SCIENCE SET
OPEN ACCESS PUBLISHERS

Research Article

Journal of Clinical and Biomedical Advances

Review on the Pre and Post-synaptic Vesicles Regarding Post-Traumatic Stress Disorder

Yang I Cao*

Director of Board, Scientific Global Limited

***Corresponding author:** Yang I Cao, Director of Board, Scientific Global Limited, Office Tower Two, Grand Plaza, 625 Nathan Road, Kowloon, Hong Kong

Submitted: 30 April 2024 **Accepted:** 06 May 2024 **Published:** 14 May 2024

Citation: *Yang I Cao (2024) Review on the Pre and Post-synaptic Vesicles Regarding Post-Traumatic Stress Disorder. J Clin Bio Med Adv 3(3), 01-05.*

Abstract

Background: *Motivated by the questions in the neurological mechanisms of post-traumatic stress disorder (PTSD), the review studies into the details of hypothalamic-pituitary-adrenal (HPA) axis. The review is supplementary to the phenomenon that COVID-19 also triggers negative psychological symptoms and suicidality.*

Methods: *The review takes γ-aminobutyric acid (GABA) beta receptors for conceptual framework in the transdisciplinary literature search.*

Results: *Evidence suggests, although interdependent, the presynaptic and postsynaptic elements of GABA activities are independent from each other in normative conditions.*

Conclusions: *I take my series of clinical trials conducted for the past 2 to 3 years for the guidance of case presentation on the interpretations of the information gathered, and there is no obvious evidence that autism spectrum disorder is associated with the GABA irregularities in PTSD and COVID-19 infections. The presynaptic interventions' slight influence to the metabolites related to GABA synthesis and degradation suggests the interrelations between GABA synapses and immune reflex.*

Keywords: Amino Acid Metabolites, Detoxification, Hydrophobic Biochemistry, Nicotinic Acetylcholine Receptors, Suicidology

Background

From my extensive and long-term clinical trials on the participant of high-functioning autism spectrum disorder (ASD), the lingering problem remains with the adrenaline intolerance of the participant in the treatment and recovering process [1]. A new hypothesis emerged during the NCT06357104 trial, with reference to the NCT05930912 trial, both registered on Clinical Trials.gov. Gupta, Guleria found that in post-traumatic disorders (PTSDs), corticotropin-releasing factor is released from the hypothalamus and stimulates the synthesis and release of adrenocorticotropic hormone (ACTH) from the pituitary, bindin to receptors in the adrenal cortex and promotes the release of glucocorticoids from the adrenal cortex [2].

This piece of information corroborates with the relatively high ACTH levels (46.62 pg/mL tested on August 3, 2023) of the participant, and the hypothesis seeks to determine if the etiology arises from the presynaptic or postsynaptic phase, or both, with the current medications of alprazolam at night and clonazepam in the morning [3, 4]. With the specific considerations for the ASD case, Jenner, Pratt found that clonazepam does not alter 5-HT synthesis but decreases 5-HT utilization in brain and blocks the egress of 5-hydroxy indole acetic acid (5-HIAA) from the brain, in which the latter is of postsynaptic nature with potentials for neurological and psychiatric biomarker [5, 6].

The purpose of the review is to determine the presynaptic and postsynaptic alterations for people with PTSD. The presynaptic elements of impact focusing on miRNAs were extensively reviewed by Zhu, Huang , while its clinical applications after cytoplasm are still vague [7]. From the psychiatric perspective, the presynaptic element of tryptophan that depends on food intake

in human bodies is anchored [6]. The postsynaptic symptoms with relation to the efferent pathways, therefore, are not regarded as etiological origination in the review, but neither are they excluded from etiological causes to presynaptic elements through responses such as the immune reflex.

Methods

The literature review puts γ-aminobutyric acid (GABA) in the spotlight regarding the peripheral vesicles. Since miRNAs' epigenetic behaviors don't necessarily follow the traditional physical anatomy of humans, the conceptualization of framework for the review is set to the GABAB receptor, prototypical heterodimers of R1 and R2 subunits [8]. Two experiments have been found in the literature search that support the positive correlations between GABA synthesis and tryptophan, with one of them emphasizing on the tryptophan hydroxylase isoform 2 (TPH2) gene [9, 10]. The exogénose element in GABA synthesis justifies the conceptual framework of the review being based upon the GABAB receptor.

