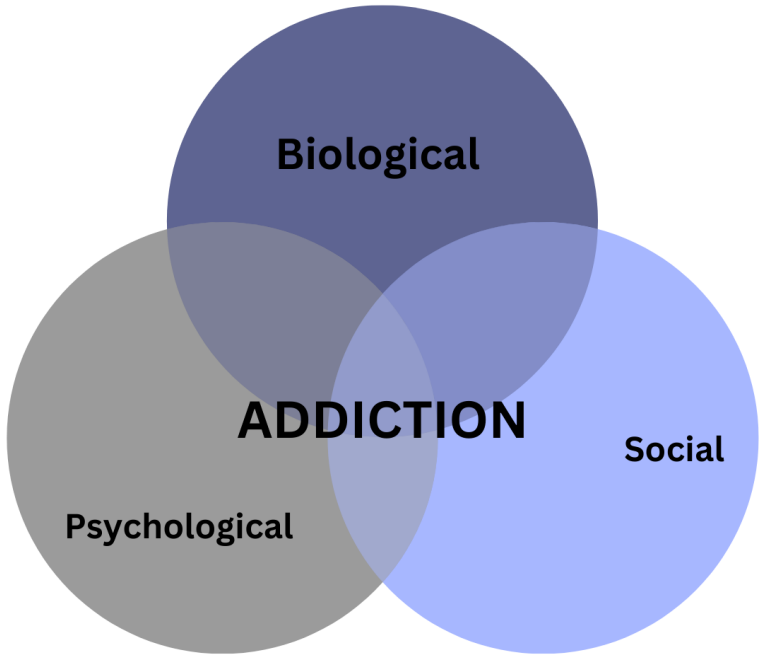
Behavioral Health in the Justice System

Jacqueline Hall

Chief Operating Officer of Wired For Addiction® & Wired BioHealth™

THE REDHEADED STEPCHILD OF HEALTHCARE

ADDICTION IS A COMPLEX DISEASE NOT A MORAL FLAW



WWW.WIREDFORADDICTION.COM

MENTAL HEALTH COMPLEXITIES ARE NOT WEAKNESSES

- 1:3 reports a mental health condition
- 1 in 7 college students report suicidal ideations
- 80% of individuals with <90 days of sobriety relapse
- COVID-19 pandemic increased prevalence of anxiety and depression by 25%
- Fentanyl poisonings and overdose related deaths are the #1 killer of Americans 18-46 years old
- Trauma is more than a way to qualify a negative experience

MENTAL HEALTH & ADDICTION IN CRIMINAL JUSTICE

The American Psychological Association reports:

- 64% of incarcerated individuals in **jail** report mental health concerns
- 54% of incarcerated individuals in **state prison** report mental health concerns
- 45% of incarcerated individuals in **federal prison** report mental health concerns

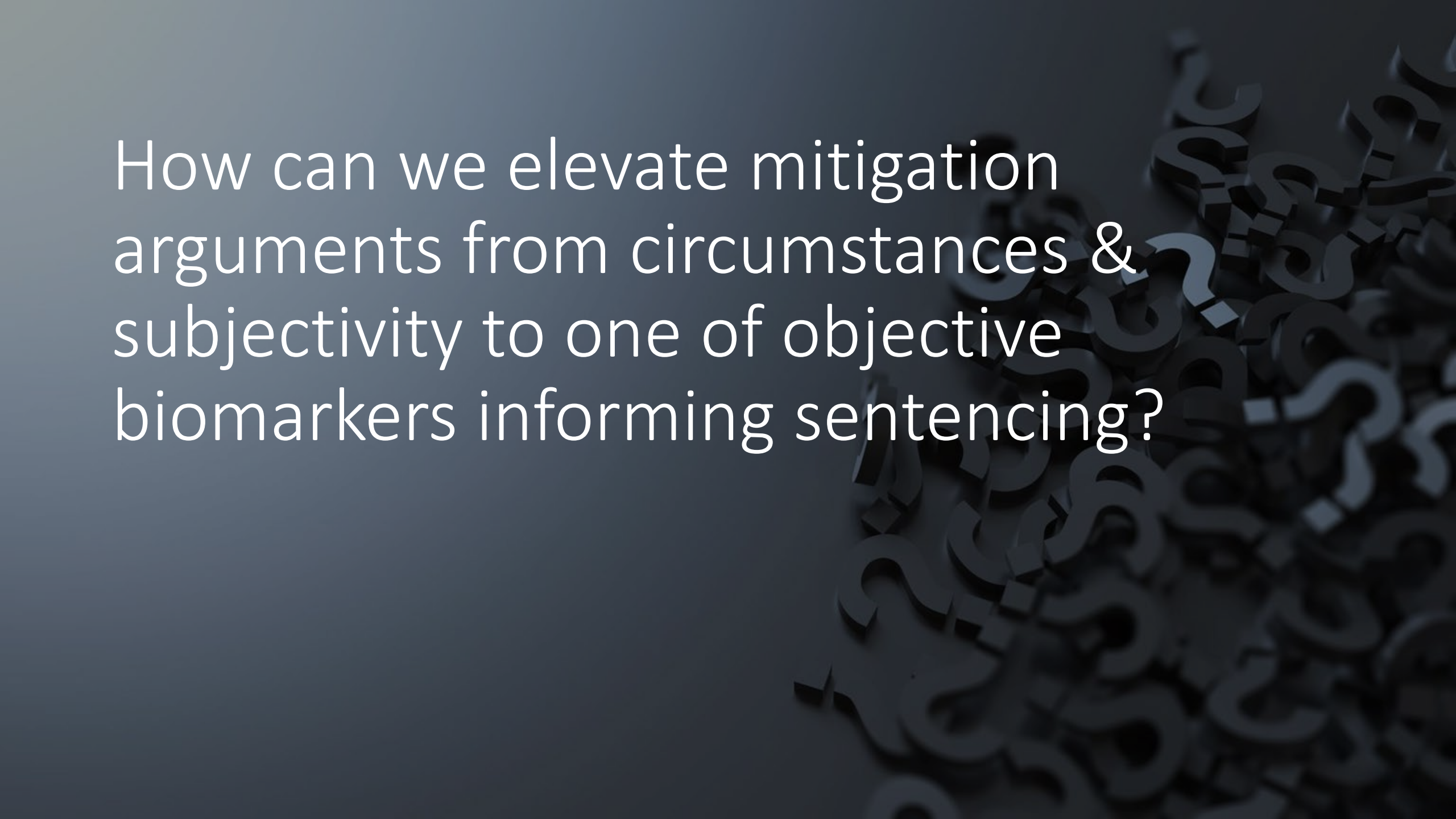
The National Council on Alcoholism and Drug Dependence, Inc. reports:

- Alcohol plays a role in 40% of all violent crimes
- 80% of offenders abuse drugs or alcohol
- 60% of individuals arrested for most types of crimes test positive for illegal drugs at arrest
- 18% of all crime is linked to the convicted individual seeking money for drugs
- 40% of all traffic fatalities are alcohol related

4/5 of children and teen arrestees in state juvenile justice systems admit having substance abuse and addiction problems.

- Only 69k of 1.9 mil receive treatment

80 Times


How can we elevate mitigation arguments from circumstances & subjectivity to one of objective biomarkers informing sentencing?

Stop Relying On **Subjective** Vocabulary & Interpretation of Aberrant Behaviors

Establish Addiction as a Biopsychosocial Disease

Addiction: A chronic, relapsing disorder characterized by compulsive drug seeking and use despite adverse consequences.

