Journal of Behavioral and Brain Science, 2020, 10, 531-536
https://www.scirp.org/journal/jbbs
ISSN Online: 2160-5874
ISSN Print: 2160-5866

BDNF Gene Frequency Distribution in Li and Han Ethnic Groups in Hainan Province and Its Comparison with Other Countries and Regions

Min Guo[1], Juncheng Guo[2], Yunsuo Gao[1], Xiaodan Wang[3*]

[1]Hainan General Hospital, Haikou, China
[2]Central South University Xiangya School of Medical Affiliated Haikou Hospital, Haikou, China
[3]School of Public Health, Hainan Medical University, Haikou, China
Email: *g2002m@163.com

How to cite this paper: Guo, M., Guo, J.C., Gao, Y.S. and Wang, X.D. (2020) BDNF Gene Frequency Distribution in Li and Han Ethnic Groups in Hainan Province and Its Comparison with Other Countries and Regions. *Journal of Behavioral and Brain Science*, **10**, 531-536.
https://doi.org/10.4236/jbbs.2020.1012032

Received: October 28, 2020
Accepted: December 4, 2020
Published: December 7, 2020

Abstract

Objective: To explore the distribution characteristics of BDNF gene frequency in Li and Han nationalities in Hainan province. **Methods:** In June 2018-2019 and march to the people's hospital of Hainan province health volunteers, 152 cases (Li 80, Han, 72), the application of polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) method to detect the polymorphism of BDNF gene (rs6265), and compared with other countries and regions of ethnic comparison between BDNF gene frequency distribution. **Results:** No statistical difference was found in rs6265 genotype distribution of BDNF gene in Li and Han ethnic groups (P = 0.3358, P = 0.0892, P = 0.1549). Comparison of BDNF allele frequency between Li and other ethnic groups showed statistically significant differences with other ethnic groups in China and Europe (P = 0.0384, P = 0.0000), but not statistically significant differences with Japan (P = 0.1164). **Conclusion:** BDNF gene (rs6265) has polymorphism in both Li and Han ethnic groups in Hainan Province. Compared with ethnic groups in other countries and regions, the polymorphism distribution is ethnically different.

Keywords

BDNF Gene, The PCR-RFLP, Alleles, Genotype

1. Introduction

Brain-derived neum promoter factor gene (BDNF) located on chromosome LLPL3 encodes the small-molecule dimer protein BDNF(nerve growth factor), which is associated with neuronal growth, survival, and the construction of

functional synapses [1] [2]. It is also an important transcriptional suppressor gene, MeCP2, that ACTS as a target gene for central nervous system function [3] [4] [5]. Therefore, it is an important candidate gene for the study of the pathogenesis of neuropsychiatric diseases. At present, there are few studies on BDNF gene in Hainan province, and the distribution law and characteristics of BDNF gene polymorphism in Chinese population are still unclear. In this study, BDNF polymorphism locus RS6265 was selected to analyze the distribution of alleles and genotype frequency in Li and Han ethnic populations in Hainan province, and compared with ethnic populations in other countries and regions, aiming to provide reference data for genetic research on BDNF gene-related diseases.

2. Objects and Methods

2.1. Objects

From June 2018 to March 2019, 152 volunteers underwent physical examination in Hainan Provincial People's Hospital. All the subjects were healthy individuals without blood relationship. Among them, 80 were from the Li ethnic group, 40 males and 40 females, aged 23 - 40. There were 72 Han patients, 40 males and 32 females, aged 24 - 40. Previously healthy, no genetic disease, no neurological disease, no organic disease, no history of mental illness. This study was approved by the Ethics Committee of Hainan Provincial People's Hospital and supervised by the Ethics Committee of Hainan Provincial People's Hospital. The approval date is January 3, 2018, and the project was approved by the Ethics Committee of Hainan People's Hospital with the number 2018-06.

All subjects obtained informed consent from themselves and their family members and signed informed consent forms.

