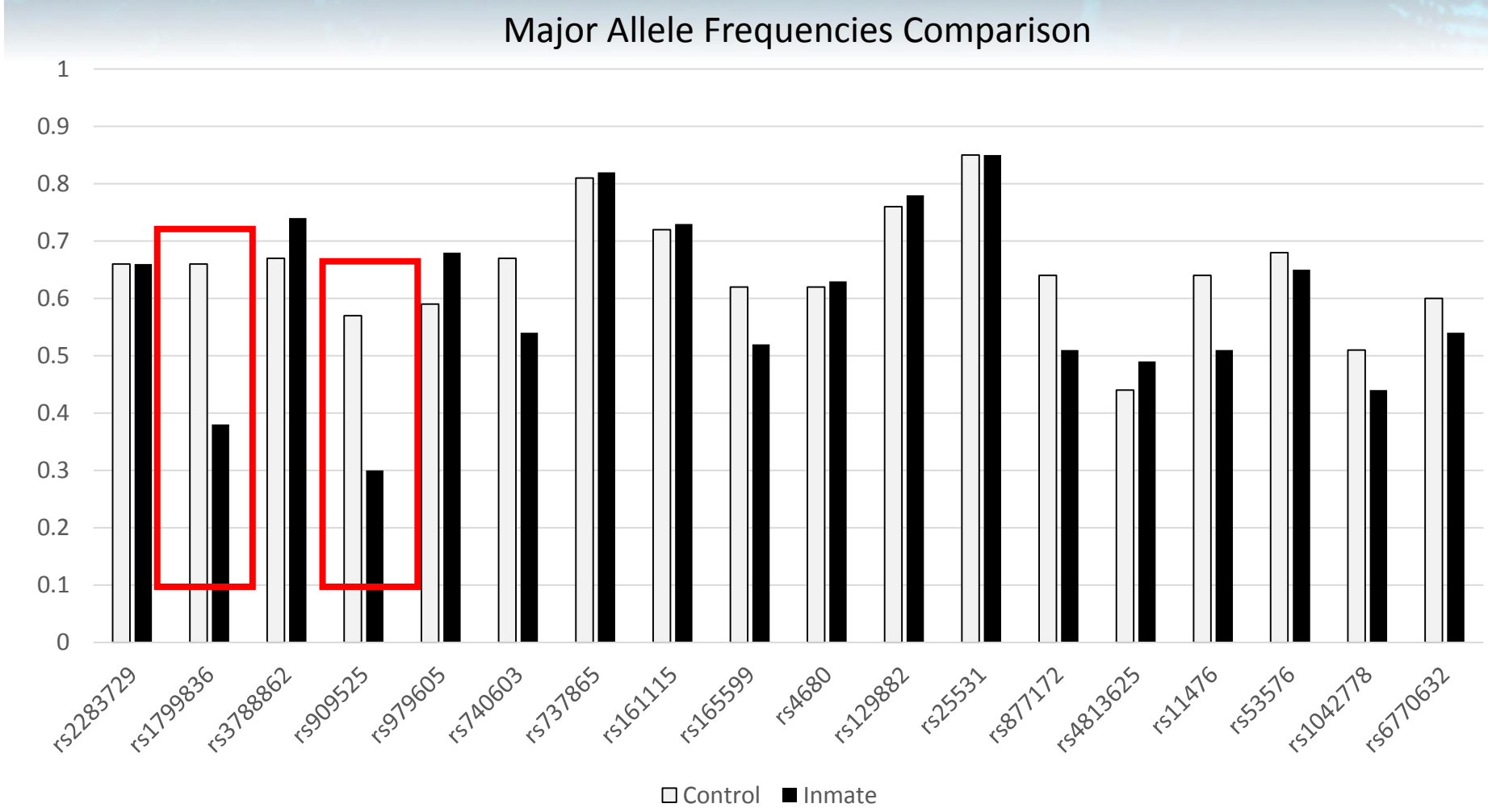
- rs25531 (SLCA4)

Oxytocin

- rs877172 (OXT)
- rs4813625 (OXT)
- rs11476 (CAV3)
- rs53576 (OXTR)
- rs1042778 (OXTR)
- rs6770632 (OXTR)

Results

Inmate – Control Analysis

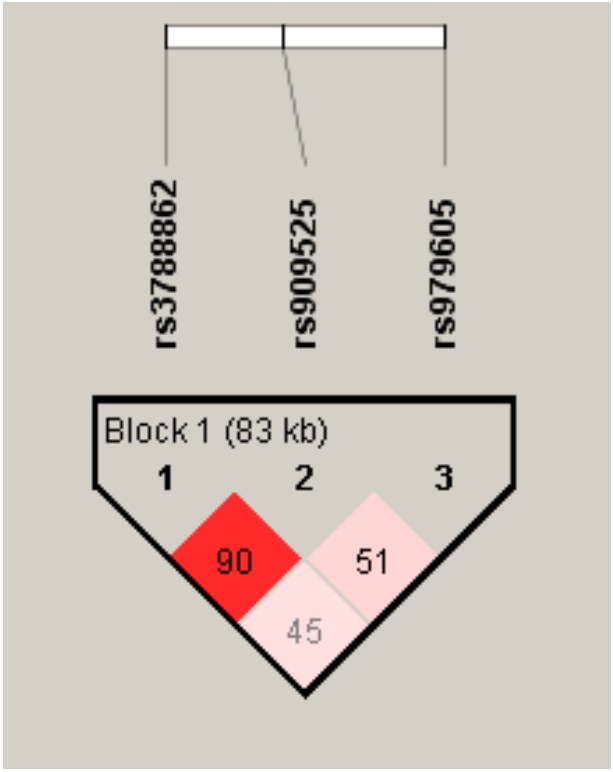


Inmate - Control Analysis

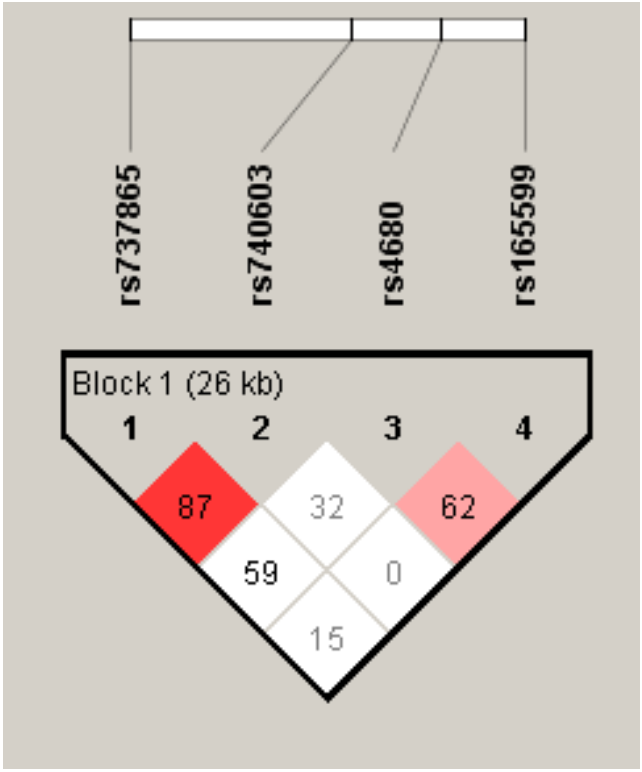
SNP	Gene	Associated Allele	Inmate : Control Ratio	Chi Square	P value
rs909525	MAOA	A	0.722 , 0.434	16.565	0.000047
rs1799836	MAOB	G	0.629 , 0.343	15.982	0.000064

