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Hormones and the Brain: the Importance of Hormones and Neurotransmitters for Proper Brain Function

The Brain is the New Heart?

- Our healthcare system is **obsessed with cardiology**. Everyone monitors their cholesterol, and heart disease is considered the number one killer in the United States.
- But lets not forget that the **head is connected to the body!**
- **All diseases affect or are affected by the brain.** Therefore, **monitoring brain health** is just as important – if not more so in many instances – than monitoring heart health.

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Core Cardiac Domains

- Valves
- Coronary Arteries
- Ejection Fraction
- Blood work
- Electrophysiological

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Core Brain domains: Integrating the Brain into Healthcare

- Electrophysiology
- Memory
- Attention
- Temperament and Type
- Axis 1 & 2
- IQs

The Edge Effect Eric Braverman 2004 Sterling Publishing Co., Inc.

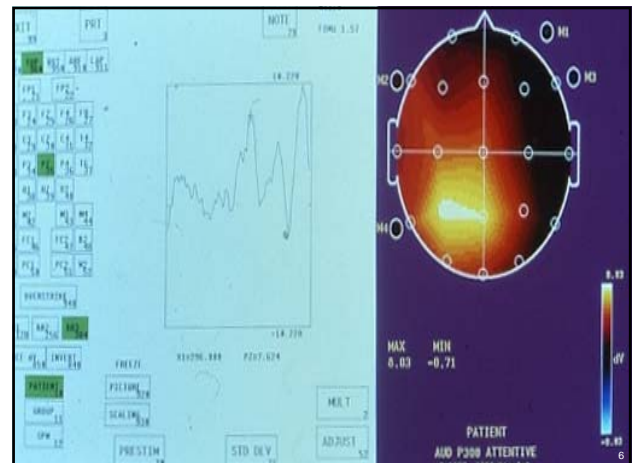
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P300 and Brain Speed

- The P300 wave is an **event related potential** that can be recorded via EEG as a positive deflection in voltage at a latency of roughly 300 + age msec.
- The **presence, magnitude, topography, and time** of this signal can measure processing speed, power, synchrony and rhythm.
- The generation of the P300 event-related potential is influenced by the **glutamatergic, GABAergic, cholinergic, noradrenergic, dopaminergic, and serotonergic systems.**
- **P300 Latency** is primarily **cholinergic**.

Neurochemical substrates and neuroanatomical generators of the event-related P300 Frodl-Bauch T, Bottlinger R, Hogert U *Neuropsychobiology* 1999;40:86-94

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P300 Wave is the New "Cholesterol Test?"

The P300 test of brain speed is becoming the cholesterol test of the brain. Someday we envision that just as how most Americans know their cholesterol levels, everyone will know their brain age, how many years they are away from dementia. Cholesterol, the first precursor to steroid hormone pathway and a marker of decline in our steroid manufacturing, is a tremendous global marker of both heart disease and physical wellbeing. *Brain processing speed delay is antecedent to both memory and attention decline, and will become the marker that every human being will measure.*

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Age and Brain Speed

Age (years)	P300 speed (msec)
5	380
10	360
20	320
30	330
40	340
50	350
60	360
70	370
80	380
90	390
100	400

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Characteristics and Mean (SE) of P300 Latency, Voltage, WMS-III, and MMSE by decade

Parameter Tested	Age 11-20 (N=44) (Mean +/-SE)	Age 21-30 (N=98) (Mean +/-SE)	Age 31-40 (N=197) (Mean +/-SE)	Age 41-50 (N=328) (Mean +/-SE)
P300 Latency	327.2 ± 4.2	317.6 ± 2.0	328.0 ± 2.4	332.8 ± 1.5
P300 Voltage	7.5 ± 0.4	7.4 ± 0.3	7.3 ± 0.3	6.3 ± 0.2
Verbal	94.8 ± 4.5	101.7 ± 2.8	100.0 ± 2.1	100.9 ± 1.6
Visual	97.8 ± 6.0	101.5 ± 2.9	96.5 ± 2.2	97.1 ± 1.5
Immediate	96.6 ± 6.3	101.7 ± 2.9	99.2 ± 2.0	98. ± 41.8
Working	91.1 ± 3.2	98.8 ± 2.4	96.7 ± 2.0	94.9 ± 1.3
MMSE	28.0 ± 0.6	26.7 ± 1.3	26.9 ± 0.8	27.2 ± 0.5

*Braverman E, Blum K. (2003) P300 Event-Related Potential: An Accurate Predictor of Memory. Clinical EEG, Vol 34, No. 3

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Characteristics and Mean (SE) of P300 Latency, Voltage, WMS-III, and MMSE by decade

Parameter Tested	Age 51-60 (N=318) (Mean +/-SE)	Age 61-70 (N=191) (Mean +/-SE)	Age 71-80 (N=216) (Mean +/-SE)	Age 81-90 (N=78) (Mean +/-SE)
P300 Latency	339.3 ± 1.6	347.6 ± 2.0	359.9 ± 2.2	371.6 ± 3.8
P300 Voltage	6.3 ± 0.2	6.0 ± 0.2	6.0 ± 0.2	5.8 ± 0.4
Verbal	102.8 ± 1.7	101.1 ± 1.9	95.4 ± 1.9	88.7 ± 2.9
Visual	99.3 ± 1.8	92.7 ± 1.7	89.0 ± 1.8	85.5 ± 3.5
Immediate	101.8 ± 1.9	95.8 ± 2.0	90.7 ± 1.9	84.6 ± 3.3
Working	94.8 ± 1.6	92.0 ± 1.5	91.5 ± 1.7	88.7 ± 2.3
MMSE	26.6 ± 0.4	27.0 ± 0.4	26.5 ± 0.4	22.9 ± 0.9

*Braverman E, Blum K. (2003) P300 Event-Related Potential: An Accurate Predictor of Memory. Clinical EEG, Vol 34, No. 3

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MMSE Groupings vs P300 Variables, WMS-III**

	P300 Latency (Mean±SE)	P300 Voltage (Mean±SE)	Verbal Memory (Mean±SE)	Visual Memory (Mean±SE)	Immediate Memory (Mean±SE)	Working Memory (Mean±SE)
Group A MMSE 0-19 Age≥40 N=24 (P<0.0001)	375.0 ± 9.0 NS*	6.7 ± 0.7 NS	77.5 ± 6.8 NS	64.1 ± 8.2 NS	65.2 ± 7.1 NS	67.5 ± 3.3 NS
Group B MMSE 20-24 Age≥40 N=64 (P<0.0001)	368.6 ± 3.5 P=0.004	6.4 ± 0.4 NS	81.4 ± 2.7 NS	80.3 ± 2.7 NS	77.7 ± 3.3 NS	78.8 ± 2.0 NS
Group C MMSE 25-27 Age≥40 N=109 (P<0.0001)	354.8 ± 3.1 NS	6.2 ± 0.3 NS	90.9 ± 2.3 NS	85.2 ± 2.1 NS	83.6 ± 2.3 NS	86.7 ± 1.7 NS
Group D* MMSE 28-30 Age≥40 N=189	350.8 ± 2.0 NS	6.0 ± 0.2 NS	101.9 ± 1.6 P=0.0001	94.6 ± 1.8 P=0.001	98.2 ± 1.7 P=0.00001	95.1 ± 1.6 P=0.00062
Group E Control Age≥40 N=489	343.4 ± 1.3 P=0.0004	6.0 ± 0.1 NS	103.4 ± 1.3 NS	98.9 ± 1.3 NS	101.9 ± 1.3 NS	96.5 ± 1.1 NS