Results

Gaba Metabolism

The three pathways for GABA metabolism are: 1. Decarboxylase, 2. Dehydrogenase, and 3. Transaminase, in which glutamates may be involved in all but dehydrogenase metabolic interactions (GABA shunt) [11]. Since the level of GABA in the brain is regulated by L-glutamate decarboxylase (GAD), it is only possible that dehydrogenase is the most important form of GABA synthesis [12]. In the experiment conducted by Bao, Cheung , trypsin inhibitor was used for GAD phosphorylation [12, 13].

The hydrophobic and hydrophilic environment in cytoplasm influences the directions in micropinocytosis. The dehydrogenase and transaminase activities of GABA are closely associated with the production of nicotinamide adenine dinucleotide (NAD+), NADH, and H+ [11]. The weak nuclear force, steric effects, and micro-polarization during cytoplasm's crowding effects are rarely temperature-dependent except for glucose-6-phosphate dehydrogenase (G6PD) [14]. This phenomenon supports the possibilities that the postsynaptic entropic GABA reactions are likely to be counteracted by enthalpic contributions with the "presynaptic" GABA synthesis through dehydrogenase [14].

An animal experiment with rabbits by Daniel, Love revealed that insulin in the blood affects free tryptophan for brain supply in opposite ways by binding to albumin in the blood or by reducing the levels in the blood of six or more of the amino acids which compete with tryptophan for transport carriers into the brain. Indeed, G6PD is regulated by insulin [15, 16]. While the gene expression is rapamycin-sensitive and requires phosphatidylinositol 3-kinase, the evidence chain is sufficient that GABA supply and consumption are interdependent, and the biochemical processes are independent from each other [16]. Figure 1 reveals the albumin-related biomarkers collected in the series of clinical trials.

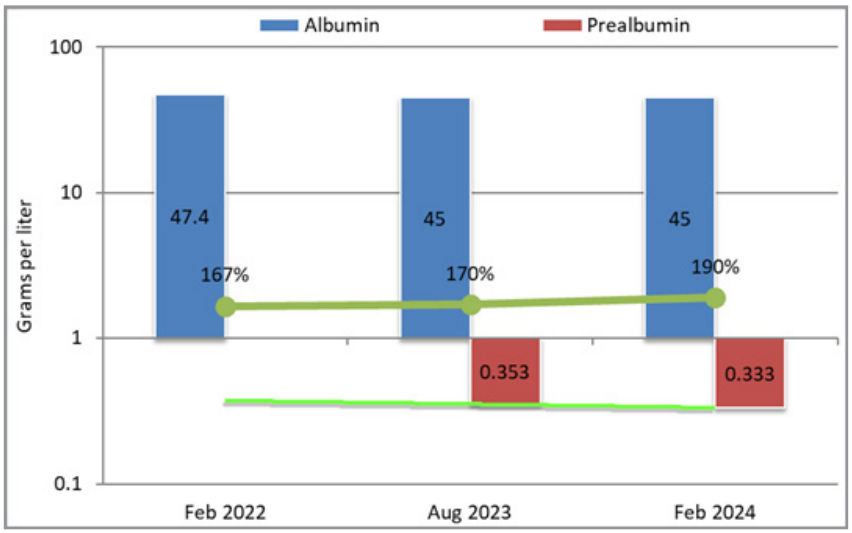

Figure 1: The participant's albumin profile in the trials.

Dehydrogenase in Phosphorylation

The bioavailability of tryptophan in the brain depends heavily on the insulin-regulated G6PD-involved phosphorylation. During phosphorylation, brain GAD is inhibited, and it can be defined as the presynaptic scenario for GABA activities [12]. In the meantime, glutamate utilization typical in GABAB receptors forms R1/R2 heterodimers to produce GABA-mediated G protein coupled receptor (GPCR) functions [8, 11].

The presynaptic scenario does not necessarily imply the simultaneous GABA synthesis. The GABA shunt pathway of NAD kinase activated NAD+ + ATP - H+ + NADP+ + ADP and NAD(P) transhydrogenase activated H+ + NAD+ + NADPH - H+ + NADP+ + NADH reactions are dependent upon conversion from dietary tryptophan [17, 18]. The hydrophobic process is closely associated with the production of reactive oxygen species (ROS) and ferroptosis [19, 20]. Dysregulations in the process instinctively reminds of the varieties of symptoms from

panic disorders to PTSDs. Therefore, the presynaptic scenarios of GABA dysfunction are narrowed down to GABA synthesis in phosphorylation.

