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Autism &Androgen receptor

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Abstract— Androgen receptor and autism which discuss one of many causes of autism which is low levels of gamma aminobutyric acid(GABA) neurotransmitter that result from low production of glutamic acid decarboxylase 65&67 enzymes from the expression process of GAD1&2 genes that needed in catalyzing glutamate to form GABA plus how using acetyl L-carnitine will affect on androgen receptors number. Discussion: Androgen receptor is found in the brain,upon activation by binding of androgen hormones and by taking acetyl l-carnitine, the number of activated AR will increase. The DNA-binding domain of activated androgen receptors will act as transcription factors(zinc finger domain) that regulate the expression of GAD1-2 genes by binding to the regulatory region of GAD1&2 genes(DNA) which called enhancer during the transcription process that leads to enhancing the transcription process of GAD1-2 genes in order to increase the amount of GAD65&67 proteins (enzymes) produced from translation process of m-RNA to protein in order to use these enzymes to catalyse enough amount of glutamate to produce enough amont of GABA neurotransmitter to help in treating or reducing symptoms of autism.

Keywords: autism, GAD1&2, GAD65&67, androgen receptor, acetyl l-carnitine

Androgen receptor (AR)

The androgen receptor (AR), also known as NR3C4 (nuclear receptor subfamily 3, group C, member 4), is a type of nuclear receptor that is activated by binding any of the androgenic hormones, including testosterone and dihydrotestosterone in the cytoplasm and then translocating into the nucleus. The main function of the androgen receptor is as a DNA-binding transcription factor that regulates gene expression

Androgen receptor location in the brain

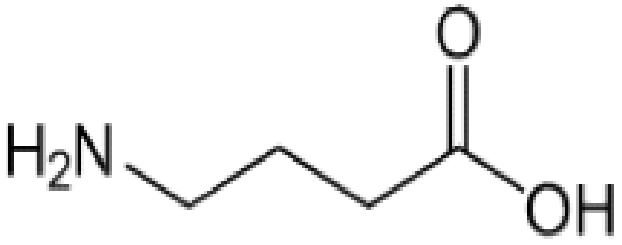
Androgen receptor located in the cerebral cortex(purkinje cells)and amaygdala and orginating in the hippocampus.

Autism

ifferences in the brain. People with ASD often have problems with social communication and interaction, and restricted or repetitive behaviors or interests. People with ASD may also have different ways of learning, moving, or paying attention.

Gamma aminobutyric acid (GABA)

Is the chief inhibitory neurotransmitter in the developmentally mature mammalian central nervous system. Its principal role is reducing neuronal excitability throughout the nervous system



Glutamic acid decarboxylase (GAD65&67) enzymes(proteins)

GAD exists in two isoforms with molecular weights of 67 and 65 kDa (GAD67 and GAD65), which are encoded by two different genes ondifferent chromosomes (GAD1 and GAD2 genes, chromosomes 2 and 10 in humans, respectively).GAD67 and GAD65 are expressed in the brain where GABA is used as a neurotransmitter

They catalyze the decarboxylation of glutamate neurotransmitter which is the metabolic precursor of gamma-aminobutyric acid (GABA) and carbon dioxide (CO2). GAD uses pyridoxal-phosphate (PLP) as a cofactor. The reaction proceeds as follows:

$$HOOC{-}CH2{-}CH2{-}CH(NH2){-}COOH \rightarrow CO2 + HOOC{-}CH2{-}CH2{-}CH2NH2$$

