



# Restore<sup>RX</sup>

*"Restore" and balance your body by understanding how your genes respond to sleep, pain, inflammation, stress & CBD metabolism.*

 **StrongDNA**

Unlock the power of your genetic code

[www.mystrongDNA.com](http://www.mystrongDNA.com)

Created for: Jane Doe

# REPORT SUMMARY



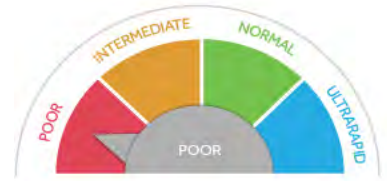
## CBD

CBD Metabolism	<b>POOR</b>	CYP3A4, CYP2C9, CYP2C19
Systemic Inflammation	<b>WELL ABOVE AVERAGE</b>	near CRP, APOC1 (APOE-CI-CII), HNF1A
Sleep Duration	<b>BELOW AVERAGE</b>	ABCC9, LOC101927400, DRD2
Pain Tolerance	<b>LOW</b>	COMT
Social Anxiety	<b>INCREASED</b>	FGD2, MTCH1
Stress Tolerance	<b>NORMAL</b>	PDE4B
Alcohol Sensitivity	<b>SENSITIVE</b>	ADH1C, ADH1B, ALDH2
Chronotype	<b>EVENING</b>	RGS16, PIGK, AK5, PRPF3, TARS2, ORAI2, RASA4, PER2, HCRTR2, EXD3, RAX, CPLX4, LMAN1, HTR6, FKBP1B, CALB1, INADL, PSME4, ACYP2

# CBD METABOLISM

## WHAT YOUR GENES SAY ABOUT YOU:

Our analysis indicates that your genetic profile exhibits characteristics that give you the likelihood of being a **POOR** CBD metabolizer. That means your CYP enzyme activity is inefficient at metabolizing CBD when you ingest it. The result is that you will have reduced CBD clearance and increased plasma concentrations, making you more sensitive to CBD. You will likely feel stronger effects for longer after taking any given dose. Though you need extremely high doses for CBD to actually be toxic, it is possible to experience negative side effects, like feeling tired and out of sorts, when you take more than you need, which is easy to do for someone with a poor metabolizing genotype. You may need considerably lower doses than others to feel the desired effect and to avoid unwanted or adverse reactions.



Your genetic profile indicates that you are likely to be a **POOR**

CBD metabolizer. This genotype means your CYP enzyme activity is not efficient and you are likely to end up with higher CBD concentrations in your system and feel stronger effects following any given dose. You will need to adjust your dosage accordingly.

Your genotype means that you clear CBD more slowly, build greater plasma concentrations, and therefore feel the effects of any given dose of CBD more strongly than those who have more efficient CBD metabolism. That means you will likely need lower doses to achieve the desired outcome and you may be more susceptible to negative side effects, such as feeling tired or experiencing GI issues, from otherwise moderate doses.

That does not mean that you will necessarily have problems with CBD use, however. Like people of all genotypes, it may just take some trial and error to achieve the results you're looking for.

## SUCCESS STRATEGIES

There are many factors, outside of genetics, that influence how you will experience CBD. Knowing them can help you optimize your benefits from CBD usage.

## RELATED GENES / SNPs

CYP3A4, CYP2C9, CYP2C19

The genes and their associated SNPs that are included in this category have been shown in studies to have significant associations with how your body metabolizes CBD after you ingest it.

When you ingest CBD, your body releases enzymes in your liver and GI tract to break it down and metabolize it. The enzymes primarily responsible for CBD metabolism are called cytochrome P450, or CYP enzymes. Their activity helps determine the strength of the effect you get and how long it lasts. This effect is most pronounced when taking pills or edibles. When you inhale cannabinoids, there is minimal metabolism by CYP enzymes in the lungs before it hits your bloodstream.

Genetics have a significant influence on CYP enzyme activity, and it can vary dramatically among individuals. For instance, activity

## CBD METABOLISM

• **The product:** The Food and Drug Administration (FDA) does not regulate the CBD industry. Unfortunately that means there are low-quality products out there that may not deliver what they promise. Make sure you buy real—not synthetic—CBD and that the company presents evidence of quality control. The company should offer detailed information on where and how they obtain their CBD oil as well as access to certified third-party lab results. If they do not, look elsewhere.

• **The dosage:** Experts recommend starting with a low dose—about 10 milligrams—of active ingredient and see how you feel. Every few days, you can increase the amount slightly until you don't feel any extra benefit. Or, if you start to feel worse or negative symptoms like fatigue, nausea, or irritability, dial back the dosage. As someone who is genetically prone to inefficient CBD metabolism, you should start at about half of what is usually recommended and work your way up gradually.

• **How you consume CBD:** CBD is found in a wide array of products and forms, including capsules, oils, edibles like gummy bears, balms, and vaping devices. The way you take it significantly impacts the timeframe, magnitude, and duration of the effects. Pills and edibles take the longest to work—generally 30 minutes or more—because you have to digest them. You also lose a little bit of the active ingredients during metabolism in the liver, which may be preferable for your sensitive genotype. Tinctures that you drop under your tongue or spray in your mouth work relatively quickly—generally in about 15 to 30 minutes—because they bypass digestion. In general people need lower dosages when using tinctures. Inhaling is by far the fastest, most potent way to take CBD. You may feel the effects in as little as 30 seconds after vaping. Because inhaled CBD allows nearly four times as much CBD to enter your system than ingesting it, plan on lowering your dose accordingly if you choose to vape. Topical treatments are designed for site-specific ailments like muscle pain, rather than general health benefits.

Multiple personal factors also influence how you will respond to CBD, including your gender (estrogen interacts with the endocannabinoid system, which can influence its effect), your age (drug metabolism in general decreases with age), and your individual endocannabinoid system (everyone has a different number of receptors).

of CYP3A4—the most important drug-metabolizing enzyme in humans—can vary more than 100-fold from person to person and genetics accounts for up to 88 percent of that variability. The gene's relatively recently discovered \*22 allele has a significant impact affecting CBD dosing. Research shows that even one copy of this allele reduces the clearance of CYP3A4-metabolized drugs like CBD by up to 40 percent. This variant is more common in Caucasians than other ethnicities, with approximately 1 in every 17 people of European descent having one copy.

The variants of other CYP genes also present differently across ethnicities. For example, the \*3 variant of the CYP2C19 gene occurs primarily in East Asians. However, the \*17 variant of the same gene is rarely found in East Asians, but more frequent in those of African and European descent. Likewise, the \*3 and \*2 variants of the CYP2C9 gene are common in people of European descent, but generally rare in those of African and Asian descent.

Our analysis investigated which genotype for each of these genes was present in your DNA. Your rating of **POOR**, **INTERMEDIATE**, **NORMAL**, **ULTRARAPID** reflects how quickly and efficiently you are likely to metabolize CBD and whether you'll feel the effects more or less strongly and for what duration



## CBD METABOLISM

---

Remember also, depending on what you're taking CBD for, it may take more or less time to feel the effect. CBD is lipophilic, which means it is fat-soluble and builds up in your body over time. Even though your genotype makes you likely to build up CBD levels more quickly, it still may take a little time to reach a certain level in your system before you notice benefits such as pain or anxiety relief.

You should also talk to your doctor before taking CBD if you are taking other prescribed drugs, since CBD may occupy your drug-clearing enzymatic activity and interfere with your metabolism of other drugs, as well.

# SYSTEMIC INFLAMMATION

## WHAT YOUR GENES SAY ABOUT YOU:

Our analysis indicates that your genetic profile exhibits characteristics that give you a likelihood of having **WELL ABOVE AVERAGE** systemic inflammation levels. That means your CRP levels are likely to fall in an elevated range, which if left unchecked, can raise your risk for age-related chronic diseases like diabetes, heart disease, as well as certain cancers. Though your genetic profile may elevate your risk, you can lower your systemic inflammation levels through healthy diet, exercise, and lifestyle practices and behaviors.