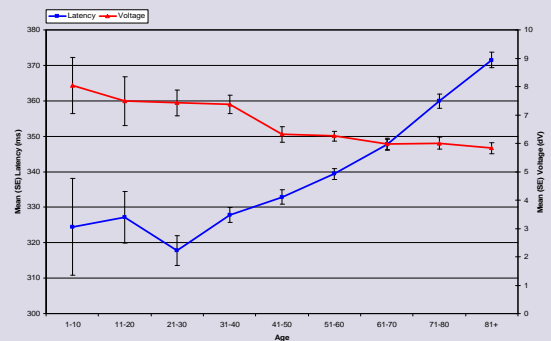
*NS=Not Significant. P Values are comparisons of B to A, C to B, D to C and E to D

** WMS-III demographics: A (N=11), B (N=44), C(N=68), D(N=123), E (N=205)

*Braverman E, Blum K. (2003) P300 Event-Related Potential: An Accurate Predictor of Memory. Clinical EEG, Vol 34, No. 3

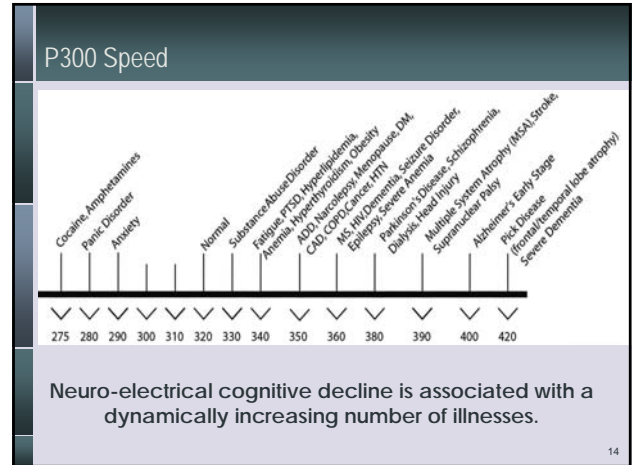
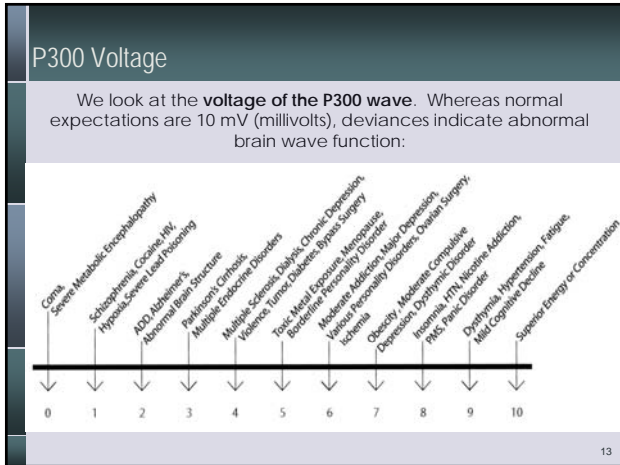
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P300 Latency and Voltage average, by age group



*Braverman E, Blum K. (2003) P300 Event-Related Potential: An Accurate Predictor of Memory. Clinical EEG, Vol 34, No. 3

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BEAM: Brain Diagnostic Evaluation

- Spectral analysis, including changes in frequency of the signal wave
- P300 voltage (strength) and latency (delay in the wave cycle)
- Evoked potentials (using visual and auditory provocations), numbers
- Grade of abnormality, Grade 1 through Grade 7
- EEG Electroencephalography
- People go on seizure medications when there are arrhythmias in their brains, which can be detected with a computerized EEG (BEAM).

Clinical significance of focal topographic changes in the electroencephalogram (EEG) and evoked potentials (EP) of psychiatric patients Gerez M, Tello A [Brain Topogr.](#) 1992 Fall;5(1):3-10

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BEAM

- EEG - (Limited Value)
- P300 Voltage - Energy, Power, Metabolism
- P300 Time - Speed, Youth, Cognition
- Evoked Potentials - *Arrhythmia* /Brain Rhythm
Anxiety, Seizures
- Spectral Analysis- *Synchrony* (On/Off Switch)
Mind-Body, Relaxation

P300 (latency) event-related potential: an accurate predictor of memory impairment. Braverman ER, Blum K [Clin Electroencephalogr.](#) 2003 Jul;34(3):124-39

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BEAM

- Voltage - Catecholamines
- Speed - Cholinergic
- Rhythm - GABAergic
- Synchrony - Serotonergic

P300 (latency) event-related potential: an accurate predictor of memory impairment. Braverman ER, Blum K [Clin Electroencephalogr.](#) 2003 Jul;34(3):124-39

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Brain Evaluation & Assessment Method

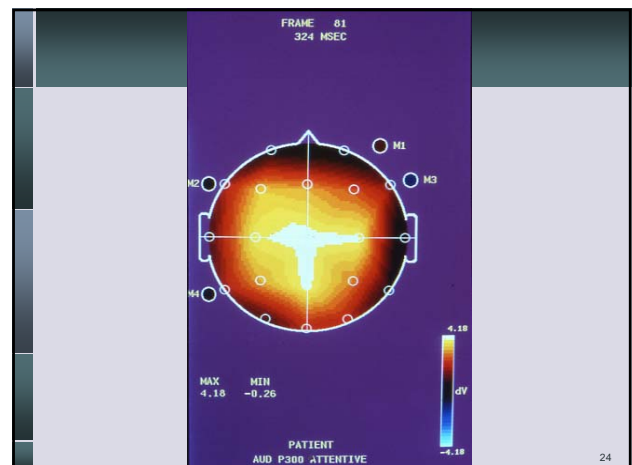
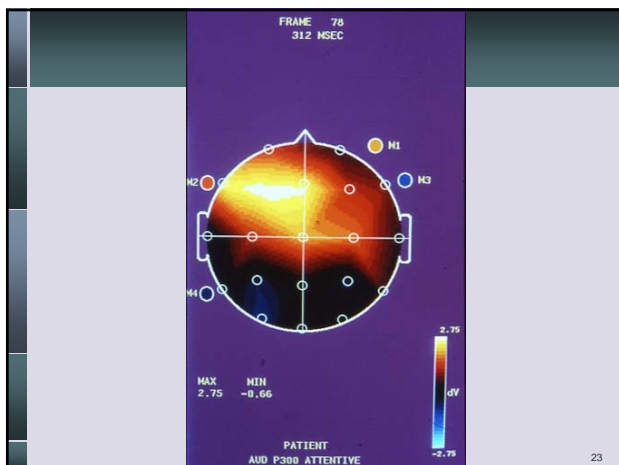
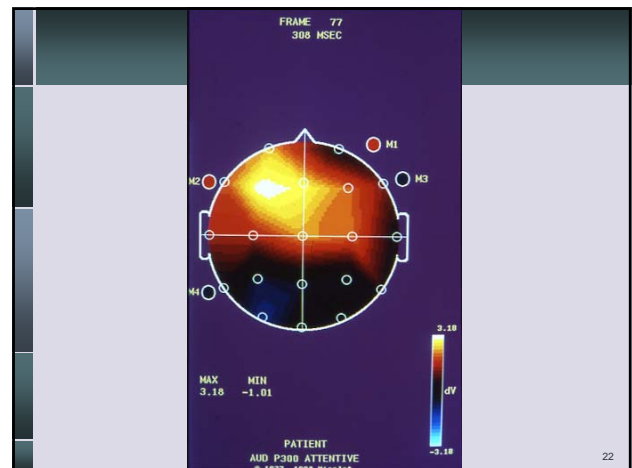
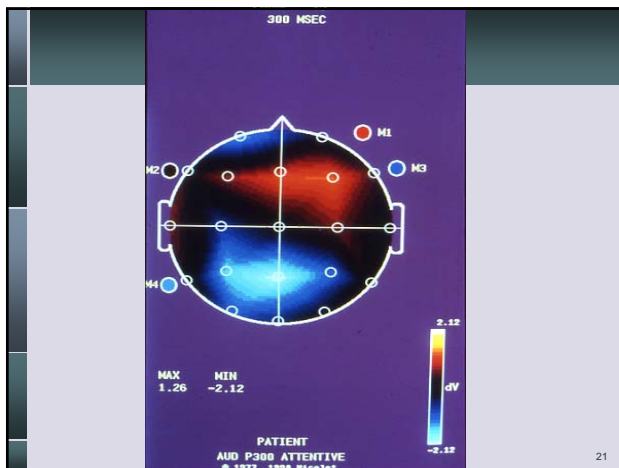
- Brain Electrical Activity Mapping (BEAM)
- McGill Clinical Multiaxial Inventory (MCMI-III)
- Myers-Briggs Type Indicator (MBTI)
- Wechsler Memory Scale-Revised (WMS-R)
- Test of Variables of Attention (TOVA)
- Cognitive IQ Assessment (GAMA)

