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The Intricate Biological Proximity of Vitamin D and Brain Serotonin

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Abstract: Background: The purpose of this article is to extend and elaborate on our current understanding of Calcitriol and Brain Serotonin synthesis; particularly on how the two may be related.
Methods: Using a 2014 study involving clinical trials to extend this hypothesis.
Results: Vitamin D (Calcitriol) activated the gene that codes for Tryptophan Hydroxylase 2, which synthesizes Brain Serotonin. It also inhibits Tryptophan Hydroxylase 1, which makes serotonin in the gut.
Conclusion: Vitamin D is closely related to the synthesis of Brain Serotonin. If furthered, it may be used as a treatment for the Serotonin Anomaly in Autistic Children.
Keywords:
1. Biochemistry
2. Genetics
3. Neuroscience
4. Physiology

I. A BRIEF BACKGROUND

Life, as we know it, is a beautiful construction of numerous factors. These factors are different for every organism, ranging from basic requirements, such as Oxygen for animals and Carbon Dioxide for plants, to some relatively complex ones, such as the secretion of hormones like insulin for the regulation of blood sugar levels in animals. Thousands of chemical reactions provide for a particular product to be synthesized, so that an overall action or function can take place. We often underestimate what the frequency of these reactions is, which forms the basis for our complex organ systems being able to sustain in the life conditions of this planet. In this report, we look at one particular type of reaction, and it's relation to another.

Vitamin D, in our body, is circulated as the hormone Calcitriol, which is performing vital functions, such as the absorption of Calcium in the body. Brain Serotonin is another hormone which is related to social behavior, sleep etc. A 'Serotonin Anomaly' exists in Autistic children, where the serotonin in the brain is reported to be at lower levels than usual, while the guy serotonin is higher than usual. This mechanism is explained by the proposed hypothesis of this article, which is already backed by multiple bodies of evidence

II. HOW VITAMIN D IS MADE

Simply put, Vitamin D is an extremely important resource for the human body. The importance of its functions is absolutely ridiculous. However, the mechanism of Vitamin D is often misunderstood. To elaborate on what this report is trying to achieve, we must first establish the basics of the photochemical conversion of Vitamin D. To set the record straight, sunlight doesn't 'contain' Vitamin D. So how is the body receiving the Vitamin D from sunlight? How this works is that Type B Ultraviolet Radiation (The type known to cause skin burns) comes in contact with a precursor to Vitamin D, which already exists in your body, and goes by the name of 7 - Dehydrocholesterol. This is an extremely crucial element of this process, as it forms the basis of the complex synthetic and usage processes that follow. An average human body's skin needs some exposure to the UVB radiation precisely in the wavelength spectrum of 270-300 nm.

Vitamin D is used in the form of a hormone. The Vitamin D (Consumed in diet and converted by skin) travels to the kidney and the liver, where it is converted into an active hormone, which is called Calcitriol. From here, it is used in a plethora of processes. The hormone is required for the absorption of Calcium from the gut into the bloodstream.

Sunlight is unparalleled in the amount of Vitamin D that it converts in the skin. Numerically speaking, one can obtain 8-12,000 IU (International Units) of Vitamin D from exposure to Sunlight for merely as much as 10 - 30 Minutes! Alternatively, it can be obtained from one's diet. However, the amount of Vitamin D that can be obtained from one's diet makes up only a fraction of what one could receive from some minutes of exposure to sunlight, estimated at 6-1200 IU. Clearly, sunlight is the ultimate source of vitamin D production in the body.

III. THE RELATION TO SEROTONIN

Serotonin ($C_{10}H_{12}N_2O$) or 5-hydroxytryptamine is a monoamine neurotransmitter. Its biological function is complex and multifaceted, modulating mood, cognition, reward, learning, memory etc. Brain serotonin is the hormone that guides social behavior, and is produced as a result of an enzyme called Tryptophan - Hydroxylase 2, which converts the amino acid tryptophan into the hormone serotonin. Tryptophan Hydroxylase 1 produces serotonin in the gut, and one requires just the perfect concentration of serotonin in the gut for homeostatic digestion.