TPH2 Gene Expression in Relation to Dehydrogenase

Indirect evidence supports that the postsynaptic GABA activities can be disrupted by the expression of TPH2 gene expression that counteracts the functions of dehydrogenase for GABA synthesis. TPH2 is responsible for the conversion of tryptophan to 5-hydroxytryptophan (5-HTP), in order for 5-hydroxytryptamine (5-HT) production [21]. The ethanol drinking experiment with mice by Zaniewska, Mosienko reveals that dehydration in the metabolic system can be sometimes necessary by instinct in sought of health, which indirectly corroborates with the insulin-regulated brain GABA supply that decreases from free tryptophan binding to albumin in the blood [21, 15].

If the etiological chain of PTSD is also consisted of postsynaptic GABA activities, over-hydration is hypothesized to be the factor for evidence. The degradation of tryptophan to 5-HTP to serotonin consumption forms the 5-HIAA, and the 5-hydroxy in the excretion process, if interdependence of chemical reactions with tryptophan synthesis were to be intruded, the postsynaptic etiology may be formed [6]. Since GABAA receptor is a ligand-gated chloride channel that mediates fast inhibitory signals through rapid postsynaptic membrane hyperpolarization, its forces in macroenvironment changes for cytoplasm directions are not negligible, such as the influences to the second round of presynaptic vesicles in the separation of glutamate and GABA by an anion exchange column [8, 14, 22].

Smoking Behaviors Involving NAD+

Liu, Ma established the GABA synthesis gene's resistance to water core-induced hypoxia such as post-interactions with GAD that can cause stress in GABA synthesis [23, 11]. In phosphorylation, superoxide dismutase is one of the most significant heterogenous relieves to the water core-induced hypoxia. Therefore, the indigenous presynaptic synthesis and postsynaptic elements are intertwined in the metabolic pathway, other than the strictly separated pre- and postsynaptic vesicles.

Conclusions

In my trials seen in Figure 1, from 2023 to 2024, albumin levels remain unchanged, even though prealbumin slightly decreased, which, in turn, substantially increased the albumin/globulin (A/G) ratio. The correlations between prealbumin changes and A/G ratio changes under the same albumin level were further profiled with lactate dehydrogenase (LDH) seen in Figure 2. The data suggests slight amelioration for GABA activities were achieved unintended during the trials, which focused on the immune reflex and autoimmune and immunodeficient etiologies.

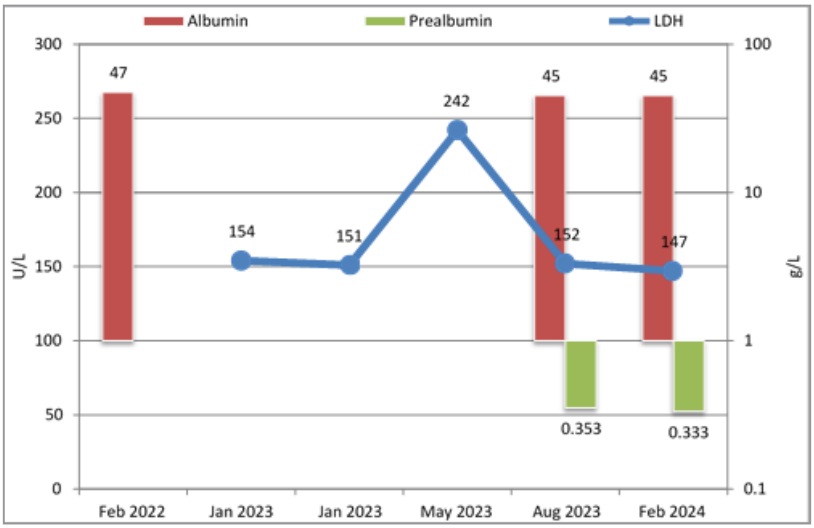

Figure 2: The LDH's influence to albumin concentrates.