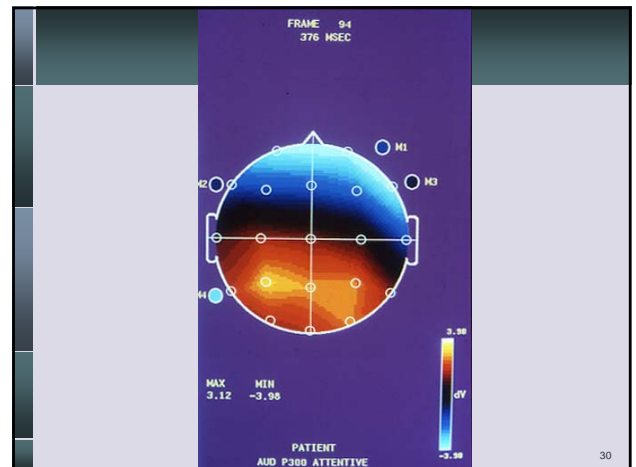
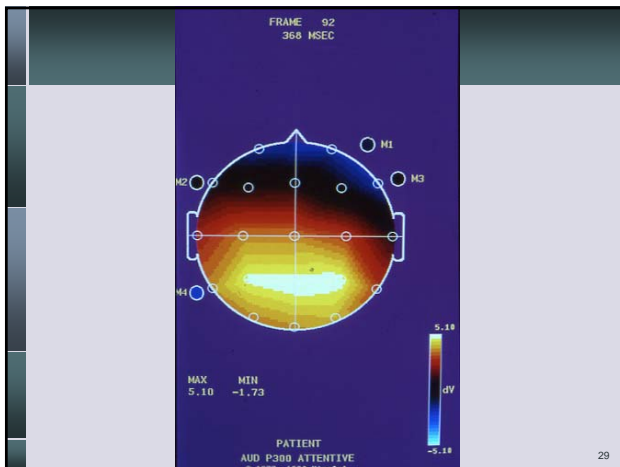
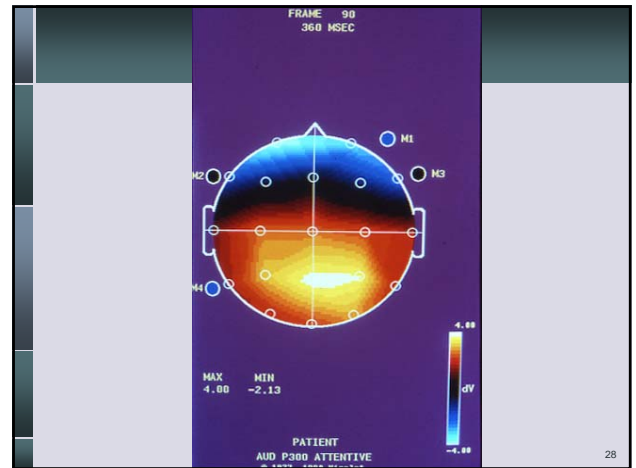
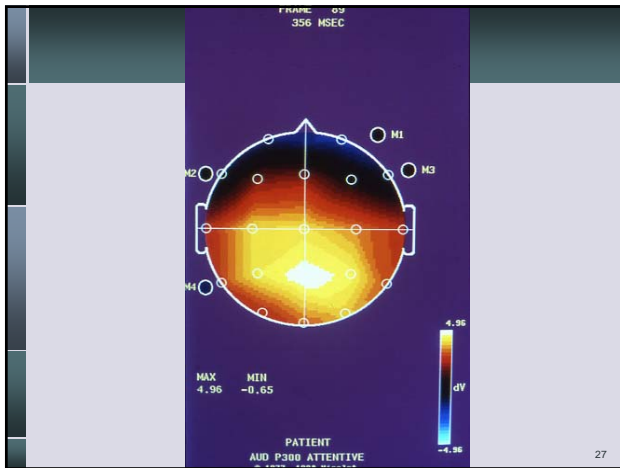
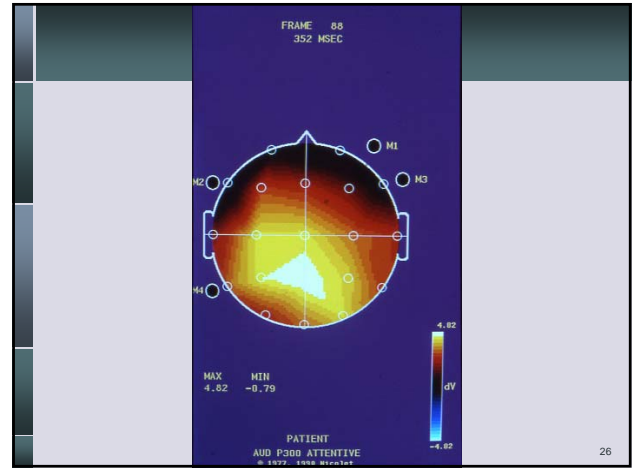
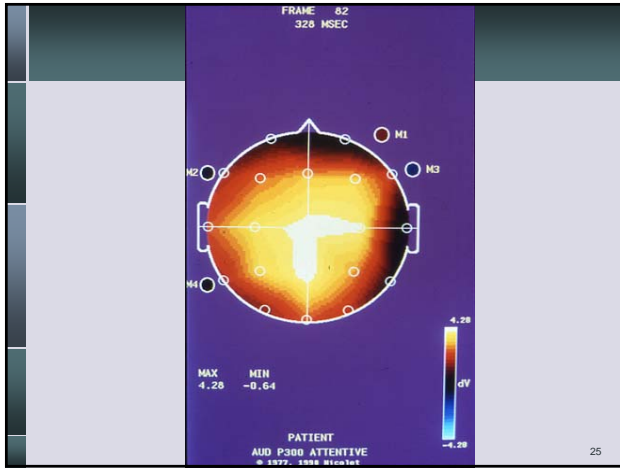
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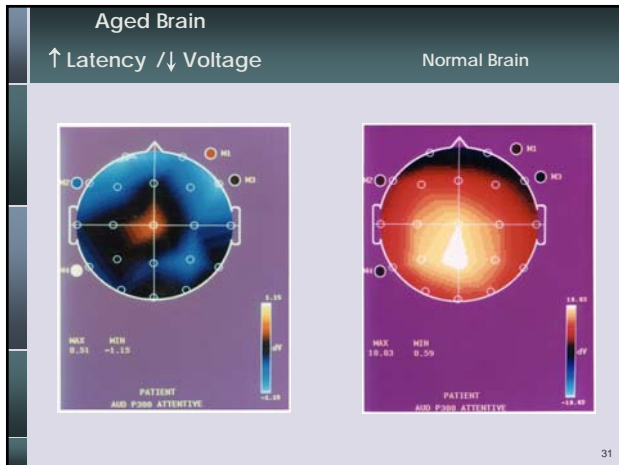
The Origins of Brain Electricity

- Electrolytes and ions
- Neurotransmitters
- Hormones
- Electromagnetic fields
- Spinal Cord to Brain "Edge"

- The P300 wave originates in the right frontal lobe, travels to the left frontal lobe and moves to the central portion of your brain and then to the parietal lobes.







