The Nervous System & Neurotransmitters

BEAUTIFUL CHAOS!

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BEAUTIFUL CHAOS!

"Make things as simple as possible, but not any simpler than that"

Albert Einstein

BEAUTIFUL CHAOS!

- HOW DO WE MAKE IT SIMPLE?
- Brain and neurotransmitters are EXTREMELY COMPLEX in function and activities.
- The total number of neurotransmitters is not known, but is well over 100
- Two broad categories: small-molecule neurotransmitters and neuropeptides.
- Small-molecule neurotransmitters mediate rapid synaptic actions, whereas neuropeptides tend to modulate slower, ongoing synaptic functions.

LARGE PICTURE

- Temptation to get bogged down in technical complexities of this world, without grasping a large picture.
- Does the size of country, organization or family predict its functioning or success?
- Obviously not! We can observe sometimes small organizations filled with chaos, and large ones functioning like best Swiss watch.
- We'll present here very PRACTICAL solution to the complexity presented.

NS – A LARGE PICTURE

- The nervous system is a CONTROL SYSTEM. Most authors use analogy of a computer or electrical wiring. I believe it's more accurate that the computer is patterned to be similar to nervous system.
- **BRAIN** similar to the **SOFTWARE**, responsible for making decisions
- NERVES the HARDWARE or wiring that communicates those decisions with the rest of the body.

LARGE PICTURE

- Surprisingly, virtually everything in the body has some sort of analogy with human life
- BRAIN Spaces we occupy, countries, factories, offices, houses.
- NEUROTRANSMITTERS Inhabitants of all those spaces.
- No space makes sense without occupants.
- LIFE IS MEANINGLESS WITHOUT NEUROTRANSMITTERS!

PURPOSE

- Why I decided to do this program?
- What is ultimate purpose of coming to these lectures?
- > We often answer rationally, broken down in details
- Ultimately how we RESPOND is greatly dependent on nervous system and neurotransmitter balance
- The response is not only superficial "feel good" moment
- Researchers have found that lawyers have the highest incidence of depression in the US. Nearly one in five attorneys suffers from alcohol or substance abuse. They often ignore the early warning signs.
 Psychology Today, May 2, 2011
- Yale Law professor's study says rates of mental health problems among lawyers are in line with doctors, dentists, and veterinarians

LARGE PICTURE

1. PURPOSE

2. FLUIDITY

3. CONTENTMENT

1. BRAIN – HARDWARE, OFFICE, HOUSE

- We are not diminishing brain complexities with the illustration, as the space you occupy should be complex, advanced, accommodating
- CLEAN
- FUNCTIONAL
- > What if, let's say, myelin sheaths are damaged?
- Heavy metals, toxins present?
- SUPPLY magnesium, B6, niacin, inositol missing?
- Brain, neurons, will not be functional
- This will help us understand neurodegenerative diseases

THE GLYMPHATIC SYSTEM

• **The glymphatic system** is a "pseudo-lymphatic" perivascular network distributed throughout the brain, responsible for replenishing as well as cleansing the brain. Glymphatic clearance is the macroscopic process of convective fluid transport in which harmful interstitial metabolic waste products are removed from the brain intima.

- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7698404/
- OMEGA 3, EXERCISE

https://www.frontiersin.org/journals/neurology/articles/10.3389/fneur.2022.885020/full

NAC

 N-acetylcysteine decreases malignant characteristics of glioblastoma cells by inhibiting Notch2 signaling

https://pubmed.ncbi.nlm.nih.gov/30606241/

SLEEP – brain waste removal time

MSM

- Methylsulfonylmethane, or MSM, is an organic compound that contains biologically active sulfur. This is important because sulfur is the fourth most plentiful mineral in the human body, and it's necessary for many critical bodily functions—including detoxification.
- In our bodies, MSM helps facilitate the detoxification process by making cells more permeable, which helps to release built up heavy metals, waste and toxins, while also making it easier for nutrients and water to enter the cells and continue the cleansing process. The sulfur contained in MSM is also an important factor in the production of glutathione, the body's "master antioxidant" and potent detoxifier.

