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Research Article

The Role of Genetic Mutations on Gene MYT1 Polymorphism (rs2273455) in Bipolar & Borderline Personality Disorder

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Abstract:

Bipolar disorder is a mood disorder that can cause extreme mood swings: at times you may be extremely "high", euphoric, irritable or energetic. This is called an episode of madness. At other times, you may feel "down," sad, apathetic, or hopeless. Cyclothymic disorder or cyclothymia also includes hypomanic and depressive symptoms. But they are not as severe and prolonged as hypomanic or depressive episodes. These symptoms usually last for at least two years in adults and one year in children and adolescents.

Keywords: bipolar disorder; borderline personality disorder; bio psychological disorder; MYT1 gene; mutation

Introduction

An introduction to bipolar disorder and borderline personality disorder

Bipolar disorder is a mood disorder that can cause extreme mood swings: at times you may be extremely "high", euphoric, irritable or energetic. This is called an episode of madness. At other times, you may feel "down," sad, apathetic, or hopeless. This part is called depression. You may have depression and anxiety symptoms together. This is called a mixed part. Along with mood swings, bipolar disorder causes changes in behavior, energy levels, and activity levels. Bipolar disorder used to be called other names, including manic depression and depressive disorder [1].

There are three types of bipolar disorder: Bipolar I involves manic episodes that last at least 7 days or manic symptoms are so severe that you need immediate hospital care. Depressive episodes are also common. These often last at least two weeks. This type of bipolar disorder can include different parts [1].

Bipolar II disorder includes episodes of depression. But instead of full-blown manic episodes, there are hypomanic episodes. Hypomania is a milder version of mania [1].

Cyclothymic disorder or cyclothymia also includes hypomanic and depressive symptoms. But they are not as severe and prolonged as hypomanic or depressive episodes. These symptoms usually last for at least two years in adults and one year in children and adolescents. With either type, having four or more manic or depressive episodes in a year is called "rapid cycling" [1].

The exact cause of bipolar disorder is unknown. Several factors are likely to contribute to this disorder. They include your genetics, brain structure and function, and your environment. You are at higher risk for bipolar disorder if you have a close relative with it. Going through trauma or stressful life events may further increase this risk. Symptoms of bipolar disorder can vary. But it includes mood swings known as mood episodes: symptoms of an episode can be mania, feeling very high, high or euphoric, feeling jumpy or wired, being more active than usual, having a very short or very short temper. seem irritable, have racing thoughts and talk very fast, need less sleep, feel unusually important, talented, or powerful, do risky things that show poor judgment, such as eating and drinking too much, spending or giving away too much money, or reckless sex [2].

Symptoms of an episode of depression can include feelings of sadness, hopelessness and worthlessness, feeling alone or disconnected from others, speaking too quietly, feeling like you have nothing to say or have forgotten a lot, having low energy, sleeping too much, eating too much or too little, not being interested in your usual activities and not even being able to do simple things, thinking about death or suicide [2].

Symptoms of a mixed episode include both manic and depressive symptoms. For example, you may be very sad, empty, or hopeless, while at the same time having a lot of energy. Some people with bipolar disorder may have milder symptoms. For example, you may experience hypomania instead of mania. With hypomania, you may feel great and find that you can do a lot. You may not feel that anything is wrong. But your family and friends may

notice changes in your mood and activity level. They may notice that your behavior is unusual for you. After hypomania, you may experience severe depression [2].

Borderline personality disorder is a mental health disorder that affects the way you think and feel about yourself and others, causing problems in everyday life. This includes self-image issues, difficulty managing emotions and behavior, and a pattern of unstable relationship [2].

With borderline personality disorder, you have a strong fear of abandonment or instability and find it difficult to tolerate being alone. However, inappropriate anger, impulsiveness, and frequent mood swings may push others away, even if you want to have loving and lasting relationships. Borderline personality disorder usually begins in early adulthood. The condition appears to be worse in younger adulthood and may gradually improve with age. If you have borderline personality disorder, don't be discouraged. Many people with this disorder get better with treatment over time and can learn to live a fulfilling life [3].