2.2. Methods (Gene Polymorphism Detection)

All subjects received 5 ml of fasting blood from the elbow vein in the morning. EDTA was sent to the central laboratory of Hainan People's Hospital for freezing at −20˚C. Genomic DNA was extracted with whole blood genomic DNA extraction kit (OMEGA, USA) centrifuge column method, and the concentration and purity detection met the requirements of PCR amplification. Primer Premier5.0 Primer design software was used to design PCR primers for BDNF gene rs6265 (**Table 1**). The primers were synthesized by Shanghai Shenggong Bio-engineering Technology Services Co.LTD.PCR amplification reaction system was 50 L, containing genomic DNA 1 L, a pair of primers 1 L (10 M), PFU enzyme 0.25 L (5 U/L), 10 × Buffer 5 L (200 mM TrisHCl, pH 8.8; 100 mm KCl; 20 mm MgS04; 160 mm (NH4) 2 s04; 1% Triton, 1 mg/mL BSA, dNTPs 1 L (10 mM), deionized water 40.75 L. PCR amplification cycle parameters: pre-denaturation at 98˚C for 3 minutes, denaturation at 95˚C for 1 minute, annealing at 60˚C for 45 seconds, elongation at 72˚C for 55 seconds, a total of 35 cycles, and elongation at 72˚C for 8 minutes. PCR kit was purchased from Shanghai Jierui Bioengineering Co., LTD. The PCR products were sent to Shanghai Sangon Biotechnology Services Co., Ltd. for sequencing.

Table 1. PCR primer sequences.

SNP		Sequence
The BDNF gene rs6265	Forward:	5'-TTTCTCCCTACAGTTCCACCAG-3'
	Reverse:	5'-CTCCAAAGGCACTTGACTACTG-3'

2.3. Statistical Analysis

1) H-W software was used to test the genetic balance coincidence of Hardy-Weinberg law.

2) SPSS15.0 statistical software was used for statistical analysis of the data: pipiro-Wilkt risk test was used for normal distribution test of the measurement data; T-test was used for group comparison of normal distribution data, and rank sum test was used for non-normal distribution data. Analysis of variance (ANOVA) was used for multiple questions comparison. The composition ratio was compared by using ×2 test. The correlation factors were analyzed by Pearson correlation analysis and partial correlation analysis.

3. Results

Genotype and Allele Frequency Distribution of BDNF Gene (rs6265) in Li and Han Ethnic Groups in Hainan Province

The hardy-weinberg equilibrium test was carried out by goodness-fit test, and the results showed that the distribution of BDNF genotypes in the subjects was in line with the hardy-weinberg equilibrium (all $P > 0.05$). The samples in this study were random and representative of the population. The rs6265 locus of BDNF gene in Li and Han nationalities was analyzed, and the frequency distribution of rs6265 gene in both groups was consistent with h-w balance (all $P > 0.05$). No statistical difference was found in genotype distribution of BDNF gene RS6265 between Li and Han ethnic groups in Hainan province, as shown in **Table 2**.

The BDNF allele frequency among Li population was compared with that of other ethnic groups. The results were shown in **Table 3**, which showed statistical significance with other ethnic groups in China and Europe, but no statistical significance with that of Japan.

4. Discussion

BDNF is the second neurotrophic factor discovered after nerve growth factor (NGF). The precursor has 247 amino acid residues, which are processed after translation to produce a mature basic protein composed of 119 amino acid residues. There are 3 pairs of disulfide bonds in the chain and they exist as dimers in the body. Neurotrophic factor BDNF is most abundant in the body, is mainly expressed in the cerebral cortex, hippocampus, striatum, etc., plays an important role in brain development, can affect the growth of neurons of the axial and the connection, mediated [7] the proliferation, differentiation and survival of neurons in the central nervous system, the synthesis of BDNF mainly in neurons, by

Table 2. Comparison of genotype and allele frequency distribution of BDNF gene (RS6265) in Li and Han ethnic groups in Hainan [N (%)].

