

Sample Client

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Personal information

NAME

Sample Client

SEX AT BIRTH

Female

HEIGHT

5ft 0" 153cm

WEIGHT

110lb 50kg



DISCLAIMER

This report does not diagnose this or any other health conditions. Please talk to a healthcare professional if this condition runs in your family, you think you might have this condition, or you have any concerns about your results.

How this works

Dopamine and norepinephrine are two of your brain's most critical neurotransmitters, working together in an interconnected pathway that influences virtually every aspect of your mental and physical well-being. From motivation and reward to focus and stress response, these chemical messengers orchestrate the complex dance between your thoughts, emotions, and behaviors.

The journey begins with the amino acid **phenylalanine**, which your body converts to tyrosine, then to **L-DOPA**, and finally to **dopamine**. Dopamine itself serves as the precursor to **norepinephrine** (and subsequently epinephrine), creating a cascade of neurotransmitter production that must be carefully balanced.

This pathway requires several key enzymes, including phenylalanine hydroxylase (PAH), tyrosine hydroxylase (TH), aromatic L-amino acid decarboxylase (DDC), and dopamine beta-hydroxylase (DBH), each serving as a critical checkpoint in the production process.

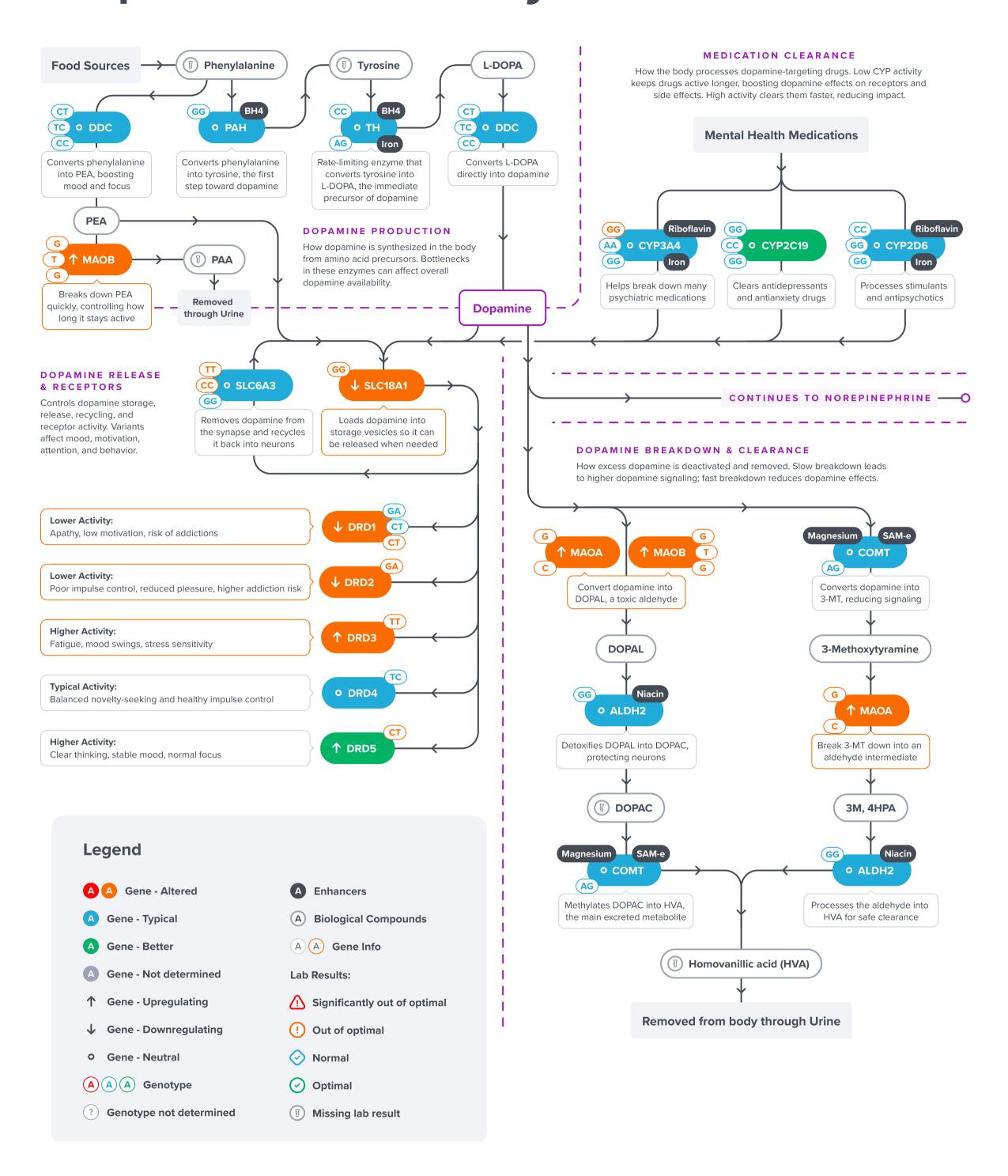
Once produced, these neurotransmitters must be properly packaged, released, and cleared from the synaptic space where they transmit their signals. Transporters like **DAT1** and **NET** regulate how long dopamine and norepinephrine remain active, while various receptors determine the strength and nature of their effects. The breakdown process, managed by enzymes like MAOA, MAOB, and COMT, ensures that neurotransmitter levels don't become excessive, while also generating byproducts that must be safely cleared from your system.

Your genetic blueprint contains variations that influence every step of this intricate pathway. Some variants may accelerate enzyme activity while others slow it down. Some affect how efficiently your brain responds to these neurotransmitters, while others influence how quickly medications are metabolized. Understanding your unique genetic profile provides invaluable insights into your brain chemistry, helping explain individual differences in mood, cognition, energy levels, and even your response to stress and medications.

This report examines your specific genetic variants across the entire dopamine and norepinephrine pathway, offering personalized recommendations to help optimize your neurochemical balance.

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Dopamine Pathway



Norepinephrine Pathway

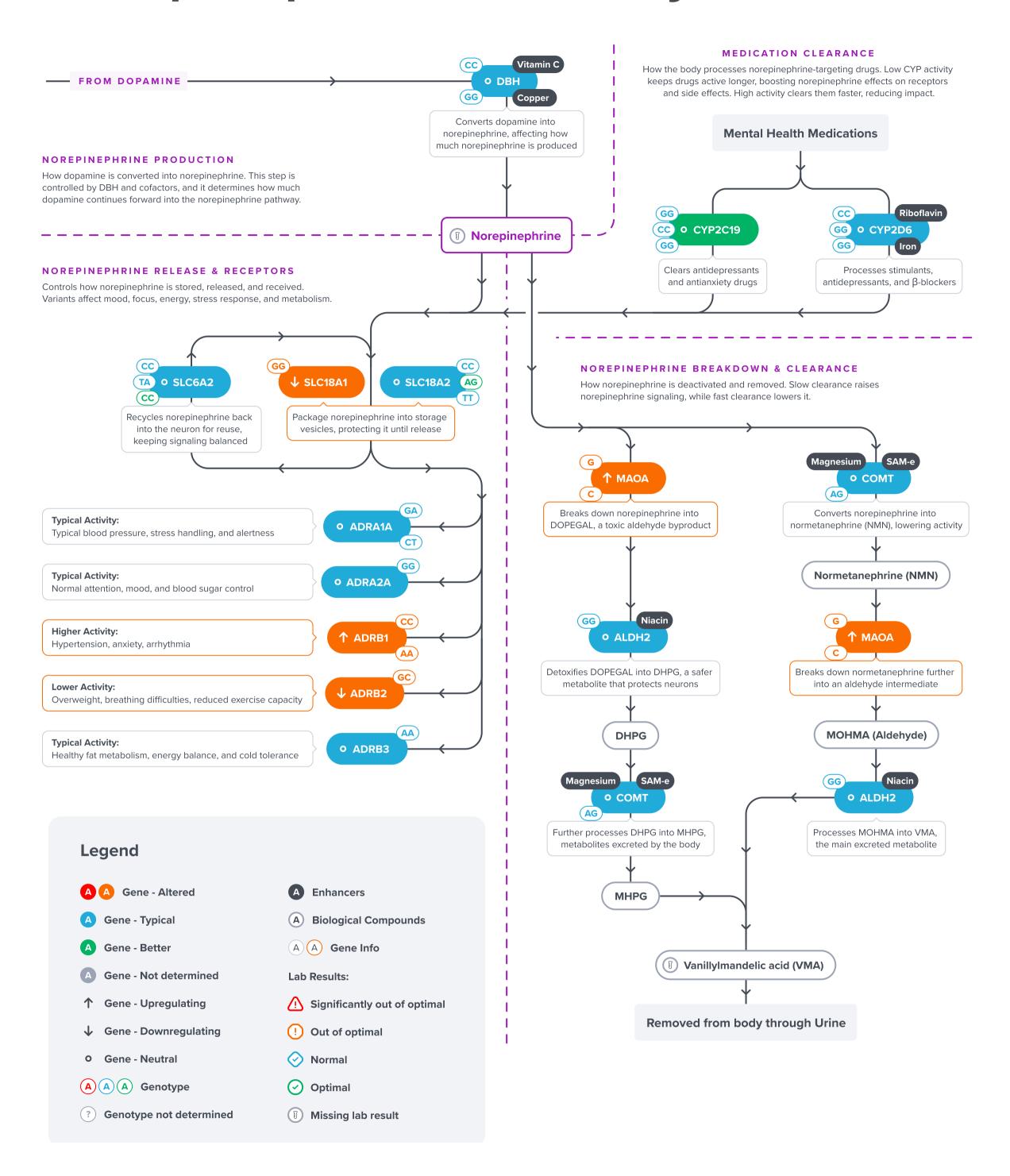


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Results Overview

Dopamine Pathway

Gene - SNP Summary

	rs 686	o GA
DRD1	rs 5326	↓ ст
	rs4532	o CT
SLC18A1	rs1390938	↓ GG
СОМТ	rs4680	o AG
DDC	rs 921451	o CT
	rs11575542	o CC
	rs3735273	o TC
SLC6A3	rs6347	↑ TT
	rs11564750	o GG
	rs27072	↑ CC

DRD2	rs1800497	↓ GA
MAOA	rs6323	↑ G
	rs 909525	↑ C
ALDH2	rs 671	o GG
CYP2D6	rs3892097	o CC
	rs1065852	o GG
	rs28371706	o GG
DRD4	rs1800955	o TC
rs6356 TH rs10770141	rs6356	o CC
	rs10770141	o AG
DRD5	rs6283	↓ СТ

DRD3 rs6280 ↑ T	
	Γ
rs3027452	
MAOB rs2283729 ↑ G	
rs1799836	
rs35599367 o G	G
CYP3A4 rs12721627 o G	G
rs 55785340 o A	Α
PAH rs1522305 o G	G
rs4244285 o G	G
CYP2C19 rs4986893 o G	G
rs12248560 o C	С

Labs Summary

(1) Glucose, Fasting
(1) Iron
(1) Cortisol, Saliva
(1) Homovanillic Acid (HVA), Random Urine
(1) Norepinephrine, Plasma

(1) Norepinephrine, Random Urine
(1) Prolactin
(1) Vanillylmandelic Acid (VMA), Random Urine
(1) Vitamin B12
(1) Vitamin B2 (Riboflavin), Plasma

(1) Vitamin D, 25-Hydroxy, Total
(1) Zinc

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Norepinephrine Pathway

Gene - SNP Summary

ADDB4	rs1801253	↑ CC
ADRB1	rs1801252	↑ AA
ADRA1A	rs1048101	o GA
ADRATA	rs1383914	о СТ
CYP2D6	rs3892097	o CC
	rs1065852	o GG
	rs28371706	o GG
CYP2C19	rs4244285	o GG
	rs4986893	o GG
	rs 12248560	• сс

ADRB2 rs1042714 ↓ GC SLC18A1 rs1390938 ↓ GG ADRA2A rs553668 o GG ALDH2 rs671 o GG rs1611115 o CC			
ADRA2A rs553668 o GG ALDH2 rs671 o GG rs1611115 o CC	ADRB2	rs1042714	↓ GC
ALDH2 rs671 o GG rs1611115 o CC	SLC18A1	rs1390938	↓ GG
rs1611115 o CC	ADRA2A	rs 553668	o GG
	ALDH2	rs671	o GG
DDU	DBH	rs1611115	o CC
rs1108580 o GG		rs1108580	o GG
rs3785143 o CC	SLC6A2	rs 3785143	o CC
SLC6A2 rs3785157 \$\dpsycdot\ \cdot\ CC		rs3785157	↓ cc
rs28386840 o TA		rs28386840	о ТА

MAOA	rs6323	↑ G
	rs909525	↑ C
ADRB3	rs4994	о АА
СОМТ	rs4680	o AG
SLC18A2	rs363276	o CC
	rs363387	o TT
	rs 363371	↑ AG

Labs Summary

- Adiponectin
- **Blood Pressure (Diastolic)**
- **Blood Pressure (Systolic)**
- I BMI Cortisol, Saliva
- **1** Homovanillic Acid (HVA), Random Urine

- **U** Leptin
- **Magnesium**
- Norepinephrine, Plasma
- **Norepinephrine, Random Urine**
- **(I)** Resting Heart Rate

(I) Vanillylmandelic Acid (VMA), Random Urine

VO2 Max

Your recommendations

Your recommendations are prioritized according to the likelihood of it having an impact for you based on your lab results, along with the amount of scientific evidence supporting the recommendation.