Borderline personality disorder affects how you feel about yourself, how you relate to others, and how you behave [3].

Signs and symptoms may include:

Intense fear of abandonment, even going to extreme lengths to avoid actual separation or rejection, or imagining a pattern of intensely unstable relationships, such as idealizing someone at one point and then suddenly believing the person does not care enough or is cruel. Rapid changes in identity and self-image that include changing goals and values, and seeing yourself as bad or as if you don't exist at all [3].

Episodes of stress-related paranoia and disconnection from reality last from minutes to hours. Impulsive and risky behaviors, such as gambling, reckless driving, unsafe sex, binge eating or drug abuse, or successful sabotage by abruptly quitting a good job or ending a positive relationship. Threats of suicide or behavior or self-harm, often in response to fear of separation or rejection. Widespread mood swings lasting from hours to days, which can include extreme happiness, irritability, shame, or anxiety [3].

Constant feeling of emptiness

Inappropriate, intense anger, such as frequent loss of temper, sarcasm or bitterness, or physical aggression. As with other mental health disorders, the causes of borderline personality disorder are not fully understood. In addition to environmental factors—such as a history of child abuse or neglect—BPD may be associated with:

Genetics Some twin and family studies suggest that personality disorders may be inherited or strongly associated with other mental health disorders in family members [4].

Brain abnormalities: Some research has shown changes in certain areas of the brain that play a role in regulating emotions, impulsivity, and aggression. In addition, certain brain chemicals that help regulate mood, such as serotonin, may not function properly [4].

risk factors:

Certain factors related to personality development can increase the risk of developing borderline personality disorder. This includes: Hereditary predisposition: If someone close to you - your mother, father, brother or sister - has the same or a similar disorder, you may be at higher risk [4].

Stressful Childhood: Many people with this disorder report being sexually or physically abused or neglected as children.

Some people have lost or become estranged from a parent or close caregiver at a young age or have a parent or guardian through substance abuse or other mental health issues. Others have been subject to hostile conflict and unstable family relationships [4].

Complications of borderline personality disorder

Borderline personality disorder can affect many areas of your life. It can negatively affect intimate relationships, work, school, social activities, and self-image, resulting in:

Frequent job changes or loss

Failure to complete education

Several legal cases, such as prison time

Relationships full of conflict, marital stress or divorce

Self-injury, such as cuts or burns, and frequent hospitalizations

Involvement in abusive relationships

Unplanned pregnancies, sexually transmitted infections, motor vehicle accidents and physical altercations due to impulsive and high-risk behaviors, attempted or completed suicide.

In addition, you may have other mental health disorders such as: depression, alcohol or other substance abuse, anxiety disorders, appetite disorders, bipolar disorder, post-traumatic stress disorder (PTSD), attention deficit/hyperactivity disorder (ADHD), other personality disorders [5,6].

Materials and Methods

In this study, blood samples were taken from 40 people suffering from bipolar disorder, 40 of whom were female and 10 of whom were male and 30 people Health, and with their written consent, molecular genetic testing was performed to check the changes in these genes. Individual information (such as age, gender, medical history) was recorded. The subjects were selected after final diagnosis by a child and adolescent psychiatrist according to DSM-V criteria, signed a written consent for blood sampling, and filled out an interview form designed to understand the contribution of genetic influence. 2 cc of blood was taken from each person and in Falcons containing EDTA as an anticoagulant; It was poured and then the falcons were gently shaken to mix to prevent blood clots from forming. Finally, the samples were stored in a -20 ° C freezer to extract DNA from blood. Saturated salt method was used to extract genomic DNA from whole blood samples. After DNA extraction, its concentration must be determined so that a certain concentration of DNA is subjected to the PCR reaction. In this case, the concentration of DNA used is constantly maintained. Two methods are used to determine the concentration and quality of the extracted DNA.

1- Spectrophotometric method

2- Electrophoresis method

Spectrophotometry is a quantitative method and electrophoresis is a qualitative method. Molecular RFLP-PCR technique was used for this study. This technique is commonly used to examine different alleles of a gene in a population. The sequence diversity of the respective gene alleles creates different cleavage sites for the restriction enzymes, resulting in fragments of different lengths. Depending on the length of the DNA fragments obtained from the cut, the change in nucleotides can be detected. One of the advantages of this method is that it is fast and does not require a probe.