Total Disease Load / Brain Function

- *Every disease wears out your head. And the more diseases you accumulate – hormonal or otherwise – the more damaged your brain function will be.*

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Disease = Accelerated Aging

- Everyone has heard of menopause.
- But *most hormones* – not just estrogen – *have a "pause."*
- The pauses we experience as we age affect *every single organ system* and lead to *uncountable diseases*.
- *Each gland* and organ system ages at a different rate in different people.
- Hormones affect and are affected by *all neurotransmitter systems*.

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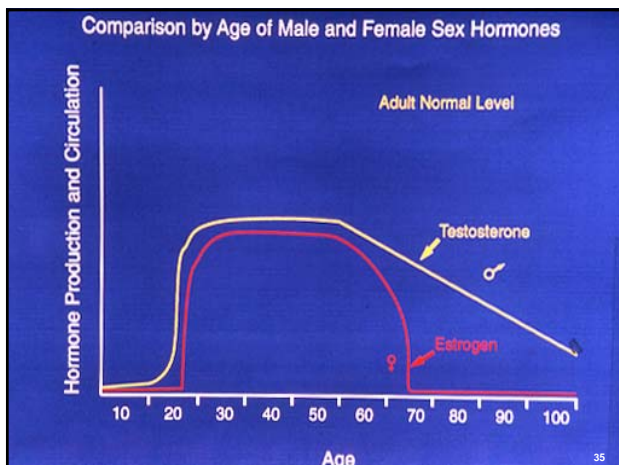
Age Prints, and Causes of Pauses?

Causes:

- Genetic & Environmental
- Endocrine disruptors
- This leads to neurotransmitter imbalances
- What we commonly consider to be "normal aging."

Each person has a unique *age print* – where their oldest parts are age accelerators and eventually lead to death.

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Genetic vs. Environmental Causes

- Some pauses are *genetic* and some are *environmental*
- *Male menopause (andropause)* is mostly caused by *environmental factors*.
- *Female menopause* is mostly caused by *genetic factors*.

Endocrine Disruptors:

- Pesticides
- Plastics and cosmetics containing phthalates
- Car exhaust, paints, plumbing, canned foods
- Hair dyes, newspaper print, tap water

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An Overview of Pauses and Their Global Nature Throughout the Body

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Pause	Decline In	Onset Age
Electropause	Electrical activity of brain waves	45
Biopause	Neurotransmitters	Dopamine: 30 Acetylcholine: 40 GAB A: 50 Serotonin: 60
Pineal Pause	Melatonin	20
Pituitary Pause	Hormone feedback loops	30
Sensory Pause	Touch, hearing, vision, taste and smell sensitivity	40
Psychopause	Personality, health and mood	30
Thyropause	Calcitonin and thyroid hormone levels	50
Parathyropause	Parathyroid hormone	50

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Pause	Decline In	Onset Age
Thymopause	Gland size and immune system	40
Cardio/Vasculopause	Blood flow	40
Pulmonopause	Lung elasticity and function with increase in blood pressure	50
Adrenopause	DHEA	55
Nephropause	Erythropoietin level	40
Somatopause	Growth hormone	30
Gastropause	Nutrient Absorption	40
Pancreopause	Blood sugar level	40

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Pause	Decline In	Onset Age
Insulopause	Glucose tolerance	40
Andropause	Testosterone in men	45
Menopause	Estrogen, progesterone, and testosterone in women	40
Osteopause	Bone density	30
Dermopause	Collagen, Vitamin D synthesis	35
Onchopause	Finger and toe nails	40
Uropause	Bladder control	45
Genopause	DNA	40

- Everyone has a unique *"pause print."*
- *Bioidentical hormone replacement* is not the same for everyone, and it is important to get a *full brain and body health check up* in order to decide which hormones will work for you.
- Remember – *you are only as young as your oldest part!* Find silent disease before it silences you.

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Hormonal Changes According to the Medical Literature

Decrease	No Change	Increase
Insulin growth factor Vitamin 25(OH) D Testosterone(m) Estradiol (f) DHEA & its sulfate Triiodothyronine 1,25(OH) ₂ Vit D Inhibin Arginine Vasopressin Pregnenolone	Epinephrine Thyroxine Glucagon Glucagon like Peptide 1 Thyrotropin Calcitonin ACTH Prolactin(f)	Insulin Vasopressin Cholecystokinin Atrial naturetic peptide Norepinephrine Epinephrine(>80yo) FSH LH(f) Parathormone Cortisol

These changes create the pauses of aging!

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P.Morrison MF: Hormones, gender and the aging brain: The endocrine basis of geriatric psychiatry, (2000) Cambridge University Press, Cambridge.

What are Hormones, Anyway?

- Hormones are chemical messengers secreted by endocrine glands.
- Hormones can be classified according to how they are synthesized.
- The three main categories are: peptide and polypeptide hormones, steroid hormones, and amine hormones (derived from tyrosine and tryptophan).

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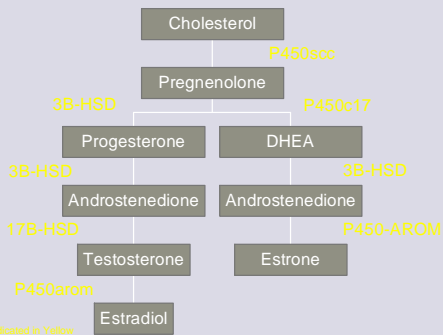
Steroid Hormones (all derived from cholesterol)

- Androstenedione
- DHEA
- DHEA-Sulfate
- Estradiol
- Estrone
- Cortisol
- Aldosterone
- Pregnenolone
- Progesterone
- Testosterone
- Vitamin D

Vander's Human Physiology: The Mechanisms of Body Function 2006 Widmaier, Raff, Strang

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Sex Steroid Synthesis in the CNS



Bates KA, Harvey AR, Cairuthers M, Martins RN. Androgens, andropause and neurodegeneration: exploring the link between steroidogenesis, androgens and Alzheimer's disease. *Cell Mol Life Sci*. 2005 Feb; 62(3):281-92.

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Peptide and Polypeptide Hormones

- Calcitonin
- Erythropoietin
- Human Growth Hormone
- IGF-1
- Incretin
- Insulin
- Parathyroid Hormone
- Oxytocin
- DDAVP (Vasopressin)

Vander's Human Physiology: The Mechanisms of Body Function 2006 Widmaier, Raff, Strang

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Amine Hormones (Tryptophan and Tyrosine derivatives)

- Melatonin
- Thyroid Hormone – Thyroxine (T4)
- Thyroid Hormone – Tri-Iodothyronine (T3)

Vander's Human Physiology: The Mechanisms of Body Function 2006 Widmaier, Raff, Strang

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The Brain Pulses out Hormones!