BRAIN glymphatic system

- Antioxidants in brain tumors: current therapeutic significance and future prospects
- https://molecular_ cancer.biomedcentral.com/articles/10.1186/s12943-022-01668-9
- N-acetylcysteine decreases malignant characteristics of glioblastoma cells by inhibiting Notch2 signaling
- https://jeccr.biomedcentral.com/articles/10.1186/s13046-018-1016-8
- https://www.science.org/content/blog-post/n-acetyl-cysteinewarning-shot
- https://pubmed.ncbi.nlm.nih.gov/17450321/

NEUROGENESIS & NEUROPLASTICITY

NEUROGENESIS

Formation of new neurons, especially important in instances of injury or illness. It was believed neurons decline drastically after birth. New studies are now showing that neurogenesis takes place throughout our lifetime and simply slows down as we age.

NEUROPLASTICITY

- Brain's own ability to reorganize itself by creating new connections.
- Neurogenesis and neuroplasticity refer to entirely different concepts that often act independent of each other.

NEUROGENESIS

Neurogenesis in the Hippocampus

- During the late 1990s, researchers at Rockefellers University in New York City conducted studies in which marmoset monkeys were injected with a tracer chemical that could differentiate between slow-dividing mature brain cells and fast-dividing new ones.1
- They found that the <u>hippocampus</u> (a brain region associated with memories, learning, and emotions) continued to create new cells without the constraint of age or time.
- Later studies using carbon-14 dating (which evaluates the age and process of cellular development) confirmed that cells in the hippocampus, while continually dying, were quickly replaced by new ones. It is only by the formation of these cells that the hippocampus can maintain its central functions.2

BRAIN AGING PREVENTION

- Curcumin anti-oxidative property, prevents rapid aging of the brain
- Caloric restriction diet can influence brain plasticity and preclude the decline of memory.
- Exercise can increase brain-derived growth factor (BDGF), vascular endothelial growth factor (VEGF0)
- With the same intensity and time duration of exercise, resistance training did not increase in BDGF in the long run, whereas running and aerobic exercise significantly improved BDGF
- Synapsin one, and tyrosine kinase activity that can expand the size of the brain, enhance the plasticity and neurogenesis.
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7586385/

NEUROGENESIS – BDNF

- Exercise-Mediated Neurogenesis in the Hippocampus via BDNF
- Exercise is known to have numerous neuroprotective and cognitive benefits, especially pertaining to memory and learning related processes. One potential link connecting them is exercise-mediated hippocampal neurogenesis, in which new neurons are generated and incorporated into hippocampal circuits.
- https://www.frontiersin.org/journals/neuroscience/art icles/10.3389/fnins.2018.00052/full

NEUROPLASTICITY

- Brain constantly thinks negative thoughts about the future and has a negative bias. The bias and discernment developed because it made man more cautious and safer
- Past research shows that people who maintain an optimistic attitude live longer and lead healthier lives than those who do not. The study suggested that being positive-minded can increase the likelihood of seeing your 85th birthday. This is because optimistic attitudes can lead to better decisions, which leads to better overall health.
- Some studies have shown that positive thinking can reduce the risk or severity of illness and boost your immune system. These studies link psychological stress to immune changes brought by stress, where there is existing vulnerability, such as HIV infection.
- Furthermore, positive thinking has been shown to magnify the effects of serotonin, dopamine, and endorphins in our brains, which is especially helpful in reducing depression.
- One of the most important benefits of practicing positive thinking is that, when you consciously practice it, it actually becomes a habit over time and eventually can even become your new natural reaction to negative or difficult situations

NEUROPLASTICITY

- You can CHANGE YOUR MIND
- > Think of other people and what you like and love about them
- The most difficult people, God loves them... what does He love about them?
- Think of you in terms of potential who you can become, as SEE YOURSELF as you are already there.
- People who are ILLOGICALLY STUBBORNLY POSITIVE, USUALLY SUCCEED
- Neuroplasticity: The Power of Positive Thinking and the Fascinating Ability of the Brain to Change Itself.
- NEUROPEPTIDES can modulate the activity of co-released neurotransmitters to either increase or decrease the strength of synaptic signaling. Within the periphery, neuropeptides can function similar to peptide hormones and modulate nearly all bodily functions.