Gene	Primer name	Primer Sequenc (5' to 3')	Length (bp)	TM (°C)	Product length(bp)
MYT1	Forward Reverse	AGTCAGAATAAGAGGTGGCG TAATGATCATGGCAGCGTCG	20 20	64	187

Table 1: Specifications of primers used in this study.

Genotype determination: MYT1

To determine the rs2273455 bi-allelic polymorphism, the intron 2 region was amplified by PCR. The characteristics of the primers are given in (Table 2-5), the PCR reaction concentration in (Table 2-6), and the PCR steps in (Table 2-7). PCR products were isolated on 2% agarose gel. Alleles were identified as 187 bp band after staining the gel with safe stain.

Investigation of MYT1 polymorphism (rs2273455) by RFLP method

After PCR reaction using the mentioned primers according to the optimal PCR conditions, a fragment with a length of 187 bp was amplified. To ensure the performance of the PCR reaction for all samples, their PCR products were electrophoresed on 2% agarose gel and stained with Safe stain. PCR products were then cut using Nla III enzyme according to the following steps:

First, all the materials needed for the RFLP reaction, which include double ionized distilled water, a specific buffer of Nla III enzyme, Nla III enzyme, are poured into microtubes containing the PCR product. Then place the microtubes in a pan at 37 ° C for 16 hours. The concentrations of the materials used to break down the Nla III enzyme site are shown in Table 2.

After this period, some of the product containing the enzyme was cut, loaded on agarose gel and electrophoresed. And in the last step, that photo was taken.

Nla III enzyme and its cleavage site

Nla III enzyme is a highly functional restriction enzyme and its cleavage site is as follows:

5 ...' G T T C ... 3'

3 '... C A A G ... 5'

The final volume in volume 30µl	Reaction material
12/5 µl	ddH2O
2 µl	Buffer(10x)
0.5 µl	*Nla* III
15 µl	PCR Product

Table 2: Concentration of components used to break down the Nla III enzyme site.

AGAAACTCTTCTCCGGTTACAACAAGTGGTCCCGACCCGTGGCCAACATCTCGGACGTGG
TCCTCGTCCG

CTTCGGCCTGTCCATCGCTCAGCTCATTGA[CGTGGTAGGTGAGGGCGTGGCCATCGTGC
ACTGTGACTGA

GGTCGCCCTGCAAGG]AGCACAGGGGTCTGGGTGGGCAGAGGGGACACAGCCATCAACA
CTCCCCGTGGCT

GTGAGTGTCCGGCCCGGGCTGGTACGTCAGAACGACAGCCACCAGCTCTGCCCCGCCTG
AGCCCCAGCCA

Figure 1: The rs2273455 primer binding site in the MYT1 gene and the Nla III enzyme identification and cleavage site: Arrow indicates the primer forward binding site; Has been).

Results

PCR-RFLP technique was used to investigate this polymorphism. The results of electrophoresis of PCR products related to amplification of rs2273455 polymorphism using appropriate specific primers and fragments of amplification of this polymorphism are shown in Figure 3. PCR fragments contain fragments of length 187 bp and fragments from RFLP-PCR with the effect of Nla III restriction enzyme in the presence of T allele at the enzyme identification site located at the site of the relevant polymorphism; It is cut into two pieces with lengths of 100 and 150 bp and in the presence of C allele it is cut into one piece 250 bp and in the presence of CT allele it is cut into three pieces with lengths of 250, 100 and 150 bp.

In this study, the association of MYT1 rs2273455 polymorphism with RFLP technique was investigated. In this regard, 40 people with Bipolar disorder and 50 healthy people without a history of Bipolar disorder as a control group in the northwestern region of Iran were studied. The characteristics of the sick and control subjects are given in Tables 3a and 3b. The genotypic distribution of rs2273455 polymorphism was calculated for patients with Bipolar disorder and the control group.