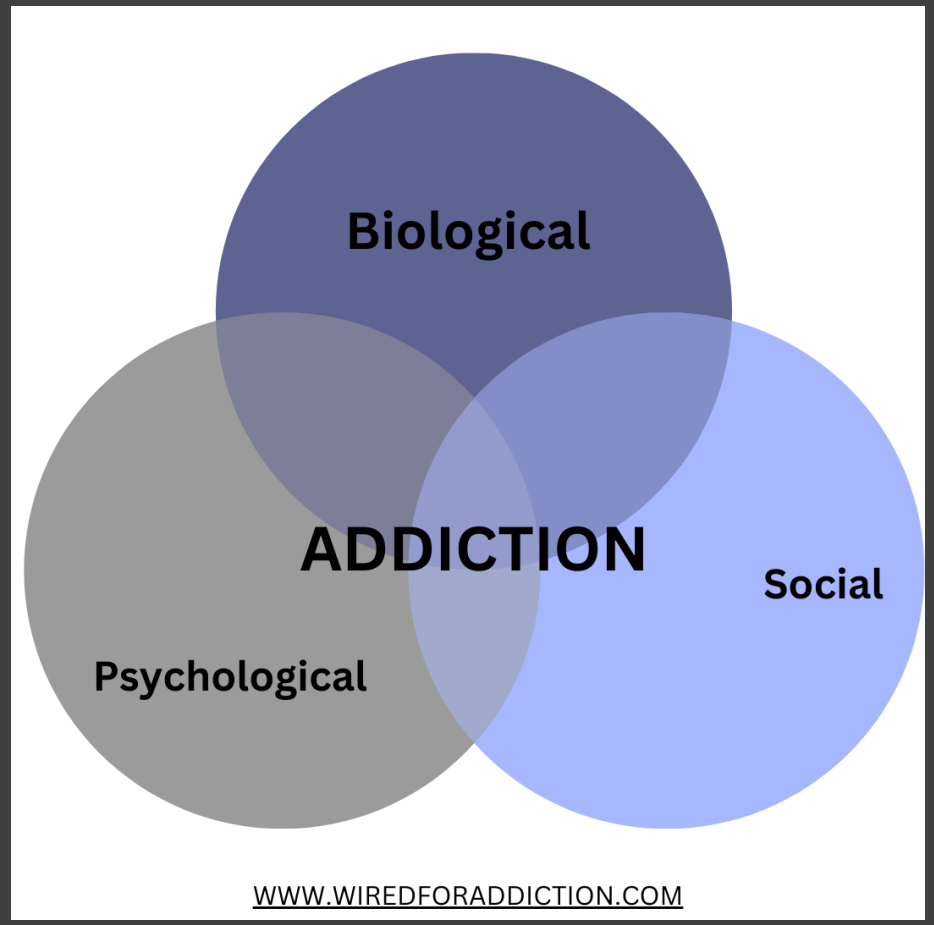
Disease: Any harmful deviation from the normal structural or functional state of an organism.

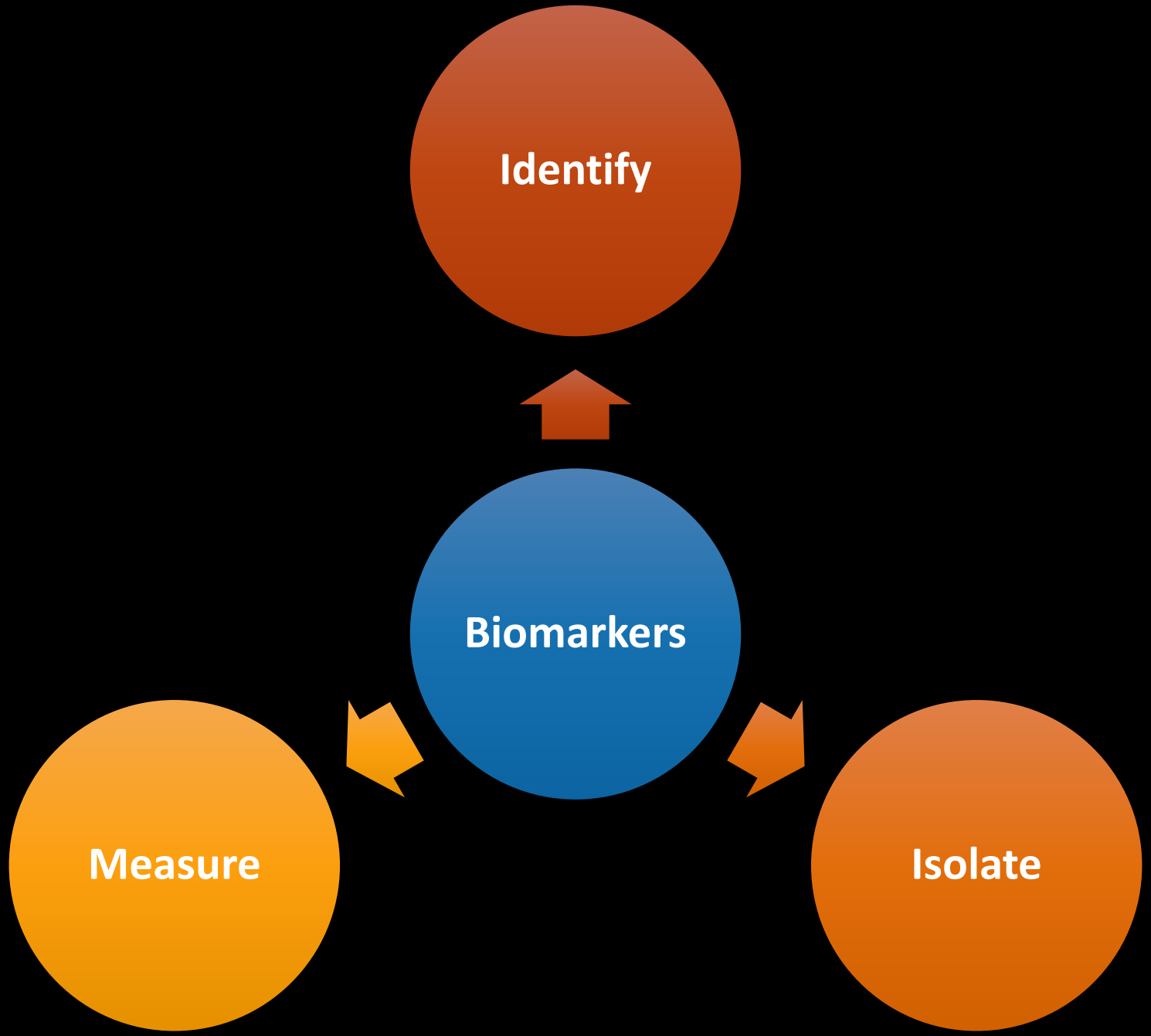
Addiction is not a single molecule disease nor is it a moral flaw.

Biopsychosocial Disease

Like feelings and behaviors, the psychological & social components can be argued & criticized.

The biological cannot as it very much meets the definition of a disease through the inclusion of *biomarkers.*




Identify
Biomarkers
Measure
Isolate

Biometrics vs Biomarkers

Biometrics are data points such as heart rate variability, resting heart rate, respiratory rate, SpO2, sleep performance, and skin temperature.

Wearables collect data of sleep, recovery, and stress.

Reactive by measuring symptomatic expression.

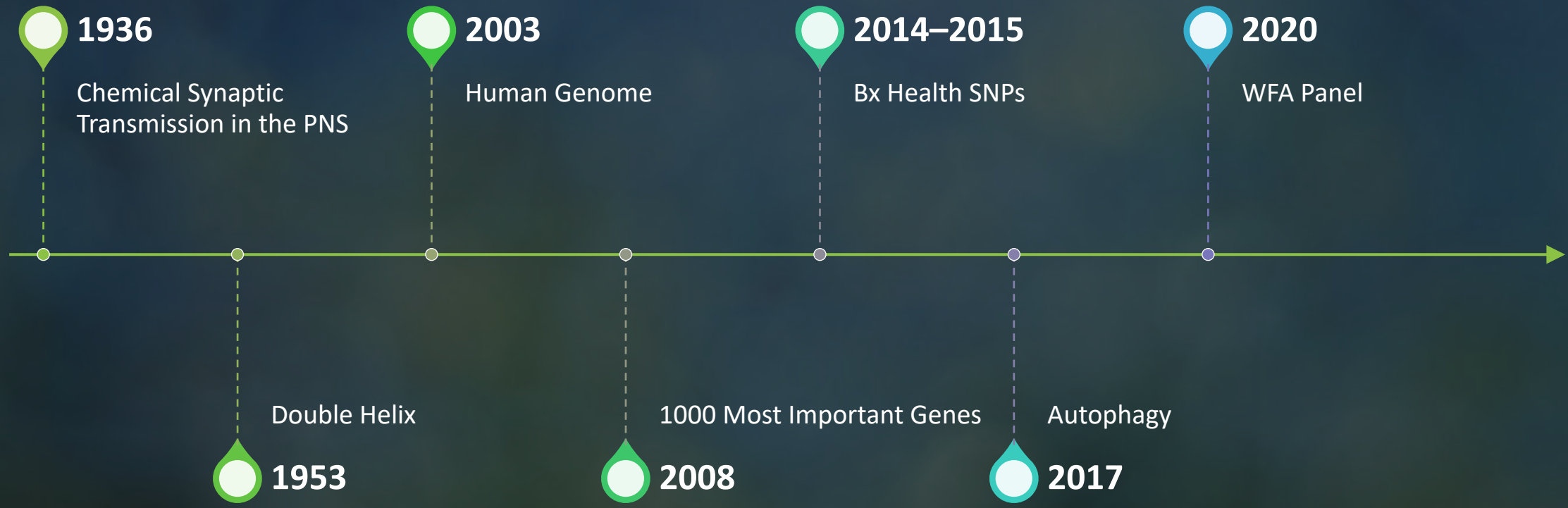
Biomarkers are molecules that indicate normal or abnormal process taking place in your body.