NUTRITION AND BBB

- A FUNCTIONAL BARRIER between the blood and the CNS. Composed of astrocytes and the endothelial wall of the capillaries found in the arachnoid layer of the meninges.
- The endothelial cells forms tight junctions to control many substances from entering the brain. Astrocytes provide nutrients, remove waste.
- BBB can become too constricted or too porous. The brain can also harbor microorganisms, viruses, parasites, toxins.

Neuron Anatomy



ARABINOGALACTANS

Allergy-Protective Arabinogalactan Modulates Human Dendritic Cells via C-Type Lectins and Inhibition of NF-Kb

Protection of the brain through supplementation with larch arabinogalactan in a rat model of vascular dementia

- The results of this study support our hypothesis that cell wall polysaccharides consisting of arabinose are effective at protecting white matter injury, regardless of their origin. Moreover, LAG has the potential for development as a functional food to prevent vascular dementia.
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5621360/
- Nutrition research and practice, 2007

BRAIN NUTRITION – GENERAL

- Unprocessed fats, carbohydrates, protein, fiber
- Water, low surface tension, deuterium free
- IAG
- MSM
- Probiotics
- BioGlycozyme Forte multi 2=3 daily F
- Tyrosine
- Phytonutrients,
- Glandular tissues, Cytozyme B etc
- BIOMEGA 1000
- Phosphatidyl Serine, choline

2. NEUROTRANSMITTERS

- PEOPLE
- Father Glutamate
- Mother GABA
- Grandmother Serotonin
- Grandfather Acetylcholine
- ► And all the colorful, unpredictable children dopamine, endorphins, oxytocin etc. ☺

CONTENTMENT, SATISFACTION

"There are some days when I think I'm going to die from an overdose of satisfaction"

Salvador Dali

SATISFIED MIND

How many times have you heard someone say "If I had his money, I could do things my way?" But little they know that it's so hard to find One rich man in ten with a satisfied mind

Money can't buy back your youth when you're old Or a friend when you're lonely, or a love that's grown cold The wealthiest person is a pauper at times Compared to the man with a satisfied mind

When life has ended, my time has run out My friends and my loved ones, I'll leave, there's no doubt But there's one thing for certain, when it comes my time I'll leave this old world with a satisfied mind

Death and Life... topic I discuss with everyone

HOW MUCH DO WE KNOW

Neurotransmitters: Elusive glutamate receptors

Current Biology, Volume 4, Issue 1, 1 January 1994,

Mapping neurotransmitter systems to the structural and functional organization of the human neocortex, 27 October 2022

- Neurotransmitter receptors support the propagation of signals in the human brain. How receptor systems are situated within macro-scale neuroanatomy and how they shape emergent function remain poorly understood, and there exists no comprehensive atlas of receptors.
- https://www.nature.com/articles/s41593-022-01186-3#authorinformation



Types of Neurotransmitters

Neurotransmitters are broken up into 4 main groups

1. Amino Acid

- 2. Biogenic Amines
- 3. Neuropeptides
- 4. Gaseous (NO)

TYPES OF NEUROTRANSMITTERS



SUPERSTARS?

 Superstar neurotransmitters (NT) get the most attention, dopamine, serotonin etc.

80% Neurotransmission, mother & father:

- GLUTAMATE 60% most important daily NT for alertness.
- GABA 20%
- Depletion of Glutamate can lead to low GABA. Depletion can come from stress, overtraining, glutamine deficiency.

1. GLUTAMATE

- GLUTAMINE demand driven
- A physiological way to reduce circulating glutamine levels is through exercise
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7114859/#:~:text=A cute%20and%20Long%2DTerm%20Exercise,glutamine%20levels%20is%2 0through%20exercise
- Glutamine, beans, fish, eggs, nuts, soya, kefir, dark leafy veg, meats
- Fasting, dieting can deplete glutamine glutamate GABA
- Body Builders often emphasize BCAA, neglecting glutamine. Serious exercise depletes glutamine
- GI Resolve 30 days will increase alertness and energy, besides gut healing