In the series of trials, I also noticed the dose-independent agomelatine's amelioration effects on smoking behaviors in the male participant [24]. It is reported that nicotine consumption rebalances NAD+ homeostasis in the metabolites by enhancing nicotinamide phosphoribosyl transferase (NAMPT) activity [25]. The reduction behavior in nicotine consumption in the case, therefore, is inferred to have been caused from the improved conditions in the metabolites in NAD+ homeostasis, even though it has not eliminated the participant's nicotine dependence. Thereby, the postsynaptic etiology of PTSD still results from 5-TH consumption's influences to the presynaptic activities.

The review proves the null hypothesis that both the presynaptic and postsynaptic vesicles can impact on PTSD. The postsynaptic impacts mainly act and effect on the presynaptic domain in the metabolite tracts. Therefore, intervention in GABAB receptors can be the ultimate mediating benefactor.

The calcium signals during the acute symptoms of SARS-CoV-2 are not metabolic indicators, but GABA indicators with calcium phosphate [26, 27]. This explains the agomelatine's dose-independent effects in smoking behavior reduction, where the calcium rebalances acted upon nicotinic acetylcholine receptors [24, 28, 29]. The recycled utilization of nicotinamide from the met-

abolic fate of tryptophan in degradation may be further studied for nicotine addiction [30]. Therefore, detoxification of SARS-CoV-2 proteins is related to the central nervous system and can be intervened with metabolite-combined therapies, evidenced by the data collected in the progression of the series of clinical trials.

Acknowledgments

I thank the officers reviewing the records on ClinicalTrials.gov who pushed my boundaries to the realm of central nervous system research.

Funding

No funding is acquired for the research.

Conflict of Interest

No conflict of interest is perceived by the author.

Data Availability

Relevant clinical trials NCT06107348, NCT05711810, NCT05839236, NCT05930912, and NCT06357104 can be accessed on ClinicalTrials.gov.

