

May Deficiency of Catecholamine Catabolizer Renalase be the Underlying Primary Reason of Autism?

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Editorial

Autism disease is biochemically characterized with the increase of norepinephrine which is among the members of catecholamines. Renalase enzyme is responsible for metabolization of catecholamines including epinephrine. If there is not enough renalase enzyme, it causes a set of pathologies such as autism since catecholamines cannot be extinguished at appropriate period of time [1]. Accordingly we tried to hypothesize the possible relationship of autism disease with renalase enzyme for the first time in this editorial and we laid emphasis on the fact that renalase might be a new agent for the treatment and diagnosis of autism disease.

Autism is a development disorder in which the patient is alone with his/her inner world (social communication, interaction and behavior disorder). Autism develops natively and it has a genetical transition background, a complicated neurobiological basis and it generally arises before 3 ages [2,3]. Due to American Ministry of Health data, 1 of 88 children in school age is diagnosed as autism [2]. Autism is observed 3-4 fold more in boys than girls [2,3]. Even though major improvements are recorded about autism, underlying biochemical mechanisms cannot completely enlighten yet.

In biochemical investigations which are executed in order to reveal the underlying reasons of autism, increased level of norepinephrine is detected in autism patients and their relative's blood and low level of dopamine beta-hydroxylase activity is notified [4]. These findings demonstrate the hyper-function of noradrenergic system in autistic patients. Other clues indicating the hyper-functional of noradrenergic system in these patients are occurrence of cardiovascular abnormalities-in other words high rate of pulse and high blood pressure in autistic children [5].

When we select the aforementioned findings as a baseline, we hypothesize in this editorial that high norepinephrine levels and high blood pressure may be related to inadequacy of catecholamine catabolizing renalase enzyme in autistic patients. Dopamine, epinephrine and norepinephrine molecules are known as catecholamines [6]. Renalase enzyme which is a flavine/adenine/dinucleotide dependent amine oxidase,

extinguish these catecholamines by converting epinephrine and norepinephrine to 3-methoxy-4-hydroxymandelic acid (VMA) and dopamine to homovanilic acid [7]. Renalase enzyme was discovered in kidney tissue in 2005 for the first time [7] and it was notified to be synthesized in various biological tissues including heart, liver and brain [8,9]. Normal level of renalase enzyme in circulatory system is stated to range within 3-5 µg/ml [8]. It can be concluded that lower and higher levels out of this range may cause a pathological situation. Renal levels in circulation may decrease in autism patients. Renalase level is strictly detected by at least three factors such as renal function, renal perfusion and catecholamines. If the primary renalase synthesizer organ kidneys lose their function, a decrease in renalase levels takes place [7,9]. Decrease in renalase levels causes a rise in blood pressure by causing the high rate of catecholamines in the circulation. As it can be remembered that high rate of blood pressure may originate from inadequate releasing of renalase from biological tissues including kidneys. We should remind that noradrenergic (and adrenergic) cells locate at locus caeruleus and pons [10]. Axones of these neurons are projected to cerebral cortex, limbic system, thalamus and hypothalamus with median forebrain bunches [10]. We also know that common developmental disorders (CDD) (including autism) are related to catecholamine levels. In this case, quantities of catecholamine levels in brain have bigger pathological importance than the quantity of catecholamines in circulation. Renalase cannot pass blood-brain barrier because it is a 3.8 kDa big molecule [8]. Accordingly, renalase levels synthesized in brain as a result of the degradation of catecholamines are related to renalase amount. Epinephrine is observed in high concentrations in case of autism [4]. This means that epinephrine catabolism may be less or inadequate because of inadequate synthesis of renalase in brain parts because of an atrophy. Epinephrine levels may be high in autism patients for this reason. This kind of patients may have a resistance to renalase enzyme and they may have a problem in catabolizing catecholamines because of this. But no matter what the reason is, epinephrine reducing drugs in brain or increasing the activity of renalase enzyme seems like a new treatment approach in autism patients. In addition, investigating the levels of catecholamine and renalase in autistic individuals will help diagnosis and will provide data for researching the treatment

options. There are promising results in autistic children with imipramine which is a tricyclic compound hindering reverse oscillation of norepinephrine and 5HT and with methysergide which is a non-selective 5HT antagonist [11]. Renalase enzyme seems like an agent with a potential of being an alternative option in autism patients.

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