Your genetic profile indicates that you are inclined to have **WELL ABOVE AVERAGE**

systemic inflammation levels. We recommend that you begin following an anti-inflammatory diet and engaging in healthy lifestyle behaviors that are known to lower CRP levels and minimize inflammation in the body. You also can consider supplementing with CBD, which acts to reduce inflammation.

## SUCCESS STRATEGIES

Normal CRP levels vary from laboratory to laboratory, but generally there are no or very low levels of CRP detectable in the blood. According to the American Heart Association, you are at a low risk for developing heart disease if your CRP levels are less than 1.0 mg/L; your risk is considered average if your levels are between 1.0 mg/L and 3.0 mg/L, and your risk is high if your levels are higher than 3.0mg/L.

According to data from the Physicians Health Study of nearly 15,000 healthy adult men, a high level of CRP was associated with a heart attack risk three times higher than average. Some medical professionals believe that taking measures to lower your CRP levels can lessen your risk for heart attack and stroke. You can find out your levels with a simple blood test. Ask your doctor to have your CRP levels screened along with your cholesterol, triglycerides

## RELATED GENES / SNPs

HNF1A, CRP, APOC1 (APOE-CI-CII)

The genes and their associated SNPs that are included in this category have been shown to have significant associations with a person's systemic inflammation levels. That's low-level inflammation we don't see, which, left unchecked, can damage our blood vessels and lead to many serious chronic diseases like heart disease, diabetes, stroke, neurodegenerative diseases like Alzheimer's, and some cancers. Exercise enthusiasts like runners and CrossFit participants will also find that chronic inflammation hinders recovery from exercise and training and hinders performance.

Doctors use C-reactive protein (CRP) levels as a general marker of systemic inflammation. CRP is a protein found in your blood plasma that binds to the surface of dead or dying cells and certain bacteria to clear them from your body. When there's a lot of cellular damage to clean up, CRP levels



## SYSTEMIC INFLAMMATION

and other blood markers. Request a high-sensitivity C-reactive protein (hs-CRP) test, which is more sensitive than the standard test and also can be used to evaluate your risk for developing coronary artery disease.

Along with tracking your CRP levels, practice healthy diet, exercise and lifestyle behaviors to reduce inflammation in your body.

**Be mindful of your BMI.** As someone with a genetic inclination for significantly higher than average systemic inflammation, you want to make it a priority to achieve a healthy weight if you have pounds to lose. Body mass index (BMI), which is a measure of body fat based on height and weight, is the main non-genetic determining factor for CRP levels. Carrying excess fat, particularly around the midsection where it is most metabolically active, is known to induce chronic low-grade inflammation. It also can switch on your at-risk genes that are associated with systemic inflammation. Maintaining a healthy weight is one of the best ways to keep systemic inflammation in check. If you're overweight, even modest weight loss can have a significant positive impact on CRP levels. One study found that losing just 5 percent of body weight can result in measurable reductions in CRP levels. Those who lost weight by dieting and exercising were able to reduce their CRP levels by more than 41 percent in a year.

**Exercise daily.** Physical fitness is protective against inflammation. As fitness levels decline, CRP levels rise, according to a study from Johns Hopkins. Regular physical activity helps reduce inflammation by up to 60 percent and can keep CRP levels in check. One decade-long study of nearly 4,300 men and women by British researchers found that those who got just the minimum recommended amount of exercise—2 ½ hours a week—had measurably lower CRP levels than those who got less physical activity. For the best results, aim for at least 20 to 30 minutes of moderate exercise every day.

**Eat an anti-inflammatory diet.** The food you eat heavily influences your inflammation levels. Avoid high glycemic foods that predominantly consist of flour and/or sugar, as they've been shown to spike blood sugar and insulin levels and induce inflammation. Opt instead for a Mediterranean-style diet that is naturally rich in monounsaturated fats and inflammation-reducing polyunsaturated omega-3 fatty acids. Focus your diet around antioxidant-rich fruits and vegetables, nuts, seeds, olive oil and moderate amounts of meat, healthy fats and red wine. Eat at least 8 ounces of fatty fish a week and minimize your intake of red meat.

**Get enough sleep.** Researchers at the Emory University School of Medicine found that people who reported getting less than 6 hours of sleep a night had significantly higher CRP levels than those who slept between 6 and 9 hours a night. People who reported sleeping

rise. Unsurprisingly, high CRP levels have been linked to a higher risk of mortality.

There are many culprits behind systemic inflammation, including autoimmune diseases, being overweight (especially if you carry your excess fat in your abdomen, where it is most metabolically active), poor fitness, a diet that is high in sugar and other inflammatory foods, sleep deprivation, as well as exposure to secondhand smoke and other pollutants.

CRP is also significantly influenced by genetics. Researchers estimate that the heritability of CRP levels is up to 40 percent. In a recent genome wide association analysis of more than 82,700 men and women, scientists identified a half a dozen genetic variations that were significantly associated with CRP levels. When they ranked the study participants according to their at-risk CRP genetic makeup, those in the highest gene score group had an average CRP level that was more than double the average level of those in the lowest gene score group.

Our analysis investigated which genotype for this gene was present in your DNA. Your rating of **NORMAL**, **ABOVE AVERAGE** or **WELL ABOVE AVERAGE** reflect whether or not your genotype include those that increase your risk for elevated systemic inflammation levels.

## SYSTEMIC INFLAMMATION

---

poorly also had more inflammation than their better-rested peers.

**Eat more fish.** Fish is rich in inflammation reducing omega-3 fatty acids. If you don't like fish, regular use of fish oil supplements can reduce CRP levels by 16 percent according to a study from the Fred Hutchinson Cancer Research Center in Seattle.

**Consider a CBD supplement.** CBD is widely prescribed and used as an anti-inflammatory. The human body has an endocannabinoid system (ECS) that helps regulate functions like sleep, mood, pain, and the immune system, and you have receptors for endocannabinoids throughout your body. There are two major cannabinoid receptors in your nervous system—CB1, which is mainly found in the brain and spinal cord and CB2, which is concentrated in immune cells. Studies show CBD has a significant impact on CB2 receptors, and when CB2 receptors are activated they work to reduce inflammation.

Research on CBD and inflammation is ongoing and looks promising. A 2011 study published in *Free Radical Biology and Medicine* concluded that CBD showed promise for lowering inflammation related to free radical stress. A review study published in *Future Medicinal Chemistry* found that phytocannabinoids like CBD suppress the inflammatory response and can be an effective treatment for reducing inflammation.

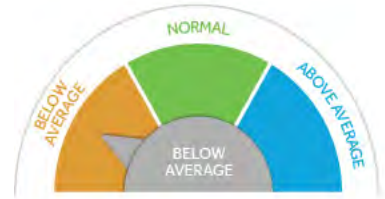
**Drink moderately.** If you drink, do so in moderation. Too much is bad for you, but research shows that moderate amounts, such as a drink a day lowers your CRP levels more than totally abstaining. It's not a reason to start drinking, of course. But good news for those who enjoy alcohol in moderation.



# SLEEP DURATION

## WHAT YOUR GENES SAY ABOUT YOU:

Our analysis indicates that your genetic profile exhibits characteristics that make you likely to get a **BELOW AVERAGE** amount of sleep per night. That means you are more likely to be at risk for short sleep duration related health risks such as weight gain, heart disease, and diabetes. The good news is that the majority of factors that influence sleep duration are well within your control and by taking a few simple measures, including practicing good sleep hygiene you can get more rest and reap the many health benefits associated with regularly getting a good night's rest.