- The four main neurotransmitter systems: *Cholinergic, Catecholaminergic, Serotonergic, GABAergic*. Each system affects different *hormones* in *different ways*.
- In some instances, "neurotransmitters" behave more like *hormones* (e.g. *epinephrine and norepinephrine*, and *dopamine* when it acts as a *releasing hormone* from the pituitary gland)

Neurotransmitter regulation of anterior pituitary hormones Tuomisto J, Mannisto P *Pharmacol Rev*. 1985 Sep; 37(3):249-332

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Hormones Involved with the Catecholamine System: Brain Voltage

- Testosterone/ Estrogen
- DHEA
- Thyroid
- Cortisol
- HGH
- Erythropoietin

- Insulin
- TRH
- IGF-1
- Cholecystakinin
- HCG
- Prolactin
- GnRH

Neurotransmitter regulation of anterior pituitary hormones Tuomisto J, Mannisto P *Pharmacol Rev.* 1985 Sep;37(3):249-332
 Hypoinsulinemia regulates amphetamine-induced reverse transport of dopamine. Williams JM, Owens WA, Turner GH, Saunders C, Dipace C, Blakey RD, France CP, Gore JC, Daws LC, Avison MJ, Galli A *PLoS Biol* 2007 Oct 16;5(10):2349-78
 Dopamine D2 receptors contribute to increased avidity for sucrose in obese rats lacking CCK-1 receptors Hajnal A, De Jonghe BC, Covasa M *Neuroscience*, 2007 Aug 24;148(2):584-92
 Stimulating effect of erythropoietin on the release of dopamine and acetylcholine from the rat brain slice Yamamoto M, Koshimura K, Kawaguchi M, Sotmiya M, Murakami Y, Kato Y *Neuroscience letters* 2000;vol. 292, 2, pp.131-3
 Norepinephrine regulates human chorionic gonadotrophin production by first trimester trophoblast tissue in vitro Shi CZ, Zhuang LZ *Placenta*, 1993 Nov-Dec;14(6):683-93

Hormones Involved with the Cholinergic System – Brain Speed

- Human Growth Hormone
- Vasopressin
- DHEA
- Calcitonin

- Parathyroid Hormone
- Estrogen
- Prolactin
- T3 & T4

Neurotransmitter regulation of anterior pituitary hormones Tuomisto J, Mannisto P *Pharmacol Rev.* 1985 Sep;37(3):249-332
 Role of brain acetylcholine in vasopressin release during osmotic stimulation and hemorrhage Iltake K, Share L, Brooks DP, Crofton JT, Ouchi Y *Experimental Brain Research*, Vol 75, number 1 Mar 1989
 Enhanced plasma DHEAS, brain acetylcholine, and memory mediated by steroid sulfatase inhibition Rhodes ME, Li PK, Burke AM, Johnson DA *Brain Res.* 2997 Oct 31;773(1-2):28-32
 Effect of parathyroid hormone and calcitonin on acetylcholine release in rat sympathetic superior cervical ganglion Stern JE, Cardinali DP *Brain Res.* 2994 Jul 11;650(2):267-74
 Cognitive Status in Hypothyroid Female Patients: Event-Related Evoked Potential Study Anjana Y, Tandon OP, Vaney N, Madhu SV *Neuroendocrinology* 2008 Feb 19

Acetylcholine & Catecholamines

- Donepezil, an acetylcholinesterase inhibitor used in the treatment of Alzheimer's disease, improves P300 latency
- Clark Randt showed that catecholamines help memory and impacts brain voltage and speed to a degree.

Event related potentials and psychopharmacology, cholinergic modulation of P300. Dierks T, Frolich L, Ihl R, Maurer K *Pharmacopsychiatry* 1994;27:72-74
 P300 auditory event-related potentials and neuropsychological study during donepezil treatment in vascular dementia Paci C, Gobatto R, Carboni T, Sanguigni S, Santone A, Curatola L *NeuroSci*, 2006 Feb;26(6):435-7
 Norepinephrine biosynthesis inhibition: effects on memory in mice Randt CT et al *Science* 1971 Apr 30;172(982):498-9

Hormones Involved with the Serotonergic System – Brain Synchrony

- Progesterone
- Human Growth Hormone
- Pregnenolone
- Melatonin

- Leptin
- Aldosterone
- Prolactin
- Estrogen

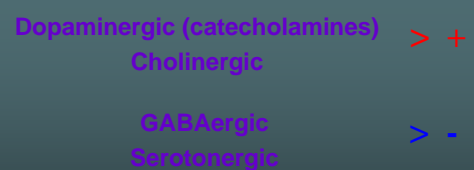
Neurotransmitter regulation of anterior pituitary hormones Tuomisto J, Mannisto P *Pharmacol Rev.* 1985 Sep;37(3):249-332
 Progesterone pretreatment enhances serotonin-stimulated BDNF gene expression in rat c6 glioma cells through production of 5 alpha-reduced neurosteroids Morita K, Her S *J Mol Neurosci* 2008;34(3):193-200
 Involvement of serotonin in leptin-induced hypophagia in mice Hirose H, Sugimoto Y, Yamada J *Jpn J Pharmacol* vol. 88, supplement 1 page 137 (2002)
 The effect of different body allowances of aldosterone on serotonin and Camp metabolism in the tissues of rats with a disordered trophic function of the nervous system Azhpa Ial, Egorova LK *Izv Akad Nauk Ser Biol*, 1992 May-Jun;(3):417-3
 Effect of parathyroid hormone and calcitonin on acetylcholine release in rat sympathetic superior cervical ganglion Stern JE, Cardinali DP *Brain Res.* 2994 Jul 11;650(2):267-74
 Melatonin and serotonin effects on gastrointestinal motility Thor PJ, Krolczyk G, Gil K, Zurowski D, Nowak L *J Physiol Pharmacol*, 2007 Dec;58 Suppl6:97-103

Hormones Involved with the GABAergic System – Brain Rhythm

- Progesterone
- Pregnenolone
- GHRH
- Prolactin
- Estrogen

Neurotransmitter regulation of anterior pituitary hormones Tuomisto J, Mannisto P *Pharmacol Rev.* 1985 Sep;37(3):249-332
 Sex steroids effects on the content of GAD, TH, GABA(A), and Glutamate Receptors in the Olfactory Bulb of the Male Rat, Guerra-Araiza C, Miranda-Martinez A, Neri-Gomez T, Comacho-Arroyo I *Neurochem Res*, 2008 Mar 25
 Ovarian hormones and migraine headache: understanding mechanisms pathogenesis – part I Martin VT, Behbehani M *Headache* 2006;46(1):3-23

The Binary Neuroelectrochemical System: the Order



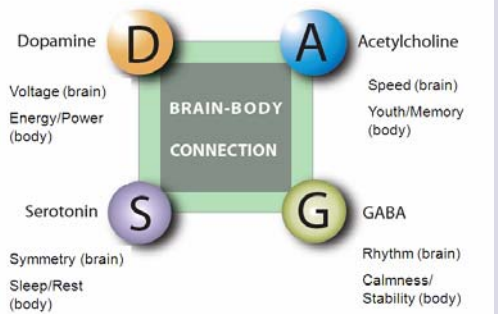
Endorphins – “spare tires”
 Clark Randt showed that *adrenaline* helps with *memory*.

$$E=MC^2$$

$$\text{Cognitive Energy} = \text{Brain Speed} \times (\text{Voltage})^2$$

Brain cyclic AMP and memory in mice Randt CT et al *Pharmacol Biochem Behav*, 1982 Oct; 17(4):677-80

The EDGE Effect



Fixing more than one part of the brain results in a synergistic (EDGE) effect

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Chemicals Influence all Neurotransmitter Systems

For example, *nicotine* has effects on all of the following systems:

Acetylcholine: arousal, cognitive enhancement

Dopamine: pleasure, appetite suppression

Serotonin: mood modulation, appetite suppression

GABA: reduction of anxiety and tension

Nicotinic acetylcholine receptors of the ventral tegmental area are involved in mediating morphine-state-dependent learning. Rezaeifard A, Darbandi N, Zarrindast MR *Neurobiol Learn Mem.* 2008 Apr 25

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The 4 Brain Humors: Brain and Body Repair Mechanisms