You'll likely find common healthy recommendations at the top of the list because they are often the most impactful and most researched.

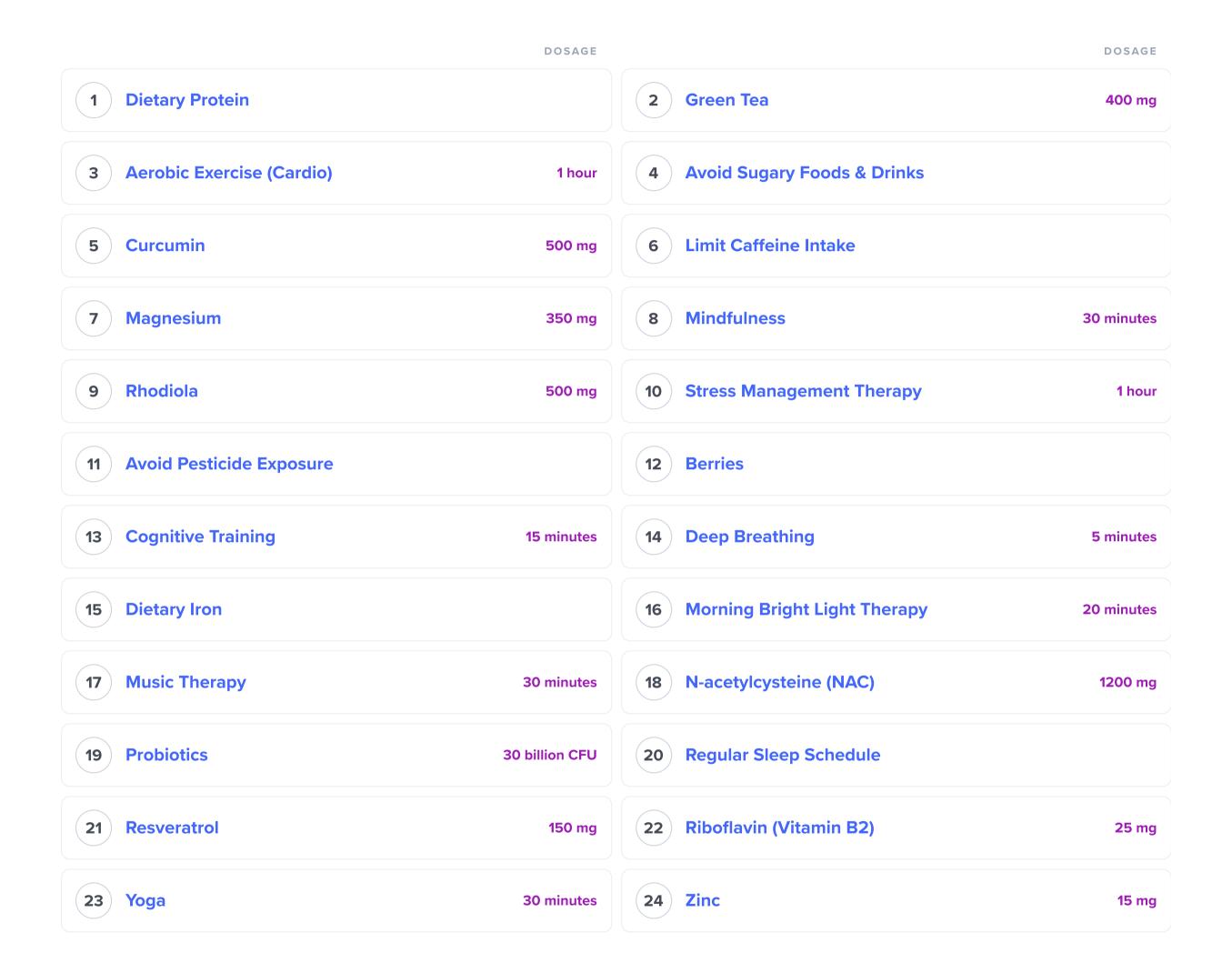


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Dietary Protein C

How to implement

Include a variety of protein sources such as meat, fish, eggs, dairy, beans, and nuts in your diet every day, aiming for at least 0.8 grams of protein per kilogram of body weight. For more active individuals or those looking to build muscle, increase intake to 1.2 to 2.0 grams per kilogram of body weight daily, spread out over all meals to maximize absorption.

How it helps

Protein provides the amino acid building blocks (like tyrosine and phenylalanine) that your brain needs to manufacture dopamine and norepinephrine. Without adequate protein intake, your brain simply can't produce enough of these neurotransmitters, which can lead to low motivation, poor focus, and mood issues.

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Getting enough protein may counteract this variant by improving leptin sensitivity and weight control.



Ensure adequate dietary protein to supply precursor amino acids for neurotransmitter synthesis (phenylalanine/tyrosine).



High-protein foods provide crucial amino acids for dopamine production and help maintain focus.



Green Tea 🔼



How to implement

Consume 400 mg of green tea extract daily. This can be taken in the form of capsules or tablets available that specify the amount of green tea extract. Ensure the supplement is taken according to the product's specific instructions, usually once a day with water.

TYPICAL STARTING DOSE 400 mg

How it helps

Green tea contains L-theanine and a moderate amount of caffeine, which work together to support focus and calm alertness by influencing dopamine and norepinephrine activity. The antioxidants in green tea, particularly EGCG, also help protect brain cells from damage and may support healthy aging of the dopamine system.

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Green tea contains moderate amounts of caffeine, which promotes adrenergic activity and supports fitness and weight control.



Green tea is a mild natural MAO-A inhibitor, which may help with your high-activity variant and boost mood.



EGCG from green tea can raise extracellular dopamine partly by inhibiting reuptake with DAT/SLC6A3 (and by COMT inhibition).



Aerobic Exercise (Cardio)



How to implement

Engage in at least 150 minutes of moderate-intensity aerobic exercise or 75 minutes of vigorous-intensity activity each week. Distribute this time over at least 3 days per week, avoiding consecutive days of vigorous exercise to allow for recovery.

TYPICAL STARTING DOSE 1 hour

How it helps

Cardiovascular exercise increases blood flow to the brain and triggers the release of dopamine and norepinephrine, giving you that "runner's high" feeling. Regular cardio also promotes the growth of new brain cells and protects existing neurons, making it one of the most powerful brain health interventions available.

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Regular cardio may counteract your variant by improving sympathetic tone, weight control, and fitness.



Moderate aerobic exercise can increase catecholamine production and release.



Avoid Sugary Foods & Drinks **2**

How to implement

To avoid sugary foods, eliminate or significantly reduce consumption of foods and beverages high in added sugars such as sodas, candies, baked goods, and sugary cereals from your diet. Instead, opt for natural sugar sources like fruits. Aim to do this daily for ongoing health benefits.

How it helps

Consuming high amounts of sugar causes rapid spikes and crashes in blood sugar, which can lead to dopamine surges followed by depletion, potentially creating a cycle similar to addiction. Over time, excessive sugar intake can reduce dopamine receptor sensitivity (making you need more stimulation to feel good), promote brain inflammation, and impair the healthy functioning of your reward and motivation systems.

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Refined sugar may downregulate D2 receptors.



Limit high-sugar foods that can overactivate D3 pathways and cause sugar crashes.



Curcumin **2**



How to implement

Take a 500 mg curcumin supplement daily with food. To enhance absorption, take it with a meal that contains fats or oils since curcumin is fat-soluble.

TYPICAL STARTING DOSE

500 mg

How it helps

Curcumin, the active compound in turmeric, is a powerful anti-inflammatory and antioxidant that may protect dopamineproducing neurons from damage and degeneration. It may also help increase levels of dopamine and norepinephrine in the brain while supporting overall brain health through multiple protective mechanisms.

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Curcumin is a mild natural MAO-B inhibitor, which may help with your high-activity variant and boost mood.



Curcumin may increase dopamine by mild MAO and DAT/SLC6A3 reuptake inhibition.



Limit Caffeine Intake **2**



Limit your caffeine consumption to less than 200 milligrams per day, equivalent to about two 6-ounce cups of coffee. Aim to avoid caffeine-containing foods and beverages such as tea, chocolate, and some soft drinks, especially in the late afternoon and evening to minimize sleep disturbances.

How it helps

While moderate caffeine can boost dopamine and norepinephrine to improve focus and alertness, excessive intake can lead to tolerance, dependence, and eventual depletion of these neurotransmitters. Limiting caffeine helps prevent the cycle of overstimulation followed by crashes, allowing your brain's natural dopamine system to function more optimally without relying on constant external stimulation.

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Excess caffeine may worsen the impact of this variant by increasing sympathetic tone and worsening cardiovascular health.



Excess caffeine may overstimulate dopamine receptors and worsen fatigue in the long run by disrupting sleep.



Magnesium 2



How to implement

Take up to 350 mg of magnesium daily as a supplement, preferably with a meal to enhance absorption.

TYPICAL STARTING DOSE

350 mg

How it helps

Magnesium plays a crucial role in regulating the nervous system and helps calm brain activity by supporting the balance of neurotransmitters. It can help reduce stress and anxiety while supporting healthy dopamine function, and many people don't get enough from their diet alone.

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Magnesium can calm the sympathetic tone and improve cardiovascular health.



Magnesium is needed for ATP and vesicular pumps; deficiency can impair vesicle loading by VMAT/SLC18A1.



Mindfulness 2



How to implement

Set aside 5-10 minutes each day to practice mindfulness meditation. Find a quiet place, assume a comfortable seated position, close your eyes, focus on your breathing, and observe your thoughts and sensations without judgment.

TYPICAL STARTING DOSE 30 minutes

How it helps

Mindfulness meditation helps regulate the brain's stress response and can increase dopamine release in reward centers while promoting better balance of norepinephrine for improved focus. Regular practice may actually change the structure of brain regions involved in attention and emotion regulation, supporting healthier neurotransmitter function and reducing the wearand-tear that chronic stress causes on these systems.

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Mindfulness may help alleviate the drops in neurotransmitters due to high MAO-A and boost mood.



Mindfulness may help improve ADHD symptoms while gently supporting dopamine pathways.



Rhodiola 2



How to implement

Take 500 mg of rhodiola supplement daily, preferably in the morning to avoid potential interference with sleep.

TYPICAL STARTING DOSE

500 mg

How it helps

Rhodiola is an adaptogenic herb that may help increase the sensitivity of neurons to dopamine and norepinephrine, allowing your brain to make better use of these neurotransmitters. It's particularly known for reducing mental fatigue and improving focus during stressful periods.

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Rhodiola is a mild natural MAO-A inhibitor, which may help with your high-activity variant and boost mood.



Rhodiola rosea has indirect dopamine-enhancing and reuptake-modulating effects. These may subjectively improve motivation and mood in someone with high DAT/SLC6A3.

Rhodiola rosea has indirect dopamine-enhancing and reuptake-modulating effects. These may subjectively improve motivation and mood in someone with high DAT/SLC6A3.



Stress Management Therapy **2**

How to implement

Engage in stress management therapy sessions, such as cognitive-behavioral therapy (CBT), for at least 1 hour per week over a course of 8 to 12 weeks. Techniques can include mindfulness, deep breathing exercises, and identifying stressors to develop coping strategies.

TYPICAL STARTING DOSE 1 hour

How it helps

Chronic stress depletes dopamine and norepinephrine over time while flooding the brain with cortisol, which can damage brain cells. Therapy techniques like cognitive behavioral therapy (CBT) help rewire stress responses and protect your brain's neurotransmitter systems from burnout.