Your genetic profile indicates that you may be likely to get a **BELOW AVERAGE**

number of hours of sleep per night. You will be more likely to get the recommended 7 to 8 hours of restorative sleep each night if you implement lifestyle, behavior, and diet habits that are conducive to good sleep.

Sleep is essential for physical and psychological health. Research shows that sleep plays a critical role in immunity, metabolism, learning, memory, and a host of vital functions. Getting too little sleep (6 hours or less) doesn't just make you feel drowsy and irritable during the day, but also, short sleep duration has been linked with an increased risk for heart disease, diabetes, poor cognitive function, getting sick, and weight gain. Research shows that adults sleeping 5 or fewer hours a night have 55% greater odds of becoming obese and succumbing to metabolic disease. We recommend that you make improving your sleep a priority. Good sleep hygiene can nudge the needle in a positive direction and ensure you get more of the restorative sleep you need.

## SUCCESS STRATEGIES

**Consider CBD.** People are increasingly turning to CBD to help them sleep. In a recent national survey by Consumer Reports, the organization found that 10 percent of Americans who reported trying CBD said they tried it to help them sleep, and most who had tried it for better sleep said it helped.

## RELATED GENES / SNPs

ABCC9, LOC101927400, DRD2

The genes and their associated SNPs that are included in this category have all been shown in studies to have significant associations with sleep duration.

Research shows that Americans currently average 6.8 hours of sleep a night, with 26 percent averaging 6 hours or less and 14 percent averaging 5 hours or less. Many factors including age, gender, lifestyle, diet, caffeine and alcohol consumption, occupation, light exposure, and general health, including anxiety and chronic pain, influence how much (or little) sleep we get each night. Your genes may also play a role in sleep duration.

Studies show the inheritability of sleep duration to be anywhere between 9 and 44 percent. Variations in the genes, or alleles, listed above influence sleep duration, with each allele increasing or decreasing sleep by

## SLEEP DURATION

Though CBD research is still very new, a small body of emerging research supports its use as a sleep aid, especially when sleep is being disrupted by anxiety. In one study published in *The Permanente Journal*, Colorado researchers studied the health records of 72 men and women who were treated with CBD (mostly 25mg/d in capsule form, though a few people received higher doses) for anxiety or poor sleep. After a month on CBD, 79 percent and nearly 67 percent of the patients experienced an improvement in anxiety and sleep, respectively (though 15 percent and 25 percent experienced worsening symptoms in anxiety and sleep, respectively, so results do vary).

How CBD may improve sleep is still not understood. Some studies like the one above suggest that it helps lull you into slumber by calming your anxious mind. Similarly, a 2017 review of cannabinoid literature published in *Current Psychiatry Reports*, reported that CBD could improve sleep in people with chronic pain.

Some scientists have hypothesized that CBD interacts with receptors in your brain that help regulate the sleep-wake cycle. However, 2018 research published in *Frontiers in Pharmacology* reported that CBD does not interfere with normal sleep architecture in healthy adults (though the question remains if it influences the sleep-wake cycle in those with sleep disorders caused by depression and anxiety).

In the study on anxiety and sleep, the most commonly prescribed dose was 25mg/d in capsule form. It's also worth noting that smaller doses may have the opposite effect, as one study reported that 15 mg of CBD appeared to increase alertness and wakefulness.

**Check your caffeine habit.** Caffeine is the most widely used drug in the world and used moderately has many mental and physical performance benefits. It's easy to overdo, however, especially late in the day. Caffeine works by binding to your brain's nerve receptors, speeding them up, which triggers your pituitary glands to secrete adrenaline. Hence the energy buzz. The half-life of caffeine is about six hours, so if your last mug is at 4 p.m., by 10 p.m., you still have a shot of espresso's worth flowing through your system, which research shows can reduce your sleep by an hour. Have your last cup before 4:00, so you can wind down and fall asleep more easily.

**Go easy on evening alcohol.** That nightcap may make you feel drowsy initially, but too much alcohol close to bedtime disrupts your sleep architecture. Alcohol within an hour of bedtime lengthens your non-REM sleep and shortens your REM sleep during the first half of the night, so you are in more wakeful territory longer. As your liver clears the ethanol from your bloodstream, your body can go into

3 to 4 minutes. Compared to other factors, genes may not move the needle on sleep in a giant way, but even small amounts of additional sleep if you are typically a short sleeper can improve your wellbeing. Consider that research shows just a 10 minute nap is sufficient for significantly improving alertness and cognitive performance for more than two hours and just three minutes of stage 2 sleep (the stage where we drift off and become less aware of our surroundings) has recuperative benefits.

Trending your sleep duration in a healthy direction may also set the stage for improved sleep hygiene and better sleep duration long term, which may trigger a cascade of further genetic outcomes. One British study reported that there are approximately 500 genes that are affected by sleep duration. When volunteers who typically slept 7 ½ hours shaved an hour off their nightly rest, the genes associated with inflammation, immune response, stress, diabetes and risk of cancer became more active. The opposite occurred when the volunteers who typically slept 6 ½ hours added an hour of sleep.

Our analysis investigated which genotype of each of these genes was present in your DNA. Your rating of **NORMAL**, **BELOW AVERAGE**, or **ABOVE AVERAGE** reflects whether your genotypes include those that carried a risk of reduced healthy sleep duration.



## SLEEP DURATION

---

a bit of withdrawal during the second half of the night, making you restless and more likely to toss and turn. Stick to one or two drinks and avoid alcohol an hour or two before bedtime.

**Dim the lights—and electronics.** Too much light exposure late in the evening suppresses your melatonin—a hormone produced in the pineal gland of the brain that is critical for your natural sleep-wake cycle—so your body temperature doesn't dip and your body doesn't get the signals that it is time to start the stages of sleep. That includes your smartphone or tablet, which also emit blue wavelength light, which has been shown to be especially harmful to circadian rhythm function. Dim the lights and shut down all electronics 30 minutes before you want to be asleep. Also consider downloading a blue light-filtering app if you must be on your device at night.

**Set the stage for sleep.** Humans sleep best in cool, dark, quiet conditions. Set your thermostat to between 60 and 67 degrees for the optimum ambient sleeping temperature. Consider black out curtains if outside light enters your bedroom. Earplugs or white noise machines can block out disruptive noise.

# PAIN TOLERANCE

## WHAT YOUR GENES SAY ABOUT YOU:

Our analysis indicates that your genetic profile exhibits characteristics that make you likely to have **LOW** COMT (Catechol-O-Methyltransferase) activity and therefore a lower pain threshold. You are likely to find painful stimulation less tolerable and more emotionally distressing than genotypes with higher COMT activity. From sore muscles after a hard workout to injuries to achy joints, pain is a part of life. As someone with a genetically low pain threshold, you may want to find healthy strategies for managing pain so you are not overwhelmed by it.



Your profile indicates that you may be likely to have **LOW**

pain threshold. That means that you will process painful stimulus more intensely and feel more physical discomfort and experience more emotional distress from pain than other genotypes. Healthy pain management may be important.

Pain is a complex, very unpleasant sensation that is caused when your brain perceives injury to your body's tissues and produces physical and emotional reactions. It's your brain's way of saying something is wrong. We all experience pain differently depending on our environment, overall emotional and physical state, and our genetics.

Pain is generally classified by the kind of damage that causes it. Broadly speaking there is pain caused by tissue damage called nociceptive pain; pain caused by nerve damage called neuropathic pain, and psychogenic pain, which may or may not have physical origins, but is heavily influenced by psychological factors. How well pain responds to any form of treatment depends on what is causing it, as well as other individual factors.