Haplotype Analysis

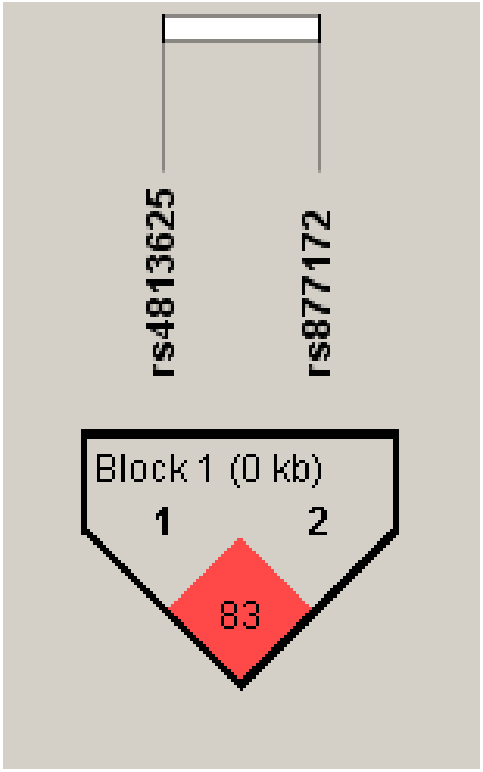
MAOA



COMT



OXT

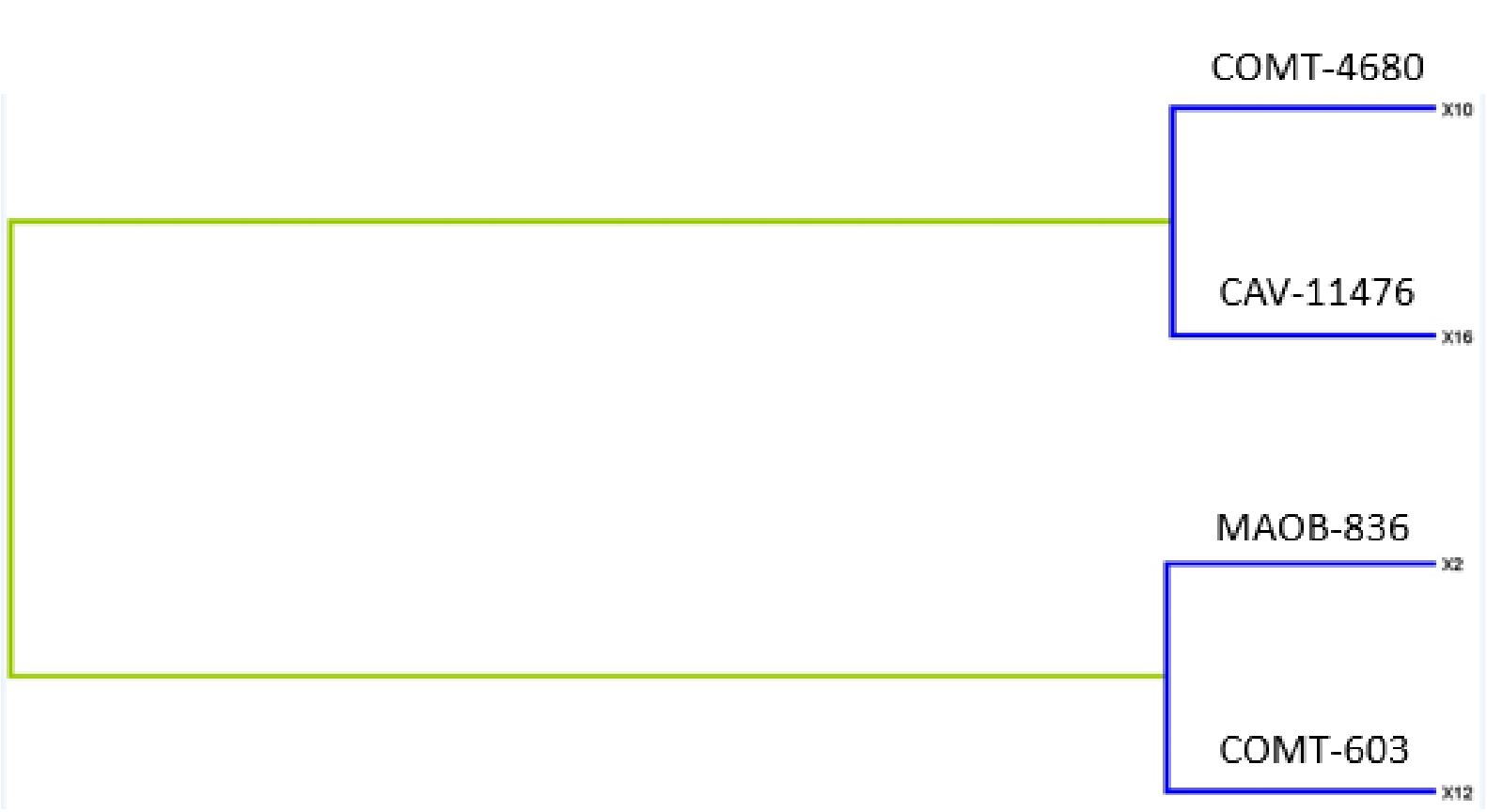


Haplotype	Freq.	Case, Control Ratios	Chi Square	p value
Haplotype Associations				
Block 1				
GAC	0.464	0.546, 0.384	5.205	0.0225
AGT	0.179	0.155, 0.202	0.75	0.3865
GAT	0.097	0.165, 0.030	10.147	0.0014
AGC	0.087	0.093, 0.081	0.089	0.7658
GGT	0.087	0.000, 0.172	18.238	1.949E-5
GGC	0.071	0.031, 0.111	4.749	0.0293
AAC	0.010	0.010, 0.010	0.0	0.9884

Name	Chi Square	Permutation p-value
rs909525	16.565	0.0000E0
Block 1: GGT	18.238	0.0000E0
Block 1: GAT	10.147	0.0150
Block 1: GAC	5.205	0.1260
Block 1: GGC	4.749	0.1950

P-value Bonferroni:
0.05/18 : **0.0028**

Multifactor Dimensionality Reduction



Within-Inmate Analysis

- Aggressive violence
- Serious ASB
- Low self control
- Prior violent crime rate
- Prior property crime rate
- Prior drug crime rate

How often have you…	NEVER	HARDLY EVER	SOMETIMES	OFTEN	ALWAYS OR ALMOST ALWAYS
Yelled at others when they have annoyed you	❑	❑	❑	❑	❑
Had fights with others to show who was on top	❑	❑	❑	❑	❑
Reacted angrily when provoked by others	❑	❑	❑	❑	❑
Taken things from other students	❑	❑	❑	❑	❑
Had temper tantrums	❑	❑	❑	❑	❑
Vandalized something for fun	❑	❑	❑	❑	❑

Previous Findings – Student Population

SNP	Gene	Behavior	Population	P value
rs6314	HTR2A	Antisocial	Hispanic	0.008
rs877172	OXT	Antisocial	Caucasian	0.001

P-value Bonferroni:
0.05/5 : **0.01**

Understanding Behavior

1. Genetic studies

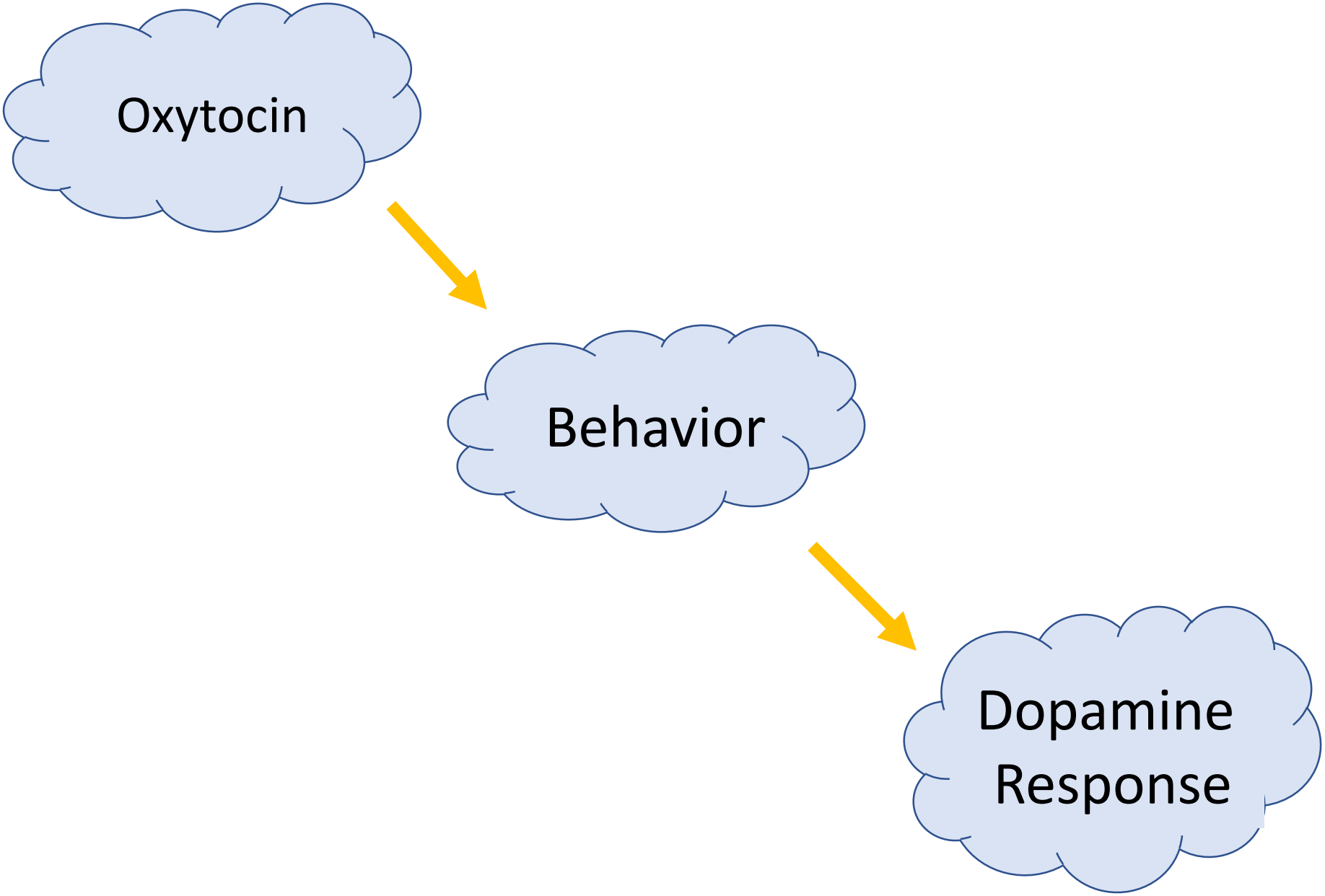
2. Behavioral tests

3. Measurements of neurotransmitters and metabolites

Next Objectives

- Test the influence of central oxytocin on aggression and sociability using behavioral tests in mice

