**# Gene symbol**

SLC6A4

**# Full name of gene**

Sodium-dependent serotonin transporter

**# What does the <gene\_symbol> gene do?**

The SLC6A4 gene creates the Sodium-dependent serotonin transporter protein. The protein transports serotonin to be recycled. This protein is targeted by many antidepressants in the SSRI and Tricyclic classes. Variants in this gene can cause 5%-95% loss of serotonin uptake activity, and may cause alcoholism and many mood disorders including obsessive compulsive disorder, depression, and bipolar disorder.

This gene is located on chromosome 17. The protein it creates acts in your brain and nervous system.

<body part brain >

<gene\_expression\_location location="D001921;">

**# What are some common mutations of <gene\_symbol>?**

There are 3 well known variants in this gene: <variant list?>

<A3609G variant view with A to G transformation>

This variant is a change at a specific point in the <gene\_symbol> gene from adenine (A) to guanine (G), resulting in reduced enzyme activity. This substitution of a single nucleotide is known as a missense variant.

<T463G variant view with T to G transformation>

This variant is a change at a specific point in the <gene\_symbol> gene from thymine (T) to guanine (G), resulting in reduced protein creation. This substitution of a single nucleotide is known as a mis-sense mutation.

< 5-HTTLPR add in VNTR>

This variant changes the number of repeated sections in the gene. It is called a variable number tandem repeats variant (VNTR).

```

<user variant viewer>

<user what does this mean>

<user gene list>

<UserGenotypeBox gene="comt">

<Genotype name=" G158A (A;G)">

<line\_graph level="moderate">

# What does this mean?

People with this variant have one copy of the G158A variant. This substitution of a single nucleotide is known as a mis-sense mutation.

# What is the effect of this variant?

You are in the Moderate Loss of Function category. See below for more information

# How common is this gene in the general population?

<pie\_chart level=" G158A (A;G)", frequency>

<frequency> of the population has a moderate loss of function

</Genotype>

<Genotype name=" G158A (G;G)">

<line\_graph level="severe">

# What does this mean?

People with this variant have two copies of the G158A variant. This substitution of a single nucleotide is known as a mis-sense mutation.

# What is the effect of this variant?

You are in the Severe Loss of Function category. See below for more information

# How common is this gene in the general population?

<pie\_chart level=" G158A (G;G)", frequency>

<frequency> of the population has a severe loss of function

<pie\_chart level=" G158A (G;G)", frequency>

You are in the Severe Loss of Function category. See below for more information

</Genotype>

<Genotype name="G158A (A;A)”>

# How common is this gene in the general population?

<pie\_chart level="G158A (A;A), frequency>

Your <gene\_name> is found to have no variants. A normal gene is referred to as a "wildtype" gene.

</Genotype>

<Genotype name=" C62T (T;G)">

<line\_graph level="moderate">

# What does this mean?

People with this variant have one copy of the C62T variant. This substitution of a single nucleotide is known as a mis-sense mutation.

# What is the effect of this variant?

You are in the Moderate Loss of Function category. See below for more information

# How common is this gene in the general population?

<pie\_chart level="C62T (T;G)", frequency>

<frequency> of the population has a moderate loss of function

</Genotype>

<Genotype name="C62T (G;G)">

<line\_graph level="severe">

# What does this mean?

People with this variant have two copies of the C62T variant. This substitution of a single nucleotide is known as a mis-sense mutation.

# What is the effect of this variant?

You are in the Severe Loss of Function category. See below for more information

# How common is this gene in the general population?

<pie\_chart level="C62T (G;G)", frequency>

<frequency> of the population has a severe loss of function

<pie\_chart level="C62T (G;G)", frequency>

You are in the Severe Loss of Function category. See below for more information

</Genotype>

<Genotype name="C62T (T;T)”>

# How common is this gene in the general population?

<pie\_chart level="C62T (T;T), frequency>

Your <gene\_name> is found to have no variants. A normal gene is referred to as a "wildtype" gene.

</Genotype>

<Genotype name=" 5-HTTLPR (L;L)">

<line\_graph level="moderate">

# What does this mean?

People with this variant have two copies of the 5-HTTLPR variant with 16 repeated sections inserting 44 base pairs. It is called a variable number tandem repeats variant (VNTR).

# What is the effect of this variant?

You are in the Moderate Loss of Function category. See below for more information

# How common is this gene in the general population?

<pie\_chart level="5-HTTLPR (L;L)", frequency>

<frequency> of the population has a moderate loss of function

</Genotype>

<Genotype name="5-HTTLPR (S;L)">

<line\_graph level="severe">

# What does this mean?

People with this variant have the 5-HTTLPR variant with 16 and 14 repeated sections. It is called a variable number tandem repeats variant (VNTR).

# What is the effect of this variant?

You are in the Severe Loss of Function category. See below for more information

# How common is this gene in the general population?

<pie\_chart level="5-HTTLPR (S;L)", frequency>

<frequency> of the population has a severe loss of function

You are in the Severe Loss of Function category. See below for more information

</Genotype>

<Genotype name=" 5-HTTLPR (S;S)">

<line\_graph level="moderate">

# What does this mean?

People with this variant have two copies of the 5-HTTLPR variant with 14 repeated sections. It is called a variable number tandem repeats variant (VNTR).

# What is the effect of this variant?

You are in the Moderate Loss of Function category. See below for more information

# How common is this gene in the general population?

<pie\_chart level="5-HTTLPR (S;S)", frequency>

<frequency> of the population has a moderate loss of function

</Genotype>

# How sure are you?

<user gene chip graph level="user gene surity">

We have <user gene surity> confidence in the read of the gene due to the coverage of our chipset process.

</UserGenotypeBox>

# How sure are you?

<if chipset to low graph>

<level graph>

We have low confidence of this gene due to the data our chipset provides.

<else if chipset to medium graph>

<level graph>

We have medium confidence of this gene due to the data our chipset provides.

<else check chipset to high graph>

<level graph>

We have high confidence of this gene due to the data our chipset provides.