May indicate a disease state or developing condition.

Identify, isolate, and measure the biology creating the symptomatic expression.

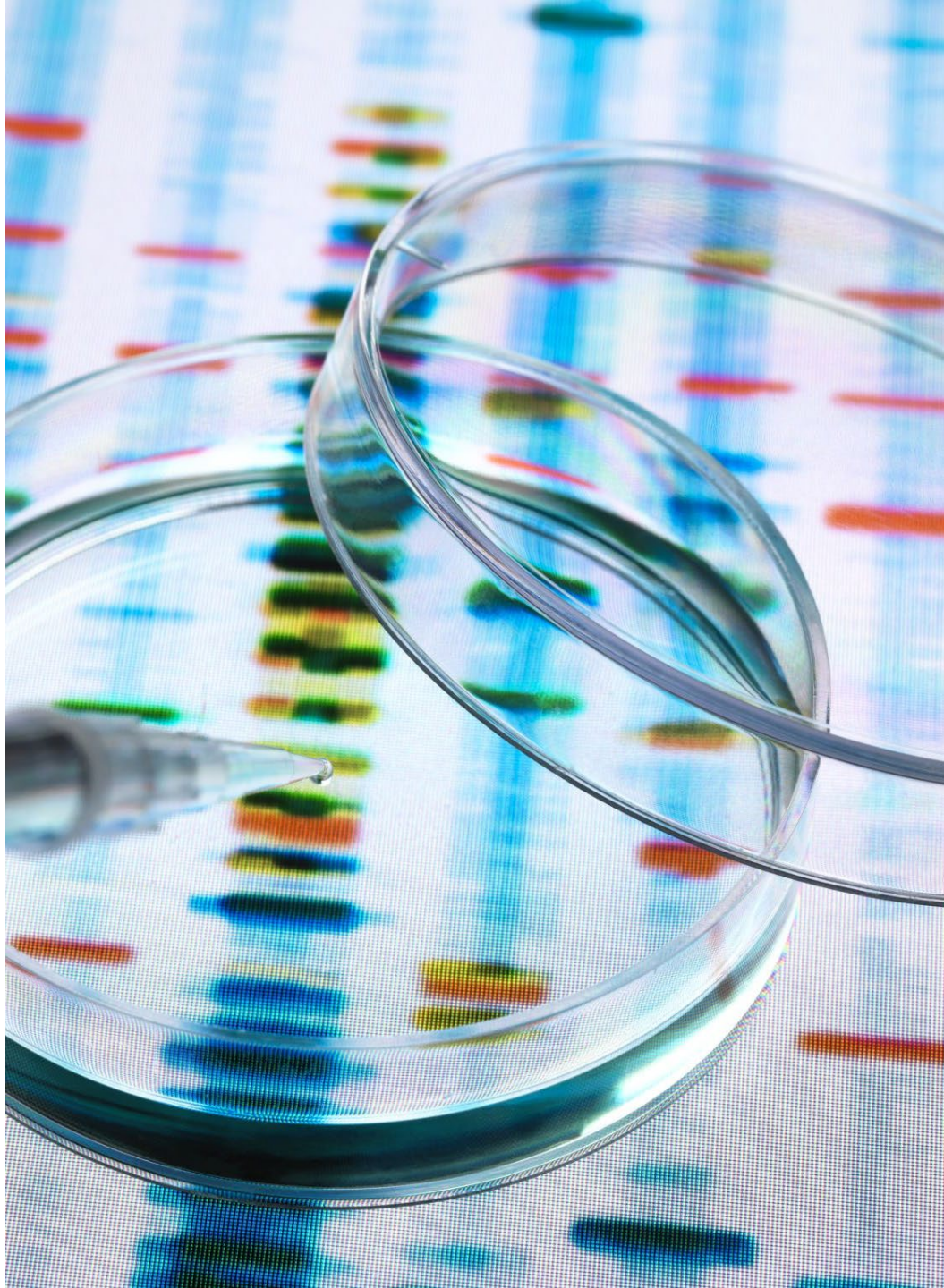
Proactive by measuring physiology creating biometrics that wearable capture.

The Biomarkers in Behavioral Health



Genetic Single Nucleotide Polymorphism

- Previously science thought that our genes were static. We now know what we can modify the expression of our genes.
  - SNP is an error in genetic coding which can lead to aberrant behaviors: risk taking, impulse control, anxiety, depression, and addiction.
  - Can measure the level of the error: no clinical abnormality, heterozygous, homozygous.
  - Genes linked to defects in methylation, autophagy, detoxification, inflammation, neuropsych, and others.



SNPs as Biomarkers in Behavioral Health

SLC6A4

Gene encodes the serotonin transporter, SERT.

Responsible for clearing the serotonin neurotransmitter from the synaptic space.

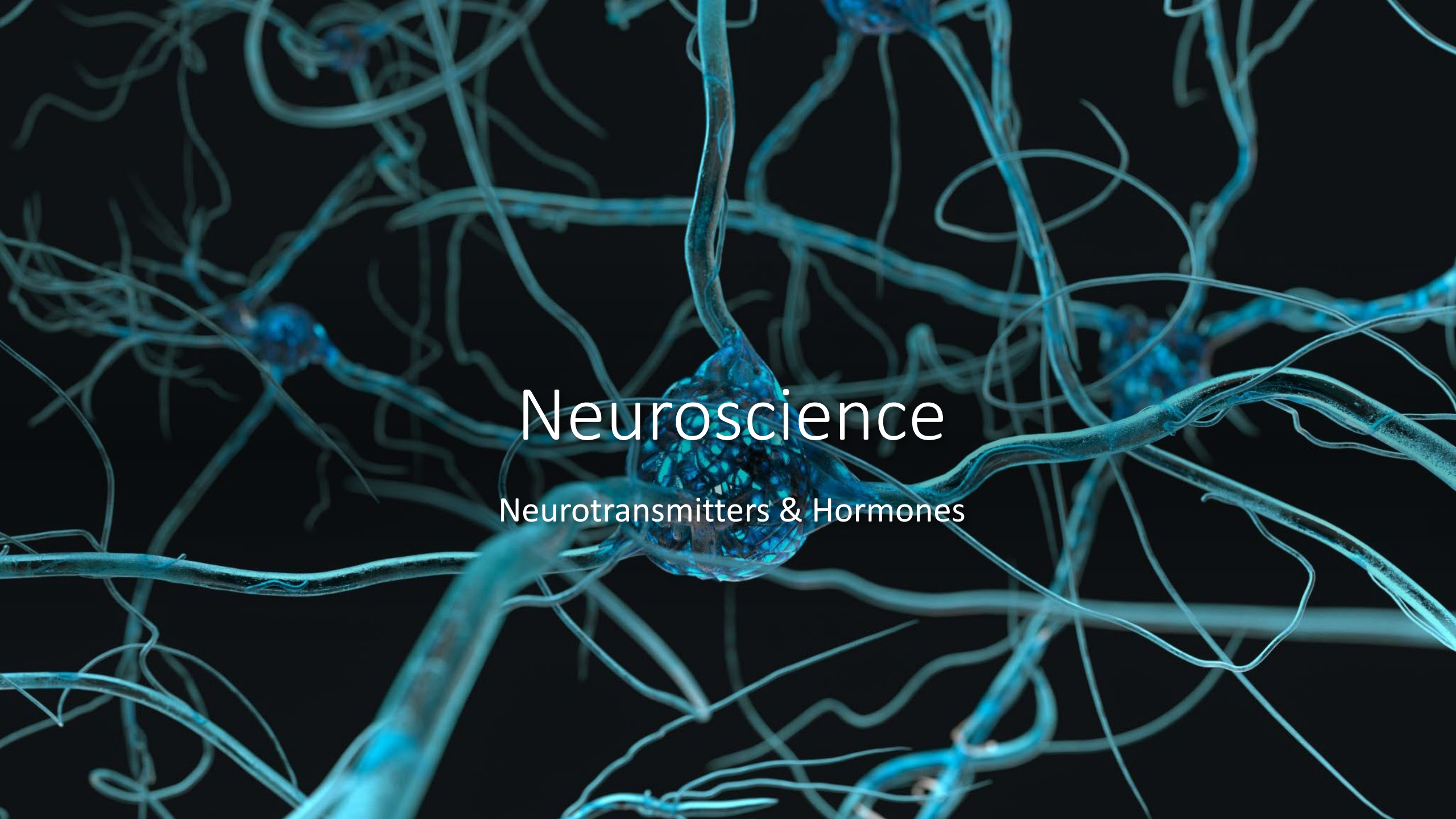
SERT is the target of many therapeutic drugs.

