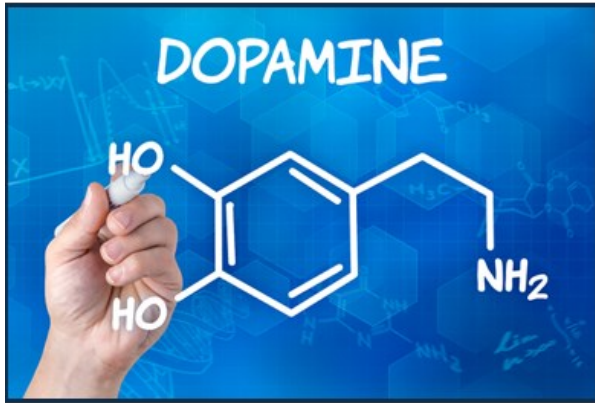


## WHAT IS DOPAMINE ?



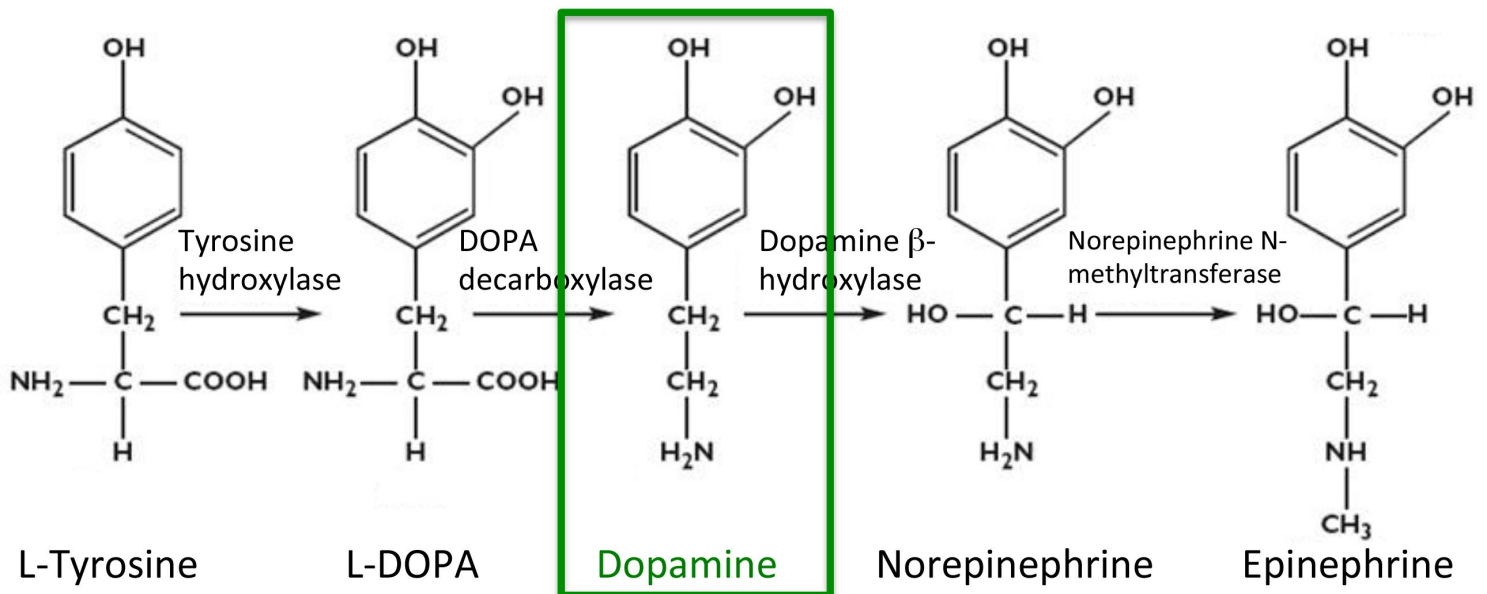
Dopamine is a neurotransmitter synthesized by your body from the dietary intake of an amino acid called tyrosine, found in protein-rich foods such as meats and cheeses. Dopamine is also a precursor molecule to two other important body chemicals--epinephrine and norepinephrine, sometimes called adrenaline and noradrenaline. The brain and nervous system utilize neurotransmitters to send messages in the form of electrochemical impulses throughout your body and, thus, regulate all of your body's functions.