```

**# What are the effects of variants in <gene\_symbol>?**

For the vast majority of people, the overall risk associated with the common <gene\_symbol> variants is small, and do not impact treatment. It is possible that variants in this gene interact with other gene variants, which is the reason for our inclusion of this gene in the gene panel.

**<call variants with the multiple categories>**

G158A (G;G)

**<function meter level="wildtype">**

**<efficiency level = "100%" >**

**<variant and population data>**

**# Normal Function**

The higher COMT enzymatic activity increases dopamine levels. It also causes [normal pain tolerance] (https://www.ncbi.nlm.nih.gov/pubmed/12595695?dopt=Abstract) and allows better thinking under stress. However, thinking ability is reduced outside of stressful situations. Other issues include:

* [1.4X increased risk of breast cancer](<https://www.ncbi.nlm.nih.gov/pubmed/18194538?dopt=Abstract>)
* [Greater risk of psychotic symptoms and schizophrenia when using cannabis](<https://www.ncbi.nlm.nih.gov/pubmed/15866551?dopt=Abstract>)
* [Poor response to antidepressant paroxetine](<https://www.ncbi.nlm.nih.gov/pubmed/18989660?dopt=Abstract>)
* [2X risk of schizophrenia compared with AA]( <https://www.ncbi.nlm.nih.gov/pubmed/22208661?dopt=Abstract>)
* 1.5 times more common in [alcohol-dependent]( <https://www.ncbi.nlm.nih.gov/pubmed/22208661?dopt=Abstract>) cases.

**# What should I do about this?**

Users should consider using other antidepressant medications than paroxetine. They should also not drink alcohol or use cannabis.