Polymorphisms are associated with increased risk of anxiety, depression, and less effective response to SSRI medications

GAD1

Enzyme responsible for conversion of glutamic acid (a stimulant neurotransmitter) to GABA (a calming neurotransmitter).

Deficiency of GABA from polymorphisms in this enzyme are associated with sleep disorders, "half glass empty" syndrome, dysphoria, and spasticity.



Neuroscience

Neurotransmitters & Hormones

Neuroscience Biomarkers

Neurotransmitters

Brain chemicals responsible for mood regulation, appetite, focus, sleep, pain, libido, drive…

Reference range based on age and gender.

Urine: bioavailable vs pathological

Speed: Text Message

Hormones

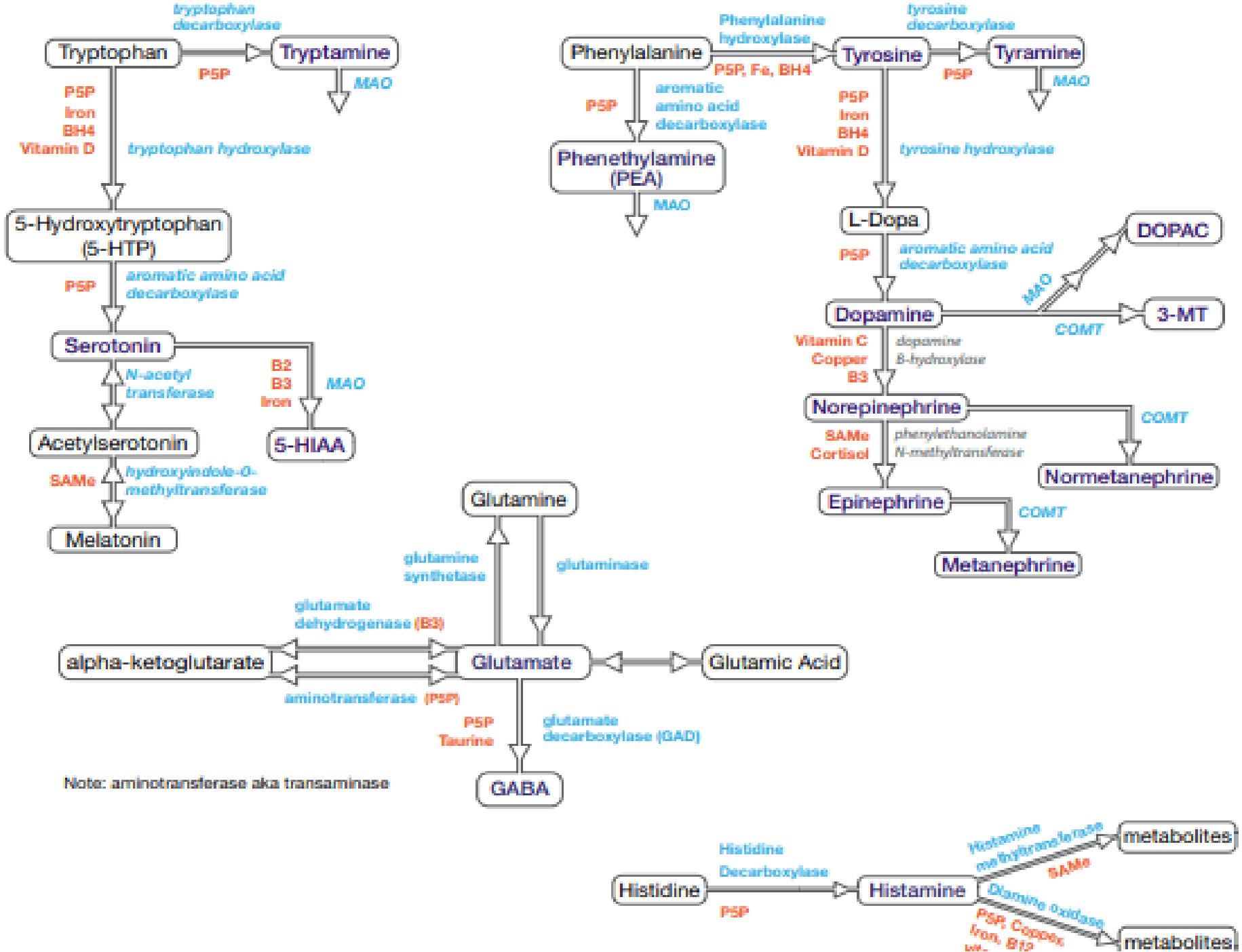
DHEA, sex hormones, cortisol

Reference range based on age and gender.

Saliva: bioavailable vs pathological

Speed: Carrier Pigeon

Neurotransmitter Biochemical Pathways



Neurotransmitters as Biomarkers in Behavioral Health

High Serotonin

Associated with symptoms of, increased anxiety, agitation and diarrhea (IBS-like symptoms).

Commercialized as the feel-good chemical and more is better…

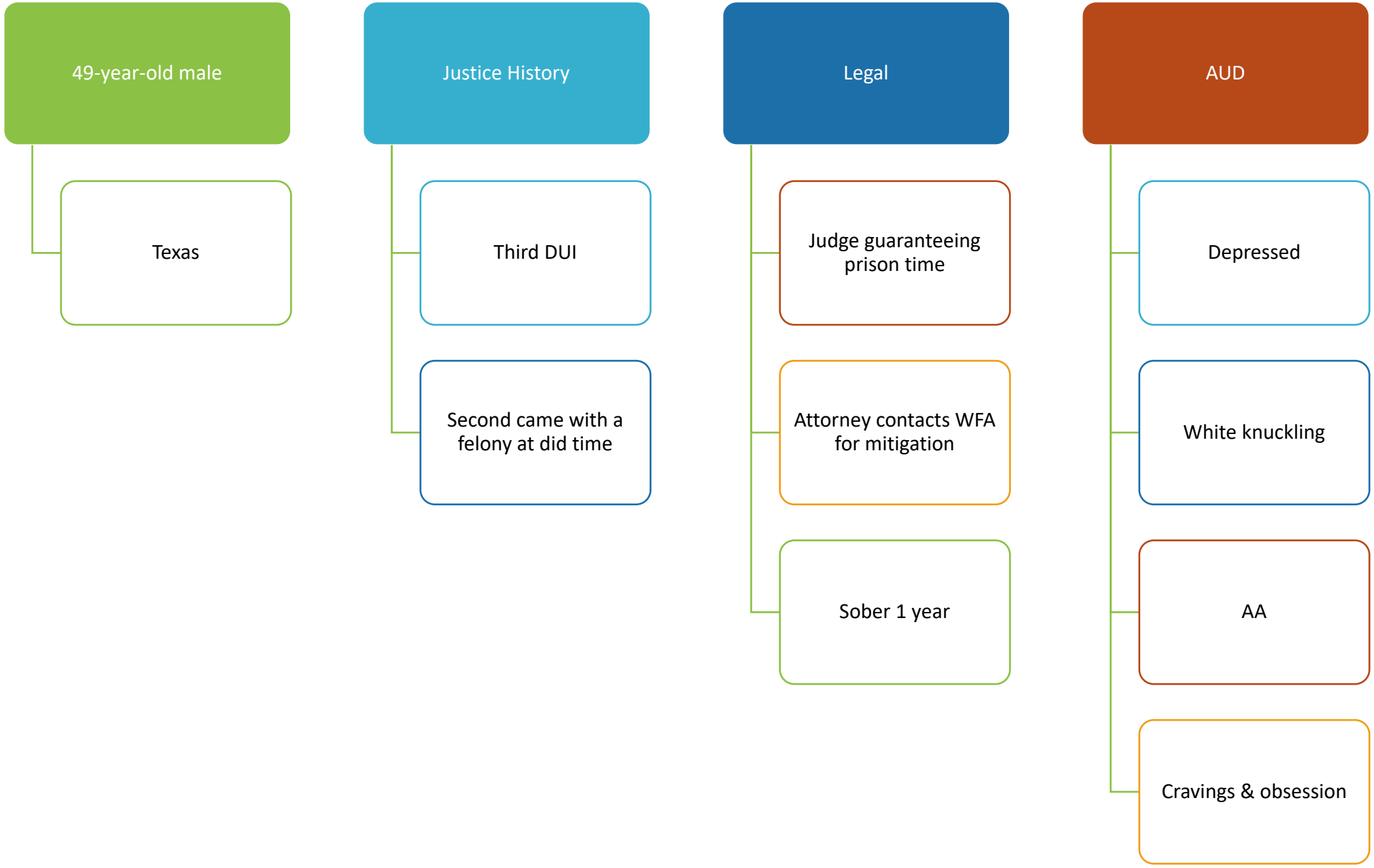
Low Serotonin

Contribute to mood concerns including anxiety, OCD, depression, anger and a sense of discontentment.