## SUCCESS STRATEGIES

You should always see your doctor for new and/or extreme pain. To manage everyday flare-ups or prolonged episodes of pain related to known conditions,

## RELATED GENES / SNPs

### COMT

The gene and its associated SNPs that are included in this category have been shown in studies to have significant associations with pain sensitivity and pain threshold.

It's well known that one person's pain is another person's minor discomfort. There are many reasons for that. Experience is one: an office worker will feel more pain getting tackled to the ground than a pro football player. Genetics is another.

Research shows that variations in the COMT gene can make a significant difference in how people withstand and react emotionally to pain. Your body's COMT enzyme, which is encoded by the COMT gene, helps regulate aspects of your brain chemistry including activity of the mood-regulating neurotransmitters dopamine and norepinephrine. Lower COMT activity results in higher dopamine activity, and when the

## PAIN TOLERANCE

you can try various forms of self care. Some tried and true methods include:

**Exercise.** From back pain to arthritis, physical activity is key for improving circulation, lowering inflammation, reducing stress, and breaking the pain cycle. Try gentle exercise like cycling, walking, or swimming.

**Cold and heat.** Cold packs help keep inflammation in check while heat promotes blood flow and helps muscles relax. You can also alternate between the two during one session.

**Stress management.** You feel pain more keenly when you're stressed out, because your muscles are tense and your brain is on high alert. Stress management techniques like mindful meditation and yoga and tai chi can help manage pain, too.

**CBD supplementation.** CBD oil also may help quell flare ups and break the cycle of prolonged pain. Though research is ongoing and more trials are needed to draw firm conclusions on the type of pain CBD is best for and who benefits most, there is good evidence that it may help reduce pain in a few ways.

For one, research shows that CBD binds to specific receptors that are involved in anxiety (serotonin 5-HT1A) and pain (vanilloid TRPV1), so is able to provide both pain and stress relieving properties—key to genotypes with high pain sensitivity. And it doesn't seem to take much to provide relief. Animal studies using 2 mg/kg of body weight of CBD per day for seven days demonstrated decreased anxiety and pain.

CBD is also a known anti-inflammatory, as cannabinoids, such as CBD attach themselves to specialized receptors called CB2 receptors that are instrumental in managing pain and inflammation.

Finally, CBD prevents the body from absorbing of anandamide, a compound named for the Sanskrit word **ananda**, meaning bliss, which is associated with regulating pain and other mental processes. It's also been linked to the "runner's high" some people feel during intense exercise. Increased levels of anandamide may in turn reduce the amount of pain a person experiences.

You can use CBD in capsules or as a topical ointment, depending on your needs. The FDA does not regulate doses. Experts with the arthritis foundation (which assists millions of people suffering with joint pain) suggest starting with low doses (e.g. 5 to 10mg twice a day), as they seem to work best for pain relief, and increasing if you feel no relief. It may take some trial and error to find the form and dosage that works best for you. Always let your doctor know what you're taking, especially if you're already taking medications for pain or other conditions.

dopamine system is highly active, the brain reduces production of its natural pain killing chemicals, leaving you more susceptible to any pain-inducing stimulus.

In one study published in the journal Science, researchers conducted a series of tests, including genetic screening, brain imaging, and controlled, sustained pain administered via an irritating solution injected into masseter muscle (a "chewing" muscle on the side of the jaw).

They found that participants who carried two copies of the "met" form of the COMT gene experienced a more intense response to pain all the way around than those with two copies of the "val" form of the gene, who withstood a higher level of painful stimulus while reporting feeling less pain and fewer pain-related negative emotions than their peers. Those participants who carried one copy of each of the COMT genes had a pain response that fell between the other genotypes.

Our analysis investigated which genotype was present in your DNA. Your rating of **LOW**, **NORMAL**, or **HIGH** reflects whether your genotype includes those that carry a risk of experiencing a low pain threshold and therefore being more sensitive to painful stimulus.

# SOCIAL ANXIETY

## WHAT YOUR GENES SAY ABOUT YOU:

Our analysis indicates that your genetic profile exhibits characteristics that make you likely to have an **INCREASED** susceptibility to experiencing social anxiety. That means you have a higher likelihood than someone with a more 'favorable' genotype to experience social anxiety that interferes with your daily life. This trait is found in about 10 percent of Caucasians and, though your genes are not your destiny, it's important to know what to do should you become one of the 15 million Americans affected by this common anxiety disorder.



Your genetic profile indicates that you are likely to have an **INCREASED**

susceptibility to experiencing extreme social anxiety that interferes with daily life. Though your genotype doesn't guarantee you will experience social anxiety, you should know what to do should you be affected by this common disorder.

People who have social anxiety are extraordinarily fearful of embarrassing themselves and of being watched and judged by others. It can cause physical symptoms, such as racing heartbeat, sweating, trembling, nausea, and in extreme cases even panic attacks. People with social anxiety find it very difficult to make eye contact and talk to people they don't know, even if they wish they could.

Social anxiety can become chronic and cause people who experience it to avoid social situations, which can worsen the anxiety overtime. A healthy social life is important for good mental and physical health. Being mostly relaxed in social situations also increases your quality of life in that it makes it easier to meet people, network for job and career opportunities, and engage in enjoyable activities held in public spaces. Treatment can help you control symptoms and be more comfortable and relaxed in social situations. Delaying treatment can make social anxiety more difficult to manage.

## RELATED GENES / SNPs

FGD2 and MTCH1

The genes and their associated SNPs that are included in this category have been shown in studies to have significant associations with the susceptibility to experiencing social anxiety.

Everybody feels nervous in social situations sometimes. But for people with social anxiety, or social phobia, everyday social interactions cause significant anxiety, fear, and self-consciousness that interfere with daily routine, like work, school, and gatherings that should otherwise be enjoyable.

The National Institute of Mental Health estimates that 12 percent of U.S. adults will experience social anxiety disorder at some point in their lives. Social anxiety is somewhat more common in women than in men. Risk factors include past negative social experiences, especially in childhood and an overactive amygdala, the part of the brain



## SOCIAL ANXIETY

### SUCCESS STRATEGIES

Exercising, eating a healthy diet, and following healthy lifestyle behaviors like getting enough sleep and not overdoing alcohol or caffeine can help prevent some anxiety. Therapy, like talk therapy or cognitive behavioral therapy can be very effective for treating social anxiety. Doctors also sometimes prescribe medications such as SSRIs (antidepressants).

Research also shows that CBD oil can quell social anxiety, making you feel more relaxed and even changing the way your brain responds to anxiety. In one study published in the *Journal of Psychopharmacology*, researchers gave a group of people with social anxiety disorder either 400 mg of CBD or a placebo pill and then rated their anxiety and performed brain-imaging scans. Later they performed the tests again, this time switching who got the dummy pills and who got the CBD supplements. Relative to the tests after taking the placebos, the volunteers enjoyed significantly decreased feelings of anxiety, and brain scans revealed altered activity in their limbic brain area, which is key for regulating emotions and anxiety.

In another study of 24 adults with social anxiety disorder, those given a single dose of 600 mg of CBD had significantly reduced anxiety, cognitive impairment, and negative feelings about themselves before performing public speaking test than their peers with anxiety who received a dummy supplement, who had elevated levels of anxiety, discomfort, and cognitive impairment. In fact, the CBD-taking public speakers' anxiety before the test was similar to a group of healthy adults who did not have social anxiety disorder.

A 2015 literature review found that evidence supports the use of CBD as a treatment for a variety of anxiety disorders, including panic disorder, generalized anxiety disorder, obsessive compulsive disorder, and social anxiety disorder.

that governs the fear response. It also runs in families and research shows it can be a genetically inherited trait.

In the first ever genome-wide association analysis published in 2018, researchers confirmed that there is a genetic basis for social anxiety and that your genotype can slightly or even significantly increase your likelihood of experiencing social anxiety.