- Measure the response of dopamine and metabolites to oxytocin from filtrate of homogenized brain tissue

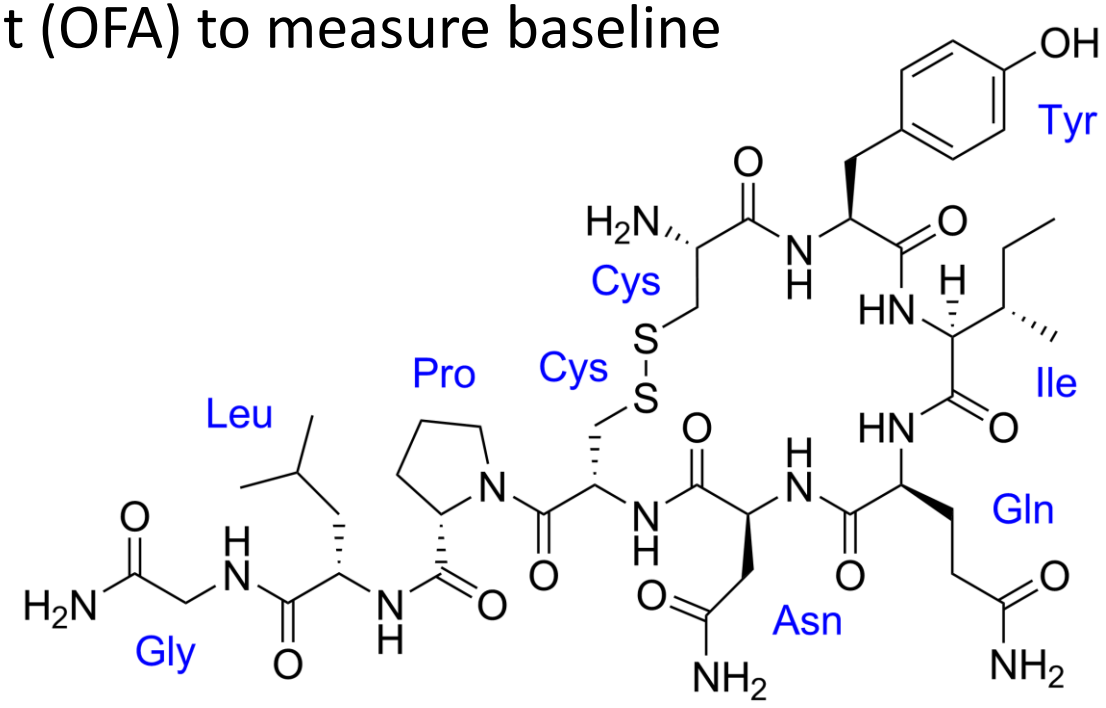

Oxytocin
Behavior
Dopamine
Response

Oxytocin & Dopamine

- Accumulated data has shown the neuroactive properties of oxytocin and its capability to reduce the abuse potential in drugs
  - Oxytocin inhibits the development of tolerance (acute and chronic) to heroin
  - It was reported that oxytocin antagonized the increased utilization of dopamine in studies with cocaine
  - Oxytocin decreases the release and receptor binding of dopamine in the mesolimbic structures of the brain

Behavioral Assessment

- Test the influence of central oxytocin on aggression and sociability using behavioral tests in mice (C57)
  - Open field assessment (OFA) to measure baseline



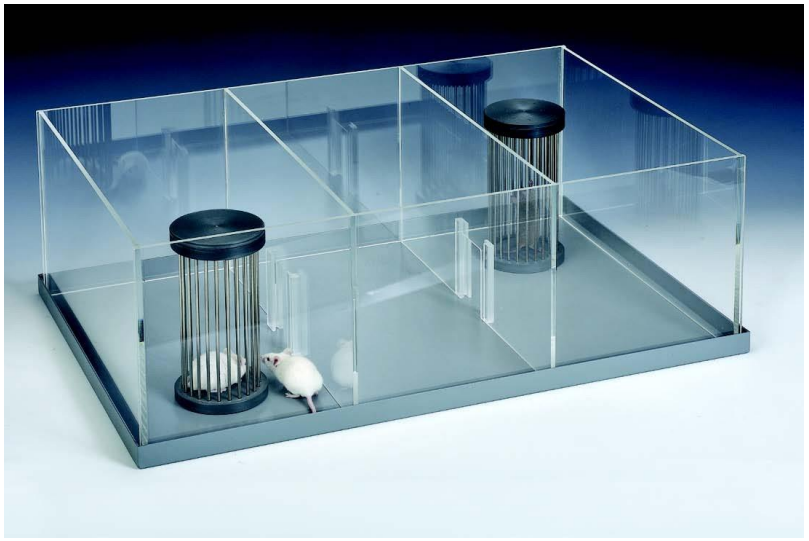
Resident Intruder Test

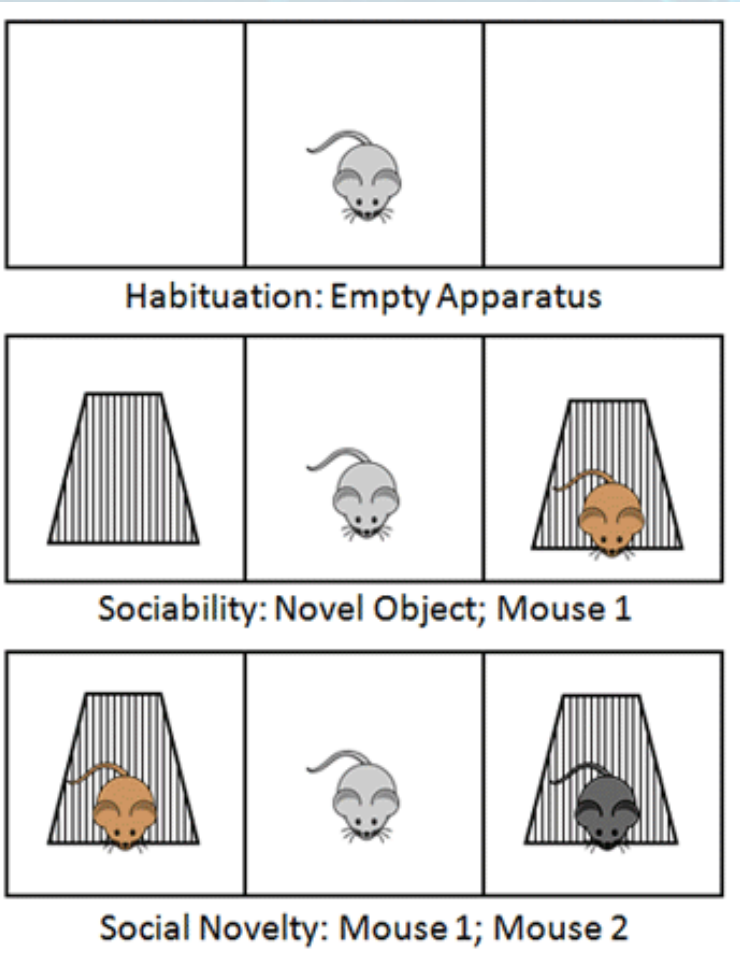
- Test for aggression

- **Day 1: juvenile intruder mouse is introduced into the cage**
  - **Interaction is recorded for 2 min**
- **Day 2: experiment is repeated with same intruder mouse**
- **Day 3: experiment is repeated with new juvenile intruder**