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Practice stress-reduction techniques and ensure adequate sleep to regulate neurotransmitter turnover.



Stress hormones can increase DAT/SLC6A3 activity.



Avoid Pesticide Exposure 2



How to implement

Purchase organic produce when possible, wash fruits and vegetables thoroughly under running water, and peel them if not organic. Use natural pest control methods instead of chemical pesticides at home and garden. Limit the use of non-organic lawn and garden chemicals.

How it helps

Many pesticides can damage the neurons that produce dopamine and norepinephrine, with some pesticides linked to increased risk of Parkinson's disease and other brain disorders. Reducing exposure by choosing organic produce when possible and avoiding pesticide use in your home can help protect these vulnerable brain cells from toxic damage.

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Pesticides disrupt VMAT/SLC18A1 and impair brain chemistry.



Berries C



How to implement

Incorporate a variety of berries such as strawberries, blueberries, raspberries, and blackberries into your daily diet. Aim for at least one cup of fresh or frozen berries every day, either as a snack, part of your breakfast (such as in oatmeal or yogurt), or as a dessert.

How it helps

Berries are packed with antioxidants called flavonoids that protect brain cells from oxidative damage and inflammation, helping preserve the neurons that produce dopamine and norepinephrine. Regular berry consumption has been linked to slower cognitive decline with aging and may support healthy brain signaling and neurotransmitter function.

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Berries contain flavonoids with mild MAO-B inhibitor activity, which may help with your high-activity variant and boost mood.



Cognitive Training C



How to implement

Engage in exercises that challenge your brain for at least 15 minutes per day, five days a week. This can include puzzles, memory games, learning a new language, or playing a musical instrument.

TYPICAL STARTING DOSE

15 minutes

How it helps

Mental exercises like puzzles, learning new skills, or brain training games stimulate dopamine release as you solve problems and achieve goals, reinforcing neural pathways. Regular cognitive challenges can strengthen the brain's executive function networks and may help maintain healthy dopamine system function as you age.

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Cognitive training exercises may help improve attention and compensate for reduced D5 signaling.



Deep Breathing C



How to implement

Practice deep breathing exercises for 5-10 minutes at least twice a day, ideally in the morning and before bed. Sit or lie down in a comfortable position, slowly inhale through your nose, allowing your chest and lower belly to rise, hold the breath for a moment, and then exhale slowly through your mouth or nose.

TYPICAL STARTING DOSE

5 minutes

How it helps

Deep breathing exercises activate your parasympathetic nervous system, which helps calm your brain and counteract stress. This practice can help balance norepinephrine levels, reduce cortisol, and create a more optimal environment for healthy neurotransmitter function.

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Deep breathing may improve ADRB2 activity, airway function, and fitness.



Dietary Iron

How to implement

Incorporate iron-rich foods into your daily meals, such as red meat, chicken, turkey, fish, beans, lentils, tofu, cooked spinach, and fortified cereals. Aim for at least 18 mg of iron per day for adult women and 8 mg per day for adult men. It's also beneficial to pair these foods with vitamin C-rich foods like oranges, strawberries, or bell peppers to enhance iron absorption.

How it helps

Iron is essential for the enzymes that produce dopamine and norepinephrine from their precursors, and deficiency can significantly impair neurotransmitter synthesis. Low iron levels are particularly associated with attention problems, fatigue, and restless leg syndrome, all of which may be related to disrupted dopamine function.

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Iron helps support CYP3A4 function and maintains cognitive function.



Morning Bright Light Therapy 2

How to implement

Expose yourself to a light therapy box, which mimics natural sunlight, for about 20-30 minutes each morning within the first hour of waking up. It's important to do this daily, especially during months with less natural sunlight, to help manage symptoms of Seasonal Affective Disorder (SAD) or other conditions influenced by light exposure.

TYPICAL STARTING DOSE 20 minutes

How it helps

Bright light exposure, especially in the morning, helps regulate your circadian rhythm and can boost dopamine and norepinephrine production, which is why light therapy is effective for seasonal affective disorder. Light influences the brain regions that control mood and alertness, and getting adequate bright light during the day (while avoiding it at night) helps maintain healthy neurotransmitter patterns.

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Light therapy may help alleviate the drops in neurotransmitters due to high MAO-A and boost mood, especially during the winter.



Music Therapy **2**



How to implement

Engage in music therapy sessions for at least 30 minutes a day, three times a week. These sessions can involve listening to music, playing an instrument, singing, or writing songs, facilitated by a certified music therapist if possible.

TYPICAL STARTING DOSE 30 minutes

How it helps

Listening to or creating music activates the brain's reward system and triggers dopamine release, which is why music can be so emotionally powerful and mood-boosting. Music therapy can help reduce stress, improve focus, and support emotional regulation by modulating both dopamine and norepinephrine activity in ways that promote well-being.

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Listening to uplifting music, especially during exercise, can boost dopamine and PEA transiently, reducing the effect of MAO-B.



N-acetylcysteine (NAC)

How to implement

Take 600 mg of N-Acetylcysteine (NAC) supplement daily with water. It can be taken at any time of the day, but try to take it at the same time each day for best results.

TYPICAL STARTING DOSE

1200 mg

How it helps

NAC is a supplement that boosts your body's production of glutathione, a master antioxidant that protects brain cells from damage. It may also help regulate dopamine levels and has shown promise for supporting brain health in conditions where dopamine balance is disrupted.

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NAC has shown promise in addiction and impulse-control disorders. It may help reduce cravings and normalize dopamine signaling.



Probiotics C

How to implement

Take a probiotic supplement containing 10 billion or more live cultures once daily, preferably with a meal or as directed by the packaging or a healthcare provider.

TYPICAL STARTING DOSE

30 billion CFU

How it helps

Probiotics support the gut microbiome, which communicates with the brain through the "gut-brain axis" and can influence dopamine production—in fact, much of your body's dopamine is actually produced in the gut. A healthy gut microbiome may help reduce inflammation, support mood regulation, and optimize neurotransmitter balance throughout the body and brain.

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Include probiotics and fermented foods to support the gut-brain axis, which influences D2 receptor expression.



Regular Sleep Schedule 🕑

How to implement

Go to bed and wake up at the same time every day, even on weekends and holidays. This helps regulate your body's internal clock, leading to better sleep quality. Aim for 7-9 hours of sleep per night.

How it helps

Maintaining a consistent sleep-wake schedule helps regulate your brain's natural dopamine and norepinephrine rhythms, which follow a daily cycle that's crucial for mood, motivation, and alertness. Poor or irregular sleep disrupts these neurotransmitter systems, impairs the brain's ability to clear out toxins, and can lead to decreased dopamine receptor sensitivity, making it harder to feel motivated and focused during the day.

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Establish regular sleep routines and limit evening screen time to reduce overstimulation and boost energy levels.



Resveratrol **2**

How to implement

Take 150-500 mg of resveratrol as a supplement daily, preferably with meals to enhance absorption. This dosage range is based on studies for various health benefits, and it's advised to not exceed 500 mg per day without medical supervision.

TYPICAL STARTING DOSE

150 mg

How it helps

Resveratrol is an antioxidant compound found in red grapes and berries that may protect dopamine-producing neurons from age-related damage and oxidative stress. It appears to have neuroprotective properties and may help maintain healthy dopamine levels, though most research has been in animals and more human studies are needed.

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Resveratrol is a mild natural MAO-A inhibitor, which may help with your high-activity variant and boost mood.



Riboflavin (Vitamin B2)



How to implement

Take a riboflavin (vitamin B2) supplement daily, with a dose ranging from 5mg to 400mg, depending on the specific health concern or advice from a healthcare provider. Swallow the supplement with water, preferably with a meal to enhance absorption. This regimen can be continued long-term or as directed by a healthcare professional.

TYPICAL STARTING DOSE

25 mg

How it helps

Riboflavin is necessary for energy production in brain cells and plays a supporting role in the pathways that create neurotransmitters including dopamine. While deficiency is uncommon, adequate riboflavin helps ensure the brain has the energy and enzymatic support needed for optimal neurotransmitter production.

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Riboflavin helps support CYP3A4 function and protects the nerves.



Yoga 🕑



How to implement

Practice yoga for at least 20 to 30 minutes a day, most days of the week. Choose a style that matches your fitness level and goals, and consider attending a class or using online resources to guide your practice.

TYPICAL STARTING DOSE 30 minutes

How it helps

Yoga combines physical movement, breath control, and meditation to reduce stress hormones while supporting healthy dopamine and norepinephrine balance. Regular practice can increase GABA (a calming neurotransmitter), reduce inflammation in the brain, and help regulate the nervous system's stress response, creating an environment where neurotransmitter systems can function optimally.

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Yoga helps reduce sympathetic tone, relieve stress, and improve cardiovascular health.



Zinc 🗠

How to implement

Take a 15 mg zinc supplement daily, ideally with a meal to enhance absorption.

TYPICAL STARTING DOSE

15 mg

How it helps

Zinc is an essential mineral that helps regulate dopamine activity in the brain and is necessary for proper neurotransmitter function. Deficiency in zinc can impair dopamine signaling and has been linked to mood and attention issues, making adequate zinc intake important for optimal brain chemistry.

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Zinc may modulate the dopamine transporter; it can bind to DAT/SLC6A3 and reduce its activity at synapses. Ensuring adequate zinc intake may improve attention.

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ADRB1



The <u>ADRB1</u> gene encodes the beta-1 adrenergic receptor, which is bound and activated by the neurotransmitter <u>norepinephrine</u> [R].

Norepinephrine is part of the sympathetic nervous system, which manages the body's response to stress. It is one of the "fight or flight" hormones, along with its close relative epinephrine. Some amount of norepinephrine is required for good health, but too much can cause problems [R].

Norepinephrine increases <u>heart rate</u> and blood pressure, triggers the release of <u>glucose</u> from energy stores, increases blood flow to skeletal muscle, reduces blood flow to the gastrointestinal system, blocks urination, and slows the rate at which food moves through the gut [R, R, R].

Norepinephrine has multiple receptors. Of these, ADRB1's function is to increase heart rate and the strength of the heart's contractions. Increased ADRB1 activity is associated with increased blood pressure [R, R, R].

rs1801253 Arg389

Alleles
G: Reduced ADRB1 activity

C: Increased ADRB1 activity

Your Genotype

个CC

Your genotype is linked to increased ADRB1 activity and

worse cardiovascular health

Intro and Health Effects

The main ADRB1 polymorphism is $\underline{rs1801253}$ (Arg389). Its 'C' allele may increase the activation of the beta-1 adrenergic receptors and has been associated with \underline{R} :

- Higher blood pressure [R, R, R, R, R]
- Increased risk of cardiovascular disease [R, R, R, R]
- Increased risk of sudden cardiac death [R]
- Higher LDL cholesterol levels [R]
- Lower training-induced exercise tolerance [R]
- Increased risk of postoperative pain [R]

On the bright side, carriers may have a decreased risk of adverse effects in response to blood pressure medication (beta blockers) [R, R].

SNP

rs1801252 Ser49Gly

Alleles

A: Increased ADRB1 activity

G: Reduced ADRB1 activity

Your Genotype

TAA

Your genotype is linked to increased ADRB1 activity and worse cardiovascular health

Intro and Health Effects

Another variant, 'A' of rs1801252 (Ser49Gly), may increase ADRB1 stability and has been associated with [R]:

- Higher blood pressure [R]
- Increased risk of cardiovascular disease [R]
- Increased risk of sudden cardiac death [R]
- Lower odds of LVEF recovery in heart failure patients [R]
- Lower renin levels [R]

On the bright side, this variant has also been associated with a better response to beta blockers [R, R].

ADRB2



The <u>ADRB2</u> gene encodes the beta-2 adrenergic receptor, a vital part of the sympathetic nervous system. This receptor binds catecholamines, especially adrenaline (epinephrine), which increase cAMP levels [R].

The beta-2 receptors cause relaxation of the airways and smooth muscles (such as lungs) while contracting skeletal muscles (such as biceps). Their activity promotes breathing and circulation, slows down digestion, and improves physical performance [R, R].

Catecholamines control fat burning and energy expenditure, especially during caloric restriction (fasting) and <u>exercise</u>. Along with the primary beta-3 receptors in fat tissue, beta-2 receptors stimulate fat burning, resulting in energy and temperature release [R, R, R].