GLUTAMATE

- GLUTAMINE WEIGHT LOSS
- https://www.healthline.com/nutrition/l-glutamine-weightloss#effectiveness
- 6-week study in 66 people with type 2 diabetes found that taking 30 grams of glutamine powder daily improved multiple risk factors for heart disease and reduced both belly and body fat.
- Similarly, a 2-week study using the same amount of glutamine observed decreased waist circumference, a marker for belly fat, in 39 people with overweight or obesity.
- In another small study, 6 women who took glutamine supplements for 4 weeks experienced significant reductions in body weight and belly fat without making other dietary or lifestyle changes.
- MECHANISM?
- Microbiome, Inflammation, Immune system, Improves blood sugar control, enhances insulin sensitivity

GLUTAMATE TO GABA conversion

- GABA function as NT, it has structure of amino acid so it's called AANT
- > Synthesis mostly in brain but also in pancreas
- GABA is synthesized from the precursor glutamate by the enzyme glutamate decarboxylase, an enzyme which uses vitamin B6 (pyridoxine) as a cofactor.
- MSG
- Mg and B6 crucial for Glutamate to GABA conversion. Most people deficient in both.

2. GABA

- Besides the nervous system, GABA is also produced at relatively high levels in the insulin-producing beta cells (β-cells) of the pancreas. The β-cells secrete GABA along with insulin and the GABA binds to GABA receptors on the neighboring islet alpha cells (α-cells) and inhibits them from secreting glucagon (which would counteract insulin's effects).
- GABA can promote the replication and survival of β -cells and also promote the conversion of α -cells to β -cells, which may lead to new treatments for diabetes.
- Alongside GABAergic mechanisms, GABA has also been detected in other peripheral tissues including intestines, stomach, fallopian tubes, uterus, ovaries, testicles, kidneys, urinary bladder, the lungs and liver, albeit at much lower levels than in neurons or β-cells

GABA

- Administration of GABA can suppress inflammatory immune responses and promote "regulatory" immune responses, such that GABA administration has been shown to inhibit autoimmune diseases.
- AUTOIMMUNE Type 1 diabetes, immune system attacks and destroy insulin-secreting pancreatic beta cells and the pancreas stops producing insulin
- dysfunctional β cells can recover in patients with T2D with proper management, such as diet, exercise,... can be restored to normal function through the removal of excess fat in the cells
- Exercise, fat loss, GABA... restoration of beta cells

GABA – OPTIMIZATION

- SN vs PSN balance. Meditation, Prayer, transcendental thinking
- Exercise increases: Dopamine (DA), noradrenaline (NE), and serotonin (5-HT), GABA
- Intense exercise increases levels of two common neurotransmitters -- glutamate and gamma-aminobutyric acid, or GABA -- that are responsible for chemical messaging within the brain.
- The Journal of Neuroscience, 2016
- https://www.sciencedaily.com/releases/2016/02/160225101241 .htm#:~:text=Intense%20exercise%20increases%20levels%20of,ch emical%20messaging%20within%20the%20brain

GABA B3, ADAPTOGENS

- Adaptogens: BioAshwagandha, ADHS, Balanced B8
- Research indicates that niacinamide and inositol enhance the effects of GABA
- Niacinamide's potent role in alleviating anxiety with its benzodiazepine-like properties: A case report
- June 2004, Journal of Orthomolecular Medicine 19(2):104-110
- Niacinamide possess benzodiazepine-like effects, 38, 39 which stimulate the GABA system and theoretically would reduce seizure activity.

GABA – INOSITOL

- Inositol helps boost serotonin and dopamine receptor density. Improving the effectiveness of serotonin, GABA, glutamate and dopamine neurotransmitters in your brain. Neurotransmitters: Inositol improves the effectiveness of major neurotransmitters in your brain.
- Neurobiology and Applications of Inositol in Psychiatry: A Narrative Review
- It has been suggested that the therapeutic activity of inositol may be related to the modulation of serotonin and/or norepinephrine receptors

GABA RECEPTOR

- GABA binds to GABA receptor
- Benzodiazapines and alcohol very high affinity for the GABA receptor they can cause addictions. Rx and alcohol disrupt the Sleep architecture so you don't get a lot of deep sleep on these drugs.
- VHP Valerian binds to GABA receptors without addiction