References

1. Pachankis YI (2023) Adrenaline Intolerance in ASD Curing From Autoimmune Pathogens —Sebaceous Immunobiology in Autoimmune Pathogen Research. Biomedical Review: Journal of Basic and Applied Medical Sciences 10: 8-14.
2. Gupta S, Guleria RS, Szabo YZ (2021) MicroRNAs as biomarker and novel therapeutic target for posttraumatic stress disorder in Veterans. Psychiatry Res 305: 114-252.
3. Basit H, Kahwaji CI (2024) Clonazepam in StatPearls. Treasure Island.
4. George TT, Tripp J (2024) Alprazolam in StatPearls.Treasure Island.
5. Jenner P, Pratt JA, Marsden CD (1986) Mechanism of action of clonazepam in myoclonus in relation to effects on GABA and 5-HT. Adv Neurol 43: 629-643.
6. Jayamohananan H, Manoj Kumar MK, Aneesh TP (2019) 5-HIAA as a Potential Biological Marker for Neurological and Psychiatric Disorders. Adv Pharm Bull 9: 374-381.
7. Ziyu Zhu, Xuekang Huang, Mengran Du, Chenrui Wu, Jiayuanyuan Fu, et al. (2023) Recent advances in the role of miRNAs in post-traumatic stress disorder and traumatic-brain injury. Molecular Psychiatry 28: 2630-2644.
8. Terunuma M (2018) Diversity of structure and function of GABA(B) receptors: a complexity of GABA(B)-mediated signaling. Proc Jpn Acad Ser B Phys Biol Sci 94: 390-411.
9. Sonya Siragusa, Maria De Angelis, Raffaella Di Cagno, Carlo Giuseppe Rizzello, et al. (2007) Synthesis of gamma-aminobutyric acid by lactic acid bacteria isolated from a variety of Italian cheeses. Appl Environ Microbiol 73: 7283-90.
10. Nora Preuss, Basira Salehi, Jan Willem, van der Veen, Jun Shen, Wayne C Drevets, et al. (2013) Associations between prefrontal gamma-aminobutyric acid concentration and the tryptophan hydroxylase isoform 2 gene a panic disorder risk allele in women. Int J Neuropsychopharmacol 16: 1707-1717.
11. Barry J Shelp, Alan W Bown, Michael D McLean (1994) Metabolism and functions of gamma-aminobutyric acid. Trends Plant Sci 4: 446-452.
12. Bao J, Cheung WY, Wu JY (1995) Brain L-Glutamate Decarboxylase INHIBITION BYPHOSPHORYLATION AND ACTIVATION BY DEPHOSPHORYLATION Journal of Biological Chemistry 270: 6464-6467.
13. Brennan EF, Rocha V (1978) Trypsin peptide patterns of tryptophan synthase beta2 proteinamong four species of the Enterobacteriaceae J Bacteriol 136: 790-794.
14. Luby Phelps K (2013) The physical chemistry of cytoplasm and its influence on cell function: anupdate. Mol Biol Cell 24: 2593-2596.
15. Daniel PM, Love ER, Moorhouse SR, Pratt OE (1981) The effect of insulin upon theinflux of tryptophan into the brain of the rabbit. J Physiol 312: 551-562.
16. Wagle A, Jivraj S, Garlock GL, Stapleton SR (1998) Insulin Regulation of Glucose-6-phosphate Dehydrogenase Gene Expression Is Rapamycin-sensitive and Requires Phosphatidylinositol 3-Kinase. Journal of Biological Chemistry 273: 14968-14974.
17. Oka Si, Allen Sam Titus, Daniela Zablocki, Junichi Sadoshima (2023) Molecular properties and regulation of NAD+ kinase (NADK). Redox Biology 59: 102561.
18. Information, N.C.f.B. PubChem Pathway Summary for Pathway NADPHOS-DEPHOS-PWY-1, NAD phosphorylation and dephosphorylation. PubChem 2024; Available from: https://pubchem.ncbi.nlm.nih.gov/pathway/BioCyc:HUMAN_NADPHOS-DEPHOS-PWY-1.
19. Chen YR, Zweier JL (2014) Cardiac Mitochondria and Reactive Oxygen Species Generation. Circulation Research 114: 524-537.
20. Hao S, Bishan Lianget, Qiong Huang, Shumin Dong, Zhenzhen Wu (2018) Metabolic networks in ferroptosis (Review). Oncol Lett 15: 5405-5411.
21. Zaniewska M, Valentina Mosienko, Michael Bader, Natalia Alenina (2022) Tph2 Gene Expression Defines Ethanol Drinking Behavior in Mice. Cells 11: 874.
22. Jin H, Heng Wu, Gregory Osterhaus, Jianning Wei, Kathleen Davis, et al. (2003) Demonstration of functional coupling between gamma -aminobutyric acid (GABA) synthesis and vesicular GABA transport into synaptic vesicles. Proc Natl Acad Sci USA 100: 4293-4298.
23. Liu X, Hao Ma, Jing Liu, Jing Liu, Chunlei Wang, et al. (2023) The γ-Aminobutyric Acid (GABA) Synthesis Gene Regulates the Resistance to Water Core-Induced Hypoxia Stress for Pear Fruits. Agronomy 13: 1062.
24. Pachankis YI (2023) Unexpected Findings on Agomelatine's Substitutive Effects in Smoking Behavior Reduction. Clinical Endocrinology and Metabolism 2: 6.
25. Yang L, Junfeng Shen, Chunhua Liu, Zhonghua Kuang, Yong Tang, et al. (2023) Nicotine rebalances NAD(+) homeostasis and improves aging-related symptoms in male mice by enhancing NAMPT activity. Nat Commun 14: 900.
26. Singh VP, Badiger NM, Huseyin Ozan Tekin, Ümit Kara (2017) Photon absorption of calcium phosphate-based dental biomaterials. in ISSSD 2017: 17 international symposium on solid state dosimetry. Mexico: Sociedad Mexicana de Irradiacion y Dosimetria.
27. Berlansky S, Matthias Sallinger, Herwig Grabmayr, Christina Humer, Andreas Bernhard, et al (2022) Calcium Signals during SARS-CoV-2 Infection: Assessing the Potential of Emerging Therapies. Cells 11: 253.

28. Dani JA (2015) Neuronal Nicotinic Acetylcholine Receptor Structure and Function and Response to Nicotine. Int Rev Neurobiol 124: 3-19.
29. Serhatlioglu I, Batuhan Bilgin, Emine Kacar, Sibel Ozcan, Sinan Canpolat, et al. (2019) Agomelatine modulates calcium signaling through protein kinase C and phospholipase C-mediated mechanisms in rat sensory neurons. J Cell Physiol 234: 10741-10746.
30. Deacon AC (2016) The Measurement of 5-Hydroxyindoleacetic Acid in Urine. Annals of Clinical Biochemistry. International Journal of Laboratory Medicine 31: 215-232.