SNP

rs1042714 Q27E, Gln27Glu

Alleles

G: Reduced ADRB2 activity

C: Normal ADRB2 activity

Your Genotype

↓GC

Your genotype is linked to reduced ADRB2 activity and worse fitness

Intro and Health Effects

The <u>rs1042714</u> variant (also known as Q27E or Gln27Glu) has been most widely researched when it comes to weight. Its minor 'G' allele (Glu, E) was associated with approximately 20% higher odds of obesity in a meta-analysis of 18 studies [R].

An older meta-analysis came to a similar conclusion. However, the authors observed a significant link between rs1042714-G and obesity only in populations with lower frequencies of this allele, such as Asians and Native Americans. In two studies with 150 women, those with the 'G' allele had more fat mass and impaired burning [R, R, R].

This variant has also been linked to:

- Reduced exercise performance and VO2 max [R]
- Increased risk of cardiovascular events in coronary artery disease patients [R]
- Increased risk of Graves' disease in Caucasians [R]

On the bright side, people with this variant tend to lose weight more easily when they reduce calorie intake. However, given the link of this variant with obesity under regular conditions, there is a potential risk of weight regain ("yo-yo" effect) after dieting [R, R].

Normally, leptin helps burn excess fat stores by stimulating the sympathetic activity in fat tissue. However, according to one clinical trial, this pathway may be suppressed in people with the above SNP. The 'G' allele carriers had higher leptin levels, indicating leptin resistance [R].

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DRD1



The <u>DRD1</u> gene helps make <u>dopamine</u> D1 receptors. Those are proteins on the surface of brain cells that bind dopamine. DRD1 is the most abundant dopamine receptor, found in regions such as the neostriatum, basolateral amygdala, cerebral cortex, hypothalamus, and thalamus [R].

DRD1 is involved in neuronal growth and behavior, mediates some behavioral and cognitive aspects, and modulates $\underline{DRD2}$ -mediated events. It also stimulates adenylate cyclase \underline{R}].

By controlling dopamine functions in the brain, D1 receptors play a role in conditions such as [R, R]:

- Addictions
- Mental disorders such as schizophrenia or OCD
- Mood disorders such as bipolar disorder or depression

SNP	Your Constyne
rs686	Your Genotype o GA
Alleles A: Increased DRD1 activity G: Reduced DRD1 activity	Your genotype is linked to typical DRD1 activity and brain chemistry

Intro and Health Effects

The main DRD1 variant is <u>rs686</u>. Its 'G' allele, which reduces DRD1 expression, has been associated with [R]:

- Increased risk of nicotine dependence [R, R]
- Increased risk of bipolar disorder [R]
- Increased risk of sleep bruxism [R]
- Worse depressive symptoms [R]

On the bright side, it's linked to:

- Decreased risk of opioid dependence [R, R]
- Decreased risk of alcohol dependence [R]
- Decreased risk of schizophrenia [R]
- Decreased risk of visual hallucinations in Parkinson's disease patients [R]

Lower aggression levels in people with traumatic brain injury [R]

SNP

rs5326

Alleles

C: Typical DRD1 activity

T: Reduced DRD1 activity

Your Genotype

↓CT

Your genotype is linked to reduced DRD1 activity and altered brain chemistry

Intro and Health Effects

Another *DRD1* polymorphism is <u>rs5326</u>. Its 'T' allele may decrease dopamine levels in certain brain areas and has been associated with [R]:

- Increased risk of heroin addiction [R]
- Increased risk of schizophrenia [R]
- Increased risk of OCD [R]
- Increased risk of heroin dependence [R]
- Poorer cognition and worse strategic planning [R]

SNP

rs4532

Alleles

C: Reduced DRD1 activity

T: Increased DRD1 activity

Your Genotype

o CT

Your genotype is linked to typical DRD1 activity and brain chemistry

Intro and Health Effects

The 'C' allele of $\underline{rs4532}$ decreases *DRD1* expression and has been associated with $[\underline{R}, \underline{R}]$:

- Increased risk of treatment-resistant schizophrenia [R]
- Worse behavioral and cognitive symptoms in people with ADHD [R]
- Increased risk of hypertension [R]

On the other hand, it's linked to:

- Better response accuracy in complex tasks [R]
- Decreased risk of paranoid schizophrenia (in Chinese) [R]
- Decreased risk of autism [R]

DRD2



The <u>DRD2</u> gene helps make <u>dopamine</u> D2 receptors. Those are proteins on the surface of brain cells that bind dopamine [R].

The functions of D2 receptors are complex. They depend on the brain region and the position of receptors on brain cells. For the most part, these receptors are inhibitory, which means they prevent excessive dopamine release [R].

By controlling dopamine functions in the brain, D2 receptors play a role in:

- Social interactions [R, R, R]
- Motivation and reward [R, R]
- Novelty seeking [R]
- Substance dependence [R, R]
- Cognitive function [R, R]

SNP rs1800497

Alleles

A: Reduced DRD2 activity

G: Typical DRD2 activity

Your Genotype

JGA

Your genotype is linked to lower DRD2 activity and altered dopamine signaling

Intro and Health Effects

When it comes to the DRD2 gene, the most studied variant is <u>rs1800497</u>, also known as Taq1A. Interestingly, this variant is found in another gene, <u>ANKK1</u>, which controls the activity of DRD2 [R, R, R].

The "A" ("A1") allele of this variant is linked to different pleasure-seeking behaviors, such as:

- Alcohol and substance misuse [R, R, R]
- Food cravings and emotional eating [R, R, R, R]
- Other addictive behaviors [R]

This allele is linked to a 30% lower number of D2 receptors in brain regions responsible for motivation and reward. People with this allele may seek more pleasure from alcohol, high-calorie foods, drugs, and other addictive substances and behaviors [R, R, R].

This variant may also be linked to [R, R, R, R]:

• Depression

- Negative feelings
- Chronic pain
- PTSD

On the positive side, people with this variant may be more motivated and have better <u>cognitive function</u> [R, R, R].

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DRD3



The <u>DRD3</u> gene encodes dopamine receptor D3, a receptor that is activated by the chemical messenger (neurotransmitter) dopamine [R].

Among its many roles, dopamine is involved in regulating the sleep-wake cycle. While activation of certain types of dopamine receptors (such as dopamine receptor D1) has been shown to promote alertness and arousal, preliminary research has reported that dopamine receptor D3 activation may induce sleepiness [R, R, R].

Indeed, mice that lack dopamine receptor D3 have been observed to be hyperactive, suggesting that dopamine receptor D3 is necessary for suppressing active behaviors such as wakefulness [R].



Intro and Health Effects

The 'T' allele of rs6280 (Ser9Gly) has been associated with chronic fatigue syndrome, an illness characterized by prolonged low energy. This variant may increase the sensitivity or production of dopamine receptor D3, which may result in excessive fatigue when activated by dopamine [R].

MAOA



The MAOA gene codes for monoamine oxidase, an enzyme that helps break down the following chemical messengers [R]:

- <u>Dopamine</u>
- Serotonin
- Norepinephrine (noradrenaline)

Collectively, these chemicals are called monoamine neurotransmitters. Monoamine oxidase also breaks down other compounds with a monoamine structure, such as <u>phenethylamine</u> and tyramine [R].

Monoamine neurotransmitters control multiple biological processes such as cognition, mood, and behavior. Their activity and rapid breakdown are essential for the correct functioning of the brain. Alternatively, their breakdown by MAOA produces toxic byproducts that cause oxidative stress and inflammation. Hence, the importance of maintaining a balanced MAOA activity [R, R].

By deaminating monoamines, MAOA controls the turnover of dopamine and norepinephrine; high MAOA activity accelerates breakdown, leading to lower neurotransmitter levels.

Your Genotype

rs6323

Alleles

G: Increased MAOA activity

T: Typical MAOA activity

Your genotype is linked to increased MAOA activity and lower monoamine levels

Intro and Health Effects

There are multiple MAOA variants affecting enzyme activity. While low-activity variants lead to increased levels of the monoamine neurotransmitters dopamine, serotonin, and norepinephrine, variants with high activity decrease them. The main one is <u>rs6323</u>, and its "**G" allele** encodes a MAO-A protein with **higher activity** [R].

Variants with high activity lead to reduced dopamine, serotonin, and norepinephrine levels. These variants have been associated with the following conditions:

- Depression [R, R, R, R]
- Panic disorder [R, R]
- Obsessive-compulsive disorder [R, R]
- ADHD [R, R, R, R, R]
- Tourette syndrome [R, R]
- Heavy smoking [R, R, R]

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- Parkinson's disease [R, R]
- Migraines [R, R]
- Chronic fatigue syndrome [R]

Drugs that block MAOA can improve several of these conditions and are commonly prescribed for mood disorders [R, R].

In contrast, traits associated with lower MAOA activity include:

- Aggression [R, R, R, R]
- Autism [R, R, R]
- Schizophrenia [R, R, R]
- Suicidal behavior [R, R, R]
- Alcoholism [R, R, R]
- Substance use disorder [R, R]
- Obesity [R, R, R]

SNP

rs909525

Alleles

C: Increased MAOA activity

T: Typical MAOA activity

Your Genotype

个C

Your genotype is linked to increased MAOA activity and lower monoamine levels

Intro and Health Effects

Another important variant is <u>rs909525</u> (C=higher activity), but it's often inherited together with rs6323, so it may not be an independent genetic factor.

Variants with high activity lead to reduced dopamine, serotonin, and norepinephrine levels. These variants have been associated with the following conditions:

- Depression [R, R, R, R]
- Panic disorder [R, R]
- Obsessive-compulsive disorder [R, R]
- ADHD [<u>R</u>, <u>R</u>, <u>R</u>, <u>R</u>, <u>R</u>]
- Tourette syndrome [R, R]
- Heavy smoking [R, R, R]
- Parkinson's disease [R, R]
- Migraines [R, R]
- Chronic fatigue syndrome [R]

Drugs that block MAOA can improve several of these conditions and are commonly prescribed for mood disorders [R, R].

In contrast, traits associated with lower MAOA activity include:

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- Aggression [R, R, R, R]
- Autism [R, R, R]
- Schizophrenia [R, R, R]
- Suicidal behavior [R, R, R]
- Alcoholism [R, R, R]
- Substance use disorder [R, R]
- Obesity [R, R, R]

MAOB



The $\underline{\mathsf{MAOB}}$ gene codes for monoamine oxidase B, an enzyme that helps break down compounds such as $\underline{\mathsf{dopamine}}$ and $\underline{\mathsf{phenylethylamine}}$ [R].

Dopamine is a neurotransmitter with many roles in the brain. Phenylethylamine can indirectly stimulate the release of dopamine and other chemical messengers, including <u>serotonin</u> and <u>norepinephrine</u> (noradrenaline). Collectively, serotonin, dopamine, and norepinephrine are referred to as monoamines [R, R, R].

Monoamine neurotransmitters control multiple biological processes such as cognition, mood, and behavior. Interestingly, some of these neurotransmitters also have the ability to modulate one another's activity. For example, dopamine and norepinephrine can both induce arousal and alertness, while serotonin can inhibit the activity of these two neurotransmitters to induce sleepiness [R].

Variants in MAOB have been linked to [R, R, R, R, R, R]:

- Chronic fatigue
- Depression and antidepressant response
- High blood pressure
- Parkinson's disease
- Schizophrenia

MAO-B preferentially degrades dopamine and phenethylamine; high activity lowers synaptic dopamine, potentially leading to mood or cognitive issues.



Intro and Health Effects

A higher amount of monoamine oxidase B implies lower monoamine levels (due to increased breakdown), and vice versa. MAOB variants with increased activity have been associated with <u>chronic fatigue syndrome</u> [R, R].

The main variants associated with this condition are [R]:

• 'G' at <u>rs3027452</u>

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- 'G' at <u>rs2283729</u>
- 'T' at rs1799836

The 'G' allele of rs3027452 is linked to lower blood pressure and higher mood improvement in response to tryptophan treatment [R, R].

SNP

rs2283729

Alleles

A: Reduced MAOB activity

G: Increased MAOB activity

Your Genotype

个G

Your genotype is linked to increased MAOB activity and lower monoamine levels

Intro and Health Effects

A higher amount of monoamine oxidase B implies lower monoamine levels (due to increased breakdown), and vice versa. MAOB variants with increased activity have been associated with <u>chronic fatigue syndrome</u> [R, R].

The main variants associated with this condition are [R]:

- 'G' at <u>rs3027452</u>
- 'G' at <u>rs2283729</u>
- 'T' at <u>rs1799836</u>

SNP

rs1799836

Alleles

C: Reduced MAOB activity

T: Increased MAOB activity

Your Genotype

个T

Your genotype is linked to increased MAOB activity and lower monoamine levels

Intro and Health Effects

A higher amount of monoamine oxidase B implies lower monoamine levels (due to increased breakdown), and vice versa. MAOB variants with increased activity have been associated with chronic fatigue syndrome [R, R].