Medications indicated for use in treating COMT issues include: [Clonidine, BIA, Diethylstilbestrol, Dobutamine, Dopamine, Entacapone, Methyldopa, Micafungin, Nialamide, S-Adenosylmethionine, Testosterone Propionate, and Tolcapone.](http://www.uniprot.org/uniprot/P21964#pathology\_and\_biotech)

G158A (A;G)

**<function meter level="moderate">**

**<efficiency level = "25%" >**

**<variant and population data>**

**# Moderate loss of function**

This variant decreases COMT enzymatic activity by as much as 25%, and increases dopamine levels. It also decreases the pain threshold and causes worse thinking under stress. However, information processing is more better under non-stressful conditions. Other issues include:

* [Greater COMT gene activation lasting from 0.5 to 48 hours after moderate exercise, correlating with muscle fatigue and pain.](<https://www.ncbi.nlm.nih.gov/pubmed/19647494>)
* [Diminished pain tolerance with high sensory and affective ratings of pain and a negative internal affective state](<https://www.ncbi.nlm.nih.gov/pubmed/12595695?dopt=Abstract>)
* Higher risk of metabolic syndrome for women taking antipsychotics like [clozapine ](<https://www.ncbi.nlm.nih.gov/pubmed/24448899?dopt=Abstract>)
* [Intermediate response to antidepressant paroxetine](<https://www.ncbi.nlm.nih.gov/pubmed/18989660?dopt=Abstract>)
* [Increased susceptibility for cocaine dependence]( <https://www.ncbi.nlm.nih.gov/pubmed/18704099?dopt=Abstract>)
* [ 1.3X increased risk of breast cancer](<https://www.ncbi.nlm.nih.gov/pubmed/18194538?dopt=Abstract>)

**# What should I do about this?**

To improve cognition, users should avoid stress. Avoid moderate levels of exercise and practice pacing or monitoring to reduce muscle fatigue and pain. Consider medications other than clozapine and paroxetine, and moniter homocysteine levels. Users should also avoid cocaine. Users should be checked regularly for breast cancer and consider [drinking green tea](<https://www.ncbi.nlm.nih.gov/pubmed/19074205?dopt=Abstract>)

Medications indicated for use in treating COMT issues include: [Clonidine, BIA, Diethylstilbestrol, Dobutamine, Dopamine, Entacapone, Methyldopa, Micafungin, Nialamide, S-Adenosylmethionine, Testosterone Propionate, and Tolcapone.](http://www.uniprot.org/uniprot/P21964#pathology\_and\_biotech)

G158A (A;A)

**<function meter level="severe">**

**<efficiency level = "25%" >**

**<variant and population data>**

**# Severe Loss of Function**

the (A) substitution polymorphism changes the amino acid to a methionine. This alters the structure of the resultant enzyme such that its activity is only 25% of the wild type. As a result, A allele carriers have more dopamine in their prefrontal cortex

Worrier. Met, more exploratory, lower COMT enzymatic activity, therefore higher dopamine levels; lower pain threshold, enhanced vulnerability to stress, yet also more efficient at processing information under most conditions

For adolescents, the [AA genotype](<https://www.ncbi.nlm.nih.gov/pubmed/21059181>) is more common in CFS patients, and is also associated with POTS during tilt table testing.

[After a sustained moderate exercise, CFS patients showed greater COMT gene activation lasting from 0.5 to 48 hours. This correlates to muscle fatigue and pain.](<https://www.ncbi.nlm.nih.gov/pubmed/19647494>)

AA [systematically worse on all psychological and functional variables in fibromyalgia](<https://www.ncbi.nlm.nih.gov/pubmed/21895373?dopt=Abstract>)

AA[ 10.4% increase in homocysteine and increased risk of venous thrombosis](<https://www.ncbi.nlm.nih.gov/pubmed/18064318?dopt=Abstract>)

Higher risk of metabolic syndrome for women taking antipsychotics like [clozapine ](<https://www.ncbi.nlm.nih.gov/pubmed/24448899?dopt=Abstract>)

AA [ Better response to antidepressant paroxetine](<https://www.ncbi.nlm.nih.gov/pubmed/18989660?dopt=Abstract>)

AA[No increased risk of psychotic symptoms and schizophrenia when using cannabis](<https://www.ncbi.nlm.nih.gov/pubmed/15866551?dopt=Abstract>)