Based on statistical calculations and genotypic distribution between patients and controls, no correlation was found because the calculated P-value for different genotypes is greater than 0.05, which means that the hypothesis of the association of this polymorphism with Bipolar disorder is rejected (0.5 = P-value). The genotypic frequency distribution of rs2273455 polymorphism of MYT1 gene was calculated in the whole patient and control groups.

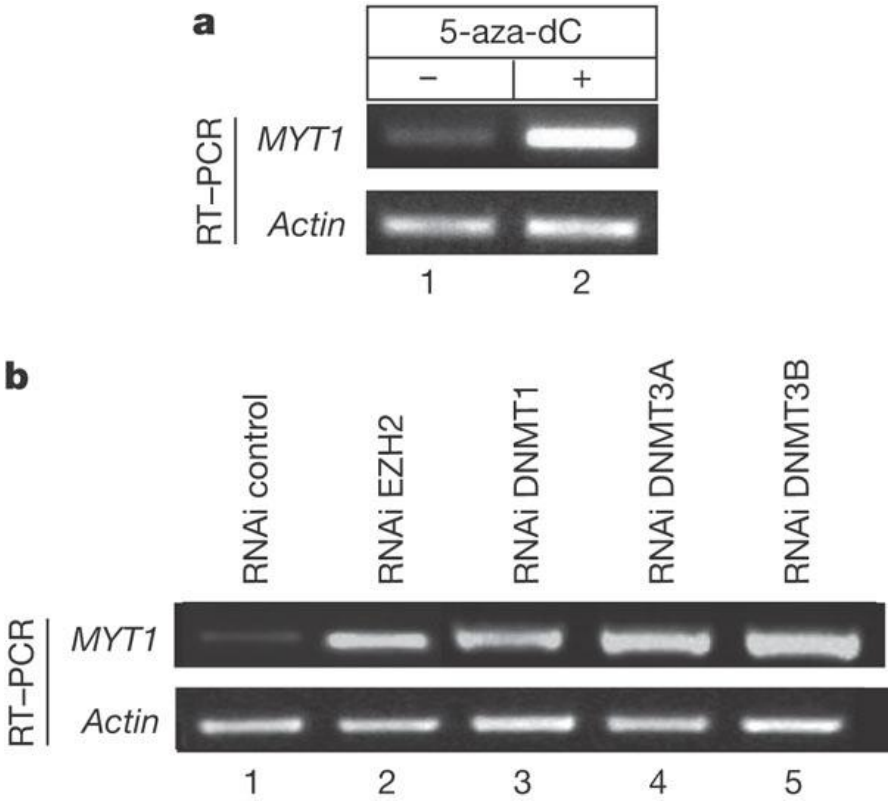

Figure 2: Image of binding pattern of MYT1 gene in gel electrophoresis by RT-PCR technique.

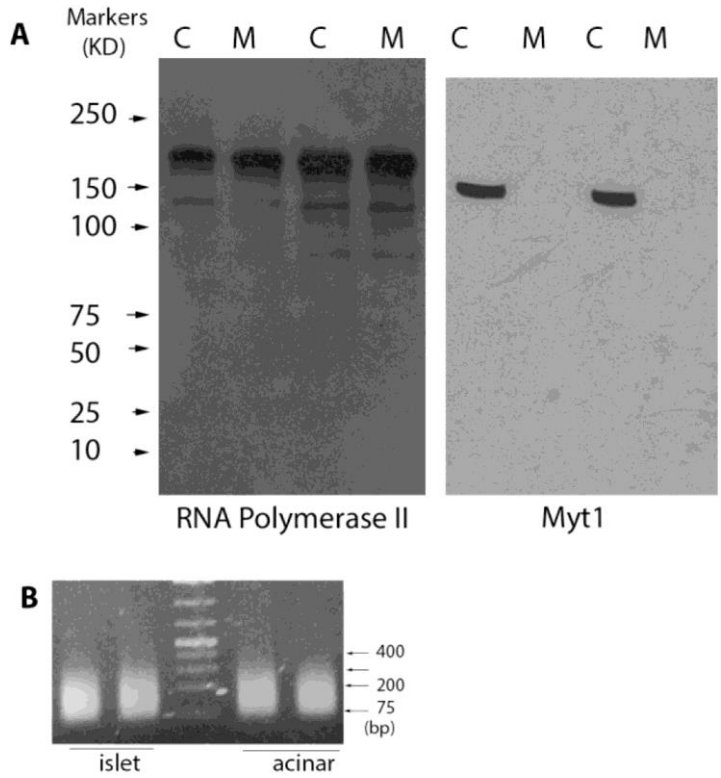

Figure 2: Image of binding pattern of MYT1 gene in gel electrophoresis by RT-PCR technique and detection of nucleotide base pairs.