The main variants associated with this condition are [R]:

- 'G' at <u>rs3027452</u>
- 'G' at <u>rs2283729</u>

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• 'T' at <u>rs1799836</u>

The 'T' allele of rs1799836 is also associated with higher anger [R].

SLC18A1



The <u>SLC18A1</u> gene encodes the vesicular monoamine transporter 1 (VMAT1), which acts to accumulate monoamines, such as <u>norepinephrine</u>, epinephrine, <u>dopamine</u>, and <u>serotonin</u>, into sacs (vesicles). By doing so, it helps ensure the correct functioning of the monoaminergic system [R, R].

The gene is primarily expressed in the brain, especially in the pituitary gland and the adrenal glands [R].

VMAT1 also plays an important role in the uptake and secretion of serotonin in the gut, which is critical for digestive function [R].

Variants in this gene disrupt the levels of monamine neurotransmitters and have been associated with psychiatric disorders such as schizophrenia and bipolar disorder [R].



Intro and Health Effects

The main SLC18A1 polymorphism is $\underline{rs1390938}$, commonly referred to as Thr136IIe. Its minor 'A' allele has been linked to higher VMAT1 and monoamine transport activity. This variant has been associated with a **decreased risk** of [R]:

- Autism spectrum disorder [R]
- Anxiety, affective, and alcohol use disorders [R, R]
- Severe alcohol withdrawal [R]
- Damaging neurological changes in alcoholics [R]
- Bipolar disorder [R]
- Low sperm motility [R]

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ADRA1A



The <u>ADRA1A</u> gene encodes the alpha-1A adrenergic receptor. This is a receptor for epinephrine (also called adrenaline), one of the major signals responsible for the fight or flight response [R, R].

The effects of epinephrine include increased <u>heart rate</u>, breathing rate, and blood flow to the muscles, to name a few. For this reason, it is also used as a medication for several conditions, such as cardiac arrest, serious allergic reactions, and asthma [R, R, R, R].

The adrenal glands make most of the epinephrine in the body, but small amounts are also produced in other tissues, like some neurons and the kidneys [R].

People with <u>chronic fatigue syndrome</u> are suspected to have significantly reduced epinephrine signaling. This lack of epinephrine may worsen symptoms, such as fatigue, difficulty thinking, and muscle pain [R, R].

SNP

rs1048101

Alleles

A: Reduced ADRA1A activity

G: Increased ADRA1A activity

Your Genotype

o GA

Your genotype is linked to typical ADRA1A activity and typical odds of chronic fatigue

Intro and Health Effects

A large association study identified an association between two ADRA1A gene variants, 'A' at $\underline{rs1048101}$ and 'T' at $\underline{rs1383914}$, and chronic fatigue. The authors of another more focused study suggested that these variants may change the way that epinephrine and its receptor bind together, making it more difficult for the body to receive epinephrine signals [R, R].

In line with the association of these variants with chronic fatigue, another study associated rs1048101 with increased disability in patients with fibromyalgia [R].

SNP

rs1383914

Alleles

C: Increased ADRA1A activity

T: Reduced ADRA1A activity

Your Genotype

o CT

Your genotype is linked to typical ADRA1A activity and typical odds of chronic fatigue

Intro and Health Effects

A large association study identified an association between two ADRA1A gene variants, 'A' at rs1048101 and 'T' at rs1383914, and chronic fatigue. The authors of another more focused study suggested that these variants may change the way that epinephrine and its receptor bind together, making it more difficult for the body to receive epinephrine signals [R, R].

In line with the association of these variants with chronic fatigue, another study associated rs1383914 with fibromyalgia [R].

ADRA2A



The <u>ADRA2A</u> encodes an alpha-2-adrenergic receptor. These receptors have a critical role in regulating neurotransmitter release from the "fight or flight" system (sympathetic nerves and adrenergic neurons) in the brain [R].

The ADRA2A receptor plays important roles in brain and heart function [R].

It modulates cardiovascular function by way of central inhibition of sympathetic/fight or flight activity or inhibition of norepinephrine release from sympathetic neurons [R].

When activated, these receptors induce low heart rate, low blood pressure, and sedation. Activated ADRA2A receptors stop the breakdown of fat cells by inhibiting hormone-sensitive lipase [R].

Animal and cell-based studies have associated this protein with decreased glucose tolerance and insulin secretion, suggesting the ADRA2A may be a candidate gene for type 2 diabetes [R, R].

SNP

rs553668

Alleles

A: Increased ADRA2A activity

G: Typical ADRA2A activity

Your Genotype

o GG

Your genotype is linked to typical ADRA2A activity and metabolic health

Intro and Health Effects

The main ADRA2A variant is <u>rs553668</u>. Its minor 'A' allele may increase the number of ADRA2A receptors.

This allele has been associated with higher fasting glucose and increased risk of type 2 diabetes (especially in Europeans) in multiple studies [R, R, R, R, R, R, R, R].

ADRB3



The <u>ADRB3</u> gene encodes the beta-3 adrenergic receptor. This receptor binds catecholamines and activates the sympathetic nervous system by increasing cAMP levels [R].

Beta-receptors impact vital processes such as breathing and blood flow, but also have diverse metabolic roles. They control fat metabolism, insulin release, glucose production, and more [R, R].

Unlike beta-1 and beta-2, expressed throughout the body, the beta-3 receptor is mainly located in fat tissue. Once activated by catecholamines, It stimulates fat burning and heat production [R].

Leptin is a crucial metabolic hormone that helps burn fat stores by stimulating sympathetic activity and raising catecholamine levels. These pathways are often blunted in obesity due to underactive beta receptors, leptin resistance, or other factors [R, R, R, R].

SNP

rs4994

Alleles

A: Typical ADRB3 activity

G: Reduced ADRB3 activity

Your Genotype

ο ΔΑ

Your genotype is linked to typical ADRB3 activity and metabolic health

Intro and Health Effects

Over 100 studies have examined the relationship between one ADRB3 variant—rs4994 or Trp64Arg— and body-weight measures. The A>G switch at rs4994 changes one amino acid in the beta-3 receptor structure. The "mutant" receptor had a reduced ability to produce cAMP and burn fat in test tubes [R, R, R].

One meta-analysis included 97 studies, involving 44,800 participants. Among East Asians, those with the "G" allele had, on average, 0.31 units higher body mass index, which would equal 0.8-1 kg. In European descendants, the difference was four times smaller and wasn't statistically significant [R].

The same group of authors conducted the largest study of 4,854 European (UK) subjects and confirmed the lack of association between this SNP and BMI [R].

In a meta-analysis of 16 studies and 12,500 children and adolescents, rs4994-G correlated with 23% higher obesity rates. Once again, the effect stemmed from East Asian subjects, who had 47% higher odds of obesity per copy of the "G" allele [R].

Research has associated the same variant with other conditions, such as:

- Diabetes [R, R]
- High blood pressure [R]
- Heart disease [R]

Those genetic effects were also more pronounced in East Asians.

ALDH2



The <u>ALDH2</u> gene encodes for part of an enzyme named aldehyde dehydrogenase (ALDH), which is involved in the breakdown of alcohol in the liver.

ADH enzymes are responsible for the first step of alcohol metabolism, where alcohol is converted to potentially toxic acetaldehyde. **ALDH** enzymes are responsible for the second step, breaking down acetaldehyde to acetic acid.

Certain ALDH2 variants produce fewer or less active ALDH enzymes, and may reduce the enzyme activity to zero, largely reducing the rate at which acetaldehyde is converted to acetic acid. This can lead to a build-up of acetaldehyde following alcohol consumption. Acetaldehyde build-up is toxic and bad for your health, and can result in negative effects such as [R, R, R]:

- Flushing
- Sweating
- Nausea
- Accelerated heart rate
- Vomiting

Low ALDH2 activity reduces clearance of aldehyde metabolites from dopamine and norepinephrine, leading to accumulation of reactive aldehydes that can damage neurons and contribute to oxidative stress.

Enhancers:

Vitamin B3 (Niacin)

SNP

rs671

Alleles

A: Reduced ALDH2 activity

G: Typical ALDH2 activity

Your Genotype

o GG

Your genotype is linked to typical ALDH2 activity and aldehyde clearance

Intro and Health Effects

A study of 251 Japanese people found that carriers of an 'A' allele at the ALDH2 <u>rs671</u> variant were more likely to experience a hangover. As a result, carriers drink less and are less likely to be alcohol-dependent than non-carriers [R].

Carriers of the 'A' allele have been reported to get drunk faster and are more likely to experience a hangover, especially if they have a <u>vitamin B12</u> deficiency. Vitamin B12 can assist in acetaldehyde breakdown. Variant carriers who drink alcohol with this

deficiency may be more at risk of the negative health effects associated with acetaldehyde buildup [R, R].

Besides acetaldehyde, ALDH2 helps clear other aldehyde metabolites, such as those formed by dopamine and norepinephrine breakdown.

The rs671 SNP is most prevalent in Asian populations and is almost non-existent in other populations. Enzyme activity is completely reduced in those who carry two copies of the 'A' allele, and by 50-70% for those who carry one [R, R].

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COMT



The $\underline{\mathsf{COMT}}$ gene helps make an enzyme called catechol-O-methyltransferase (COMT). The COMT enzyme helps break down chemical messengers in the body. These include [R, R, R]:

- <u>Dopamine</u>
- Norepinephrine (noradrenaline)
- <u>Epinephrine</u> (adrenaline)

Dopamine triggers feelings of pleasure and reward. It is also important for many cognitive functions, such as memory and attention. Norepinephrine and epinephrine support the "fight or flight" stress response [R, R, R, R].

In addition, COMT helps break down other compounds such as <u>estrogen</u> byproducts, bioflavonoids (e.g., <u>quercetin</u> and <u>fisetin</u>), tea catechins, and certain drugs (e.g., <u>L-DOPA</u> and dobutamine) [R, R].

The activity of the COMT enzyme may influence [R, R, R, R]:

- Stress response
- Mental health
- Cognitive function
- Pain sensitivity

COMT provides a major degradation pathway for catecholamines, particularly in tissues like the prefrontal cortex. Low COMT activity slows dopamine/norepinephrine clearance, possibly causing heightened arousal or anxiety.

Enhancers:



SNP

rs4680

Alleles

A: Reduced COMT activity

G: Increased COMT activity

Your Genotype

o AG

Your genotype is linked to typical COMT activity and stress resilience

Intro and Health Effects

One common variant of the COMT gene, <u>rs4680</u>, may affect COMT enzyme activity. Some people call rs4680 the "worrier or warrior" variant [R, R].

The "G" allele of this variant is linked to a higher COMT enzyme activity. People with two copies of this allele (GG) have been nicknamed the "warriors." They break down stress-related chemical messengers more quickly. This may help improve their performance under stress [R].

On the negative side, "warriors" may have lower cognitive performance under relaxed conditions [R, R, R].

People with two copies of the "A" allele (AA) may have lower COMT enzyme activity. They have been nicknamed the "worriers." They break down stress-related chemical messengers more slowly in the brain. For this reason, they may be more vulnerable to stress. This includes an increased susceptibility to heart disease, possibly due to the effects of these chemical messengers on blood pressure and heart rate [R, R, R].

The good news is that "worriers" may become more emotionally resilient with age. They also tend to have enhanced cognitive performance under relaxed conditions. Interestingly, "worriers" seem to have a more pronounced placebo response due to higher dopamine levels [R, R, R, R, R].

People carrying both alleles (AG) tend to be in between the described extremes [R, R].

CYP2D6



The <u>CYP2D6</u> encodes a member of the cytochrome P450 monooxygenase superfamily of enzymes. These proteins eliminate most drugs from the body. CYP2D6 catalyzes reactions involved in drug metabolism and the synthesis of cholesterol, steroids, and other lipids [R].