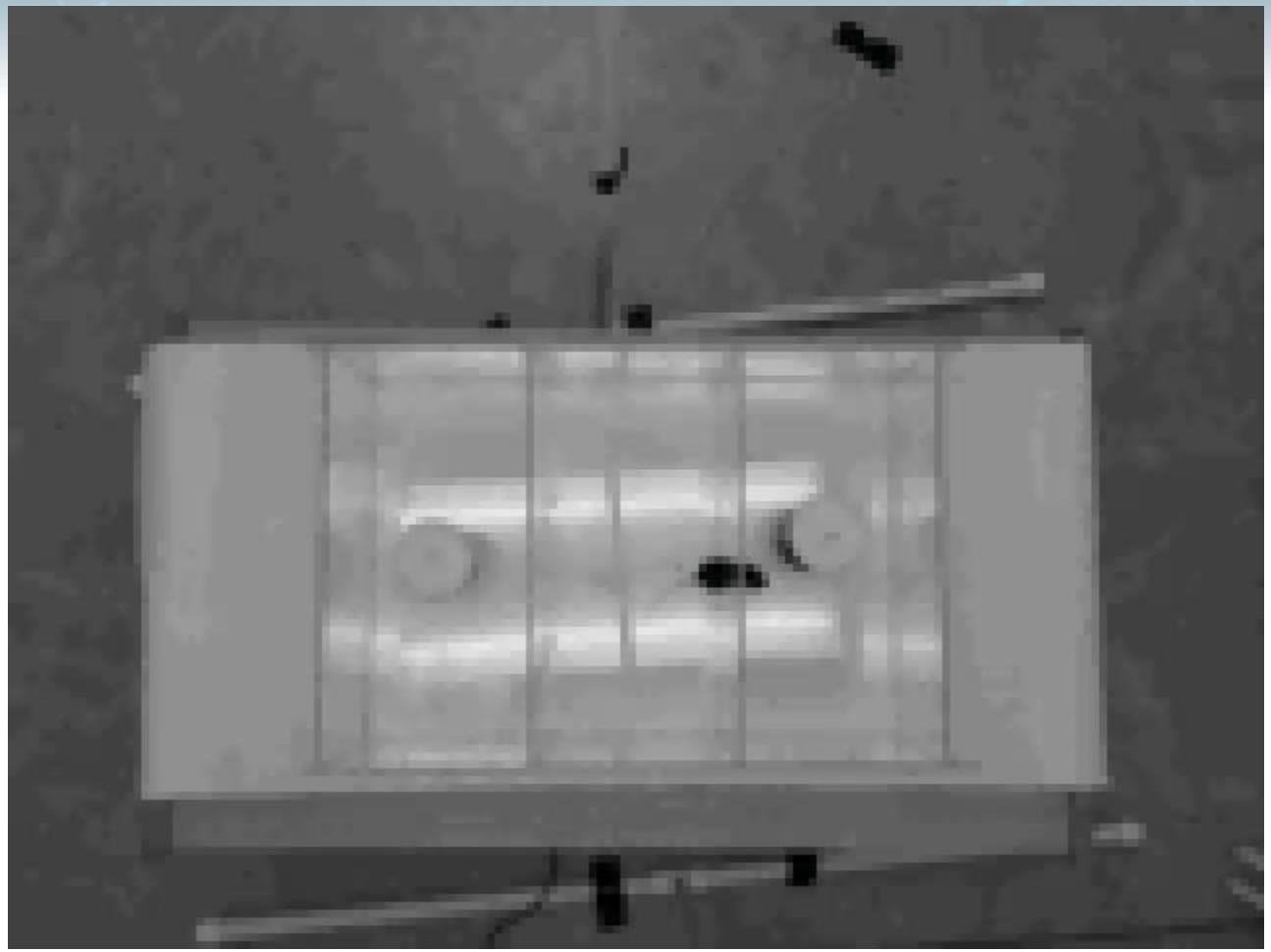
Three-Chambered Sociability Test

- Test for sociability

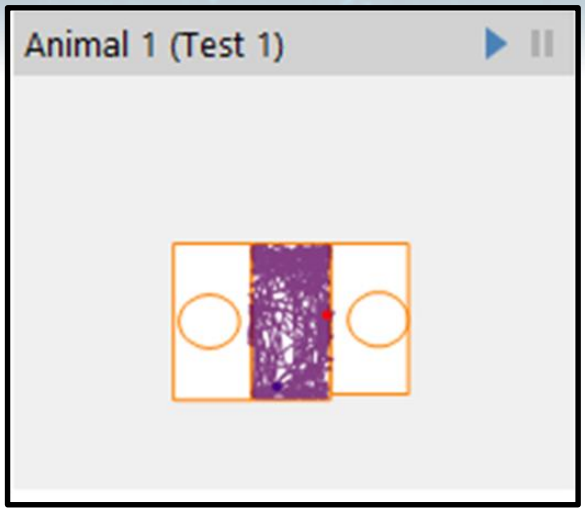


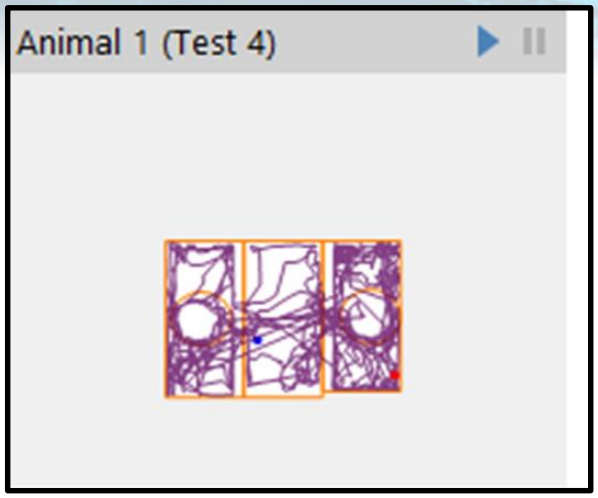


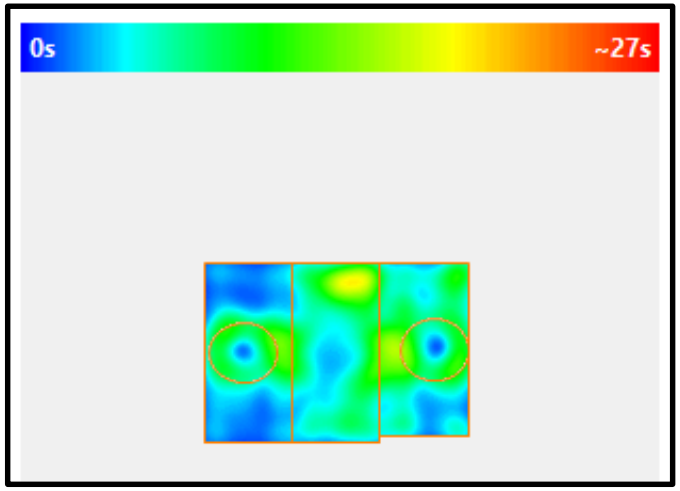
Sociability Apparatus



ANY-maze Software







Pilot Sociability Data

Phase	Average Time Spent in Zone M	Average Time Spent in Zone O
Habituation	-	-
Sociability (Mouse / Object)	96.88 s	66.06 s
Social Novelty (Mouse + New Mouse)	66.76 s	90.44 s