A. 2014 STUDY - DR. Rhonda Patrick and Dr. Bruce Ames

A study by Rhonda Patrick, PhD and Bruce Ames, PhD of Children's Hospital Oakland Research Institute (CHORI) demonstrates the impact that Vitamin D may have on social behavior associated with Autism Spectrum Disorder (ASD). Dr. Patrick and Dr. Ames have shown that serotonin, oxytocin, and vasopressin, the three brain hormones that affect social behavior, are all activated by vitamin D hormone. Autism, which is characterized by abnormal social behavior, has previously been linked to low levels of serotonin in the brain and to low vitamin D levels, but no mechanism has linked the two until now.

In this study, Dr. Patrick and Dr. Ames show that vitamin D hormone activates the gene that makes the enzyme tryptophan hydroxylase 2 (TPH2), that converts the essential amino acid tryptophan, to serotonin in the brain. This suggests that adequate levels of vitamin D may be required to produce serotonin in the brain where it shapes the structure and wiring of the brain, acts as a neurotransmitter, and affects social behavior. They also found evidence that the gene that makes the enzyme tryptophan hydroxylase 1 (TPH1) is inhibited by vitamin D hormone, which subsequently halts the production of serotonin in the gut and other tissues, where when found in excess it promotes inflammation.

This mechanism explains many of the known, but previously not understood, facts about autism including the "serotonin anomaly": low levels of serotonin in the brain and high levels in the blood of autistic children. The Patrick/Ames mechanism is relevant to the prevention of autism, and likely its treatment.

The current guidelines for adequate vitamin D levels are concentrations above 30 ng/ml. Most Americans' vitamin D is made in the skin from exposure to UltraViolet - B radiation; however, melanin pigment and sunscreen inhibit this action. This is an important cause of the well-known widespread vitamin D deficiency among dark-pigmented Americans, particularly those living in Northern latitudes. The most recent National Health and Examination survey reports that greater than 70% of U.S. population does not meet this requirement and that adequate vitamin D levels have plummeted over the last couple of decades. This precipitous drop in adequate levels of vitamin D in the US is concurrent with the rise in autism rates.

IV. METHODS OF THIS STUDY

Aim: To establish a relationship between Vitamin D and Brain Serotonin.

For further information on this study, such as the characteristics of participants, processes used etc., head on to the source cited in the Works Cited page.

As Dr. Rhonda Patrick (who conducted this study) puts it, “Serotonin and vitamin D have been proposed to play a role in autism; however, no causal mechanism has been established. Here, we present evidence that vitamin D hormone (Calcitriol) activates the transcription of the serotonin-synthesizing gene Tryptophan Hydroxylase 2 (TPH2) in the brain at a vitamin D response element (VDRE) and represses the transcription of TPH1 in tissues outside the blood-brain barrier at a distinct VDRE. The proposed mechanism explains 4 major characteristics associated with autism: the low concentrations of serotonin in the brain and its elevated concentrations in tissues outside the blood-brain barrier; the low concentrations of the vitamin D hormone precursor 25-hydroxyvitamin D [25(OH)D3]; the high male prevalence of autism; and the presence of maternal antibodies against fetal brain tissue. Two peptide hormones, oxytocin and vasopressin, are also associated with autism and genes encoding the oxytocin-neurophysin I preproprotein, the oxytocin receptor, and the arginine vasopressin receptor contain VDREs for activation. Supplementation with vitamin D and tryptophan is a practical and affordable solution to help prevent autism and possibly ameliorate some symptoms of the disorder,” (Patrick in Vitamin D hormone regulates serotonin synthesis. Part 1: relevance for autism)