Our analysis investigated which genotype of each of these genes was present in your DNA. Your rating of **NORMAL**, **SLIGHTLY INCREASED**, or **INCREASED** reflects whether your genotypes include those that carried a risk of experiencing social anxiety.



# STRESS TOLERANCE

## WHAT YOUR GENES SAY ABOUT YOU:

Our analysis indicates that your genetic profile exhibits characteristics that make you likely to have **NORMAL** levels of stress resilience. That means you are more likely than those with 'favorable' genotypes to experience stress and anxiety in the face of everyday challenges. You're far from alone: statistics show that about 75 percent of people regularly experience physical and psychological symptoms caused by stress; 33 percent feel like they are living with extreme stress, and nearly half say their stress has increased in the past five years. As stress and anxiety-inducing situations can be a normal part of everyday life, you would benefit from finding healthy stress-management strategies, so stress and anxiety does not overwhelm you.



Your profile indicates that you are likely to have **NORMAL**

levels of stress resilience. You may need to manage your stress more often than other, more stress-resilient genotypes. You should develop healthy stress management strategies to better cope with anxiety-inducing times and situations.

There's no getting around it: stress is part of daily life and, according to statistics from the American Institute of Stress, more than three-quarters of us experience it regularly. That's not all bad news, because stress can be motivating. It is bad when it becomes so high that it is debilitating, however. Unchecked, stress can wreck your sleep, health, and relationships.

## SUCCESS STRATEGIES

Try one of these scientifically proven healthy techniques to reduce stress both in the immediate and long-term:

**Exercise:** Physical activity is one of the most well-established ways to manage stress. Even just 20 minutes of exercise can ameliorate anxiety for hours.

**Use your social network:** Talk to trusted friends and family members can help you work through your woes and alleviate anxiety.

## RELATED GENES / SNPs

### PDE4B

The gene and associated SNP in this category have been shown in studies to have significant associations with stress resilience and the overall susceptibility to feeling stress and anxiety.

Though we tend to think of stress emotionally, it comes from a physical place—the hypothalamic-pituitary-adrenal (HPA) axis or by stimulation of the sympathetic nervous system and adrenalin secretion as part of our natural "fight or flight" response. Spending too much time in that state can lead to hypertension, GI issues, headaches, and mood and emotional disturbances.

How resilient (or susceptible) you are to stress depends upon a host of factors including your experience with stress, past traumatic experiences, your social support network, and your general health and well being. Your tendency for stress resilience is



## STRESS TOLERANCE

**Practice mindfulness:** Mindful meditation can help you let go of stressful emotions. Apps like Headspace can walk you through the steps to help get you started.

**CBD supplementation:** Many people with frequent stress and anxiety also use CBD supplementation. In one survey of more than 2,000 Americans conducted with the Harris Poll, the online business journal Quartz found that half of those who had tried CBD did so specifically for stress and anxiety relief. Current research into the endocannabinoid system indicates CBD may indeed be effective for that purpose.

It's well established that the endocannabinoid system plays a key role in mediating behavioral, neurochemical, and molecular responses to stress. Specifically, it serves to constrain HPA axis activity and reduce stress and anxiety. Research suggests that targeting the endocannabinoid system with cannabinoids like CBD can help reduce anxiety and mitigate the stress response.

One research analysis of 49 studies published in the journal *Neurotherapeutics* concluded that studies support the potential for CBD as a treatment for anxiety and that research found that doses of CBD in the 300 to 600 mg range reduced anxiety in healthy people during scientific studies.

also coded in your DNA.

In a study published in *JAMA Psychiatry*, an international team of researchers examined data from nearly 32,000 Danish individuals participating in the Lundbeck Foundation's "Initiative for Integrative Psychiatric Research" (iPSYCH) study, comparing genotypes in 12,655 Danish individuals with anxiety and stress-related diagnoses to 19,225 people without stress or anxiety issues. After poring through the data, the research team found a strong association between anxiety and stress related disorders and SNPs in PDE4B, a gene that influences important mood regulating hormones in the brain. They concluded that PDE4B may serve as a target in future treatments for anxiety and stress-related conditions.

Our analysis investigated which genotype was present in your DNA. Your rating of **HIGHER**, **SLIGHTLY HIGHER**, or **NORMAL** reflects whether your genotype includes those that carry the likelihood of having higher resilience to stress and anxiety.

# ALCOHOL SENSITIVITY

## WHAT YOUR GENES SAY ABOUT YOU:

Our analysis indicates that your genetic profile exhibits characteristics that make you likely to be **SENSITIVE** to alcohol. That means you may quickly end up with more of the unpleasant byproducts of alcohol metabolism, such as flushing and stomach upset and may be more prone to bad hangovers, than people who are less sensitive and more efficient at fully metabolizing alcohol. This trait is found in about 25 percent of Caucasians and can make drinking alcohol unpleasant. The upside of this genetic tendency is that you may be less likely to drink to excess. You also may be less likely to develop alcohol dependence.

Because you find drinking unpleasant, you may choose to find other ways to relax and unwind, besides using alcohol.



Your genetic profile indicates that you are likely to be **SENSITIVE**

to the byproducts of alcohol metabolism. This means you are more likely to find drinking alcohol unpleasant and may have a reduced likelihood of drinking to excess and/or becoming alcohol dependent. You may wish to find alternative ways to relax.

As someone with a genetic tendency to experience the negative effects of alcohol metabolism, such as flushing and stomach upset more quickly and acutely, you are more likely to not drink to excess, which is good news as excessive drinking can be harmful to your health. If you like the relaxing effects of alcohol, you may wish to find an alternative to avoid the unpleasant side effects.

## SUCCESS STRATEGIES

CBD can be a healthier alternative to alcohol, especially for people who are alcohol sensitive, to help lower stress and promote relaxation. CBD combats stress in a few ways. For one, it triggers your body's endocannabinoid system, which is in charge of regulating sleep and mood, and has been shown in studies to promote relaxation and improved sleep. Research shows it also affects 5-HT1A receptors, which control levels of the feel good chemical serotonin and can blunt the body's responses to stress by interfering with the secretion of the stress hormone cortisol. CBD is also

## RELATED GENES / SNPs

ADH1C, ADH1B, ALDH2

The genes and associated SNPs included in this category have been shown to have significant associations with a person's alcohol sensitivity, or how the byproducts of alcohol metabolism affect you—a trait that has a direct impact on how likely you are to consume alcohol to excess, a behavior that can be harmful to your health.

When you drink, your liver goes to work using enzymes like alcohol dehydrogenase and acetaldehyde dehydrogenase to break down the alcohol into acetaldehyde (which is toxic) and then acetate (a non-toxic substance similar to vinegar). That metabolic process works at different speeds and more or less efficiently for different people, and it can have a profound impact on how you feel after a drink or two...or more.

People who are considered sensitive to alcohol quickly end up with the unpleasant

## ALCOHOL SENSITIVITY

known to have an anxiolytic effect, in that it inhibits anxiety.

Unlike alcohol, which can have a sedative effect and help you fall asleep, only to disrupt your sleep in the middle of the night and leave you feeling groggy in the morning, CBD may help improve your overall sleep.

Like alcohol, which produces both stimulation and sedation depending on factors including dosage and blood alcohol concentration, CBD also has biphasic properties, in that it appears to have different effects depending upon the dose. At lower levels—research shows about the 15 mg range—CBD interacts with the endocannabinoid system in ways that can make you feel energetic and alert. In higher concentrations, it produces more of a calming and sedating effect.

If and/or when you do drink, drink in moderation (which should be easier with your favorable genotype). Smart drinking strategies include:

**Know the standards.** When someone says, “I just had one drink” they very often had two (maybe three or more!) without realizing it, because a “drink” is officially defined as less booze than many bartenders (and friends and family) pour. One standard drink is scientifically defined as 5 ounces of wine, 12 ounces of beer, or 1.5 ounces of spirits like vodka and rum. One martini is two standard drinks. One Long Island Iced Tea is four.