Dopamine regulates a variety of functions within your brain and body. It helps to regulate blood flow through the arteries, modulates eating habits, contributes to learning and high cognitive functioning, reinforces behavior and regulates motor activity. It is also involved in regulating the secretion of hormones from the pituitary gland and contributes to the function of the autonomic nervous system.

Increasing dopamine production is the target of many drugs such as cocaine, ritalin, coffee, etc...

## How is dopamine synthesized ?

Before going in depth into your genetic results, it is important to know how the dopamine is synthesized inside of your brain.



**IMPORTANT NOTE:** L-Tyrosine is an amino acid naturally found in protein-rich foods (meat, fish, almonds, etc...). If you don't get enough L-tyrosine in your diet, or your body doesn't properly convert it, you won't manufacture adequate dopamine. On the other side, eating lot of L-tyrosine via natural foods doesn't mean that you will get lot of dopamine, because L-Tyrosine will be in competition with lot of other amino acids contained in these foods to cross the blood-brain barrier !

## GENETICS &amp; DOPAMINE

- **TH gene (Tyrosine Hydroxylase, Function: as seen above converts L-tyrosine to L-DOPA):** In various studies<sup>1, 2</sup>, the A allele of the SNP rs10770141 is predictive of elevated levels of dopamine and norepinephrine. Moreover, individuals with this allele had lower scores of novelty seeking (= engagement in high-risk activities and extreme sports or who abuse drugs). Finally, the A allele carriers had higher TH activities and retain higher levels of catecholamines (adrenaline, noradrenaline) in the brain.