V. RESULT

Vitamin D is first converted to 25-hydroxyvitamin D [25 (OH)D3], which is the major stable circulating form of vitamin D, and then to the biologically active steroid hormone 1,25-dihydroxyvitamin D (84). We recently proposed an underlying mechanism that describes how vitamin D hormone, which appears to control >900 genes, is a key regulator of brain serotonin synthesis through TPH2, which contains a VDRE consistent with activation

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VI. DISCUSSION

Clearly, there is relatively sufficient reason to believe that Vitamin D affects serotonin production in the human body. As a way of reinforcing this idea, a proposal for an experiment follows. This is a two-part experiment, which borrows from a prospective observational study mechanism and an experimental one.

VII. THE EXPERIMENT

A. *Methods*

1) Hypothesis : An increase in Vitamin D content is related to a higher serotonin secretion.

Aim: To further the establishment of a relationship between Brain Serotonin and Vitamin D.

All the processes, characteristics of the participants etc. are described below.

There are two parts of the study that is to be conducted, to really support the mentioned hypothesis.

a) Conduct a prospective observational study of 100-150 volunteers living in the following cities - San Francisco, CA, Yuma, AZ and Pittsburgh, PA. (Volunteers must represent people from all sectors of life - gender, community, where they live in the city etc.)

b) Regularly (On a monthly basis) measure their Vitamin D and Brain Serotonin levels over a period of 6 months. - Record findings in the table given below_

Area	Calcitriol levels (6 Month average on the basis of the monthly records)	Serotonin levels (6 Month average on the basis of monthly records)	Conclusion
Pittsburgh, PA			
Yuma, AZ			
San Francisco, CA			

c) Additionally, create a group of 50-100 volunteers. Maximize their daily sun exposure (required for production of adequate Vitamin D - Over 30 Ng/ml) over a period of 2-3 months. Measure their brain serotonin levels regularly.

d) Create a group of another 50-100 volunteers. Minimize their daily exposure to UVB (keep it just enough for a vitamin D uptake of over 20 Ng/ml) for a month. Provide them with Vitamin D supplements if necessary. Record their brain serotonin levels regularly.

This experiment clearly establishes a control (step 3) and an experimental (step 4) group.

Prediction: The brain serotonin levels of the volunteers in step 3 will be greatly higher than the brain serotonin levels of the volunteers in step 4.

Notes: The data gathered in Yuma, AZ and Pittsburgh, PA should correspond to steps 3 and 4 of the experiment to justify the hypothesis.

The values in the table are, of course, to be determined.

In the event that the results of this experiment prove otherwise, it will provide clarity as to what we should eliminate from our understanding of mechanisms that depend on the two hormones' relation, including the serotonin anomaly in autistic children, as mentioned earlier.

VIII. CONCLUSION

Therefore, it can be concluded by saying that a beginning has been made with the study conducted by Dr. Rhonda Patrick and Dr. Bruce Ames. It aims to explain many of the previously known but unexplained human body mechanisms which occur in neural dysfunction. If furthered, future research on this could lead to a treatment and perhaps, cure for autistic traits developed by children due to the 'Serotonin Anomaly', as mentioned in the study.

A. Declarations

1) Ethical Approval and Consent to participate: Not Applicable to this study. However, as the author, I hereby declare that I have adhered to the accepted ethical standards of a genuine research study.

2) Consent for publication - I hereby declare that I consent to the requirements of the publication process of the Journal of Biomedical Science

3) Availability of data and materials - This data can be accessed in the following resources: https://www.sciencedaily.com/releases/2014/02/140226110836. https://pubmed.ncbi.nlm.nih.gov/25713056/

4) Competing interests - Not Applicable to this article

5) Funding - Not Applicable to this article

6) Authors' contributions - This research was entirely done by AM.

7) Acknowledgements - Dr. Rhonda Patrick and Dr. Bruce Ames for their contributions in the 2014 study.