**Stay within healthy limits.** Moderate drinking is defined as two standard drinks a day for men and one for women. Recent studies have questioned whether that amount is higher than it should be for optimal health, since alcohol consumption has been linked to chronic diseases like certain cancers.

byproducts of alcohol metabolism, such as flushing and stomach upset and are more prone to bad hangovers after relatively small amounts of alcohol, than those who are less sensitive and more efficient at alcohol processing. Unsurprisingly, people who are more sensitive to alcohol's adverse effects are also less likely to enjoy drinking or to become alcohol dependent, compared to those who are not sensitive, who may be prone to drinking to excess and/or becoming alcohol dependent.

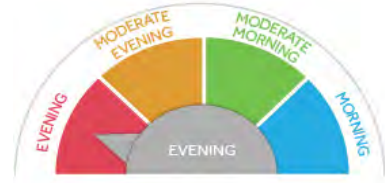
Genetics plays a significant role in alcohol metabolism and whether or not someone is sensitive to alcohol consumption. One genome-wide association study including more than 86,600 adults reported that individual DNA impacts the drinking habits of people around the world. In fact, research finds that 40 to 60 percent of alcohol dependence syndrome (ADS) is genetically determined, and DNA accounts for about half of the variance in alcohol consumption from one person to the next.

Our analysis investigated which genotype for these genes was present in your DNA. Your rating of **SENSITIVE**, **MODERATELY SENSITIVE**, or **NOT SENSITIVE** reflects whether your genotype included those that carried the likelihood of being sensitive to the negative effects of alcohol metabolism, and therefore your predisposition to avoid or consume alcohol.

# CHRONOTYPE

## WHAT YOUR GENES SAY ABOUT YOU:

Our analysis indicates that your genetic profile exhibits characteristics that make you likely to be an **EVENING** person. That means you have a strong genetic tendency to feel more awake into the evenings and to sleep later in the mornings. People with late chronotypes are at higher risk for depression; are more prone to higher levels of tobacco and alcohol use; tend to have less healthful diets, and have higher levels of metabolic disease than earlier chronotypes. Some of those health risks appear to be related to living out of sync with “normal” working/sleeping hours. The good news is there are steps you can take to nudge your internal clock toward an earlier sleep/wake cycle and ameliorate some of the downsides of your night owl genotype.



Your genetic profile indicates that you have a strong genetic tendency to be an **EVENING**

person. A late chronotype can increase your risk for weight gain, depression, and metabolic diseases, especially if you don't get sufficient sleep. Shifting your internal clock earlier may help improve your sleep and well-being.

Being a night owl can make daily life challenging. Unless you work late hours, you're expected to be up and functional with the early birds. When your internal clock doesn't shift into waking gear until late morning that means you can spend much of the workday not feeling your best.

It also can have metabolic consequences like weight gain, diabetes, and heart disease, as well as increase your risk for depression. A recent study from Aachen University in Germany also found structural differences in the brains of people with different sleep-wake tendencies. Specifically, compared to earlier risers, late chronotypes had reduced integrity in some of their brain's white matter, which can hinder cognitive function and increase risk for mood disorders.

The researchers speculated that these changes in white matter may be a result of chronic “social jet lag,” meaning that by constantly fighting their natural sleep/wake cycle, they were chronically sleep deprived and fending

## RELATED GENES / SNPs

RGS16, PIGK, AK5, PRPF3, TARS2, ORAI2, RASA4, PER2, HCRTR2, EXD3, RAX, CPLX4, LMAN1, HTR6, FKBP1B, CALB1, INADL, PSME4, ACYP2

The genes and associated SNPs in this category have been shown in studies to have significant associations with chronotype—whether you're a morning person, an evening person, or an intermediate chronotype who falls between the two ends of the spectrum.

Most of us have a fairly well established preference for waking and sleeping times, with some people being more toward “larks” or morning people and others skewing toward “owls” or night people. Our circadian rhythms control more than our sleep-wake cycles; they also influence our metabolism and physiological functions.

In general, night owls are at higher risk for depression, substance abuse, and other metabolic disruptions that can lead to weight gain and chronic disease (perhaps in part

# CHRONOTYPE

off the same fatigue, daytime sleepiness, and fuzzy-headedness associated with jet lag.

On the plus side, research has found that night owls have higher education, greater reasoning and analytical abilities, tend to achieve greater professional success than naturally early risers. One study even found that people with higher IQs tended to have more nocturnally oriented chronotypes.

So it's a matter of finding a balance between your natural tendencies and the schedule your life demands that you keep..

## SUCCESS STRATEGIES

The good news is that genetics is only one factor influencing your circadian rhythms. Your lifestyle and daily behaviors also have a significant impact on your sleeping/waking tendencies. Research shows your behavior and lifestyle habits also play an important role, so if you do find that you are struggling with a late chronotype, there are steps you can take.

In a study published in *Sleep Medicine* researchers put a group of 22 healthy night owls with an average bedtime of 2:30 a.m. and wake-up time of 10:15 a.m. on a clock-shifting intervention to see if they could change their circadian rhythms. For a period of three weeks participants in the group were asked to:

- Wake up 2 to 3 hours earlier than their usual waking time and maximize outdoor light during the mornings.
- Go to bed 2 to 3 hours before their usual bedtime and limit light exposure in the evening.
- Keep sleep/wake times fixed on both workdays and free days. No naps after 4 p.m.
- Eat breakfast as soon as possible after waking up, eat lunch at the same time each day, and refrain from eating dinner after 7 p.m.
- Avoid caffeine after 3 p.m.

By the end of the study, the group had successfully shifted their circadian rhythms: their levels of sleep-inducing melatonin and awakening cortisol hormones both shifted to earlier in the day, moving their internal body clock up by two hours without disrupting the amount of sleep they got each night.

because of sleep disruption or too little sleep trying to work into “normal” work hours).

Many factors influence our internal rhythms or circadian clocks, including age, gender, social constraints, occupation, and environmental factors. Whether or not you tend to be more of a lark or an owl is also encoded in your DNA.

Multiple genome-wide association studies, including analyses from the UK Biobank study—a large scale research project that combines detailed measurements and lifestyle questionnaire data with genetic data in 128,266 British adults—have identified numerous genes and genetic variants that influence your internal clock. Those genes and SNPs include those that modulate brain chemistry, core circadian rhythms, and photosensitive retinal cells, which are known to communicate with your brain's primary circadian pacemaker.

Our analysis investigated which genotype for each of these genes was present in your DNA. Your rating of **EVENING**, **MODERATE EVENING**, **MODERATE MORNING**, or **MORNING** reflects whether your genotypes included those that increase your likelihood of being a morning or evening person.



## CHRONOTYPE

---

They also felt better. They reported feeling less stressed and depressed, scored higher on cognitive tests, and performed better in physical strength tests during what had typically been their “suboptimal” morning hours. Their peak performance times also shifted from evening to afternoon.

CBD might also help you optimize your circadian rhythms and sleep. The endocannabinoid system plays a role in regulating circadian rhythm, including the maintenance and promotion of sleep. By taking it, you may be able to regulate your sleep/wake cycle (which is why it is sometimes prescribed for insomnia.)

It's important to get the dosage right when going the CBD route, especially if taking it at a desired bedtime. Research shows that low doses in the 15 mg range have a stimulating effect and can promote wakefulness. Studies find that moderate to higher doses, on the other hand, have a more sedating effect and may increase and/or improve sleep.



# LINKS TO RELATED STUDIES

## CBD METABOLISM

Pharmacol Ther. 2013 Apr;138(1):103-41. doi: 10.1016/j.pharmthera.2012.12.007. Epub 2013 Jan 16.