- **DDC gene (Dopa Decarboxylase, Function: as seen above converts L-DOPA to Dopamine):** A study<sup>3</sup> tested seven single nucleotide polymorphisms (SNPs) within the DDC gene for association with attention, which was assessed by the Attention Network Test to detect three networks of attention, including alerting, orienting, and executive attention, in a healthy Han Chinese sample (N=451). This study found that alerting was associated with rs10499695. An other study<sup>4</sup> revealed that this same variant from the DOPA decarboxylase gene, rs10499695, to be significantly associated with poorer cognitive performance in type 2 diabetes, meaning that higher blood sugar levels could significantly alter the dopamine synthesis in persons who have this variant.
- **DRD2 TaqI (Dopamine receptor 2, Function: when dopamine is released, in order to exert his action, it has to bind to receptors. DRD2 is one of them and is associated with cognitive processes and mental disorders.):** There are two types of DRD2 receptors : DRD2 long isoform (DRD2L) and DRD2 short isoform (DRD2S). Unlike DRD2L which increases dopamine activity, DRD2S is an autoreceptor (= modulates dopamine release by inhibiting dopamine release upon activation). The TaqI polymorphism in the DRD2 gene has been demonstrated in various studies<sup>5</sup> to significantly modulate DRD2S/DRD2L production. The A allele carriers are likely to produce significantly lower DRD2S and are more likely to have addictive behaviors with food or any drug/lifestyle that could increase dopamine levels. This is due to the fact that, as they produce less DRD2S, the dopamine signal is turned always on when increasing their dopamine levels leading to a greater wellbeing feeling (= addictive effect). DRD2S may also inhibit TH synthesis (as seen above, TH converts L-Tyrosine to L-Dopa)<sup>6</sup>. Interestingly, an other study<sup>7</sup> found that in A allele carriers, during reward anticipation, more motivation leads to a significantly higher working memory performance, whereas the carriers of two C alleles did not. An association of DRD2 gene TaqI polymorphism with mood disorders was found in overall population<sup>8</sup>, and the individuals with AA genotype were more susceptible to mood disorders in comparison to those with AC and CC genotypes. In addition, Kazantseva A. research team<sup>9</sup> demonstrated that CC genotypes have higher odds for higher novelty seeking and lower reward dependence. In contrast, A allele carriers are more prone to neuroticism.  
**Want to go more in depth?** Whereas the overall DRD2 receptor number modulates GABA-mediated inhibition of striatal neurons, inhibition of glutamate release preferentially involves the DRD2S variant. Thus, reduced DRD2S expression is expected to increase excitability of striatal medium spiny neurons. The results of a study demonstrate that the A allele associated with low DRD2S production is also associated with greater activity in human striatum and other regions during working memory. This observation, in turn, is associated with lower performance in cognitive/attentional tasks.<sup>12</sup>. In addition, a very old study (1998)<sup>13</sup> found a statistically significant reduction in D2 receptor availability reflecting an alteration in receptor density which was observed in the A/C or A/A genotype group compared to the C/C group.
- **COMT rs4680 (Function: degradation/reuptake of the neurotransmitter dopamine.):** The famous rs4680 polymorphism encode COMT proteins with either a valine (Val) or methionine (Met) at amino acid 158. The Val version of COMT (G at rs4680) is associated with higher COMT enzyme activity, and therefore lower levels of dopamine in the brain, while the Met version (A at rs4680) is associated with lower enzyme activity and higher dopamine levels. In experiments carried out mainly in younger people, the Met version of COMT has been shown to be associated with better cognitive function. Fiocco, et al., however, found<sup>10</sup> that it was the Val version of COMT that was associated with less cognitive decline over the course of eight years in the elders they studied. In both white and black subjects, the Val version correlated with smaller reductions in Digit Symbol Substitution test scores. In white subjects only, the Val version was also associated with smaller declines in Modified Mini-Mental State Examination scores.  
 Green tea is able to increase energy expenditure and fat oxidation via inhibition of COMT by catechins. However, this does not always appear unanimously because of large inter-individual variability. A small 2014 study<sup>11</sup> looked at the differences in fat oxidation and energy expenditure with green tea based on COMT genotype. Those with the rs4680 GG genotype, who naturally have a higher COMT activity, had significantly increased energy expenditure and fat oxidation with green tea through inhibition of COMT activity, while those with the AA genotype had no increase (probably because they already have a natural lower COMT activity).  
 A 2015 study<sup>14</sup> of cognitively normal older adults found that those with GG genotype had lower Neuroticism scores and higher Agreeableness and Conscientiousness scores than those with AG or AA.

## YOUR GENETIC BREAKDOWN

Gene	Your results	Effects
TH (rs10770141)	AG	High TH activity leading to a higher conversion of dietary L-tyrosine to L-dopa = higher odds of having elevated levels of dopamine & catecholamins (epinephrine and norepinephrine).
DDC (rs10499695)	TT	Negatively associated with alerting.
DRD2(TaqI)	AC	Significantly lower DRD2S production (more info above) leading to a higher dopamine activity but also to a higher dopamine-resistance (we will explain it in your recommendations); higher addictive behaviors because of a higher reward dependence; likely very high glutamate activity and lower gaba activity.
COMT(rs4680)	AG	Mid-level COMT activity = Average dopamine reuptake/clearance = Average dopamine levels in the brain especially the prefrontal cortex. average cognitive function in young age, and average cognitive decline when getting old. In older adults, associated with higher Neuroticism scores and lower Agreeableness and Conscientiousness scores

## OVERALL CONCLUSION ON YOUR DOPAMINE SYSTEM:

Lower dopamine system

Your genetic test results indicate the possibility of a decreased dopamine system. See the section below to increase it.