Associated with poor sleep quality, appetite changes, chronic fatigue, rheumatoid arthritis, and over-all lassitude.

Justice Impacted Case Study

Justice through objective biomarker evaluation & individualized biochemical pathway support.



Behavioral Health Equity Through Objectivity

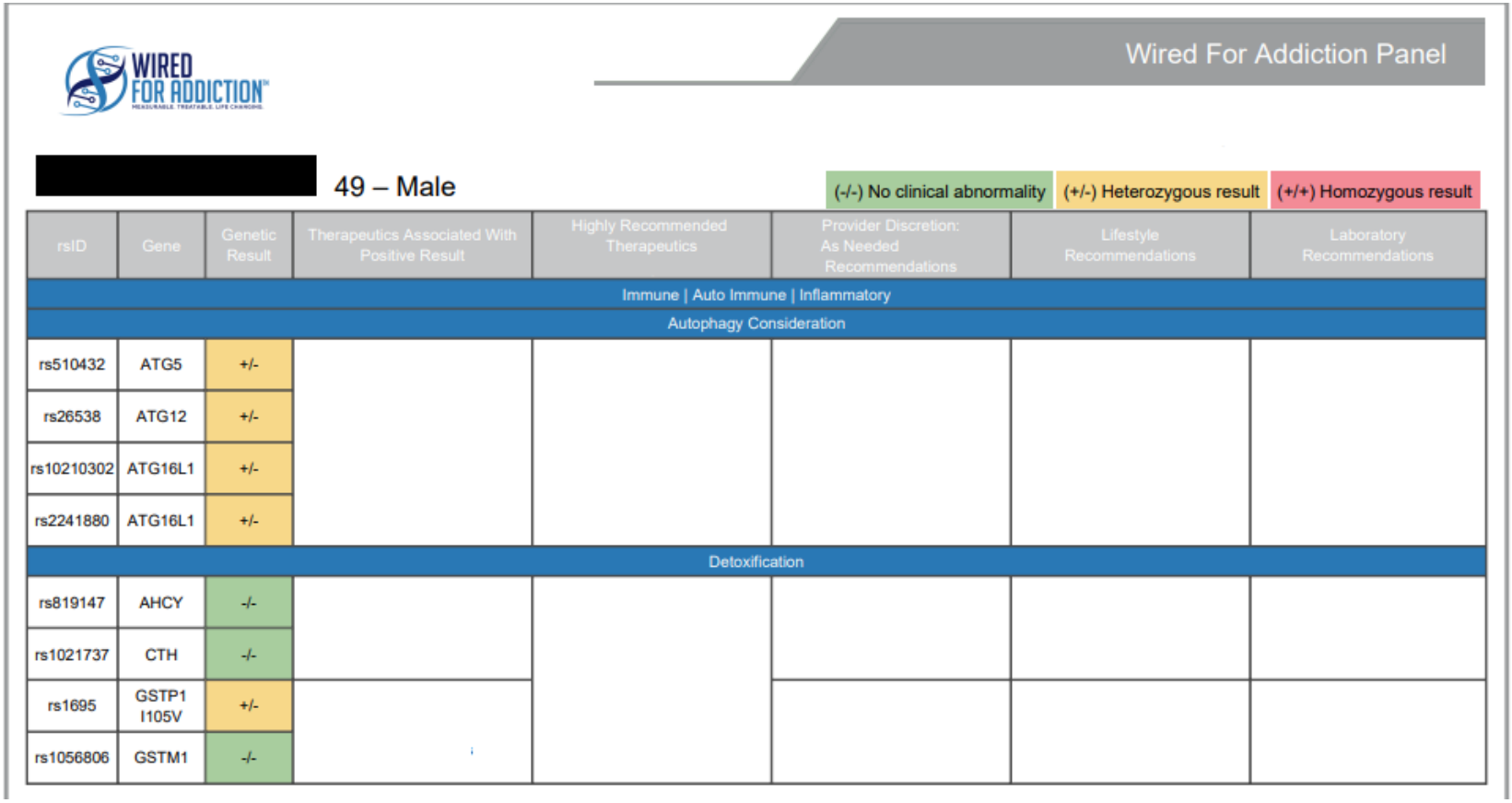
Therapeutic Class	Standard Precautions	Caution / Info	Change recommended
Anti-ADHD Agents	Atomoxetine Guanfacine	Amphetamine Dexmethylphenidate Dextroamphetamine Lisdexamfetamine Methylphenidate (COMT)	
Anticonvulsants	Clobazam Phenytoin		
Antidementia Agents	Donepezil		
Antidepressants	Amitriptyline (CYP2D6) Amoxapine Clomipramine (CYP2D6) Desipramine Doxepin (CYP2D6) Duloxetine Imipramine (CYP2C19, CYP2D6) Mirtazapine Moclobemide Nortriptyline Protriptyline Trazodone Trimipramine Trimipramine (CYP2C19) Venlafaxine Vortioxetine		
Antipsychotics	Aripiprazole Brexpiprazole Clozapine Flupenthixol		

Behavioral Health Equity Through Objectivity

- Monoamine oxidase: associated with increased aggression, mood disorders and drug addiction.
- Catechol-O-methyltransferase: COMT (+/-) sluggish ability to alter anxiety or depression episodes.
- SLC6A4: polymorphisms are associated with increased risk of anxiety and depression and less effective response to SSRI medications.

Neurotransmitters / Mood					
rs4680	COMT V158M	+/-	Taurine, Choline, Trimethylglycine (TMG), Dimethylglycine (DMG), Methionine, SAMe, Inositol		May Bene if Anxiety
rs769407	GAD1	-/-	Prescription Amantadine, Glycine, N-Acetyl-Cysteine (NAC), Zinc, Magnesium, Elderberry, L-Theanine, Melatonin		
rs3828275	GAD1	-/-			
rs6323	MAO-A	+/NA	B2 (Riboflavin), Methyl Donors (Taurine, Choline, Trimethylglycine (TMG), Dimethylglycine (DMG), Inositol, Methionine		
rs1799836	MAO-B	-/NA	Methyl Donors (Taurine, Choline, Trimethylglycine (TMG), Dimethylglycine (DMG), Inositol, Methionine		
rs6313	HTR2	-/-	5-HTP (Hydroxytryptophan)		May Benef Anxiety o
rs1042173	SLC6A4	+/+			

Behavioral Health Equity Through Objectivity



WIRED FOR ADDICTION

Wired For Addiction Panel

[redacted] 49 – Male

(-/-) No clinical abnormality | (+/-) Heterozygous result | (+/+) Homozygous result

rsID	Gene	Genetic Result	Therapeutics Associated With Positive Result	Highly Recommended Therapeutics	Provider Discretion: As Needed Recommendations	Lifestyle Recommendations	Laboratory Recommendations
Immune | Auto Immune | Inflammatory							
Autophagy Consideration							
rs510432	ATG5	+/-					
rs26538	ATG12	+/-					
rs10210302	ATG16L1	+/-					
rs2241880	ATG16L1	+/-					
Detoxification							
rs819147	AHCY	-/-					
rs1021737	CTH	-/-					
rs1695	GSTP1 I105V	+/-					
rs1056806	GSTM1	-/-					

WIRED FOR ADDICTION™
MEASURABLE. TREATABLE. LIFE CHANGING.