System	Natural	Pharmaceutical	Hormonal	Electrical Treatments & Lifestyle Changes
Dopamine "Voltage, Energy & Power"	Caffeine Rhodiola Rosea Folic Acid Tyrosine	Wellbutrin Tenuate Provigil Cymbalta Adderall	Testosterone/Estrogen DHEA Thyroid	Weight bearing exercise Teas Spices: Cumin, etc
Serotonin "Symmetry, Sleep & Rest"	Fish Oils Tryptophan Magnesium	Paxil Effexor Meridia	Progesterone Pregnenolone	CES/TENS Sleep Complex Carbs
Acetylcholine "Speed, Youth & Memory"	Fish Oils Choline Lipoic Acid Acetyl-Carnitine	Aricept Exelon Statin Drugs Namenda	Estrogen Parathyroid	Aerobics Spices: Sage Eggs, etc
GABA "Rhythm, Calmness & Stability"	Inositol CoQ Theanine	Depakote Topamax Tegretol	Progesterone Human Growth Hormone	CES Spices: Cinnamon

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Guide to Brain Chemistry

Test	Brain-Mind Domain	Dopamine • Power •	GABA • Calming •	Acetylcholine • Speed •	Serotonin • Rest •
BEAM	Electrophysiology	Voltage	Rhythm	Speed	Synchrony
MBTI	Dominant Temperament	NT	SJ	NF	SP
WMS	Memory Dominance	Working	Verbal	Immediate	Visual
TOVA, CNSVS	Attention Measure	Variability	Commissions	Omissions	Reaction Time
GAMA	IQ Dominance	Abstract	Emotional	Creative	Perceptual

Braverman ER. Neurological Function and the Aging Process. *Nutritions.* February 2003.

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Dopamine-Driven Personalities

- Power and energy characterize a balanced dopamine nature.
- Personality issues that are associated with a dopamine imbalance are: histrionic (+), schizoid (+), aggressiveness (+), anti-social personality (+), schizotypal (-), borderline personality (+)

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Acetylcholine-Driven Personalities

- Creativity, open-mindedness, and adventurousness characterize those with acetylcholine natures.
- Personality issues that are associated with an acetylcholine imbalance are: perfectionism (-), procrastination (-).

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GABA-Driven Personalities

- Stability and organization characterize a balanced GABA nature.
- Personality issues that are associated with a GABA imbalance are: anxiety (-), anti-social personality (+), shyness (-), desirability (+), histrionic (-), self-defeating (-), borderline personality (-), perfectionism (+)

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Serotonin-Driven Personalities

- Living in the moment and enjoying life (though not to the extent of sacrificing the future) characterize a balanced serotonin nature.
- Personality issues that are associated with a serotonin imbalance are: depression (-), shyness (+), narcissistic (+), procrastination (+), self-defeating (+), delusional (+), paranoid (-)

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Personality Disorders: When Brain Chemicals Become Imbalanced

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Schizotypal "Eccentric" Personality Disorder

Deficits in interpersonal relatedness, and peculiarities in ideation, appearance, and behavior, including:

- No close friends or confidants.
- Odd speech (depressive, vague, inappropriately abstract).
- Inappropriate or constricted affect.
- Suspicious or paranoid ideation
- Ideas of reference
- Excessive social anxiety
- Odd beliefs or magical thinking, inconsistent with cultural norms
- Unusual perceptual experiences

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The Neurochemical Relationship

- The schizotypal, "eccentric" personality disorder is marked by *low levels of dopamine, acetylcholine, and serotonin*

Schizotypy, attention deficit hyperactivity disorder, and dopamine genes Ettinger U, Joober R, DE Guzman R, O'driscoll GA *Psychiatry Clin Neurosci*, 2006 Dec;60(6):764-7

Initial Phase 2 Trial of a Nicotinic Agonist in Schizophrenia Freedman R, Olincy A, Buchanan RW, Harris JG, Gold JM, Johnson L, Allersworth D, Guzman-Bonilla A, Clement B, Ball MP, Kutnick J, Pender V, Martin LF, Stevens KE, Wagner BD, Zerbe GO, Soti F, Kern WR *Am J Psychiatry*, 2008 Apr 1

Selective serotonin re-uptake inhibitor augmentation in the treatment of negative symptoms of schizophrenia Silver H *Expert Opin Pharmacother*, 2004 Oct;5(10):2053-8

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Loner or Schizoid Personality Disorder

Social detachment and restricted expression of emotions, including:

- No close friends or confidants
- Constricted affect (e.g. aloof, cold, rarely reciprocates, smiles or nods)
- Appears or claims to be indifferent to the praise and criticism of others
- Little if any desire to have sexual experiences with another person
- Little desire for enjoyment of close relationships, including being part of a family
- Almost always chooses solitary activities
- Claims to experience anger rarely, if ever
- Is uninterested in the feelings of other people.

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The Neurochemical Relationship

- The loner or schizoid personality disorder is marked by *low levels of dopamine*, and *high levels of serotonin and GABA*.

Schizoid psychosis during cannabis intake (Case report) Gaszner P, Csernus I, Fulop B, Gaszner G
Neuropsychopharmacol Hung, 2004 Jun;6(2):90-2

Schizoid neurochemical pathology-Induced membrane Na(+)-K+ ATPase inhibition in relation to neurological disorders
Kurup RK, Kurup PA Int J Neurosci, 2003 Dec;113(12):1705-17 67

Painfully Shy or Avoidant Personality Disorder

Social discomfort, fear of negative evaluation, and limidity, such as:

- No close friends or confidants
- Feelings easily hurt by criticism or disapproval
- Unwilling to get involved with people unless certain of being liked
- Avoids social or occupational activities that involve significant interpersonal contact
- More fearful than most people of having a new experience
- Afraid of appearing foolish or being embarrassed
- Afraid of losing control or giving in to an unacceptable impulse
- Exaggerates the potential dangers or risks in everyday situations
- Avoids everyday activities for fear they will be too fatiguing or physically uncomfortable

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The Neurochemical Relationship

- The painfully shy or avoidant personality disorder is marked by *low levels of GABA, dopamine, and acetylcholine*, and may also show *elevated or lowered levels of serotonin*

Social anxiety disorder: psychobiological and evolutionary underpinnings. Stein DJ, Vythilingum B CNS Spectr, 2007
Nov;12(11):806-9

Changes in cholinergic activity and avoidance behavior by nicotine in differentially housed mice Essman WB Int J
Neurosci, 1971 Nov;2(4):199-205

Bulimia nervosa with co-morbid avoidant personality disorder: behavioural characteristics and serotonergic function.
Bruce KR, Steiger H, Koerner NM, Israel M, Young SN Psychol Med, 2004 Jan;34(1):113-24 69

Abuse-Me or Self-Defeating/Masochistic Personality Disorder

Feelings of martyrdom and self-demeaning behavior, such as:

- Remains in relationships in which others exploit, abuse, or take advantage of him or her despite opportunities to alter the situation
- Believes he/she almost always sacrifices own interests for those of others
- Rejects help, gifts, or favors so as not to be a burden to others
- Complains, directly or indirectly about being unappreciated
- Responds to success/positive events by feeling undeserving or worrying excessively about not being able to measure up to new responsibilities
- Always pessimistic about the future
- Thinks only about his or her worst features
- Sabotages his or her own intended goals
- Repeatedly turns down opportunities for pleasure

The Neurochemical Relationship

- The abuse-me or self-defeating/masochistic personality disorder is marked by *low levels of serotonin and dopamine*

Role of genetic factors in human sexual behavior based on studies of Tourette syndrome and ADHD probands and
their relatives Comings DE Am J Med Genet, 1994 Sep 15;54(3):227-41

Treatment of an unusual case of masochism. Shiwach RS, Prosser J J Sex Marital Ther, 1998 Oct-Dec;24(4):303-7 71

Nurturing or Dependent Personality Disorder

Dependent and submissive behavior, such as:

- Prefers others to make most or all of his or her major life decisions
- Remains in relationships with people who mistreat him or her, because of fear of being alone
- Has difficulty initiating projects or doing things on his or her own
- Volunteers to do things that are unpleasant or demeaning in order to get other people to like him or her
- Feels helpless or uncomfortable being alone or goes to great lengths to avoid being alone
- Feels devastated or helpless when a close relationship ends
- Often preoccupied with the fear of being abandoned
- Feelings easily hurt by criticism or disapproval
- Constantly seeking reassurance, approval or praise.