Understanding Behavior

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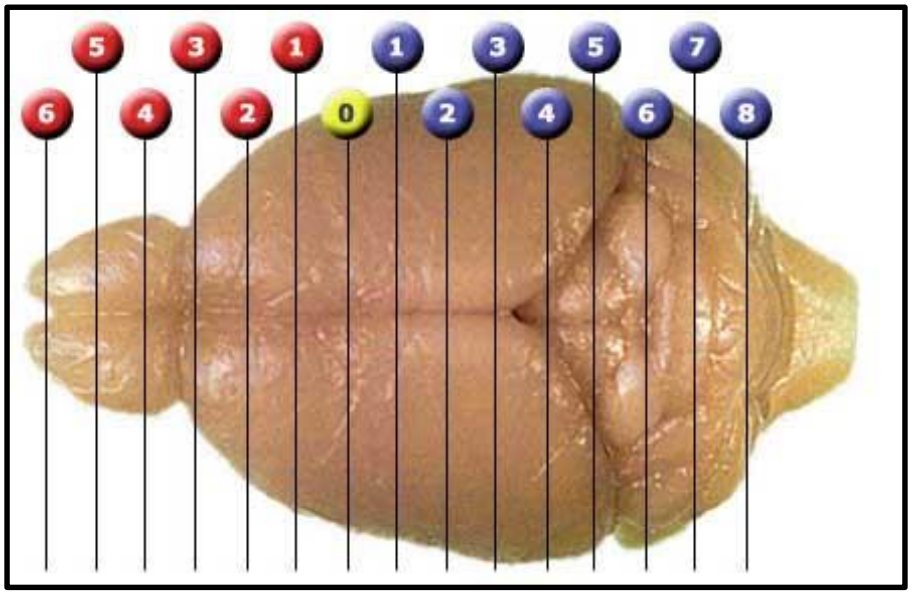
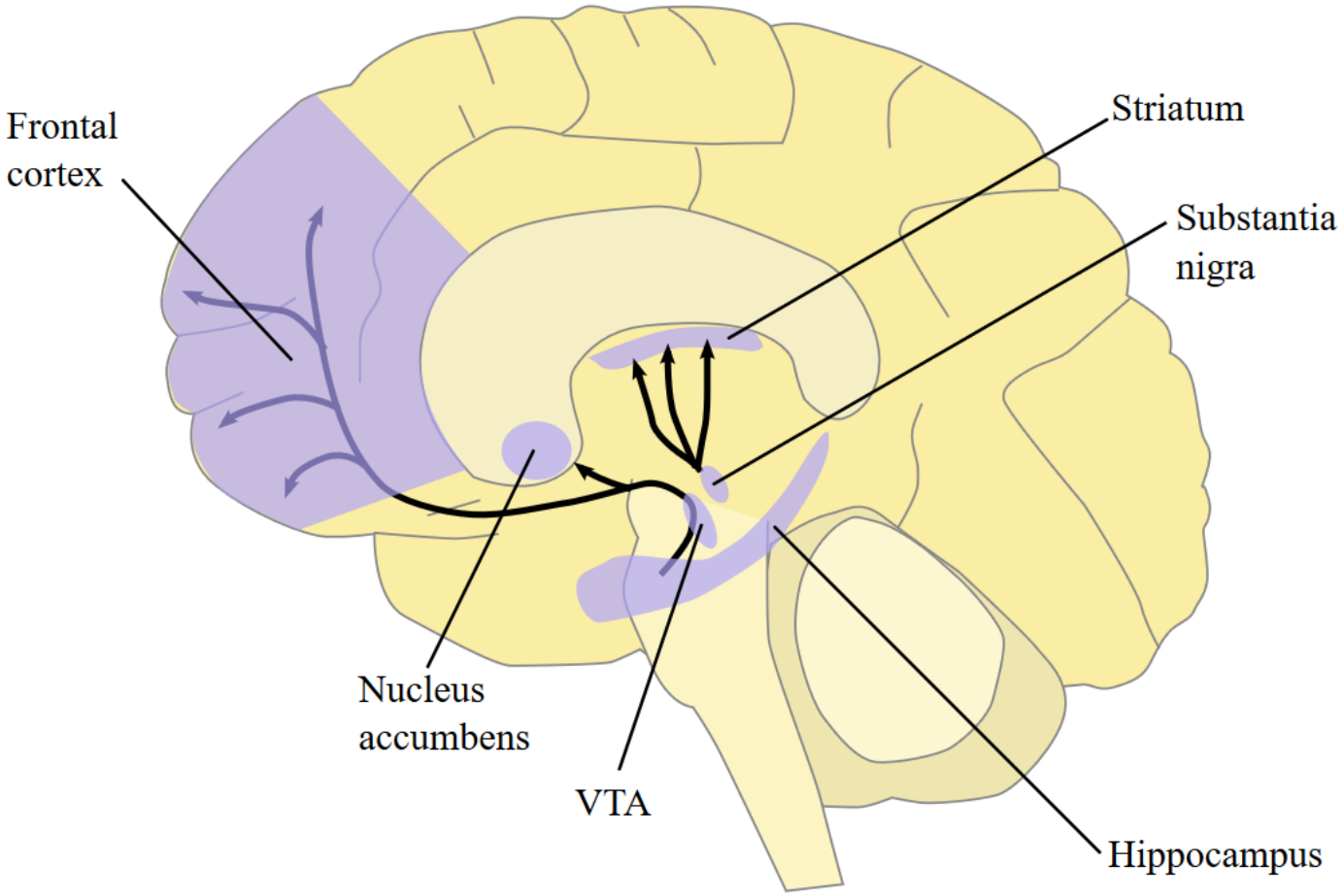
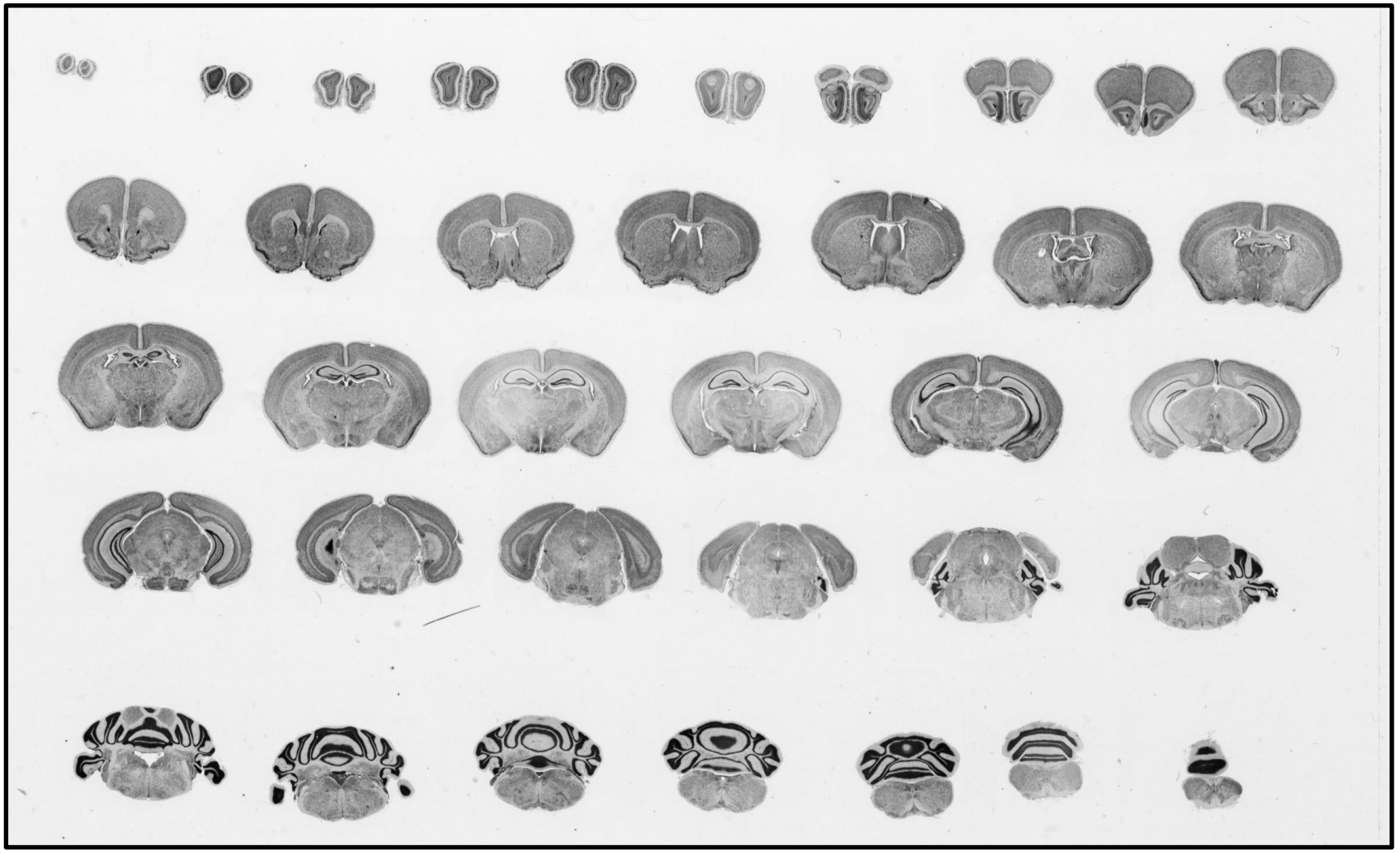


Neuroanatomy

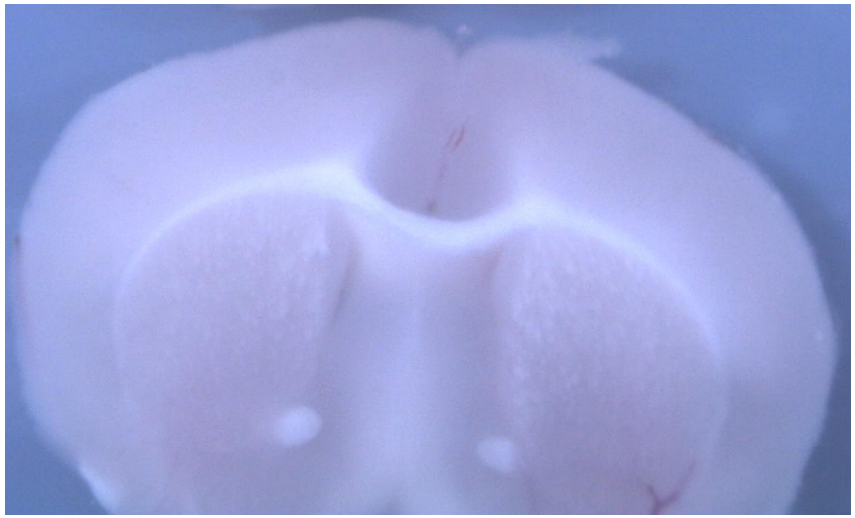


Collection Sites:

1. Motor Cortex 1 (frontal)
2. Motor Cortex 2 (frontal)
3. Cingulate cortex
4. Frontal top putamen
5. Frontal bottom putamen
6. Caudal top putamen
7. Caudal bottom putamen
8. Nucleus accumbens
9. Hippocampus frontal
10. Hippocampus caudal
11. Ventral tegmental area



Brain Slice



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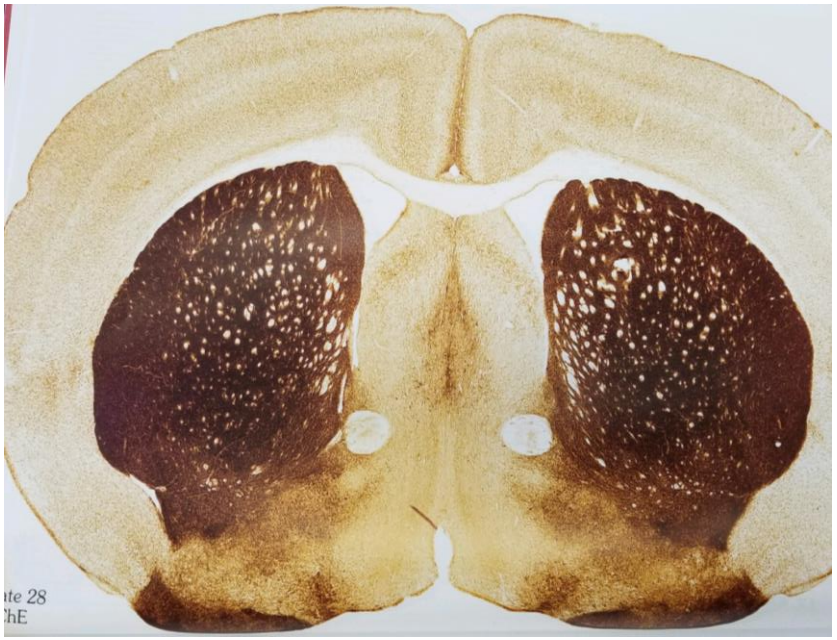

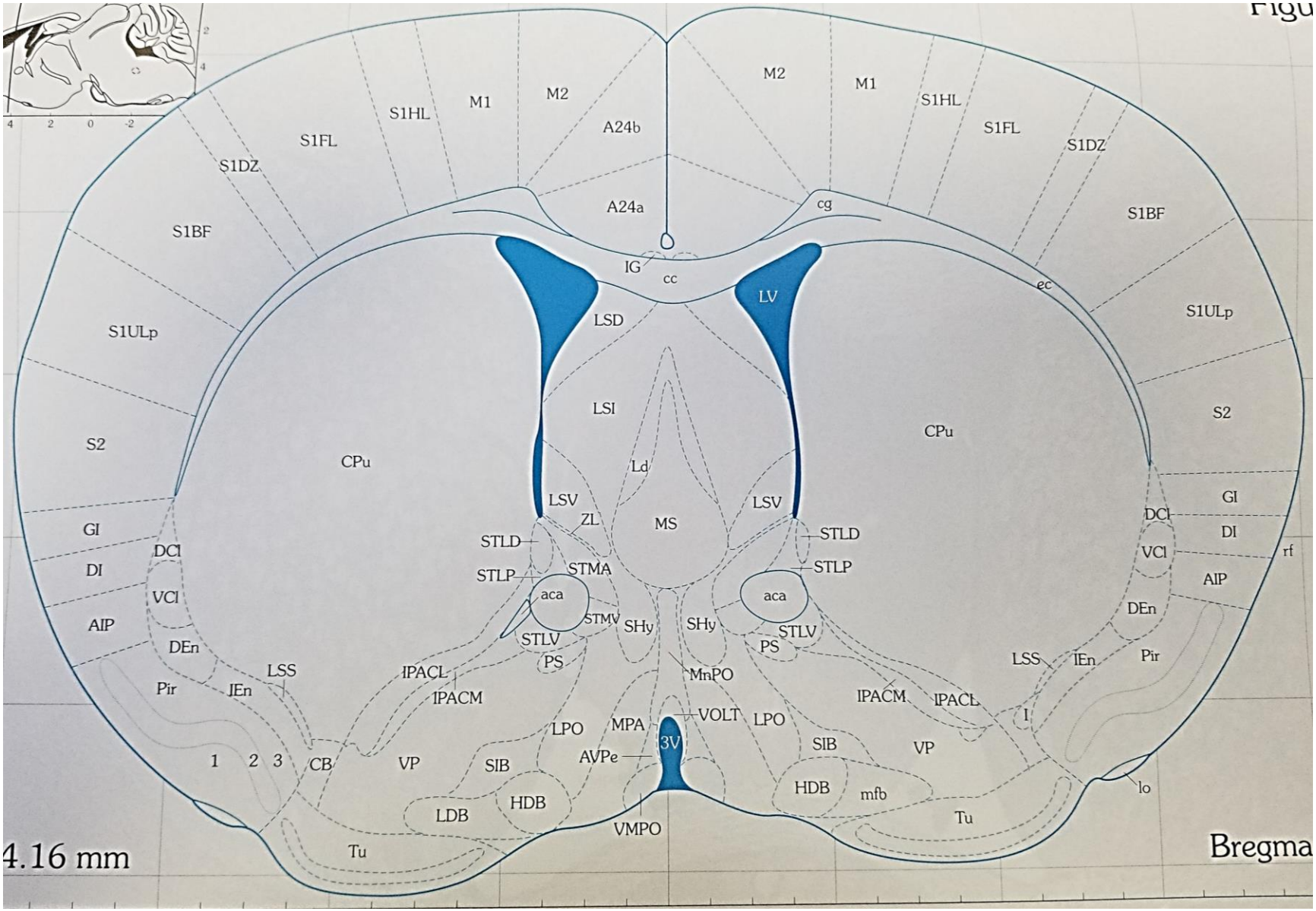
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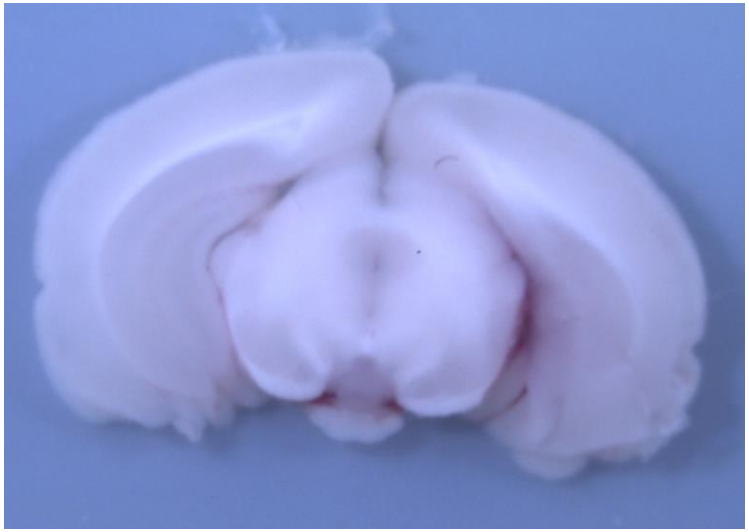