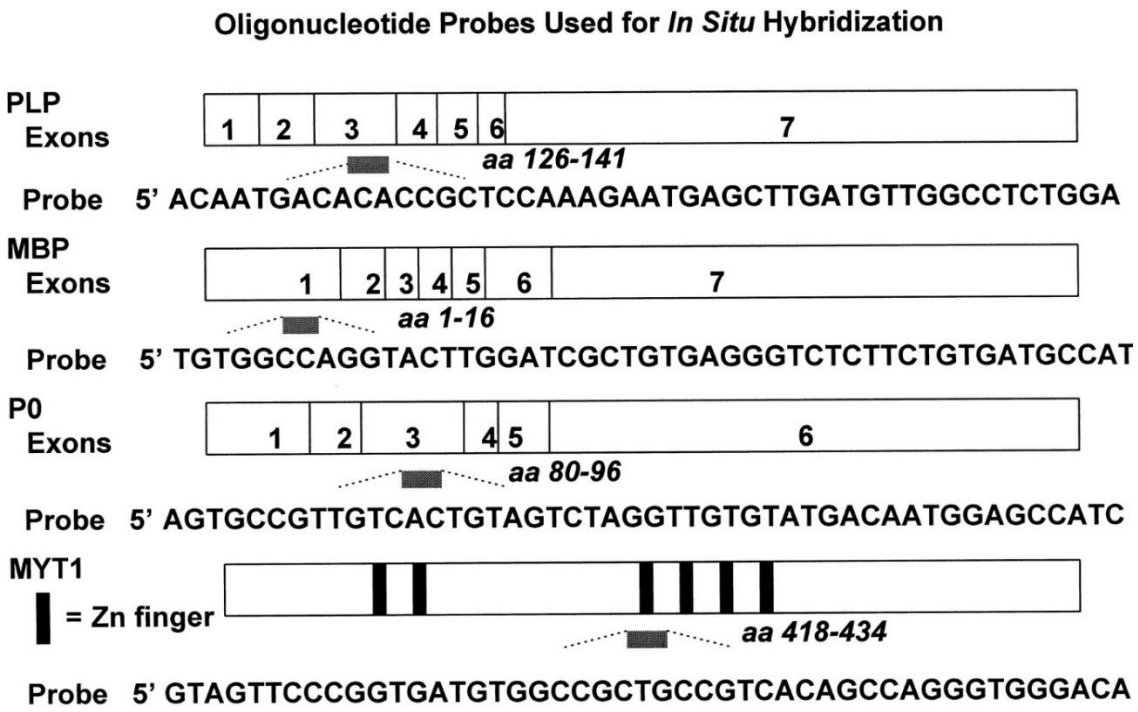

Figure 3: Schematic of the nucleotide sequence of MYT1 gene probes.

Discussion

Bipolar disorder is a mood disorder that can cause extreme mood swings: at times you may be extremely "high", euphoric, irritable or energetic. This is called an episode of madness. At other times, you may feel "down," sad, apathetic, or hopeless. This part is called depression. You may have depression and anxiety symptoms together. Cyclothymic disorder or cyclothymia also includes hypomanic and depressive symptoms. But they are not as severe and prolonged as hypomanic or depressive episodes. These symptoms usually last for at least two years in adults and one year in children and adolescents. With either type, having four or more manic or depressive episodes in a year is called "rapid cycling. Borderline personality disorder is a mental health disorder that affects the way you think and feel about yourself and others, causing problems in everyday life. This includes self-image issues, difficulty managing emotions and behavior, and a pattern of unstable relationships [7-9].

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