The Neurochemical Relationship

- The nurturing or dependent personality disorder is marked by **high levels of GABA and serotonin**, in addition to oxytocin (which is secreted in response to GABA release from synapses).

The interaction of serotonin and dopamine systems with the systems of the regulatory peptides oxytocin, vasopressin, and prolactin under normal conditions and during pregnancy Nikolaeva AA, Koroleva SV, Ashmarin IP *Vestn Ross Akad Med Nauk*, 2007;(9):37-43

CD38 regulates oxytocin secretion and complex social behavior Bartz JA, McInnes LA *Bioscience*, 2007 Sep;29(9):837-41

Maternal oxytocin triggers a transient inhibitory switch in GABA signaling in the fetal brain during delivery. Tyzio R, Cossart R, Khalilov I, Minlebaev M, Hubner CA, Represa A, Ben-Ari Y, Khazipov R *Science*, 2006 Dec 15;314(5806):1788-92

Benzodiazepines and the developing rat: a critical review Tucker JC *Neurosci Biobehav Rev*, 1985 Spring;9(1):101-11

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Anxiety Disorder/ Panic Attacks

A discrete period of intense fear or discomfort, experiences such as:

- Palpitations, pounding heart, or accelerated heart rate
- Sweating
- Trembling or shaking
- Sensations of shortness of breath or smothering
- Feeling of choking
- Chest pain or discomfort
- Nausea or abdominal distress
- Dizziness
- Derealization or depersonalization
- Fear of losing control or going crazy
- Fear of dying

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The Neurochemical Relationship

- Anxiety disorder/panic attacks are marked by **low levels of GABA**

Tonic arousal and activity: relationships to personality and personality disorder traits in panic patients. King RJ, Bayon EP, Clark DB, Taylor CB *Psychiatry Res*, 1988 Jul;25(1):65-72

Panic-disorder – psychobiological aspects of personality dimensions Draganic-Rajic S, Lecic-Tosevski D, Paunovic VR, Cvejic V, Svrakic D *Strp Arh Celok Lek*, 2005 Mar-Apr;133(3-4):129-33

The interaction of morphine and gamma-aminobutyric acid (GABA)ergic systems in anxiolytic behavior: using mu-opioid receptor knockout mice. Sasaki K, Fan LW, Tien LT, Ma T, Loh HH, Ho K *Brain Res Bull*, 2002 Mar 15;57(5):689-94

Activin tunes GABAergic neurotransmission and modulates anxiety-like behavior. Zheng F, Adelsberger H, Muller MR, Fritschy JM, Werner S, Alzheimer C *Mol Psychiatry*, 2008 Jan 8

75

Dukes-Up or Aggressive/Sadistic Personality Disorder

Strong inclination to engage in domineering, competitive, and hostile behaviors.

- Reveals satisfaction in intimidating, coercing, and humiliating others
- Unflinching, recklessly daring, thick-skinned, and seemingly unshaken by pain
- Expresses verbally abusive if not physically brutal behaviors
- Remarkably detached from an awareness of the impact of one's destructive acts
- Characterizes self as aggressively independent, vigorously energetic, and coolly calculated
- Shows paucity of sentimental memories, tender affects, conflict, shame and guilt
- Excitable and pugnacious temper
- Attracted to challenge, risk, and harm
- Exhibits a broad-ranging authoritarianism, social intolerance, and prejudice

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The Neurochemical Relationship

- The dukes-up or aggressive/sadistic personality disorder is marked by **decreased levels of serotonin and GABA**, and **increased levels of dopamine**

Neurobiology of aggression and violence Siever LJ *Am J Psychiatry*, 2008 Apr;165(4):429-42

77

Rule-Breaker or Antisocial Personality Disorder

• A pattern of irresponsible and antisocial behavior, such as:

- Inability to sustain consistent work behavior
- Failure to conform to social norms with respect to lawful behavior
- Irritability and aggressiveness as indicated by repeated physical fights or assaults
- Repeated failure to honor financial obligations as indicated by defaulting on debts, failure to provide child support, or failure to support other dependents on a regular basis
- Impulsivity
- Disregard for the truth as indicated by repeated lying
- Reckless, as indicated by driving while intoxicated or recurrent speeding
- Lacks ability to function as a responsible parent
- Has never sustained a totally monogamous relationship for more than 1 year
- Lack of remorse

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The Neurochemical Relationship

- The rule-breaker or antisocial personality disorder is marked by *decreased levels of GABA and serotonin*.

Serotonin transporter polymorphism and borderline or antisocial traits among low-income young adults Lyons-Ruth K, Holmes BM, Sasvari-Szekely M, Ronai Z, Nemoda Z, Pauls D *Psychiatr Genet*, 2007 Dec;17(6):339-43

Reward deficiency syndrome: a biogenetic model for the diagnosis and treatment of impulsive, addictive, and compulsive behaviors Blum K, Braverman ER, Holder JM, Lubar JF, Monasta VJ, Miller D, Lubar JO, Chen TJ, Comings DE *J Psychoactive Drugs*, 2000 Nov;32 Suppl1-iv, 1-112

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Posttraumatic Stress Disorder

- The person has been exposed to a traumatic event that elicited in the person intense fear, helplessness, or horror
- The traumatic event is persistently re-experienced
- There is persistent avoidance of stimuli associated with the trauma and a numbing of general responsiveness (not present before the trauma).
- There are persistent symptoms of increased arousal (not present before the trauma)
- The duration of the disturbance is more than 1 month.
- The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

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The Neurochemical Relationship

- Posttraumatic stress disorder is marked by *decreased levels of GABA, dopamine, and serotonin*.

Dopamine D2 receptor (DRD2) gene and susceptibility to posttraumatic stress disorder: a study and replication. Comings DE, Muhleman D, Gysin R *Biol Psychiatry*, 1996 Sep 1;40(5):368-72

Reduced GABAA benzodiazepine receptor binding in veterans with post-traumatic stress disorder. Gauze E, van Berckel BN, Lammersma AA, Boellaard R, de Kloet CS, Vermetten E, Westenberg HG *Mol Psychiatry* 2008 Jan;13(1):74-83.3

Posttraumatic stress disorder: characteristics and treatment Mellman T, Lydiard RB *J Clin Psychiatry*. 2008 Jan;69(1):e2

Antiepileptic drugs for the treatment of post-traumatic stress disorder Berlin HA *Curr Psychiatry Rep*, 2007 Aug;9(4):291-300

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Drama Queen or Histrionic Personality Disorder

- Excessive emotionality and attention-seeking, such as:
- Content of speech is characterized by exaggeration and hyperbole
- Constantly seeking reassurance, approval or praise
- Inappropriately sexually seductive appearance or behavior
- Overly concerned with physical appearance
- Exaggerated expressions of emotions
- Uncomfortable in situations in which he or she is not the center of attention
- Perceived by others as shallow and lacking genuineness, even if superficially warm and charming
- Egocentric and self-indulgent

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The Neurochemical Relationship

- The drama queen or histrionic personality disorder is marked by *high levels of dopamine, serotonin, GABA, and acetylcholine*.