SNP	Han group (n = 72)	Li group (n = 80)	X^2 (*P*)	*OR* (95% CI)
rs6265				
GG	38 (52.78)	33 (41.25)	Ref.	
GA	28 (38.89)	34 (42.5)	0.926 (0.3358)	1.398 (0.706 - 2.771)
AA	6 (8.33)	13 (16.25)	2.888 (0.0892)	2.495 (0.852 - 7.302)
GA + AA	34 (47.22)	47 (58.75)	2.023 (0.1549)	1.592 (0.838 - 3.025)
G	55 (72.37)	48 (62.34)	Ref.	
A	21 (26.67)	29 (37.66)	1.749 (0.1860)	1.582 (0.800 - 3.130)

SNP: Single Nucleotide Polymorphisms; OR: Odds Ratio; 95% CI: 95% confidence intervals; Ref: Reference.

Table 3. Comparison of BDNF allele frequencies between different ethnic groups and Li populations.

The crowd	Allele frequency		*Z* (*P*)
rs6265	A	G	
Li people	0.377	0.623	Ref.
Chinese [6]	0.495	0.505	2.071 (0.0384)
Japanese [6]	0.337	0.663	1.571 (0.1164)
European [6]	0.175	0.825	5.680 (0.0000)

the anterograde axoplasmic transport to the axon endings, released mainly through the high affinity receptor tyrosine protein kinase B (TrkB) ACTS on the target cells play a role, as in hippocampus BDNF mRNA content in model NGF mRNA in 20 to 30 times higher. In addition, BDNF can also be secreted by target cells acting on neurons, and reversely nutritive neurons. For example, BDNF appears more at the distal end of the nerve fracture after nerve injury in the peripheral nervous system. BDNF content in human plasma is very high, and some regions with weak blood-brain barrier, such as hypothalamus, may have BDNF passing through the blood-brain barrier. The mutual sensitivity between peripheral blood and nerve center BDNF cannot be ruled out. It is also necessary to explore whether the change of BDNF content in peripheral blood can be used as a direct indicator of anti-mental diseases. Therefore, it is widely used in the localization and linkage and association analysis of disease susceptibility genes. However, genotype and allele frequency vary greatly among different RACES, and allele polymorphisms vary greatly among different populations within the same race. Therefore, obtaining the genetic parameters of various polymorphic loci in different populations and understanding the distribution characteristics of gene polymorphisms in Li population in Hainan province will be helpful for the localization and genetic analysis of disease susceptibility genes in The Chinese population. This study shows that BDNF (rs6265) polymorphism is thought to interfere with active-dependent BDNF secretion, thus improving synaptic

strength, which may be a means to regulate specific synaptic connections [8] [9] [10]. Compared with patients with GG genotype in BDNF (rs6265), the risk of gene mutation at rs6265 of genotype (AG + AA) was increased, and BDNF expression was decreased [11]. In this study, it was found that THE AA genotype /A allele in BDNF (rs6265) was related to the differences between Li and Han populations, and was the main factor for the differences in BDNF genes between Li and Han populations. Genetically, gene flow between Li and Han in Hainan island is limited, and the genetic diversity of Li is lower than that of Han [12].

5. Limitation

Through the changes of PTSD in physiology, behavior, psychology and other aspects, we can explore the differences of BDNF gene between Li and Han populations in Hainan province. However, up to now, we have not been able to use a single genetics to explain the BDNF gene differences among Hainan nationalities. This may be because we have not yet identified the key mechanism of action, or it may itself be a combination of multiple mechanisms. By comparing allelic differences and polymorphisms of BNNF gene between Han and Li, we can better understand the genetic differences between Li and Han, and provide genetic data for anthropological, forensic identification and research on gene association between Li and Han.

Acknowledgements

This study was supported by Hainan Provincial key technology project (ZDYF-2018227) and national natural science foundation of China (81760255).