**Cytochrome P450 enzymes in drug metabolism: regulation of gene expression, enzyme activities, and impact of genetic variation**

<https://www.ncbi.nlm.nih.gov/pubmed/23333322>

Zanger UM, Schwab M.

Life Sci. 2007 Mar 20;80(15):1415-9. Epub 2007 Jan 17

**Cytochrome P450 enzymes involved in the metabolism of tetrahydrocannabinols and cannabitol by human hepatic microsomes**

<https://www.ncbi.nlm.nih.gov/pubmed/17303175>

Watanabe K, Yamaori S, Funahashi T, Kimura T, Yamamoto I

Life Sciences [16 Jun 2011, 89(5-6):165-170]

**Identification of cytochrome P450 enzymes responsible for metabolism of cannabidiol by human liver microsomes.**

<http://europepmc.org/abstract/MED/21704641>

Jiang R, Yamaori S, Takeda S, Yamamoto I, Watanabe K

Front Genet. 2013 Feb 25;4:12. doi: 10.3389/fgene.2013.00012. eCollection 2013

**Pharmacogenomics of Cytochrome P450 3A4: Recent Progress Toward the "Missing Heritability" Problem.**

<https://www.ncbi.nlm.nih.gov/pubmed/23444277>

Klein K, Zanger UM.

## SLEEP DURATION

Mol Psychiatry. 2013 Jan;18(1):122-32. doi: 10.1038/mp.2011.142. Epub 2011 Nov 22.

**A K(ATP) channel gene effect on sleep duration: from genome-wide association studies to function in Drosophila**

<https://www.ncbi.nlm.nih.gov/pubmed/22105623>

Allebrandt KV, Amin N, Müller-Myhsok B, Esko T, Teder-Laving M, Azevedo RV, Hayward C, van Mill J, Vogelzangs N, Green EW, Melville SA, Lichtner P, Wichmann HE, Oostra BA, Janssens AC, Campbell H, Wilson JF, Hicks AA, Pramstaller PP, Dogas Z, Rudan I, Merrow M, Penninx B, Kyriacou CP, Metspalu A, van Duijn CM, Meitinger T, Roenneberg T.

# LINKS TO RELATED STUDIES

Mol Psychiatry. 2015 Oct;20(10):1232-9. doi: 10.1038/mp.2014.133. Epub 2014 Dec 2.

## **Novel loci associated with usual sleep duration: the CHARGE Consortium Genome-Wide Association Study**

<https://www.ncbi.nlm.nih.gov/pubmed/25469926>

Gottlieb DJ, Hek K, Chen TH, Watson NF, Eiriksdottir G, Byrne EM, Cornelis M, Warby SC, Bandinelli S, Cherkas L, Evans DS, Grabe HJ, Lahti J, Li M, Lehtimäki T, Lumley T, Marcianti KD, Pérusse L, Psaty BM, Robbins J, Tranah GJ, Vink JM, Wilk JB, Stafford JM, Bellis C, Biffar R, Bouchard C, Cade B, Curhan GC, Eriksson JG, Ewert R, Ferrucci L, Fülöp T, Gehrman PR, Goodloe R, Harris TB, Heath AC, Hernandez D, Hofman A, Hottenga JJ, Hunter DJ, Jensen MK, Johnson AD, Kähönen M, Kao L, Kraft P, Larkin EK, Lauderdale DS, Luik AI, Medici M, Montgomery GW, Palotie A, Patel SR, Pistis G, Porcu E, Quaye L, Raitakari O, Redline S, Rimm EB, Rotter JI, Smith AV, Spector TD, Teumer A, Uitterlinden AG, Vohl MC, Widen E, Willemsen G, Young T, Zhang X, Liu Y, Blangero J, Boomsma DI, Gudnason V, Hu F, Mangino M, Martin NG, O'Connor GT, Stone KL, Tanaka T, Viikari J, Gharib SA, Punjabi NM, Räikkönen K, Völzke H, Mignot E, Tiemeier H.

Hum Mol Genet. 2016 Jan 1;25(1):167-79. doi: 10.1093/hmg/ddv434. Epub 2015 Oct 13.

## **Common variants in DRD2 are associated with sleep duration: the CARE consortium**

<https://www.ncbi.nlm.nih.gov/pubmed/26464489>

Cade BE, Gottlieb DJ, Lauderdale DS, Bennett DA, Buchman AS, Buxbaum SG, De Jager PL, Evans DS, Fülöp T, Gharib SA, Johnson WC, Kim H, Larkin EK, Lee SK, Lim AS, Punjabi NM, Shin C, Stone KL, Tranah GJ, Weng J, Yaffe K, Zee PC, Patel SR, Zhu X, Redline S, Saxena R

## SYSTEMIC INFLAMMATION

Circulation. 2011 Feb 22;123(7):731-8. doi: 10.1161/CIRCULATIONAHA.110.948570. Epub 2011 Feb 7.

## **Meta-analysis of genome-wide association studies in >80 000 subjects identifies multiple loci for C-reactive protein levels**

<https://www.ncbi.nlm.nih.gov/pubmed/?term=21300955>

Dehghan A, Dupuis J, Barbalic M, Bis JC, Eiriksdottir G, Lu C, Pellikka N, Wallaschofski H, Kettunen J, Henneman P, Baumert J, Strachan DP, Fuchsberger C, Vitart V, Wilson JF, Paré G, Naitza S, Rudock ME, Surakka I, de Geus EJ, Alizadeh BZ, Guralnik J, Shuldiner A, Tanaka T, Zee RY, Schnabel RB, Nambi V, Kavousi M, Ripatti S, Nauck M, Smith NL, Smith AV, Sundvall J, Scheet P, Liu Y, Ruokonen A, Rose LM, Larson MG, Hoogeveen RC, Freimer NB, Teumer A, Tracy RP, Launer LJ, Buring JE, Yamamoto JF, Folsom AR, Sijbrands EJ, Pankow J, Elliott P, Keane JF, Sun W, Sarin AP, Fontes JD, Badola S, Astor BC, Hofman A, Pouta A, Werdan K, Greiser KH, Kuss O, Meyer zu Schwabedissen HE, Thiery J, Jamshidi Y, Nolte IM, Soranzo N, Spector TD, Völzke H, Parker AN, Aspelund T, Bates D, Young L, Tsui K, Siscovick DS, Guo X, Rotter JI, Uda M, Schlessinger D, Rudan I, Hicks AA, Penninx BW, Thorand B, Gieger C, Coresh J, Willemsen G, Harris TB, Uitterlinden AG, Järvelin MR, Rice K, Radke D, Salomaa V, Willems van Dijk K, Boerwinkle E, Vasan RS, Ferrucci L, Gibson QD, Bandinelli S, Snieder H, Boomsma DI, Xiao X, Campbell H, Hayward C, Pramstaller PP, van Duijn CM, Peltonen L, Psaty BM, Gudnason V, Ridker PM, Homuth G, Koenig W, Ballantyne CM, Witteman JC, Benjamin EJ, Perola M, Chasman DI

# LINKS TO RELATED STUDIES

## ALCOHOL SENSITIVITY

Hepatology. 2010 Feb;51(2):491-500. doi: 10.1002/hep.23341.