Order:

Test:
Client #:
Wired For Addiction

Id:
Age: **DOB:**
Sex: Male

Sample Collection	Date/Time
Date Collected	10/27/2022
Collection Period	2nd morning void
Date Received	10/31/2022
Date Reported	11/07/2022

Analyte	Result	Unit per Creatinine	L	WRI	H	Reference Interval
Serotonin	146	µg/g				50 – 98
Dopamine	117	µg/g				110 – 200
Norepinephrine	31.2	µg/g				18 – 42
Epinephrine	7.3	µg/g				1.3 – 7.3
Norepinephrine / Epinephrine ratio	4.3					< 13
Glutamate	10	µmol/g				9.0 – 40.0
Gamma-aminobutyrate (GABA)	2.2	µmol/g				1.6 – 3.5
Glycine	793	µmol/g				350 – 1500
Histamine	17	µg/g				12 – 30
Phenethylamine (PEA)	15	nmol/g				26 – 70
Creatinine	110	mg/dL				35 – 240

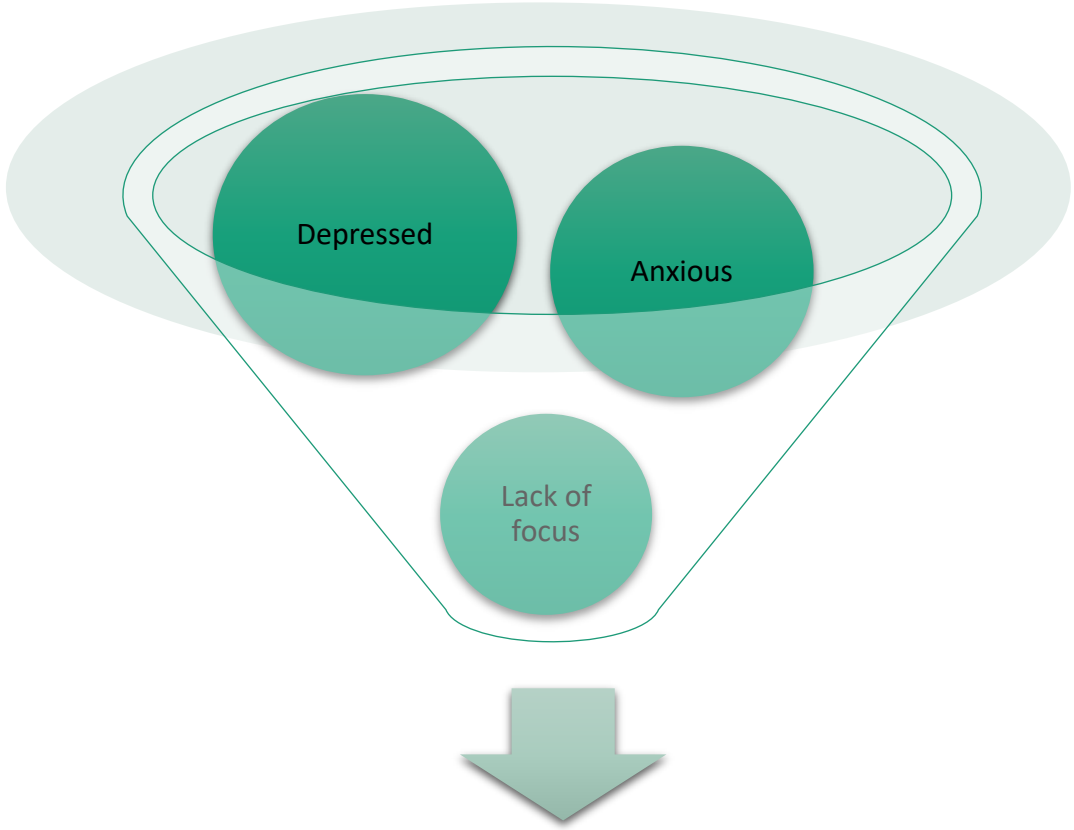
Behavioral Health Equity Through Objectivity

- Elevated serotonin: increased anxiety, agitation and diarrhea (IBS-like symptoms).
- Low range dopamine: anxiety/depression, difficulty concentrating, decreased libido and obesity, increased addiction, and other stimulation seeking activities.
- Upper range epinephrine: stress response and contributory to anxiety, agitation, irritability, insomnia and hypertension.
- Low phenethylamine: depression, attention deficits and hyperactivity, Parkinson's disease and bipolar disorder.

Depression Does Not Equal SSRI

- Without objective lab work to triage behavioral wellness complexities such as addiction, individuals are relegated to M.A.T. and empirically prescribed pharmaceuticals for behaviors derived from suboptimal physiology.
  - M.A.T. occupies a receptor site without addressing biochemical pathways.
  - Incomplete rehabilitation.

- The panel utilized in this case study allowed for the creation of a treatment-centric rather than punishment-centric approach to sentencing, in addition to a hyper-precise recovery plan based on identified, isolated, and measured biochemical pathways unique to the individual.



Diagnosed ADHD, depressed, and/or anxious depending on **vocabulary** of physician(s). Therefore, prescribed Ritalin, Zoloft, and Xanax, etc. Continue M.A.T. (Antabuse or Vivitrol) without addressing biochemical pathways and self medicate through other means (caffeine, nicotine, sugar, gambling, tobacco, relationships, drugs, etc.)

Outcome?

- Overcame judge's bias
  - Atta boy to attorney and keep up the good work to the client
- 8 days in county plus probation
  - Wired For Addiction® Biochemical Pathway Support Plan Recommendations
- "I finally feel at peace." "I can think my way through problems." "I am proud of myself."
  - Individual, family, and community have noticed a positive change beyond abstinence.

Mental Health & Criminal Justice

Mental health complexities and addiction have many biochemical factors in addition to lifestyle choices.

Diagnosing and sentencing based on vocabulary and empirical evidence is an, unnecessary, inequitable, and dangerous subjective means in a life-or-death scenario.

The purpose of incarceration is 2-fold: punish the person and protect the public. How are we protecting the public if MH contributed to the crime, no services are provided, they serve their sentence, and recidivate?

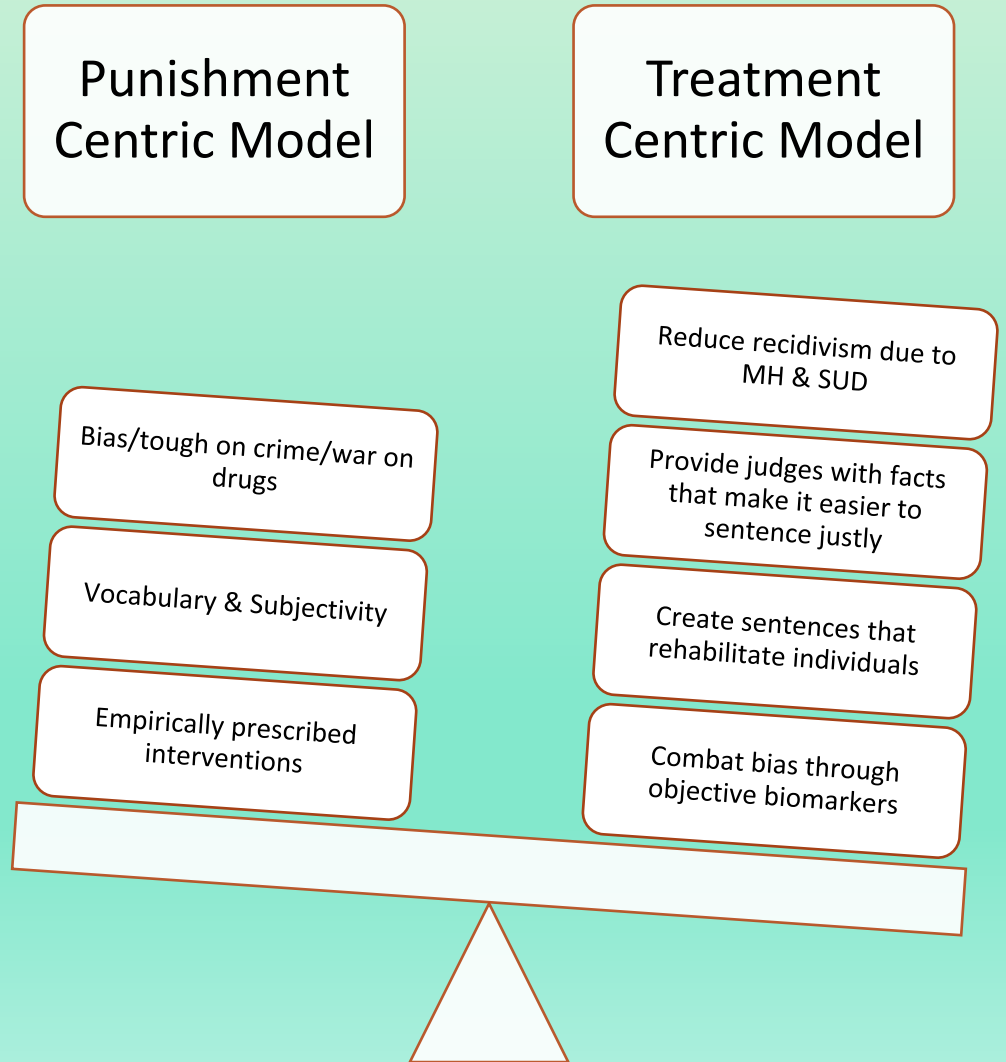
- MH & SUD diagnosed based on vocabulary.
  - Individual's vocabulary
  - Family's vocabulary
  - Judge's vocabulary
  - Counsel's vocabulary