[The low enzyme activity 158Met allele or haplotypes containing this variant might have functional effects on dopamine-derived reward processes and cortical functions resulting in increased susceptibility for cocaine dependence]( https://www.ncbi.nlm.nih.gov/pubmed/18704099?dopt=Abstract)

AA [Greatly diminished pain tolerance with higher sensory and affective ratings of pain and a more negative internal affective state](<https://www.ncbi.nlm.nih.gov/pubmed/12595695?dopt=Abstract>)

Higher proportion of patients with chronic pain or pain sensitivity have AA [(78% vs 28% of the population)](<https://www.ncbi.nlm.nih.gov/pubmed/21120493?dopt=Abstract>)

**# What should I do about this?**

To relieve POTS, consider

Users should check homocysteine levels. If elevated, users may consider taking [folate]( https://medlineplus.gov/druginfo/natural/1017.html) to reduce the levels.

Medications indicated for use in treating COMT issues include: [Clonidine, BIA, Diethylstilbestrol, Dobutamine, Dopamine, Entacapone, Methyldopa, Micafungin, Nialamide, S-Adenosylmethionine, Testosterone Propionate, and Tolcapone.](http://www.uniprot.org/uniprot/P21964#pathology\_and\_biotech)

C62T (C;C)

**<function meter level="wildtype">**

**<variant and population data>**

**# Normal Function**

The COMT enzyme allows fully functional estrogen metabolic pathways, with no increase in a risk for endometrial or breast cancer.

**# What should I do about this?**

No therapies are medically indicated at the moment.

C62T (C;T)

**<function meter level="moderate risk">**

**<risk = "25%" >**

**<variant and population data>**

**# Moderate risk**

In estrogen metabolic pathways, the COMT enzyme is related to detoxification. The slightly impaired detoxification pathway may increase the risk for [endometrial ](<https://www.ncbi.nlm.nih.gov/pubmed/18324659?dopt=Abstract>) and breast cancer.

**# What should I do about this?**

* Do regular checks for endometrial and breast cancer.
* Check the level of estrogen, and consult with your doctor to reduce elevated levels
* [Drink green tea](<https://www.ncbi.nlm.nih.gov/pubmed/19074205?dopt=Abstract>)

Medications indicated for use in treating COMT issues include: [Clonidine, BIA, Diethylstilbestrol, Dobutamine, Dopamine, Entacapone, Methyldopa, Micafungin, Nialamide, S-Adenosylmethionine, Testosterone Propionate, and Tolcapone.](http://www.uniprot.org/uniprot/P21964#pathology\_and\_biotech)

C62T (T;T)

**<function meter level="high risk">**

**<risk = "25%" >**

**<variant and population data>**

**# High Risk**

In estrogen metabolic pathways, the COMT enzyme is related to detoxification. The TT genotype is 2.39X more common in endometrial cancer patients as compared to the general population. The impaired detoxification pathway may increase the risk for [endometrial ](<https://www.ncbi.nlm.nih.gov/pubmed/18324659?dopt=Abstract>) and breast cancer.

**# What should I do about this?**

* Do regular checks for endometrial and breast cancer.
* Check the level of estrogen, and consult with your doctor to reduce elevated levels
* [Drink green tea](<https://www.ncbi.nlm.nih.gov/pubmed/19074205?dopt=Abstract>)

Medications indicated for use in treating COMT issues include: [Clonidine, BIA, Diethylstilbestrol, Dobutamine, Dopamine, Entacapone, Methyldopa, Micafungin, Nialamide, S-Adenosylmethionine, Testosterone Propionate, and Tolcapone.](http://www.uniprot.org/uniprot/P21964#pathology\_and\_biotech)

**<symptoms>**

**<references>**

**<creator comment section>**

**What should I do about this?**

<symptoms pain, muscle fatigue, POTS, stress, problems with thinking or memory, brain fog post exertional malaise, sleep disorder>

D010146; D063806; C2721712; D040701; D008569; C2721712; D012893