GABA needed during the day as well

DOPAMINE – GABA

- DOPAMINE INHIBITS GABA
- Too much cheap pleasure inhibits GABA... electronics
- Dopamine Directly Modulates GABA-A Receptors
- Paul Hoerbelt, Tara A. Lindsley and Mark W. Fleck
- Journal of Neuroscience 25 February 2015
- Our results suggest that dopamine may directly inhibit GABAa receptors that are both immediately adjacent to dopamine release sites in the striatum and activated by tonic GABA.
- Dopamine-Screen time?
- https://www.jneurosci.org/content/35/8/3525#:~:text=Our%20re sults%20suggest%20that%20dopamine,and%20activated%20by%20t onic%20GABA
- DOPAMINE DETOX

OTHER SUPERHERO NT

DOPAMINE EPINEPHRINE SEROTONIN ACETYLCHOLINE







Sleep Stages	Type of Sleep	Other Names	Normal Length
Stage 1	NREM	N1	1–7 minutes
Stage 2	NREM	N2	10–25 minutes
Stage 3	NREM	N3, slow-wave sleep (SWS), delta sleep, deep sleep	20–40 minutes

Stage 4

Sleep Cycles Through the Night



SLEEP

- Research says that early birds are happier, more punctual, do better in school, and share more conservative morals. Night owls are more impulsive, angry, and likely to become cyberbullies; they have shoddier diets and, most critically, are worse at kicking soccer balls.
- The researchers also found an association between morning people and a higher life satisfaction.
- https://psycnet.apa.org/doiLanding?doi=10.1037%2Fa0027071
- https://link.springer.com/article/10.1007/s12144-014-9246-1
- https://www.cambridge.org/core/journals/europeanpsychiatry/article/abs/novelty-seekers-and-impulsive-subjectsare-low-in-morningness/9A3BABD26BBB290E77E1A510D952994E

SLEEP

- Cell Press journal "Rapid and Reversible Control of Human Metabolism by Individual Sleep States".
- https://www.cell.com/cell-reports/fulltext/S2211-1247(21)01373-5
- Study examines REM sleep, which is associated with dreaming and high emotional content dream vs slow wave sleep, which tends to be more focused on physical repair of the body, more mundane dreams, and how those different states of mind during sleep relate to different aspects of metabolism.
- Conclusion: sleep states regulate more than 50%, of all metabolite features detected in human breath.
- We can determine if we are metabolizing more lipids or carbohydrate based on the contents of our breath. This is true during waking and during sleep.

SLEEP

- SECOND STUDY published in 2019 "Resetting the Late Timing of 'Night Owls' Has a Positive Impact on Mental Health and Performance."
- https://pubmed.ncbi.nlm.nih.gov/31202686/ Sleep Med., 2019 Aug:60:236-247
- It was human study, a randomized control trial.
- > They used non-pharmacological, practical interventions in a real world setting.
- They used targeted light exposure, consistent sleep, wake times, fixed meal times, controlled caffeine intake and exercise.
- Outcome showed significant improvements in terms of mood and far less depression and stress.

24 HR PHASES

- O-9 PHASE I from the time you wake up until about nine hours later, the neuromodulators, dopamine and epinephrine, tend to be at their highest levels
- ▶ 9–16 PHASE II Dopamine, Epinephrine subside, Serotonin rises
- 17-24 PHASE III ORGANIZED BEAUTIFUL CHAOS incredible peaks and drops in acetylcholine, dopamine and serotonin.

> This chaos will not sort itself out unless we follow 24 hour cycle

24 HR PHASES

• Acetylcholine (Ach) is under control more in terms of what we happen to be doing at any given moment, whether or not we're focusing or not focusing,

• ACh is used at the nerve to muscle synapse. The contraction of muscle fibers is exerted through the release of acetylcholine.