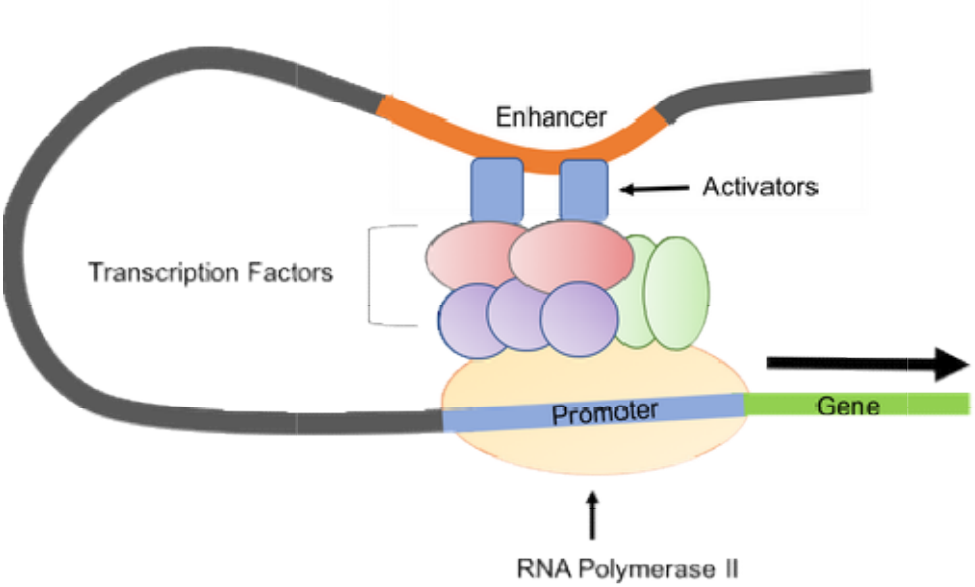
Autism

Cause relation between GABA&GAD1-2 genes

One of the autism causes is the low level of gamma aminobutyric acid (GABA) that is caused by the down regulation of glutamic acid decarboxylase GAD1 and GAD2 (genes) expression which lead to decrease levels of glutamic acid decarboxylase 65&67 enzymes (proteins) that are needed in the catalysing glutamate neurotransmitter(metabolic precursor for GABA) to produce the adequate amount of gamma aminobutyric acid (GABA).

Transcriptional factor as enhancer

In genetics, an enhancer is a short (50–1500 bp) region of DNA that can be bound by proteins (activators) to increase the likelihood that transcription of a particular gene will occur.[1][2] These proteins are usually referred to as transcription factors.



Zinc finger protein(DNA-binding domain)

Zinc finger transcription factors or ZF-TFs, are transcription factors composed of a zinc finger-binding domain and any of a variety of transcription-factor effector-domains that exert their modulatory effect in the vicinity of any sequence to which the protein domain binds

Acetyl L-carnitine

Acetyl-L-carnitine is important for many body processes. L-carnitine is made in the human brain, liver, and kidneys. The body can convert L carnitine to acetyl-L-carnitine and vice versa.

Acetyl L-carnitine mechanism for androgen receptor

Acetyl l carnitine boost the number of active androgen recptors ,which will up regulate GAD1&2 genes transcription process to produce more GAD65&67 enzymes. • acetyl l carnitine can readily cross the blood brain barrier by OCTN2 (SLC22A5), an organic cation/carnitine transporter, is widely distributed throughout the body, including the brain

Discussion

Androgen receptor is found in the brain, upon activation by binding of androgen hormones and by taking acetyl l-carnitine, the number of activated AR will increase. The DNA-binding domain of activated androgen receptors will act as transcription factors(zinc finger domain) that regulate the expression of GAD1-2 genes by binding to the regulatory region of GAD1&2 genes(DNA) which called enhancerduring the transcription process that leads to enhancing the transcription process of GAD1-2 genes in order to increase the amount of GAD65&67 proteins (enzymes) produced from translation process of m-RNA to protein in order to use these enzymes to catalyse

enough amount of glutamate to produce enough amount of GABA neurotransmitter to help in treating or reducing symptoms of autism.

Results

Studies have shown that taking 2g of acetyl l carnitine every day for 3 weeks will boost the number of actived androgen receptors in the body including the brain which will affect on the transcription process of GAD1&2 genes by enhancing the process to result in more GAD65&67 enzymes production that are needed to catalyse gltamate into GABA neurotransmitter to treat or decrease the symptoms of autism.

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