## HOW YOU CAN OPTIMISE YOUR DOPAMINE SYSTEM?

**PLEASE CONSULT WITH YOUR DOCTOR, OR OTHER QUALIFIED HEALTH CARE PROFESSIONAL BEFORE MAKING ANY CHANGE IN YOUR REGIMEN OR USING ANY PRODUCT DISCUSSED WITHIN THIS WEBSITE.**

- Whether you have a low or high dopamine system, ensure to have an optimal daily intake of vitamin D3 and C which are highly involved in the dopamine system (dosage: see your nutrition section > vitamin profile)
- You have a higher conversion of L-tyrosine to L-dopa (which is then converted into dopamine). Therefore, our first recommendation is to eat enough level of protein-rich foods daily (protein-rich foods are rich in L-tyrosine). The problem is that the amino acids contained in these foods, including L-tyrosine, will be in competition to reach the blood brain barrier so it would not be sure that enough L-tyrosine reaches the brain. Thus, in addition to these foods, also add a little supplementation in L-tyrosine when eating a meal/snack low in protein.
- You have a mid-level COMT activity, which could lead to a higher dopamine reuptake in the brain (= lower dopamine levels). You can inhibit this COMT activity through natural sources such as EGCG (found in green tea), Radiola Rosea supplement, or Quercetin (found in onion).
- You have one A1 allele inside your DRD TaqI gene which leads to a high ratio of DRD2L instead of DRD2S.

**Is it a good or a bad thing?** Even if the DRD2L is associated to a very high dopamine system, it is a bad thing.

**Why?** Because this high dopamine system leads to a high dopamine-resistance. Dopamine resistance is well-documented. Stimuli (video games, drugs, sugar, coffee, some medications, gambling, etc...) that trigger our reward centers will release dopamine, which is related to feelings of excitement and anticipation. Usually, these feelings are inhibited by the DRD2S receptor to avoid an excess of these. In contrast, having a lower production of DRD2S (like in your case) could result to an excess increase of these good feelings and then become less sensitive to these rewards. The brain becomes less sensitive to dopamine as a way to protect itself and restore balance. When the chemical stimulus is removed, the brain is still desensitized to dopamine and needs more to feel `normal`. This reduced sensitivity could push you to increase your amount of rewards stimuli (more food, more drugs, more coffee, etc...). That is probably why lot of studies demonstrated that this gene is related to cocaine abuse. Reduced sensitivity levels to various hormones and neurotransmitters have a variety of effects, but none of them are good. Fat, depressed, bored, numb, anxious, irritable... the list goes on.

**Simply stated**, you are likely to crave for rewards to have good wellness feelings and to simply feel normal. Moreover, a study<sup>7</sup> demonstrated that in people with this gene, more reward anticipation leads to a significantly higher working memory performance. That is probably why many studies identified this gene as a candidate gene for ADHD (Attention Deficit hyperactivity disorders).

**So how do we increase our sensitivity to this dopamine control system?** In some cases, less stimulation works. With less dopamine spikes, such as drinking less coffee, our circulating dopamine quickly drops, and our cells become more sensitive to the effects of dopamine. Let`s take an example: drinking coffee only 1 week out of two. Or the best solution: never drink coffee. In addition, exercise can increase both dopamine production and receptor sites. If we`re experiencing problems with motivation and excitement about life, exercise may provide a fix.

**Want to increase even more your sensitivity?** Chemically dependent people can be treated with natural dopaminergic agonists like neuroadaptogen amino-acids therapy (NAAT) to up-regulate dopamine D2 receptor density. There are many possibilities to up-regulate this density:

- A mix of these ingredients in one supplement (did you know that GenetiConcept is working on a food supplement personalisation service? Soon available!) : Supplement listed in the points above + inositol + CDP-choline + uridine + DL-phenylalanine + spirulina + Rhadiola Rosea + Forskolin.
- A supplement called SynaptaGenX (available in both oral and intravenous form) : it is a safe, natural, non-addicting, combination product that may improve the health of individuals in recovery from Reward Deficiency Syndrome, including those suffering the consequences of psychoactive chemical abuse.
- Other strategies scientifically proven: Food restriction, exercise, abstinence from sexual behaviours of any kind. Any prolonged reduction of dopamine release will cause receptor upregulation and thus higher sensitivity to dopamine.

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