Although it accounts for only 2-5% of the liver CYPs, CYP2D6 metabolizes 25% of all drugs. This includes [R, R, R]:

- Opioids: morphine, <u>hydrocodone</u>, codeine, oxycodone, tramadol [R, R, R, R, R]
- Antidepressants: <u>amitriptyline</u>, nortriptyline, <u>venlafaxine</u>, and fluoxetine [R, R, R]
- Antipsychotics: haloperidol, risperidone [R, R]
- Atomoxetine (used to treat ADHD) [R]
- Beta-blockers: carvedilol and metoprolol [R]
- Antiemetics: metoclopramide [R]
- Antitumor agents: tamoxifen and gefitinib [R, R]

Enhancers:





SNP

rs3892097 CYP2D6*4

Alleles

C: Typical CYP2D6 activity

T: Reduced CYP2D6 activity

Your Genotype

o CC

Your genotype is linked to typical CYP2D6 activity and drug clearance

Intro and Health Effects

The 'T' allele of <u>rs3892097</u> corresponds to CYP2D6*4. This is the most frequent non-functional variant in Europeans and North Americans (18.0%), accounting for 70-90% of cases [R].

SNP

rs1065852 CYP2D6*10

Alleles

A: Reduced CYP2D6 activity

G: Typical CYP2D6 activity

Your Genotype

o GG

Your genotype is linked to typical CYP2D6 activity and drug clearance

Intro and Health Effects

The 'A' allele of rs1065852 encodes the intermediate-activity CYP2D6*10 variant. This variant is especially common in Thai (50%) and East Asians (42%) [R, R].

SNP

rs28371706 CYP2D6*17

Alleles

A: Reduced CYP2D6 activity

G: Typical CYP2D6 activity

Your Genotype

o GG

Your genotype is linked to typical CYP2D6 activity and drug clearance

Intro and Health Effects

Another intermediate-activity variant is CYP2D6*17, encoded by the 'A' allele of rs28371706. This variant is most common in Africans (around 20%) [R, R].

CYP3A4



The <u>CYP3A4</u> gene encodes cytochrome P450 3A4, a member of the cytochrome P450 monooxygenase superfamily of enzymes. These proteins eliminate most drugs from the body [R, R].

CYP3A4 in particular is responsible for processing approximately 45–60% of prescribed drugs, including opiods, immunosuppressants, statins, **antipsychotics**, **and antidepressants** [R, R, R, R, R, R].

This enzyme is mainly found in the liver (\square 40% of the total liver CYP content) but also in the small intestine, prostate, breast, colon, and brain. CYP3A4 is the most active CYP enzyme in the gut, which explains why what we eat and drink has a great effect on the activity of this enzyme [R, R, R].

Enhancers:





SNP

rs35599367

Alleles

A: Reduced CYP3A4 activity

G: Typical CYP3A4 activity

Your Genotype

o GG

Your genotype is linked to typical CYP3A4 activity and drug clearance

Intro and Health Effects

The 'A' allele of $\underline{rs35599367}$, also known as CYP3A4*22, reduces CYP3A4 levels and activity by approximately half, resulting in slower drug metabolism $[\underline{R}, \underline{R}, \underline{R}, \underline{R}]$.

SNP

rs12721627

Alleles

A: Reduced CYP3A4 activity

G: Typical CYP3A4 activity

Your Genotype

o GG

Your genotype is linked to typical CYP3A4 activity and drug clearance

Intro and Health Effects

The minor allele 'C' of $\underline{rs12721627}$ (CYP3A4 $\underline{\square}16$) has been associated with lower enzyme activity $[\underline{R}, \underline{R}]$.

In combination with other variants, this may result in slower drug metabolism and a potentially higher risk of side effects.

SNP

rs55785340

Alleles

A: Typical CYP3A4 activity

G: Reduced CYP3A4 activity

Your Genotype

оДД

Your genotype is linked to typical CYP3A4 activity and drug clearance

Intro and Health Effects

The minor allele 'G' of <u>rs55785340</u> (CYP3A4*2) has been associated with lower enzyme activity [R, R].

In combination with other variants, this may result in slower drug metabolism and a potentially higher risk of side effects.

DBH



The <u>DBH</u> gene codes for dopamine beta-hydroxylase, an enzyme that converts <u>dopamine</u> to <u>norepinephrine</u> in the brain [R].

Dopamine triggers feelings of pleasure and reward. It is also important for many cognitive functions, such as memory and attention. In turn, norepinephrine supports the "fight or flight" stress response [R, R, R, R].

Low DBH activity has been associated with:

- Increased risk of ADHD [R, R, R]
- Increased neuroticism, novelty seeking, impulsivity, and aggression [R]
- Decreased risk of migraines but more frequent migraine-related side effects [R]

Enhancers:



SNP

rs1611115

Alleles

C: Typical DBH activity

T: Reduced DBH activity

Your Genotype

o CC

Your genotype is linked to typical DBH activity and norepinephrine levels

Intro and Health Effects

The best-characterized DBH polymorphism is $\underline{rs1611115}$. Its 'T' allele may decrease DBH production, resulting in higher dopamine and lower norepinephrine levels. This allele has been associated with [R]:

- Increased neuroticism, novelty seeking, impulsivity, and aggression [R]
- Decreased conscientiousness [R]
- Increased risk of adult ADHD [R]
- Decreased risk of migraines but more frequent migraine-related side effects [R]

SNP

rs1108580

Alleles

A: Reduced DBH activity

G: Typical DBH activity

Your Genotype

o GG

Your genotype is linked to typical DBH activity and norepinephrine levels

Intro and Health Effects

Another variant leading to lower DHB levels, 'A' at <u>rs1108580</u>, has been associated with [R]:

- Increased risk of ADHD [R, R]
- Increased risk of schizophrenia [R]

Decreased risk of alcohol dependence [R]

DDC



The <u>DDC</u> gene encodes the aromatic I-amino acid decarboxylase (AADC) enzyme. This enzyme takes part in the pathway that produces dopamine and serotonin. Both neurotransmitters are produced in two-step processes. First, other enzymes control the reactions that convert tyrosine to L-DOPA and tryptophan to 5-hydroxytryptophan [R].

The AADC enzyme converts L-DOPA and 5-hydroxytryptophan to dopamine and serotonin, respectively. To do this, it removes a molecular structure called a carboxyl group, consisting of a carbon atom, two oxygen atoms, and a hydrogen atom [R].

Variants in the *DDC* gene result in reduced activity of the AADC enzyme and decreased dopamine and serotonin levels. Changes in the levels of these neurotransmitters contribute to the developmental delay, intellectual disability, abnormal movements, and autonomic dysfunction seen in people with AADC deficiency [R].

SNP

rs921451

Alleles

C: Reduced DDC activity

T: Typical DDC activity

Your Genotype

o CT

Your genotype is linked to typical DDC activity and L-DOPA metabolism

Intro and Health Effects

The most widely researched DDC SNP is <u>rs921451</u>. Its minor 'C' allele has been associated with lower DDC activity. This variant has been associated with [R]:

- Increased risk of Parkinson's disease [R]
- Worse motor response to L-DOPA in patients with Parkinson's disease [R, R, R, R]
- Reduced risk of orthostatic hypotension in patients with Parkinson's disease [R]
- Greater nicotine dependence [R]

SNP

rs11575542

Alleles

C: Typical DDC activity

T: Reduced DDC activity

Your Genotype

o CC

Your genotype is linked to typical DDC activity and L-DOPA metabolism

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Intro and Health Effects

The minor 'T' allele of rs11575542, also linked to lower DDC enzymatic activity, has been associated with [R]:

- Worse somatic symptoms [R]
- Heavier drinking [R]

SNP

rs3735273

Alleles

C: Reduced DDC activity

T: Increased DDC activity

Your Genotype

o TC

Your genotype is linked to typical DDC activity and L-DOPA metabolism

Intro and Health Effects

The 'T' allele of <u>rs3735273</u> may increase DDC activity based on its opposite effects to the two previous variants. It has been associated with:

- Better response to L-DOPA in patients with Parkinson's disease [R, R]
- Increased risk of orthostatic hypotension in Parkinson's disease patients [R]
- Increased risk and severity of ADHD [R, R]
- Reduced nicotine dependence [R]

DRD4



The <u>DRD4</u> gene helps make <u>dopamine</u> D4 receptors. Those are proteins on the surface of brain cells that bind dopamine. The D4 subtype is a G-protein-coupled receptor activated by dopamine that inhibits adenyl cyclase, ultimately reducing intracellular levels of the messenger molecule cyclic AMP [R, R].

Variants in this gene have been associated with neurological and psychiatric conditions such as [R, R, R, R]:

- ADHD
- Autism
- Schizophrenia
- Addictions
- Bipolar disorder
- Parkinson's disease
- Eating disorders

This receptor is also a target for drugs that treat schizophrenia and Parkinson's disease [R].

SNP Your Genotype rs1800955 o TC Alleles C: Increased DRD4 activity Your genotype is linked to typical DRD4 activity and T: Reduced DRD4 activity dopamine function

Intro and Health Effects

The best-researched DRD4 polymorphism is rs1800955. Its 'C' allele increases DRD4 expression by 40%, potentially enhancing dopamine function. This variant has been associated with [R]:

- Increased novelty seeking [R]
- Increased extraversion [R]
- Greater positive affect [R]
- Decreased risk of heroin dependence [R]
- Decreased risk of attention deficit [R]
- Decreased risk of concussion [R]
- Decreased risk of paranoid symptoms in people with methamphetamine use disorder [R]

On the downside, it's also linked with risk-taking behavior and smoking [R, R, R]

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PAH



The \underline{PAH} gene encodes an enzyme called phenylalanine hydroxylase. This enzyme is responsible for the first step in the conversion of the amino acid phenylalanine into another amino acid, tyrosine. **Tyrosine is a building block for all proteins.** It also helps make important chemicals such as $[\underline{R}, \underline{R}, \underline{R}, \underline{R}, \underline{R}]$:

- <u>Dopamine</u>
- Norepinephrine (noradrenaline)
- <u>Epinephrine</u> (adrenaline)
- Thyroid hormones
- Melanin (skin pigment)

The PAH enzyme works with a molecule called tetrahydrobiopterin (BH4) to carry out this chemical reaction [R].

Your Genotype
rs1522305

Alleles
G: Typical PAH activity
C: Increased PAH activity

Your genotype is linked to typical PAH activity and typical odds of schizophrenia

Intro and Health Effects

A study of over 5k participants associated the minor 'C' allele of $\underline{rs1522305}$ with a **reduced** risk of schizophrenia in Caucasian populations [R].

Although studies on the functional impact of this polymorphism are lacking, the authors speculated that it may increase PAH activity. The resulting improved phenylalanine metabolism may support dopamine function in the brain.

SLC18A2



The <u>SLC18A2</u> ('solute carrier family 18 member 2') gene encodes a protein called VMAT2 ('vesicular monoamine transporter 2) that is a member of the toxin-extruding antiporter family [R].

VMAT2 is mainly located in neurons, where it acts as a pump for the release of neurotransmitters such as dopamine, norepinephrine (noradrenaline), epinephrine (adrenaline), serotonin, histamine, and GABA [R, R].

Due to its role in neurotransmitter release, VMAT2 is essential for cognitive processes such as motor control, stable mood, and autonomic function. Moreover, it protects the neurons from both internal and external toxins. In fact, it was first identified for its ability to protect from the Parkinsonism-inducing dopamine neurotoxin MPP+ [R, R, R].

Variants with decreased VMAT2 activity have been associated with:

- PTSD [R]
- Alcohol and nicotine dependence [R]
- Schizophrenia [R]
- Bipolar disorder [R]
- Parkinson's disease [R]
- Tardive dyskinesia [R]

SNP

rs363276

Alleles

C: Typical SLC18A2 activity

T: Reduced SLC18A2 activity

Your Genotype

o CC

Your genotype is linked to typical SLC18A2 activity and typical odds of PTSD

Intro and Health Effects

Several SLC18A2 polymorphisms resulting in decreased VMAT2 levels have been associated with different mental health issues. These include:

The 'T' allele of $\underline{rs363276}$: associated with an increased risk of PTSD [R, R].

SNP

rs363387

Alleles

G: Increased SLC18A2 activity

T: Typical SLC18A2 activity

Your Genotype

o TT

Your genotype is linked to typical SLC18A2 activity and typical odds of addictions

Intro and Health Effects

Several SLC18A2 polymorphisms have been associated with different mental health issues. These include:

• The 'G' allele of <u>rs363387</u>: associated with a **lower risk** of alcohol and nicotine dependence, as well as with better inhibitory control [R, R, R].

SNP

rs363371

Alleles

A: Increased SLC18A2 activity

G: Reduced SLC18A2 activity

Your Genotype

TAG

Your genotype is linked to increased SLC18A2 activity and better mental health

Intro and Health Effects

Several SLC18A2 polymorphisms resulting in decreased VMAT2 levels have been associated with different mental health issues. These include:

• The 'G' allele of <u>rs363371</u>: associated with an increased risk of Parkinson's disease and schizophrenia but a decreased risk of ALS [R, R, R, R].