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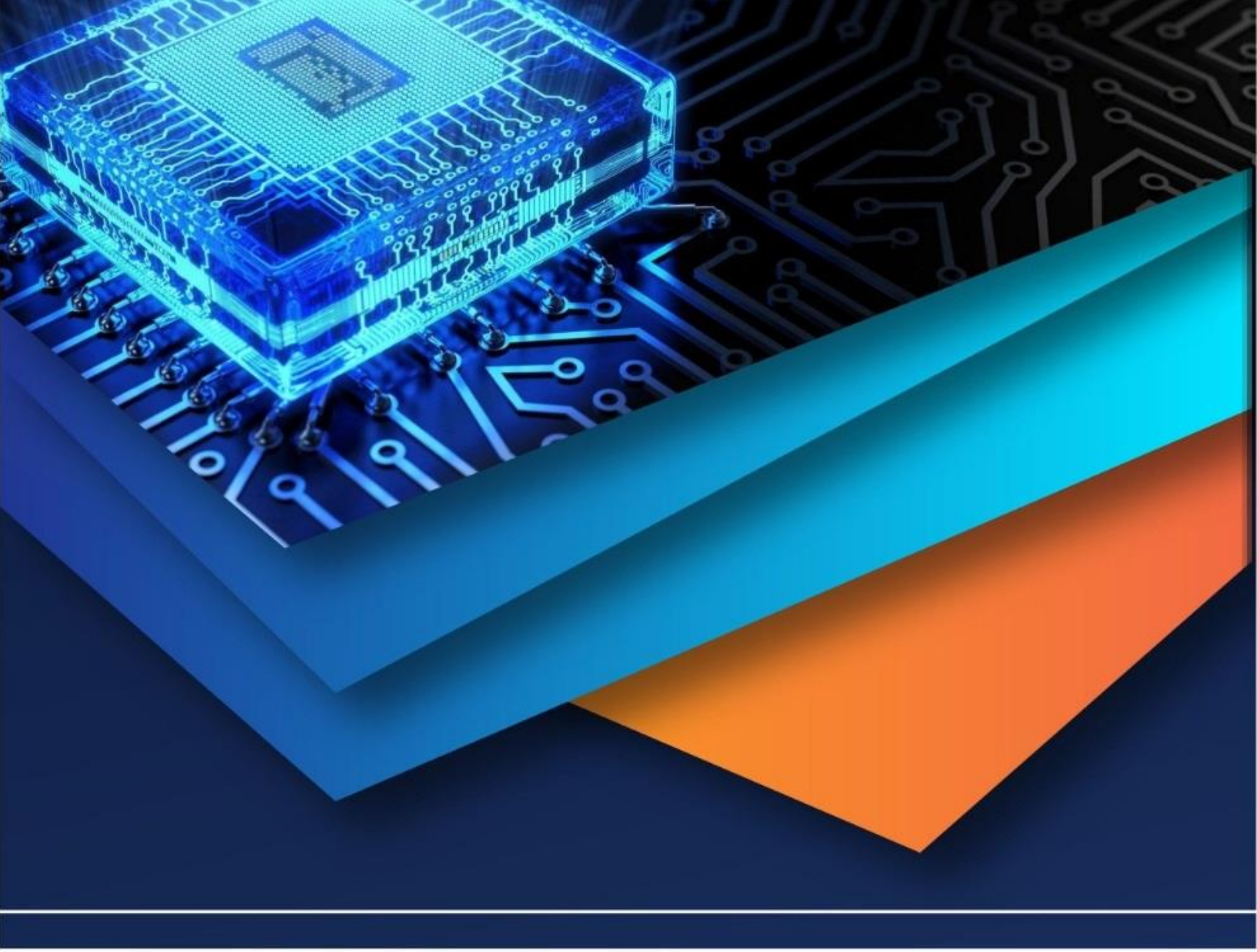

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