• Ach is at its strongest both during REM (rapid eye movement) sleep and while you are awake. It seems to help your brain keep information gathered while you are awake. It then sets that information as you sleep. So if you study or learn new information in the hours before bed, "sleeping on it" can help you remember it.

https://www.hopkinsmedicine.org/health/conditions-and-diseases/sleepwake-

ACETYLCHOLINE – wise grandfather

- Involved in states of focus, memory and learning
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2659740/
- Essential for brain **plasticity**, ability to change and learn more quickly.
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6673455/ The Journal of neuroscience, Dec 2007
- https://www.nature.com/articles/s41598-018-27393-2 "Acetylcholinemodulated plasticity in reward-driven navigation: a computational study" Scientific Reports June 2018
- Ach to communicates signals between neurons in the central nervous system (CNS) and the peripheral nervous system (PNS)
- Essential in the neocortex to learn simple tasks of discrimination.

https://www.ncbi.nlm.nih.gov/books/NBK557825/

OTHER CONNECTIONS

- Dopamine is not only about pleasure. Dopamine is about motivation, craving and pursuit... career, to mate, food, goals, things we don't have. Athletes experience this.
- Serotonin is associated with a feeling of satiety of having enough of what we already have. Now when serotonin is very, very high, people can even be sedate. They can be completely amotivated, no motivation to seek out things like food or sex or work or et cetera. Whereas when serotonin levels are very low, people can actually exhibit agitation and high levels of stress.

SUMMARY

- DOPAMINE motivation, drive and pursuit and to some extent, focus.
- EPINEPHRINE, NOREPINEPHRINE energy of having a forward center of mass, mentally and or physically.
- ▶ 3. SEROTONIN peaceful, content, sated state of being.
- 4. ACETYLCHOLINE focus in particular focus as it relates to learning and encoding new information. Brain plasticity.

OTHER CONNECTIONS

- SUNLIGHT INCREASES HORMONES. Hormones affect neurotransmitters
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4335177/
- Sex hormones affect neurotransmitters and shape the adult female brain during hormonal transition periods. Frontiers in neuroscience. 2007
- "Skin exposure to UVB light induces a skin-brain-gonad axis and sexual behavior" Cell Reports, August 2021
- https://www.cell.com/cell-reports/fulltext/S2211-1247(21)01013-5
- SKIN IS ENDOCRINE ORGAN, hormone secreting hormones are controlling those neuromodulators
- **DOPAMINE AND SEROTONIN BOTH UP**
- When your skin absorbs sunlight and produces vitamin D, that cycle triggers the production of dopamine as well as serotonin, meaning time in the sun can boost your dopamine levels. A 2018 study found that vitamin D may protect dopaminergic neurons against neuroinflammation and oxidative stress." Mar 12, 2021

https://davisphinneyfoundation.org/sunlight-and-parkinsons/

DISEASES ASSOCIATED WITH NEUROTRANSMITTERS

NEUROTRANSMITTER

- □ Acetylcholine
- Dopamine

- □ GABA
- □ Serotonin

Glutamate

Migrainestroke

Parkinson's disease
Schizophrenia

DISEASE

□ Alzheimer's

- □ Epilepsy
- MigrainesADDDepression



PURPOSE EMERGING FROM CHAOS

- Define your purpose, exercise free will, living with intention, unreasonable positive attitude
- Respect natural laws, mainly 24 hour cycle
- Sunlight
- Exercise
- Control with prefrontal cortex and free will what thoughts, desires, ideas occupy your mind
- Keep your space brain, nervous system CLEAN and organized, provide proper SUPPLY – NUTRIENTS for life to take place
- Brain waste removal and nutrients provided daily

SUPPORTING NUTRIENTS

- Mg Zyme 2 x 2 F or ActiMag 1 scoop a day
- ▶ B6 Phosphate 1–2 F
- Balanced B8 1 tsp anytime
- Tyrosine 1–2 E morning or noon (not late at night)
- Taurine 2-4 day or night, but at night assists sleep
- MSM 5 daily anytime. Combine together with:
- Mo Zyme Forte 1-2 daily
- Phosphatidyl Serine 1–2 E
- Phospatidyl Choline 1–2 F
- VHP 2x2 E
- Curcum Rx 2–4 daily anytime
- Biomega liquid 1 tsp or Biomega 1000 2 daily F
- ► IAG 1-2 tbsp E
- BioDoph7 1x2 E