**Variability in ethanol biotransformation in whites is modulated by polymorphisms in the ADH1B and ADH1C genes**

<https://www.ncbi.nlm.nih.gov/pubmed/20101753>

Martínez C, Galván S, Garcia-Martin E, Ramos MI, Gutiérrez-Martín Y, Agúndez JA

Addict Biol. 2015 May;20(3):594-604. doi: 10.1111/adb.12141. Epub 2014 Apr 16

**Genetic variants in or near ADH1B and ADH1C affect susceptibility to alcohol dependence in a British and Irish population**

<https://www.ncbi.nlm.nih.gov/pubmed/24735490>

Way M, McQuillin A, Saini J, Ruparelia K, Lydall GJ, Guerrini I, Ball D, Smith I, Quadri G, Thomson AD, Kasiakogia-Worley K, Cherian R, Gunwardena P, Rao H, Kottalgi G, Patel S, Hillman A, Douglas E, Qureshi SY, Reynolds G, Jauhar S, O'Kane A, Dedman A, Sharp S, Kandaswamy R, Dar K, Curtis D, Morgan MY, Gurling HM

Mol Psychiatry. 2017 Sep;22(9):1359-1367. doi: 10.1038/mp.2017.101. Epub 2017 May 9.

**Genetic contributors to variation in alcohol consumption vary by race/ethnicity in a large multi-ethnic genome-wide association study**

<https://www.ncbi.nlm.nih.gov/pubmed/28485404>

Jorgenson E, Thai KK, Hoffmann TJ, Sakoda LC, Kvale MN, Banda Y, Schaefer C, Risch N, Mertens J, Weisner C, Choquet H

Hum Genet. 2012 Aug;131(8):1361-74. doi: 10.1007/s00439-012-1163-5. Epub 2012 Apr 5

**Further clarification of the contribution of the ADH1C gene to vulnerability of alcoholism and selected liver diseases**

<https://www.ncbi.nlm.nih.gov/pubmed/22476623>

Li D, Zhao H, Gelernter J

Mol Psychiatry. 2014 Jan;19(1):41-9. doi: 10.1038/mp.2013.145. Epub 2013 Oct 29.

**Genome-wide association study of alcohol dependence: significant findings in African- and European-Americans including novel risk loci**

<https://www.ncbi.nlm.nih.gov/pubmed/24166409>

Gelernter J, Kranzler HR, Sherva R, Almasy L, Koesterer R, Smith AH, Anton R, Preuss UW, Ridinger M, Rujescu D, Wodarz N, Zill P, Zhao H, Farrer LA

# LINKS TO RELATED STUDIES

Alcohol Clin Exp Res. 2015 Jul;39(7):1137-47. doi: 10.1111/acer.12751. Epub 2015 Jun 3.

**Genomewide Association Study for Maximum Number of Alcoholic Drinks in European Americans and African Americans**

<https://www.ncbi.nlm.nih.gov/pubmed/26036284>

Xu K, Kranzler HR, Sherva R, Sartor CE, Almasy L, Koesterer R, Zhao H, Farrer LA, Gelernter J

## SOCIAL ANXIETY

Am J Med Genet B Neuropsychiatr Genet. 2017 Mar; 174(2): 120–131. doi: 10.1002/ajmg.b.32520

**Genetic Risk Variants for Social Anxiety**

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5325045/#R30>

Murray B. Stein, MD, MPH, Chia-Yen Chen, ScD, Sonia Jain, PhD Kevin P. Jensen, PhD, Feng He, MS, Steven G. Heeringa, PhD Ronald C. Kessler, PhD, Adam Maihofer, MS, Matthew K. Nock, PhD, Stephan Ripke, MD, Xiaoying Sun, MS, Michael L. Thomas, PhD, Robert J. Ursano, MD, Jordan W. Smoller, MD, ScD, and Joel Gelernter, MD, On behalf of the Army STARRS Collaborators

## PAIN SENSITIVITY

PLoS One. 2011;6(11):e27764. doi: 10.1371/journal.pone.0027764. Epub 2011 Nov 21

**The catechol-O-methyltransferase (COMT) val158met polymorphism affects brain responses to repeated painful stimuli**

<https://www.ncbi.nlm.nih.gov/pubmed/22132136>

Loggia ML, Jensen K, Gollub RL, Wasan AD, Edwards RR, Kong J

Science. 2003 Feb 21;299(5610):1240-3.

**COMT val158met genotype affects mu-opioid neurotransmitter responses to a pain stressor**

<https://www.ncbi.nlm.nih.gov/pubmed/12595695>

Zubieta JK, Heitzeg MM, Smith YR, Bueller JA, Xu K, Xu Y, Koeppe RA, Stohler CS, Goldman D.

## STRESS RESILIENCE

doi: <https://doi.org/10.1101/263855>

**Genome-wide Association Study of Anxiety and Stress-related Disorders in the iPSYCH Cohort**

<https://www.biorxiv.org/content/biorxiv/early/2018/02/12/263855.full.pdf>

Sandra M. Meier, Ph.D, Kalevi Tronetti, Ph.D. Thomas Damm Als, Ph.D. Mikaela Laine, M.Sc. Marianne Giørtz Pedersen, M.Sc Jonas Bybjerg-Grauholm, Ph.D.; Marie Bækved-Hansen, Ph.D. Ewa Sokolowska, Ph.D. Preben B. Mortensen, Dr.Med.Sc.; David M. Hougaard, Dr.Med.Sc Thomas Werge, Ph.D.; Merete Nordentoft, Ph.D Anders D. Børglum, M.D.; Iiris Hovatta, Ph.D. Manuel Mattheisen, M.D Ole Mors, Ph.D.

# LINKS TO RELATED STUDIES

## CHRONOTYPE

PLoS Genet. 2016 Aug 5;12(8):e1006125. doi: 10.1371/journal.pgen.1006125. eCollection 2016 Aug

**Genome-Wide Association Analyses in 128,266 Individuals Identifies New Morningness and Sleep Duration Loci**

<https://www.ncbi.nlm.nih.gov/pubmed/27494321>

ones SE, Tyrrell J, Wood AR, Beaumont RN, Ruth KS, Tuke MA, Yaghootkar H, Hu Y, Teder-Laving M, Hayward C, Roenneberg T, Wilson JF, Del Greco F, Hicks AA, Shin C, Yun CH, Lee SK, Metspalu A, Byrne EM, Gehrman PR, Tiemeier H, Allebrandt KV, Featherly RM, Murray A, Hinds DA, Frayling TM, Weedon MN

Sleep Med. 2018 Oct;50:36-41. doi: 10.1016/j.sleep.2018.04.015. Epub 2018 Jun 1

**Circadian preference and sleep timing from childhood to adolescence in relation to genetic variants from a genome-wide association study**

<https://www.ncbi.nlm.nih.gov/pubmed/29982088>

Merikanto I, Lahti J, Kuula L, Heinonen K, Räikkönen K, Andersson S, Strandberg T, Pesonen AK

Nat Commun. 2016 Feb 2;7:10448. doi: 10.1038/ncomms10448

**GWAS of 89,283 individuals identifies genetic variants associated with self-reporting of being a morning person**

<https://www.ncbi.nlm.nih.gov/pubmed/26835600>

Hu Y, Shmygelska A, Tran D, Eriksson N, Tung JY, Hinds DA

Nat Commun. 2016 Mar 9;7:10889. doi: 10.1038/ncomms10889

**Genome-wide association analysis identifies novel loci for chronotype in 100,420 individuals from the UK Biobank**

<https://www.ncbi.nlm.nih.gov/pubmed/26955885>

Lane JM, Vlasac I, Anderson SG, Kyle SD, Dixon WG, Bechtold DA, Gill S, Little MA, Luik A, Loudon A, Emsley R, Scheer FA, Lawlor DA, Redline S, Ray DW, Rutter MK, Saxena R

Sleep. 2017 Feb 1;40(2). doi: 10.1093/sleep/zsw048

**Genetic Basis of Chronotype in Humans: Insights From Three Landmark GWAS**

<https://www.ncbi.nlm.nih.gov/pubmed/28364486>

Kalmbach DA, Schneider LD, Cheung J, Bertrand SJ, Kariharan T, Pack AI, Gehrman PR