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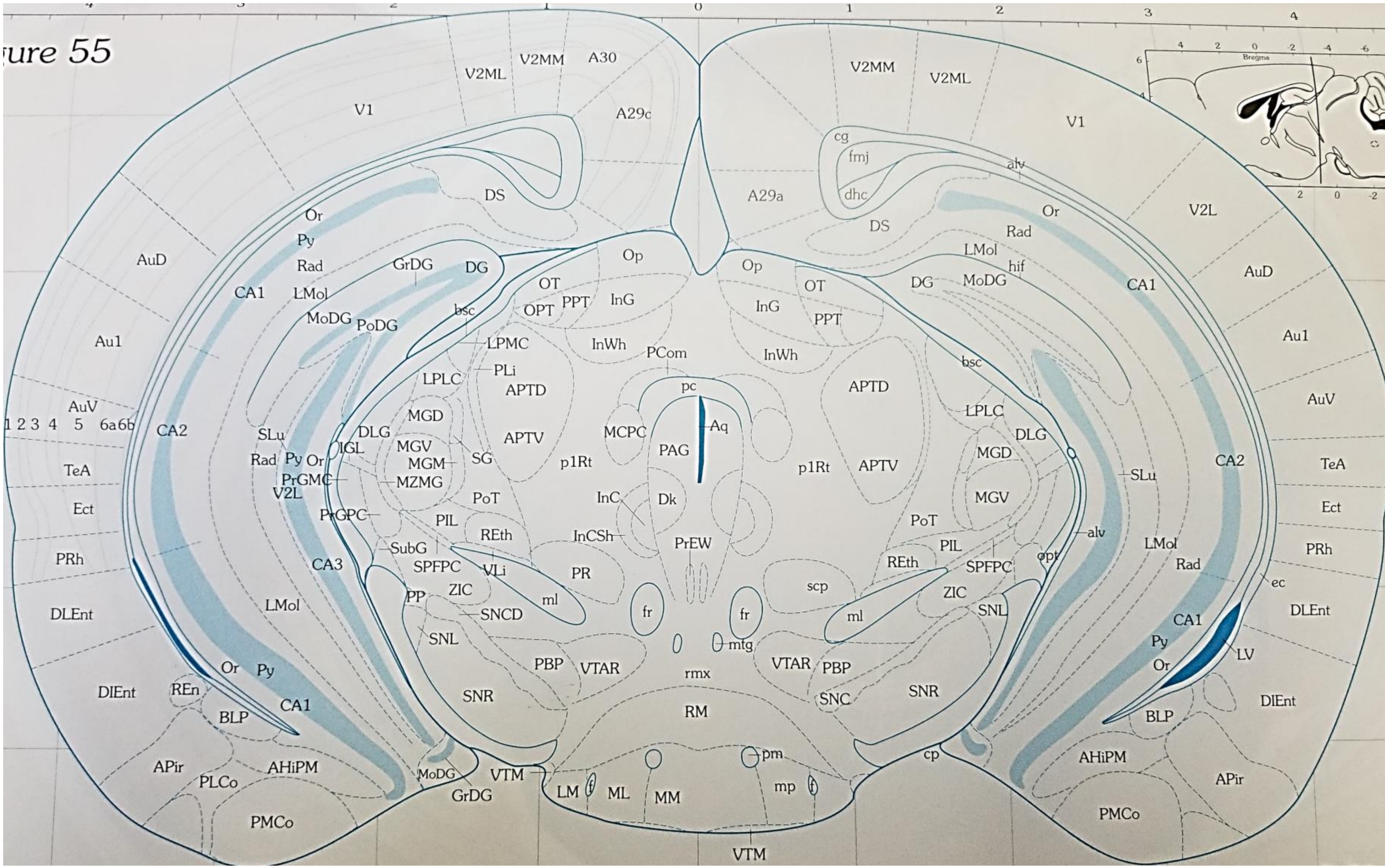

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SLu
CA2
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MGV
PoT
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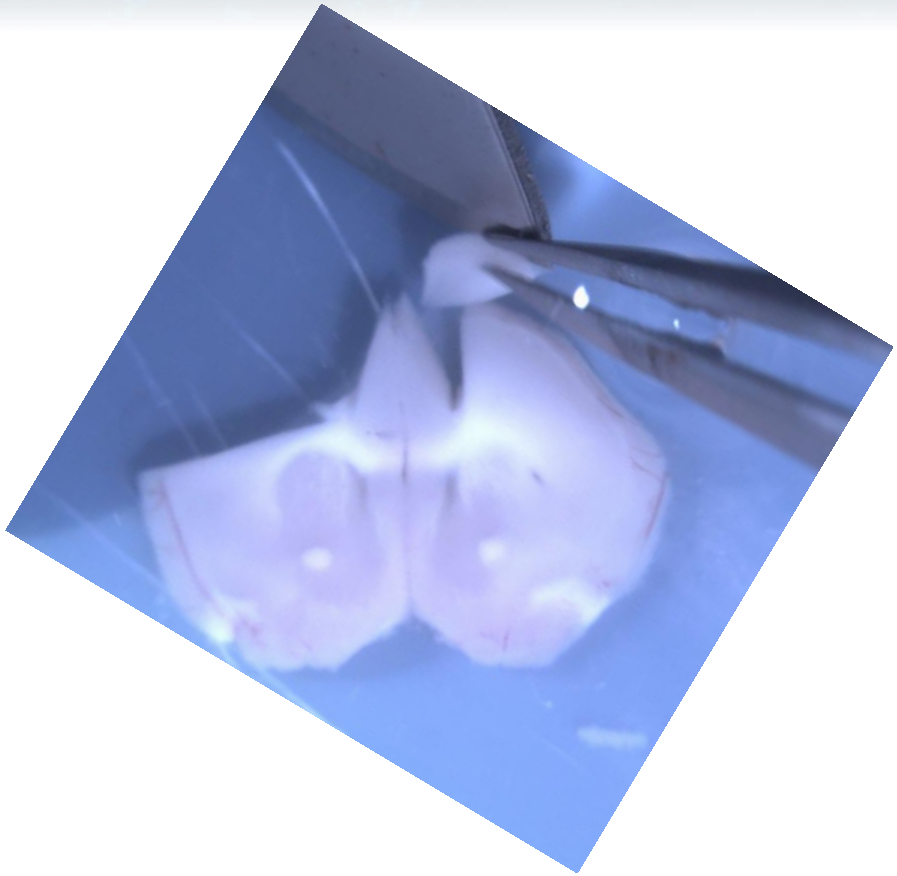
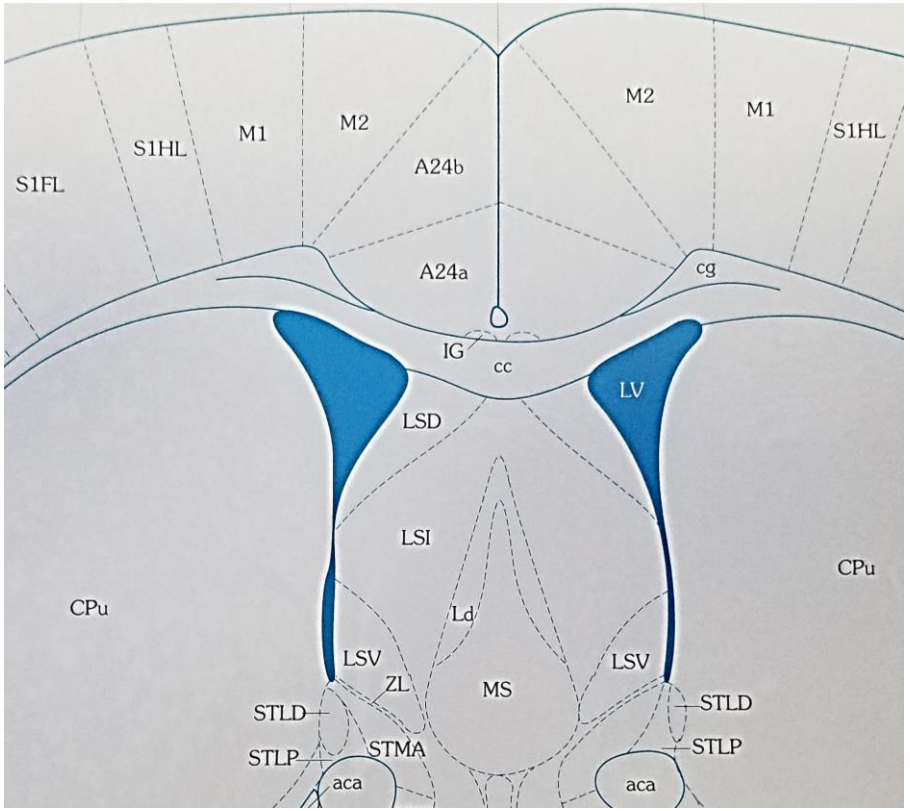
Extraction of motor cortex two (M2)





Measuring Dopamine Response

- The filtrate will be injected directly into an LC system
  - Separate compounds in a mixture based on physical and chemical properties
    - Size, charge, affinity for column