- Sentenced & Prescribed based on empirical experience.
  - Try a combo of meds & change if mental health declines or plateaus.
  - Judge's bias.
  - Counseling can upregulate or downregulate physiology, but not enough to fully optimize a biochemical pathway unilaterally.
  - Psychotropic medication to neutralize physical threat to self and others and to reduce personal required to stabilize individual. Often leads to ineffective, wasteful, and damaging repercussions.

Provide Objective Data to Support a Condition Better Treated Medically Rather Than Penalized Legally

- Pharmacogenomic Testing
  - If your client is incarcerated, ensure that the medications they're being given are compatible with their DNA.
  - More documentation to support the need to be properly medicated while being transferred/transported.
  - If aberrant behavior is being exhibited in jail, make sure it's not due to the facility improperly medicating your client and thereby jeopardizing the mental and physical health of themselves and those around him/her.
- Wired For Addiction® Custom Panel
  - Provide objective testing & interpretation to determine biological factors driving substance misuse and make the case for a treatment centric rather than punishment centric approach to sentencing.
  - Proactively recommend inclusion in probation to address the biological component of client's substance misuse.
- Address the revolving door of the criminal justice system and relapse

Using objectivity to create a treatment-centric rather than punishment-centric sentence



References

- Lotta, T. et al. Kinetics of Human Soluble and Membrane-Bound Catechol O-Methyltransferase: A Revised Mechanism and Description of the Thermolabile Variant of the Enzyme. Biochemistry (1995). doi:10.1021/bi00013a008 • Stein, M. B., Fallin, M. D., Schork, N. J. & Gelernter, J. COMT polymorphisms and anxiety-related personality traits. Neuropsychopharmacology (2005). doi:10.1038/sj.npp.1300787 • Lee, L. O. & Prescott, C. A. Association of the catechol-O-methyltransferase val158met polymorphism and anxiety-related traits: A meta-analysis. Psychiatr. Genet. (2014). doi:10.1097/YPG.0000000000000018 • Ulmanen, I. et al. Expression and intracellular localization of catechol O-methyltransferase in transfected mammalian cells. Eur. J. Biochem. (1997). doi:10.1111/j.1432-1033.1997.0452a.x • Axelrod, J. O-methylation of epinephrine and other catechols in vitro and in vivo. Science (80-.). (1957). doi:10.1126/science.126.3270.400 • Tai, C. H. & Wu, R. M. Catechol-Omethyltransferase and Parkinson's disease. Acta Medica Okayama (2002). • Grossman, M. H., Emanuel, B. S. & Budarf, M. L. Chromosomal mapping of the human catechol-O-methyltransferase gene to 22q11.1?q11.2. Genomics (1992). doi:10.1016/0888-7543(92)90316-K • Golan, D. E., Armstrong, E. J. & Armstrong, A. W. Principles of pharmacology: the pathophysiologic basis of drug therapy. (Wolters Kluwer Health, 2017). • Bonifácio, M. J., Palma, P. N., Almeida, L. & Soares-Da-Silva, P. Catechol-O-methyltransferase and its inhibitors in Parkinson's disease. CNS Drug Reviews (2007). doi:10.1111/j.1527-3458.2007.00020.x • Wichers, M. et al. The catechol-O-methyl transferase Val158Met polymorphism and experience of reward in the flow of daily life. Neuropsychopharmacology (2008). doi:10.1038/sj.npp.1301520 • Diamond, A., Briand, L., Fossella, J. & Gehlbach, L. Genetic and Neurochemical Modulation of Prefrontal Cognitive Functions in Children. Am. J. Psychiatry (2004). doi:10.1176/appi.ajp.161.1.125 • Robinson, S., Goddard, L., Dritschel, B., Wisley, M. & Howlin, P. Executive functions in children with Autism Spectrum Disorders. Brain Cogn. (2009). doi:10.1016/j.bandc.2009.06.007 • Bruder, G. E. et al. Catechol-O-methyltransferase (COMT) genotypes and working memory: Associations with differing cognitive operations. Biol. Psychiatry (2005). doi:10.1016/j.biopsych.2005.05.010 • Chen, J. et al. Functional analysis of genetic variation in catechol-O-methyltransferase (COMT): Effects on mRNA, protein, and enzyme activity in postmortem human brain. Am. J. Hum. Genet. (2004). doi:10.1086/425589

- glutamate decarboxylase 1 [Homo sapiens (human)] - Gene - NCBI. National Center for Biotechnology Information (2020). Available at: https://www.ncbi.nlm.nih.gov/gene/2571. • KELLY, C. D. et al. Nucleotide sequence and chromosomal assignment of a cDNA encoding the large isoform of human glutamate decarboxylase. Ann. Hum. Genet. (1992). doi:10.1111/j.1469-1809.1992.tb01150.x • Giorda, R., Peakman, M., Tan, K. C., Vergani, D. & Trucco, M. Glutamic acid decarboxylase expression in islets and brain. The Lancet (1991). doi:10.1016/0140-6736(91)92781-V • Dirkx, R. et al. Targeting of the 67-kDa isoform of glutamic acid decarboxylase to intracellular organelles is mediated by its interaction with the NH2- terminal region of the 65-kDa isoform of glutamic acid decarboxylase. J. Biol. Chem. (1995). doi:10.1074/jbc.270.5.2241 • Bu, D. F. & Tobin, A. J. The exon-intron organization of the genes (gad1 and gad2) encoding two human glutamate decarboxylases (gad67and gad65) suggests that they derive from a common ancestral gad. Genomics (1994). doi:10.1006/geno.1994.1246 • Demakova, E. V, Korobov, V. P. & Lemkina, L. M. Determination of gamma-aminobutyric acid concentration and activity of glutamate decarboxylase in blood serum of patients with multiple sclerosis. Klin. Lab. Diagn. (2003). • Asada, H. et al. Mice lacking the 65 kDa isoform of glutamic acid decarboxylase (GAD65) maintain normal levels of GAD67 and GABA in their brains but are susceptible to seizures. Biochem. Biophys. Res. Commun. (1996). doi:10.1006/bbrc.1996.1898 • McHale, D. P. et al. A Gene for Autosomal Recessive Symmetrical Spastic Cerebral Palsy Maps to Chromosome 2q24-25. Am. J. Hum. Genet. (1999). doi:10.1086/302237

- Kim, S. K. et al. Association study between monoamine oxidase A (MAOA) gene polymorphisms and schizophrenia: Lack of association with schizophrenia and possible association with affective disturbances of schizophrenia. Mol. Biol. Rep. (2014). doi:10.1007/s11033-014-3207-5 • Anton, R. F. et al. Pharmacogenomics. Nat Genet. 16, 268–278 (2008). • Karmakar, A. et al. Pilot study indicate role of preferentially transmitted monoamine oxidase gene variants in behavioral problems of male ADHD probands. BMC Med. Genet. (2017). doi:10.1186/s12881-017-0469-5 • Bortolato, M. & Shih, J. C. Behavioral outcomes of monoamine oxidase deficiency: Preclinical and clinical evidence. in International Review of Neurobiology (2011). doi:10.1016/B978-0-12-386467-3.00002-9

- • Johnson, B. A. et al. Pharmacogenetic approach at the serotonin transporter gene as a method of reducing the severity of alcohol drinking. Am. J. Psychiatry 168, 265–275 (2011). • SLC6A4 gene - Genetics Home Reference - NIH. U.S. National Library of Medicine (2020). Available at: https://ghr.nlm.nih.gov/gene/SLC6A4. • Anton, R. F. et al. Pharmacogenomics. Nat. Genet. 16, 268–278 (2008). • Ait-Daoud, N. et al. Preliminary Evidence for cue-induced Alcohol Craving Modulated by Serotonin Transporter Gene Polymorphism rs1042173. Front. Psychiatry 3, 6 (2012). • Landgren, S. et al. Genetic Variation of the Ghrelin Signaling System in Females With Severe Alcohol Dependence. Alcohol. Clin. Exp. Res. 34, 1519–1524 (2010).