SLC6A2



The <u>SLC6A2</u> gene encodes a member of the sodium:neurotransmitter symporter family called norepinephrine transporter (NET). As its name suggests, this protein plays a key role in norepinephrine transport and homeostasis [R].

Norepinephrine is released from noradrenergic neurons during synaptic transmission. This neurotransmitter regulates mood, arousal, memory, learning, and pain perception, and supports the "fight or flight" stress response. NET functions to transport as much as 90% of this norepinephrine, together with sodium and chloride, back into the presynaptic neuron [R, R].

Certain gene variants have been associated with ADHD [R, R].

SNP

rs3785143

Alleles

C: Typical SLC6A2 activity

T: Increased SLC6A2 activity

Your Genotype

o CC

Your genotype is linked to typical SLC6A2 activity and typical odds of ADHD

Intro and Health Effects

In line with the role of norepinephrine in several aspects of attention such as increased focus, memory recall, and alertness, dysfunction of the norepinephrine system has been linked to ADHD [R, R].

The following SLC6A2 variants have been associated with ADHD risk and worse inattention symptoms:

- 'T' at <u>rs3785143</u> (especially true for oppositional defiant disorder) [R, R, R, R, R, R]
- 'T' at <u>rs3785157</u> [R, R, R]
- 'T' at <u>rs28386840</u> [R, R, R]

These variants may increase SLC6A2 expression and reduce norepinephrine levels in the brain, potentially contributing to ADHD symptoms.

Some of these variants have also been found to affect the effectiveness of ADHD treatment. For instance, carriers of the 'T' allele of rs3785143 may not respond well to atomoxetine [R, R].

SNP

rs3785157

Alleles

C: Reduced SLC6A2 activity

T: Increased SLC6A2 activity

Your Genotype

TCC

Your genotype is linked to reduced SLC6A2 activity and lower odds of ADHD

Intro and Health Effects

In line with the role of norepinephrine in several aspects of attention such as increased focus, memory recall, and alertness, dysfunction of the norepinephrine system has been linked to ADHD [R, R].

The following SLC6A2 variants have been associated with ADHD risk and worse inattention symptoms:

- 'T' at rs3785143 (especially true for oppositional defiant disorder) [R, R, R, R, R, R]
- 'T' at <u>rs3785157</u> [R, R, R]
- 'T' at <u>rs28386840</u> [R, R, R]

These variants may increase SLC6A2 expression and reduce norepinephrine levels in the brain, potentially contributing to ADHD symptoms.

SNP

rs28386840

Alleles

A: Reduced SLC6A2 activity

T: Increased SLC6A2 activity

Your Genotype

o TA

Your genotype is linked to typical SLC6A2 activity and typical odds of ADHD

Intro and Health Effects

In line with the role of norepinephrine in several aspects of attention such as increased focus, memory recall, and alertness, dysfunction of the norepinephrine system has been linked to ADHD [R, R].

The following SLC6A2 variants have been associated with ADHD risk and worse inattention symptoms:

- 'T' at <u>rs3785143</u> (especially true for oppositional defiant disorder) [R, R, R, R, R, R]
- 'T' at <u>rs3785157</u> [R, R, R]
- 'T' at <u>rs28386840</u> [R, R, R]

These variants may increase SLC6A2 expression and reduce norepinephrine levels in the brain, potentially contributing to ADHD symptoms.

Some of these variants have also been found to affect the effectiveness of ADHD treatment. For instance, multiple studies found that children with ADHD were more likely to respond to methylphenidate if they carried the risk allele at rs28386840 [R].

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SLC6A3



About

The <u>SLC6A3</u> gene encodes the dopamine transporter DAT1. This protein is found on the membrane of brain cells, where it transports the neurotransmitter dopamine into the cell [R].

Dopamine is involved in several key functions [R, R]:

- **Reward and motivation:** dopamine is best known for its role in the brain's reward system. It regulates feelings of pleasure and reward, which are critical for motivation. Dopamine release during rewarding activities encourages us to engage in those activities repeatedly.
- **Mood regulation:** dopamine levels influence various aspects of mood and are associated with emotions of elation and happiness.
- Cognitive function: adequate dopamine levels are essential for memory, attention, and problem-solving functions.
- **Motor control:** through its action in the basal ganglia, dopamine is essential for coordinating smooth and balanced muscle movement. Deficiencies in dopamine in these areas are linked to motor control disorders such as Parkinson's disease.

To transmit signals, dopamine is released into the space between neurons (the synaptic cleft), where it binds to receptors on the surface of neighboring neurons. The DAT1 transporter brings dopamine from the synaptic cleft back into neurons for reuse. Its activity determines how much dopamine is present in the synaptic cleft and for how long. This makes the DAT1 transporter a major controller of dopamine signaling in the brain [R].

Dysfunctions of the dopamine system have been linked to ADHD. In line with this, the dopamine transporter is the target of commonly prescribed medications for ADHD. These medications can physically block the transporter so that less dopamine is transported into cells and more dopamine is available in the brain [R, R].



Intro and Health Effects

Several SLC6A3 variants have been associated with an increased risk of ADHD, as well as increased impulsivity and inattention in individuals with ADHD. These include [R, R, R, R]:

- 'T' of <u>rs6347</u>
- 'G' of rs11564750

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• 'C' of <u>rs27072</u>

While the mechanism behind this association is not clear, these variants may increase the density of the dopamine transporter in certain regions of the brain. This would decrease the amount of dopamine available in these brain regions, giving rise to ADHD and its associated symptoms [R, R].

SNP

rs11564750

Alleles

G: Typical SLC6A3 activity

C: Reduced SLC6A3 activity

Your Genotype

o GG

Your genotype is linked to typical SLC6A3 activity and typical odds of ADHD

Intro and Health Effects

Several SLC6A3 variants have been associated with an increased risk of ADHD, as well as increased impulsivity and inattention in individuals with ADHD. These include [R, R, R]:

- 'T' of <u>rs6347</u>
- 'G' of <u>rs11564750</u>
- 'C' of <u>rs27072</u>

While the mechanism behind this association is not clear, these variants may increase the density of the dopamine transporter in certain regions of the brain. This would decrease the amount of dopamine available in these brain regions, giving rise to ADHD and its associated symptoms [R, R].

SNP

rs27072

Alleles

C: Increased SLC6A3 activity

T: Reduced SLC6A3 activity

Your Genotype

个CC

Your genotype is linked to increased SLC6A3 activity and higher odds of ADHD

Intro and Health Effects

Several SLC6A3 variants have been associated with an increased risk of ADHD, as well as increased impulsivity and inattention in individuals with ADHD. These include [R, R, R, R]:

- 'T' of <u>rs6347</u>
- 'G' of rs11564750

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• 'C' of <u>rs27072</u>

While the mechanism behind this association is not clear, these variants may increase the density of the dopamine transporter in certain regions of the brain. This would decrease the amount of dopamine available in these brain regions, giving rise to ADHD and its associated symptoms [R, R].





The TH gene codes for tyrosine hydroxylase, an enzyme that catalyzes the first step in the conversion of tyrosine to dopamine. Two other catecholamine neurotransmitters, <u>norepinephrine</u> and <u>epinephrine</u>, are produced from dopamine [R, R].

As a rate-limiting enzyme in the production of catecholamines, TH plays many important roles in the body. These include [R, R, <u>R</u>]:

- Brain health
- Stress response
- Blood pressure control
- Energy production
- Muscle function

Enhancers:



SNP

rs6356

Alleles

C: Typical TH activity

T: Increased TH activity

Your Genotype

o CC

Your genotype is linked to typical TH activity and brain chemistry

Intro and Health Effects

The main TH variant is <u>rs6356</u>, whose minor 'T' allele may **increase TH activity**. Although this may seem beneficial in theory, this variant has been associated with:

- Increased risk of late-onset Parkinson's disease [R]
- Increased risk of schizophrenia [R]
- Increased risk of migraines [R]
- Increased risk of cognitive and attentional impulsivity in maltreated children [R]
- Increased risk of hypertension [R]

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SNP

rs10770141

Alleles

A: Increased TH activity

G: Typical TH activity

Your Genotype

o AG

Your genotype is linked to typical TH activity and brain chemistry

Intro and Health Effects

Another variant, the 'A' allele of $\underline{rs10770141}$, may increase TH expression. This variant has been associated with [R]:

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- Increased risk of schizophrenia [R]
- Lower novelty seeking [R]
- Lower persistence in patients with chronic fatigue syndrome [R]
- Increased risk of opioid dependence [R]
- Increased sensitivity to both "good" and "bad" effects of cocaine [R]
- Higher blood pressure in response to cold stress [R]

CYP2C19



The <u>CYP2C19</u> gene encodes a member of the <u>cytochrome P450</u> family. These enzymes are involved in the breakdown and elimination of most toxins and drugs from the body. <u>CYP2C19</u> is mostly found in the liver and metabolizes "10% of clinical drugs, including **antidepressants**, proton pump inhibitors, blood thinners, and antimalarial drugs [R, R]:

Variants in the CYP2C19 gene may alter the rate at which these drugs are broken down. An elevated CYP2C19 activity may reduce the effectiveness of the treatment (by speeding up drug clearance) but also increase it if the drug needs to be broken down to become active, as is the case for clopidogrel.

CYP2C19 is also involved in the metabolism of substances naturally produced in the body., such as <u>arachidonic acid</u> and estrogens [R, R, R, R, R, R, R, R].

SNP

rs4244285 CYP2C19*2

Alleles

A: Reduced CYP2C19 activity

G: Typical CYP2C19 activity

Your Genotype

o GG

Your genotype is linked to typical CYP2C19 activity and drug clearance

Intro and Health Effects

One of the most common polymorphisms associated with reduced CYP2C19 activity is CYP2C19*2 (<u>rs4244285</u>). Carriers of one copy of the minor 'A' allele have a reduced ability to break down drugs, including **antidepressants**, meaning they may experience more pronounced benefits but also **side effects** [R, R, R].

Those with two copies can metabolize very little or none of the drug and are classified as **poor metabolizers**, with even stronger effects on drug metabolism [R, R, R].

SNP

rs4986893 CYP2C19*3

Alleles

A: Reduced CYP2C19 activity

G: Typical CYP2C19 activity

Your Genotype

o GG

Your genotype is linked to typical CYP2C19 activity and drug clearance

Intro and Health Effects

Another important variant associated with reduced CYP2C19 activity is CYP2C19*3 (rs4986893). Carriers of one copy of the minor 'A' allele have a reduced ability to break down drugs, including antidepressants, meaning they may experience more pronounced benefits but also **side effects** [R, R, R].

Those with two copies can metabolize very little or none of the drug and are classified as poor metabolizers, with even stronger effects on drug metabolism [R, R, R].

SNP

rs12248560 CYP2C19*17

Alleles

C: Typical CYP2C19 activity

T: Increased CYP2C19 activity

Your Genotype

o CC

Your genotype is linked to typical CYP2C19 activity and drug clearance

Intro and Health Effects

The <u>rs12248560</u> polymorphism, also known as CYP2C19*17, is located in the region that controls gene expression (the promoter). Its minor allele 'T' is associated with increased gene expression and protein activity [R, R].

People with this variant are classified as ultrarapid metabolizers, meaning they may see a suboptimal effect of standard drug doses [R, R].

DRD5



The $\underline{DRD5}$ gene helps make $\underline{dopamine}$ D5 receptors. Those are proteins on the surface of brain cells that bind dopamine. The D5 subtype has a 10-fold higher affinity for dopamine than D1! D5 is also expressed more widely in the brain than D1 $[\underline{R}, \underline{R}, \underline{R}]$.

These receptors are also expressed in the kidneys and immune cells (dendritic and T helper cells). The activation of D5 receptors [R, R, R, R, R, R, R]:

- Increases BDNF in the prefrontal cortex
- Increases learning and memory
- Cause the consolidation of fear memories in the amygdala
- Reduces amphetamine-induced activity
- Increases Th17 cells and IL23
- Reduces NK cells and their activity
- Lowers blood pressure
- Increases sodium excretion



Intro and Health Effects

The most widely investigated DRD5 polymorphism is <u>rs6283</u>. Its minor 'C' allele has been associated with an **increased risk of ADHD** [R].

Because many ADHD symptoms are caused by impaired dopamine function in the brain, this variant might reduce the number of D5 receptors or their affinity for dopamine [R].