A unified biosocial theory of personality and its role in the development of anxiety states Cloninger CR *Psychiatr Dev*, 1986 Autumn;4(3):167-226

Psychogenic pseudo-asthmatic syndrome Szmidt M, Instonajt B, Fijałkowski M *Pneumonol Alergol Pol*, 1995;63(3-4):215-7

Cerebral information processing in personality disorders: I. Intensity dependence of auditory evoked potentials Wang W, Wang Y, Fu X, Liu J, He C, Dong Y, Livesley WJ, Jang KL *Psychiatry Research* 141 (2006) 173-183

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Unstable or Borderline Personality Disorder

- Instability of mood, interpersonal relationships, and self image, e.g.:
- A pattern of unstable and intense personal relationships characterized by alternating between the extremes of overidealization and devaluation
- Interpersonal exploitativeness
- Impulsivity
- Affective instability -- marked shifts from normal mood to depression, irritability, or anxiety
- Inappropriate, intense anger or lack of control of anger
- Recurrent suicidal threats, gestures or behavior, or self-mutilating behavior
- Marked and persistent identity disturbance manifested by uncertainty
- Chronic feelings of emptiness or boredom

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The Neurochemical Relationship

- The unstable or borderline personality disorder is marked by *decreased levels of GABA*

Efficacy and safety of gabapentin in Borderline Personality Disorder: a six-month, open-label study. Peris L, Szergan N, Ruiz M *Vertex*, 2007 Nov-Dec;18(76):418-22

Major Depression Episode

- The following symptoms have been present during the same 2 week period and represent a change from previous functioning:
- Depressed mood most of the day, nearly every day
- Markedly diminished interest or pleasure in all or most activities most of the day, nearly every day
- Significant weight loss when not dieting or weight gain, or decrease or increase in appetite, nearly every day
- Insomnia or hypersomnia nearly every day
- Psychomotor agitation or retardation nearly every day
- Fatigue or loss of energy nearly every day
- Feelings of worthlessness or excessive inappropriate guilt nearly every day
- Diminished ability to think or concentrate nearly every day
- Recurrent thoughts of death or suicide

86

The Neurochemical Relationship

- Major depressive disorder is marked by *decreased levels of dopamine and serotonin*

The under-recognized role of dopamine in the treatment of major depressive disorder. Montgomery SA *Int Clin Psychopharmacol*, 2008 Mar;23(2):63-9

Serotonin Transporter Gene Polymorphisms and Sertraline Response in Major Depression Patients Dogan O, Yuksel N, Ergun MA, Yilmaz A, Ilhan MN, Karlioglu HE, Koc A, Menevse A *Genet Test*, 2008 May 1

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Suspicious or Paranoid Personality Disorder

Unwarranted tendency to interpret the actions of people and events as threatening, e.g.:

- Expects, without sufficient basis, to be exploited or harmed by others
- Unjustifiably questions the loyalty or trustworthiness of friends
- Reads hidden threatening meanings into benign remarks or events
- Unjustified concern or jealousy of spouse or partner
- Reluctance to confide in others because of fear that the information will be used against him or her
- Preoccupations with unsubstantiated conspiratorial theories about contemporary events
- Easily slighted and quick to counterattack or react with anger
- Carries grudges or is unforgiving

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The Neurochemical Relationship

- Suspicious or paranoid personality disorder is marked by *high levels of dopamine and low levels of serotonin*.

Polymorphism in exon 6 of the dopamine D(2) receptor gene (DRD2) is associated with elevated blood pressure and personality disorders in men. Rosmond R, Rankinen T, Chagnon M, Perusse L, Chagnon YC, Bouchard C, Bjorntorp P *J Hum Hypertens*, 2001 Aug;15(8):553-8

Dopamine beta-hydroxylase (DBH) gene and schizophrenia phenotypic variability: a genetic association study. Yamamoto K, Cubellis JF, Gelemler J, Benkeffat C, Lalonde P, Bloom D, Lal S, Labelle A, Turecki G, Rouleau GA, Joober R *Am J Med Genet*, 2003 Feb; 117(1):33-8

The modulatory influence of polymorphism of the serotonin transporter gene on characteristics of mental maladaptation in relatives of patients with endogenous psychoses Aifirmova MV, Golimbet VE, Korovaitseva GI, Lezheiko TV, Abramova LI, Kaleda VG, Barkhatova AN *Neurosci Behav Physiol* 2008 Mar;38(3):253-8

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Self-Absorbed or Narcissistic Personality Disorder

Excessive self-involvement, hypersensitivity to the evaluation of others, and lack of empathy, e.g.:

- Reacts to criticism with feelings of rage, shame, or humiliation
- Interpersonal exploitativeness
- Grandiose or self-impairance
- Pattern of unstable and intense interpersonal relationships that characteristically alternates between the extremes of overidealization and devaluation
- Preoccupation with fantasies of unlimited success, power, brilliance, beauty or ideal love
- Requires constant attention and admiration
- Entitlement
- Belief that one's problems are unique and may be understood only by other special people
- Is aware of but indifferent to the feelings of others
- Preoccupied with feelings of envy

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The Neurochemical Relationship

Self-absorbed or narcissistic personality disorder is marked by *decreased levels of serotonin*.

Cerebral information processing in personality disorders: I. Intensity dependence of auditory evoked potentials
Wang W, Wang Y, Fu X, Liu J, He C, Dong Y, Livesley WJ, Jang K *Psychiatry Research* 141 (2006) 173-83 91

Perfectionist/Obsessive-Compulsive Personality Disorder

Perfectionism and inflexibility, e.g.,

- Restricted expression of warm and tender emotions
- Lack of generosity in giving time, money or gifts when no personal gain is likely to result
- Perfectionism that interferes with task completion
- Preoccupation with details, rules, lists, order, organization or schedules
- Stubborn insistence that others submit to precisely his or her way of doing things
- Excessive devotion to work and productivity to the exclusion of leisure activities and friendship
- Indecisiveness
- Unable to discard worn out or worthless objects even when they have no sentimental value
- Overly conscientious, scrupulous, and inflexible about matters of morality

The Neurochemical Relationship

Perfectionist/obsessive-compulsive personality disorder is marked by *increased levels of GABA, and decreased levels of serotonin and acetylcholine. Dopamine may be increased or decreased.*

Gabapentin augmentation for fluoxetine-treated patients with obsessive-compulsive disorder. Cora-Locatelli G, Greenberg BD, Martin J, Murphy DL *J Clin Psychiatry*, 1998 Sep;59(9):480-1
Serotonergic mechanisms in the treatment of obsessive-compulsive disorder. Goddard AW, Shekhar A, Whiteman AF, McDougle CJ *Drug Discov Today*, 2008 Apr;13(7-8):325-32
Nicotine augmentation for refractory obsessive-compulsive disorder. A case report. Pasquini M, Garavini A, Biondi M *Prog Neuropsychopharmacol Biol Psychiatry*, 2005 Jan;29(1):157-9
New approach to obsessive-compulsive disorder: dopaminergic theories Harsanyi A, Csigo K, Demeter G, Nemeth A *Psychiatr Hung*, 2007;22(4):248-58 93

The PATH to Achieving Total Health: Lines of Defense

4th Line of Defense:
Neuropsychoactive medications that fit your brain chemistry.



1st Line of Defense - Nutrition/lifestyle changes: regular exercise including weight-bearing and aerobic activity, following the Rainbow Diet, spiritual health.

3rd Line of Defense – Hormone Replacement with Bioidenticals:
Pause Print the Body and replace hormones as you age to keep your body and mind young.

2nd Line of Defense - Vitamins and supplements: Brain Print and the body, and follow a supplement regimen to fit your unique chemistry.

Image from: www.masteryourlife.com

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Conclusion

- *Hormones, neurotransmitters, your brain, mind and body* constantly participate in an *everlasting chain of reactions* that affects all aspects of your health and well-being.
- A *mechanical or chemical imbalance* in the chain can lead to problems *anywhere in your body* and affect your *mental health*.
- Establishing a *“brain-print”* and *“pause-print”* is extremely important in order to set up a baseline for comparison.
- *Knowing the Brain Code* and its relevance to *your specific chemistry* will enable you to *prevent or reverse disease* and *work with your personality and temperament* to achieve the *maximum quality of life*.

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