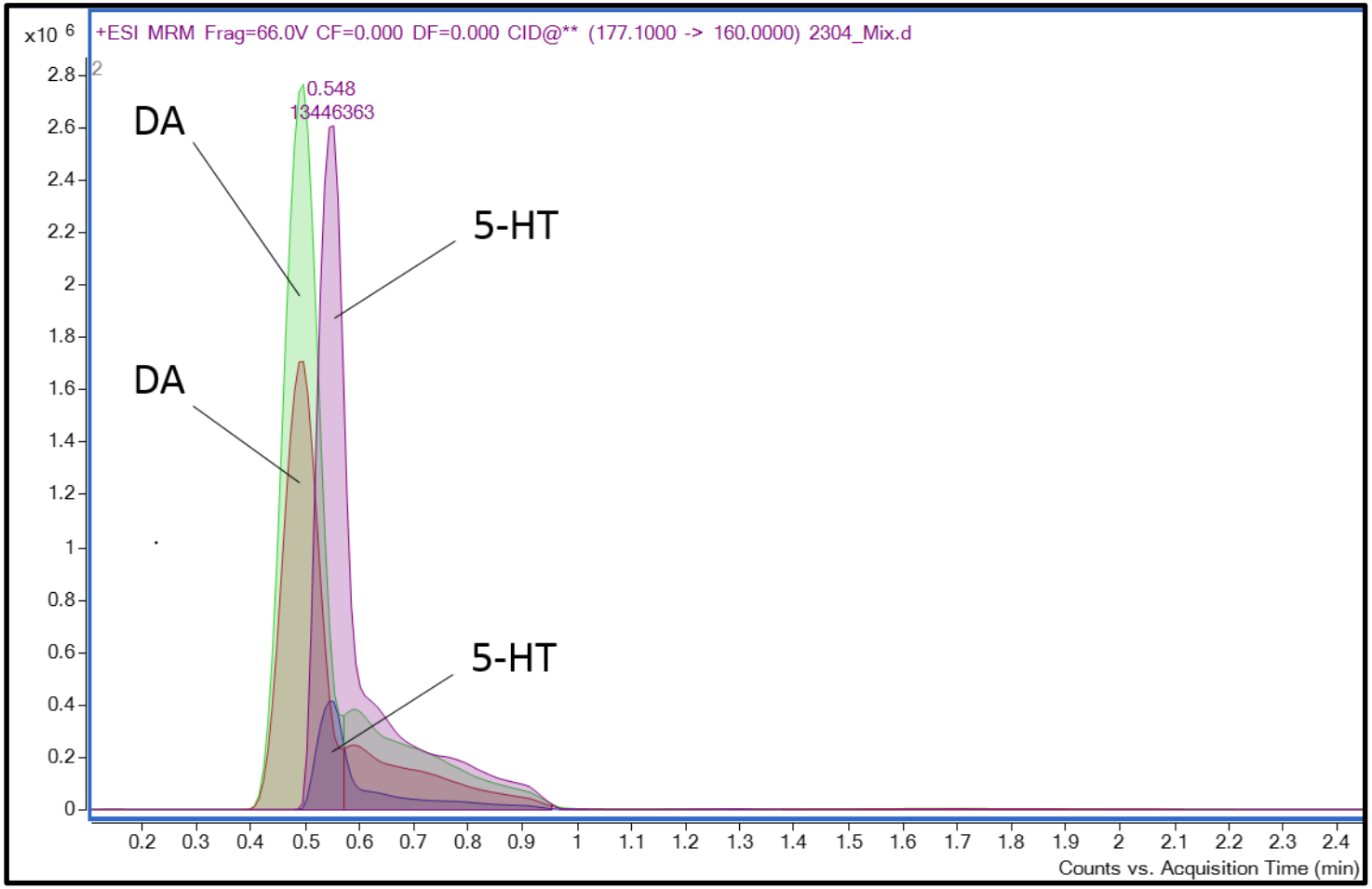
Neurotransmitters

Dopamine

- Dopamine (DA)
- 3,4-Dihydroxyphenylacetic acid (DOPAC)
- Homovanillic acid (HVA)

Serotonin

- Serotonin (5-HT)
- 5-Hydroxyindoleacetic acid (5-HIAA)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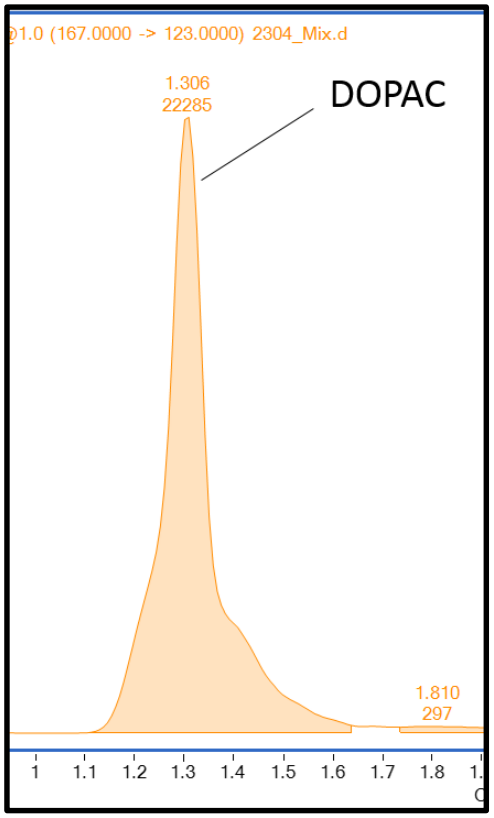
Counts vs. Acquisition Time (min)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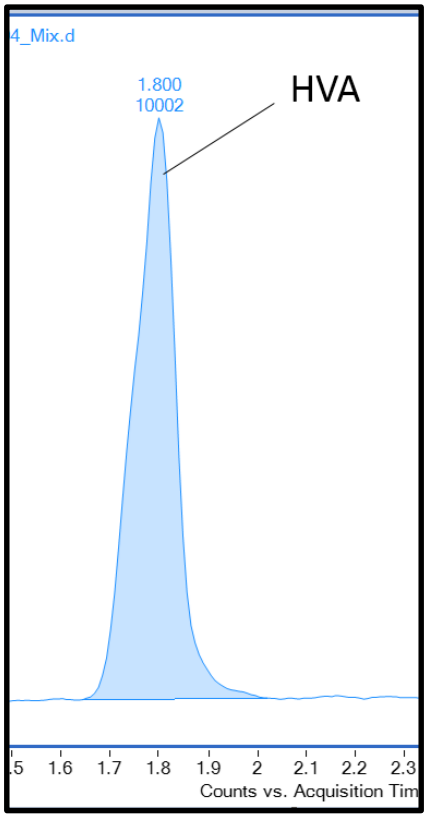
1.7
1.8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10002
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1.7
1.8
1.9
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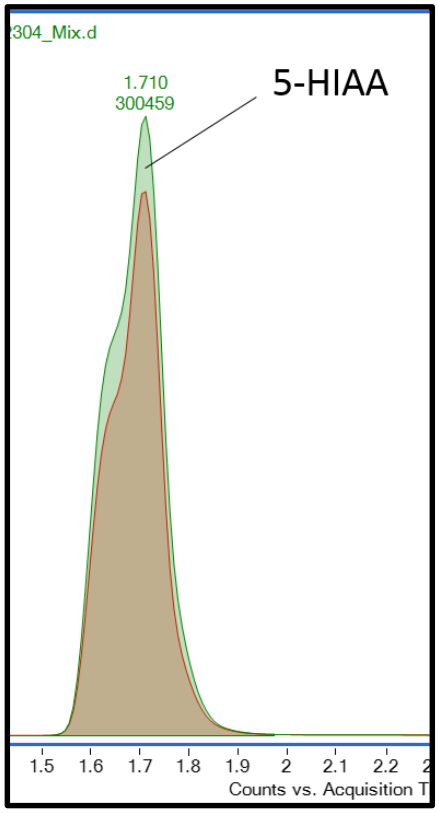
2.2
2.3
Counts vs. Acquisition Tim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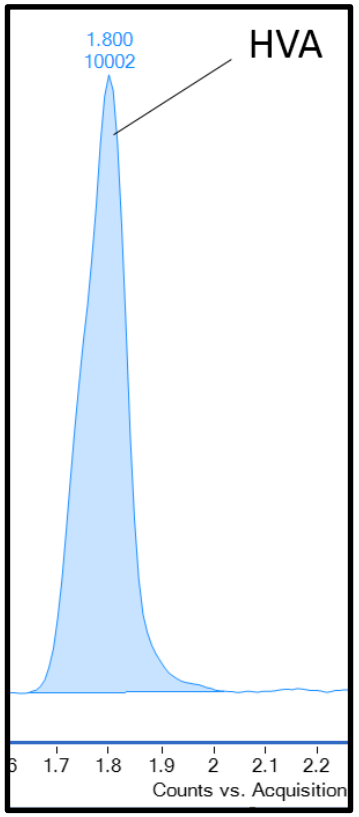
Counts vs. Acquisition T


1.800
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Counts vs. Acquisition

Potential Impact

- Better understanding of the mechanisms that influence behavior can provide opportunities for early intervention and remediation of effects
- Studies on the influence of these neurotransmitters can help predict adult mental health problems including depression, anxiety, and emotional stability
- Furthermore, it can show biological vulnerabilities and help explain how to treat deficiencies or excessiveness of these neurotransmitters

Potential Impact (cont.)

- The answer to this work may help explain:

1. Genetic influence on social behavior
2. Mechanisms and central pathways involved
3. Scientific explanation about the origin and development of aggressive and antisocial behavior

FSF Emerging Forensic Scientist Award
Paper Presentation

Acknowledgements

- Sam Houston State University:
  - Department of Forensic Science
    - Dr. David Gangitano, PhD
    - Dr. Hughes-Stamm, PhD
    - Dr. Sarah Kerrigan, PhD
    - Maddie Roman, BS
    - Britni Skillman, BS
  - Department of Criminal Justice
    - Dr. Todd Armstrong, PhD
    - Dr. Danielle Boisvert, PhD
    - Dr. Jessica Wells, PhD
  - Science Annex
    - Ed Tivador, BS
- Baylor College of Medicine
  - Department of Psychiatry
    - Dr. Ramiro Salas, PhD

Questions

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