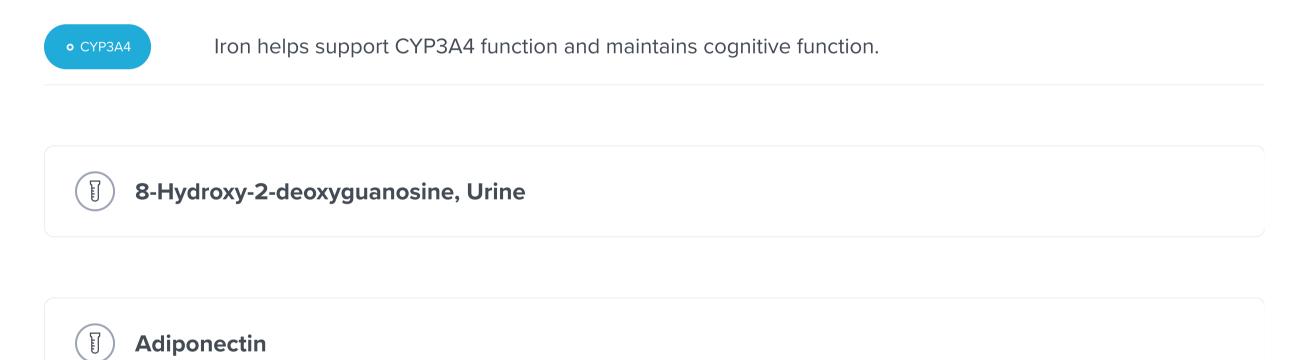
Lab markers to check



Personalized to Your Genes



Personalized to Your Genes



Personalized to Your Genes

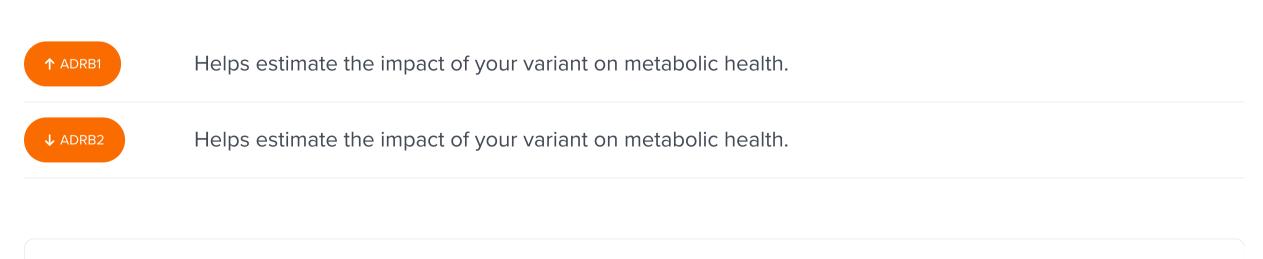


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Aldosterone



Blood Pressure (Diastolic)

Personalized to Your Genes



Helps estimate the impact of your variant on cardiovascular health.



Helps estimate the impact of this variant on fitness and cardiovascular health.



Blood Pressure (Systolic)

Personalized to Your Genes



Helps estimate the impact of your variant on cardiovascular health.



Helps estimate the impact of this variant on fitness and cardiovascular health.



BMI

Personalized to Your Genes



Helps estimate the impact of this variant on weight.

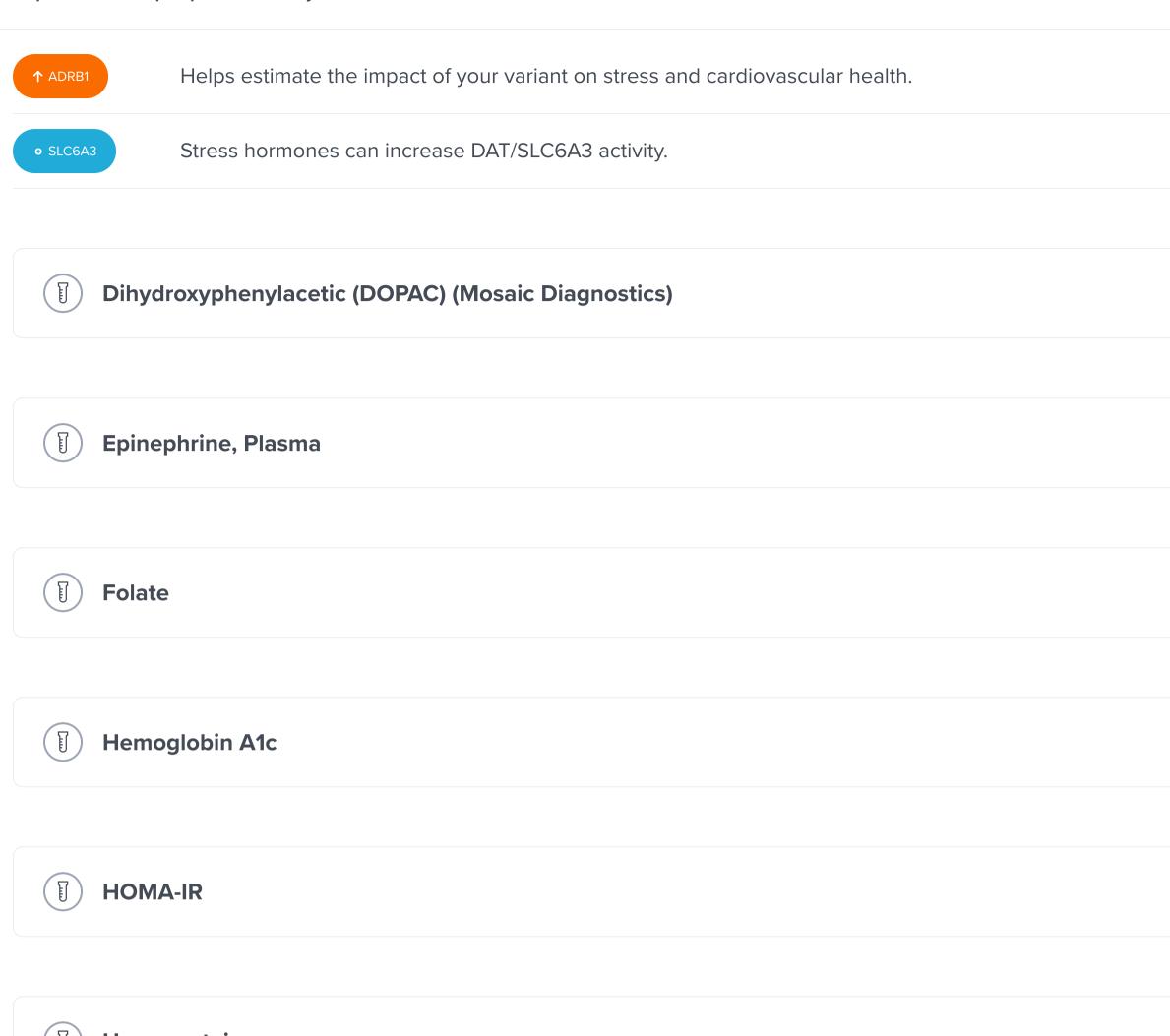


Copper, Serum



Cortisol, Saliva

Personalized to Your Genes



Homocysteine

Homovanillic Acid (HVA), Random Urine

Personalized to Your Genes

Indicates changes in dopamine levels that may affect D3 signaling. ↑ DRD3

Reflects the changes in dopamine levels due to high MAO-A.

Reflects the changes in dopamine levels due to high MAO-B. ↑ MAOB

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The main metabolite that reflects changes in dopamine levels.



Insulin, Fasting



Leptin

Personalized to Your Genes



Helps estimate the impact of your variant on metabolic health.



Helps estimate the impact of your variant on metabolic health.



Magnesium

Personalized to Your Genes



Magnesium may lessen the impact of your variant on cardiovascular health.



Malondialdehyde



Norepinephrine, Plasma

Personalized to Your Genes



High MAO-A may mildly reduce NE levels.



High MAO-B may reduce NE levels.



NE levels are important to monitor in case of VMAT/SLC18A1-related issues.



Norepinephrine, Random Urine

Personalized to Your Genes



NE levels are important to monitor in case of VMAT/SLC18A1-related issues.



Prolactin

Personalized to Your Genes



Elevated levels may indicate a lack of dopamine linked to D2 receptor issues.



Elevated levels may indicate insufficient dopamine.



Renin



Resting Heart Rate

Personalized to Your Genes



Helps estimate the impact of your variant on cardiovascular health.



Helps estimate the impact of this variant on fitness and cardiovascular health.



SAM-e, Serum



Vanillylmandelic Acid (VMA), Random Urine

Personalized to Your Genes

Reflects the changes in NE levels due to high MAO-A. ↑ MAOA

Reflects the changes in NE levels due to high MAO-B. ↑ MAOB

The main metabolite that reflects NE levels. **↓** SLC18A1

Vitamin B12

Personalized to Your Genes

Important to check in cases of chronic fatigue, which is linked to this variant. ↑ DRD3

Vitamin B2 (Riboflavin), Plasma

Personalized to Your Genes

Riboflavin helps support CYP3A4 function and protects the nerves. • CYP3A4

Vitamin B6

Vitamin C



Vitamin D, 25-Hydroxy, Total

Personalized to Your Genes



Important to check in cases of chronic fatigue, which is linked to this variant.



VO2 Max

Personalized to Your Genes



Helps estimate the impact of this variant on fitness.



Zinc

Personalized to Your Genes



Helps modulate the DAT/SLC6A3 transporter

Glossary

3-Methoxytyramine

A dopamine breakdown product created by COMT in the synapse before further clearance.

3M, 4HPA

A minor metabolite formed when dopamine is broken down, usually excreted in urine.

ADHD

A condition linked to dopamine imbalance, with symptoms like poor focus, hyperactivity, and impulsivity.

Aldehyde

A reactive byproduct formed during dopamine and norepinephrine breakdown. Some aldehydes can be toxic if not cleared.

β-blockers

Medications that block certain norepinephrine and epinephrine receptors, reducing heart rate and stress responses.

DHPG

A safer metabolite formed when toxic DOPEGAL is detoxified by ALDH2.

DOPAC

A stable breakdown product of dopamine, created after toxic aldehydes are cleared.

DOPAL

A toxic aldehyde created when dopamine is broken down. Needs to be cleared by ALDH2 to prevent damage.

DOPEGAL

A toxic aldehyde formed when norepinephrine is broken down. Detoxified into DHPG by ALDH2.

Dopamine

A neurotransmitter involved in motivation, mood, movement, and reward. Imbalances can affect mental health and behavior.

Enzyme

A protein that speeds up chemical reactions, such as making, breaking down, or modifying dopamine and norepinephrine.

Homovanillic acid (HVA)

A major dopamine end-product found in blood and urine, reflecting overall dopamine breakdown.

L-DOPA

A direct precursor to dopamine, made from tyrosine. Also used as a treatment for Parkinson's disease.

Metabolite

A substance made when the body processes or breaks down another molecule, like dopamine.

MHPG

A major breakdown product of norepinephrine, commonly measured to assess norepinephrine activity.

MOHMA (Aldehyde)

A toxic intermediate formed when normetanephrine is broken down. Cleared by ALDH2 into VMA.

Neuron

A nerve cell that sends and receives signals using neurotransmitters like dopamine and norepinephrine.

Norepinephrine

A neurotransmitter and hormone made from dopamine. Supports focus, alertness, stress response, and blood pressure control.

Normetanephrine (NMN)

A metabolite formed when norepinephrine is broken down by COMT before further clearance.

PAA (Phenylacetic acid)

A breakdown product of phenylethylamine (PEA), formed when MAO-B clears PEA from the body.

PEA (Phenylethylamine)

A natural compound made from phenylalanine. Acts like a stimulant, briefly boosting mood, focus, and energy before being quickly broken down by MAO-B.

Phenylalanine

An amino acid from protein-rich foods. It serves as the starting point for dopamine production.

Precursor

A substance that comes before another in a pathway — for example, tyrosine is a precursor to L-DOPA.

Receptor

A protein on neurons that neurotransmitters like dopamine and norepinephrine bind to, triggering effects in the body.

Synapse

The tiny gap between neurons where neurotransmitters are released to pass signals.

Tyrosine

An amino acid made from phenylalanine or found in food. It's converted into L-DOPA, a direct dopamine precursor.

Vanillylmandelic acid (VMA)

The main end-product of norepinephrine breakdown, excreted in urine.

Vesicle

A small bubble-like structure inside neurons that stores neurotransmitters like dopamine until release.