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Saito, Y., Nakao, K., Itoh, H., *et al.* (1989) Brain Natriuretic Peptide Is a Novel Cardiac Hormone. *Biochemical and Biophysical Research Communications*, **158**, 360-368. https://doi.org/10.1016/S0006-291X(89)80056-7

[2] Ballermann, B.J. and Brenner, B.M. (1986) George E. Brown Memorial Lecture. Role of Atrial Peptides in Body Fluid Homeostasis. *Circulation Research*, **58**, 619-630. https://doi.org/10.1161/01.RES.58.5.619

[3] Tsutamoto, T., Wada A., Maeda, K., Hisanaga, T., *et al.* (1997) Attenuation of Compensation of Endogenous Cardiac Natriuretic Peptide System in Chronic Heart Failure: Prognostic Role of Plasma Brain Natriuretic Peptide Concentration in Patients with Chronic Symptomatic Left Ventricular Dysfunction. *Circulation*, **96**, 509-516. https://doi.org/10.1161/01.CIR.96.2.509

[4] Christian, H. (2004) Essential Biochemistry and Physiology of (NT-pro) BNP. *European Journal of Heart Failure*, **6**, 257-260. https://doi.org/10.1016/j.ejheart.2003.12.015

[5] Keating C, Tilbrook, A.J., Rossell, S.L., Enticott, P.G. and Fitzgerald, P.B. (2012)

Reward Processing in Anorexia Nervosa. *Neuropsychologia*, **50**, 567-575. https://doi.org/10.1016/j.neuropsychologia.2012.01.036

[6] Nees, F., Witt, S.H., Dinu-Biringer, R., Lourdusamy, A., Tzschoppe, J., *et al.* (2015) BDNF Val66Met and Reward-Related Brain Function in Adolescents: Role for Early Alcohol Consumption. *Alcohol*, **49**, 103-110. https://doi.org/10.1016/j.alcohol.2014.12.004

[7] Stratta, P., Sanita, P., *et al.* (2016) Clinical Correlates of Plasma Brain-Derived Neurotrophic Factor in Post-Traumatic Stress Disorder Spectrum after a Natural Disaster. *Psychiatry Research*, **244**, 165-170. https://doi.org/10.1016/j.psychres.2016.07.019

[8] Karnik, M.S., Wang, .L, Barch, D.M., *et al.* (2010) BDNF Polymorphism rs6265 and Hippocampal Structure and Memory Performance in Healthy Control Subjects. *Psychiatry Research*, **178**, 425-429. https://doi.org/10.1016/j.psychres.2009.09.008

[9] Zhang, L., Benedek, D.M., Fullerton, C.S., *et al.* (2014) PTSD Risk Is Associated with BDNF Val66Met and BDNF Overexpression. *Molecular Psychiatry*, **19**, 8-10. https://doi.org/10.1038/mp.2012.180

[10] Zivadinov, R., Weinstock-Guttman, B., Benedict, R., *et al.* (2007) Preservation of Gray Matter Volume in Multiple Sclerosis Patients with the Met Allele of the rs6265 (Val66Met) SNP of Brain-Derived Neurotrophic Factor. *Human Molecular Genetics*, **16**, 2659-2668. https://doi.org/10.1093/hmg/ddm189

[11] Zakharyan, R. and Boyajyan, A. (2014) Brain-Derived Neurotrophic Factor Blood Levels Are Decreased in Schizophrenia Patients and Associate with rs6265 Genotypes. *Clinical Biochemistry*, **47**, 1052-1055. https://doi.org/10.1016/j.clinbiochem.2014.03.021

[12] Song, M.Y., Wang, Z., Zhang, Y.Q., *et al.* (2019) Forensic Characteristics and Phylogenetic Analysis of Both Y-STR and Y-SNP in the Li and Han Ethnic Groups from Hainan Island of China. *Forensic Science International: Genetics*, **39**, e14-e20.