- TG12 • Smith, G. S., Walter, G. L. & Walker, R. M. Clinical Pathology in Non-Clinical Toxicology Testing. in Haschek and Rousseaux's Handbook of Toxicologic Pathology (2013). doi:10.1016/B978-0-12-415759-0.00018-2 • Yuan, J. et al. Polymorphisms in autophagy related genes and the coal workers' pneumoconiosis in a Chinese population. Gene 632, 36–42 (2017). • Anton, R. F. et al. Pharmacogenomics. Nat. Genet. 16, 268–278 (2008). • Mizushima, N. Autophagy: Process and function. Genes and Development (2007). doi:10.1101/gad.1599207 • Levine, B. & Kroemer, G. Autophagy in the Pathogenesis of Disease. Cell (2008). doi:10.1016/j.cell.2007.12.018 • Antunes, F. et al. Autophagy and intermittent fasting: the connection for cancer therapy? Clinics (Sao Paulo, Brazil) (2018). doi:10.6061/clinics/2018/e814s • Takagi, A., Kume, S., Maegawa, H. & Uzu, T. Emerging role of mammalian autophagy in ketogenesis to overcome starvation. Autophagy (2016). doi:10.1080/15548627.2016.1151597 • Lindberg, S. Autophagy: Definition, Diet, Fasting, Cancer, Benefits, and More. Healthline (2014). Available at: https://www.healthline.com/health/autophagy#bottom-line.

- Mizushima, N. Autophagy: Process and function. Genes and Development (2007). doi:10.1101/gad.1599207 • Salem, M., Nielsen, O. H., Nys, K., Yazdanyar, S. & Seidelin, J. B. Impact of T300A Variant of ATG16L1 on antibacterial response, risk of culture positive infections, and clinical course of Crohn's disease. Clin. Transl. Gastroenterol. (2015). doi:10.1038/ctg.2015.47 • Begun, J. et al. Integrated Genomics of Crohn's Disease Risk Variant Identifies a Role for CLEC12A in Antibacterial Autophagy. Cell Rep. (2015). doi:10.1016/j.celrep.2015.05.045 • Cheng, J. F., Ning, Y. J., Zhang, W., Lu, Z. H. & Lin, L. T300A polymorphism of ATG16L1 and susceptibility to inflammatory bowel diseases: A meta-analysis. World J. Gastroenterol. (2010). doi:10.3748/wjg.v16.i10.1258 • Kabat, A. M. et al. The autophagy gene Atg16l1 differentially regulates Treg and TH2 cells to control intestinal inflammation. Elife (2016). doi:10.7554/eLife.12444 • Lassen, K. G. et al. Atg16L1 T300A variant decreases selective autophagy resulting in altered cytokine signaling and decreased antibacterial defense. Proc. Natl. Acad. Sci. (2014). doi:10.1073/pnas.1407001111 • Smith, G. S., Walter, G. L. & Walker, R. M. Clinical Pathology in Non-Clinical Toxicology Testing. in Haschek and Rousseaux's Handbook of Toxicologic Pathology (2013). doi:10.1016/B978-0-12-415759-0.00018-2 • Levine, B. & Kroemer, G. Autophagy in the Pathogenesis of Disease. Cell (2008). doi:10.1016/j.cell.2007.12.018 • Lindberg, S. Autophagy: Definition, Diet, Fasting, Cancer, Benefits, and More. Healthline (2014). Available at: https://www.healthline.com/health/autophagy#bottomline. • Antunes, F. et al. Autophagy and intermittent fasting: the connection for cancer therapy? Clinics (Sao Paulo, Brazil) (2018). doi:10.6061/clinics/2018/e814s • Takagi, A., Kume, S., Maegawa, H. & Uzu, T. Emerging role of mammalian autophagy in ketogenesis to overcome starvation. Autophagy (2016). doi:10.1080/15548627.2016.1151597 • Gazouli, M. et al. NOD2/CARD15, ATG16L1 and IL23R gene polymorphisms and childhood-onset of Crohn's disease. World J. Gastroenterol. (2010). doi:10.3748/wjg.v16.i14.1753 • Kuballa, P., Huett, A., Rioux, J. D., Daly, M. J. & Xavier, R. J. Impaired autophagy of an intracellular pathogen induced by a Crohn's disease associated ATG16L1 variant. PLoS One (2008). doi:10.1371/journal.pone.0003391 • Rosentul, D. C. et al. Role of autophagy genetic variants for the risk of Candida infections. Med. Mycol. (2014). doi:10.1093/mmy/myt035 • Raju, D., Hussey, S. & Jones, N. L. Crohn disease ATG16L1 polymorphism increases susceptibility to infection with Helicobacter pylori in humans. Autophagy (2012). doi:10.4161/auto.21007 • Stappenbeck, T. S. et al. Crohn disease: A current perspective on genetics, autophagy and immunity. Autophagy (2011). doi:10.4161/auto.7.4.13074 • Csöngei, V. et al. Interaction of the major inflammatory bowel disease susceptibility alleles in Crohn's disease patients. World J. Gastroenterol. (2010). doi:10.3748/wjg.v16.i2.176 • Boada-Romero, E. et al. The T300A Crohn's disease risk polymorphism impairs function of the WD40 domain of ATG16L1. Nat. Commun. (2016). doi:10.1038/ncomms11821 • Glubb, D. M. et al. NOD2 and ATG16L1 polymorphisms affect monocyte responses in crohn's disease. World J. Gastroenterol. (2011). doi:10.3748/wjg.v17.i23.2829 • Salem, M., Ammitzboell, M., Nys, K., Seidelin, J. B. & Nielsen, O. H. ATG16L1: A multifunctional susceptibility factor in crohn disease. Autophagy (2015). doi:10.1080/15548627.2015.1017187 • UsateguiMartín, R. et al. Polymorphisms in autophagy genes are associated with paget disease of bone. PLoS One (2015). doi:10.1371/journal.pone.0128984 • Messer, J. S. et al. The Crohn's disease: Associated ATG16L1 variant and Salmonella invasion. BMJ Open (2013). doi:10.1136/bmjopen-2013-002790

- • Lindberg, S. Autophagy: Definition, Diet, Fasting, Cancer, Benefits, and More. Healthline (2014). Available at: https://www.healthline.com/health/autophagy#bottom-line. • Takagi, A., Kume, S., Maegawa, H. & Uzu, T. Emerging role of mammalian autophagy in ketogenesis to overcome starvation. Autophagy (2016). doi:10.1080/15548627.2016.1151597 • Antunes, F. et al. Autophagy and intermittent fasting: the connection for cancer therapy? Clinics (Sao Paulo, Brazil) (2018). doi:10.6061/clinics/2018/e814s • Levine, B. & Kroemer, G. Autophagy in the Pathogenesis of Disease. Cell (2008). doi:10.1016/j.cell.2007.12.018 • Smith, G. S., Walter, G. L. & Walker, R. M. Clinical Pathology in Non-Clinical Toxicology Testing. in Haschek and Rousseaux's Handbook of Toxicologic Pathology (2013). doi:10.1016/B978-0-12-415759-0.00018-2 • Mizushima, N. Autophagy: Process and function. Genes and Development (2007). doi:10.1101/gad.1599207 • Anton, R. F. et al. Pharmacogenomics. Nat. Genet. 16, 268–278 (2008). • White, K. A. M. et al. Variants in autophagy-related genes and clinical characteristics in melanoma: a population-based study. Cancer Med. 5, 3336–3345 (2016). • Yuan, J. et al. Polymorphisms in autophagy related genes and the coal workers' pneumoconiosis in a Chinese population. Gene 632, 36–42 (2017). • Martin, L. J. et al. Functional Variant in the Autophagy-Related 5 Gene Promotor is Associated with Childhood Asthma. PLoS One 7, e33454 (2012)

Questions?

Jacqueline Hall

JHall@WiredForAddiction.com 202-255-1184

WiredForAddiction.com Staff@WiredForAddiction.com 1-888-841-7099