Associations Between Gene Polymorphisms and Psychological Stress in the Guangxi Minority Region of China

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To investigate whether there is an association between gene polymorphisms, genetic and environmental interactions, and psychological stress reactivity in Chinese subjects living in the Guangxi minority region.

This cross-sectional study enrolled subjects older than 18 years, living in Nandan county, Guangxi minority region, China for at least 1 year. All participants were healthy, without any mental diseases, and were able to communicate. Eligible participants were randomly selected. The Life Event Scale Questionnaire, Simplified Coping Style Questionnaire, and Social Support Rating Scale were used to measure the physiological stress, coping style, and social support, respectively, in individuals.

A total of 600 participants were recruited. A decreased risk of psychological stress was only found in TT of NPSR1 (rs324981): A allele carriers *vs.* TT genotype (OR 1.64, 95% CI 1.11, 2.42), and AT genotype *vs.* TT genotype (OR 1.76, 95% CI 1.17, 2.65). The overall coping style was positively associated with psychological stress, and no significant interactions between genetics and environment were found.

We found that the NPSR1 (rs324981) T/T genotype decreased the risk of psychological stress, while the overall coping style was a risk factor for psychological stress. However, there was no interactive effects of genes and environment on psychological stress. Our findings will improve understanding of the biological basis underlying psychological stress if the results can be replicated in further research.

MeSH Keywords: **Polymorphism, Genetic • Polymorphism, Single Nucleotide • Stress, Psychological**

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Background

Psychological stress is a complex reaction that occurs when an individual feels threats or challenges from the environment. It is generally considered as a result of the interaction between humans and the environment and is triggered by multiple complex factors [1]. In the early 1930s, Selye suggested that moderate psychological stress is not harmful [2]. However, excessive psychosocial stress beyond an individual's normal level of tolerance or physiological function can lead to physical harm. In recent decades, the roles of genetic factors in psychological and behavioral reactions have drawn worldwide attention. Twin studies and family-based studies have demonstrated the key role of genetic factors in psychological and behavioral reactions [3–5]. Mental health is recognized as a worldwide problem and the global cost of mental illness has increased rapidly in recent years. People belonging to ethnic minority groups in China may encounter more social conflicts than do people in the majority Han ethnic group; therefore, more research is required on this topic. Due to the unique cultural and traditional background, Nandan county of Guagnxi Province, located in southern China, was selected for this research. The main ethnic groups are BaikuYao, Zhuang, and Han. No previous study has investigated the association between gene polymorphisms and psychological stress in Guangxi Province, China.

The hypothalamic-pituitary-adrenocortical (HPA) axis was the first identified potential biological mechanism for psychological stress and is involved in the regulation of the psychological reaction [6–8]. Catechol-O-methyltransferase (COMT) is the major enzyme involved in the breakdown of the catecholamine, dopamine, and noradrenaline. Collip et al. observed that patients with the Met/Met genotype of COMT Val108/158Met showed significantly more psychotic and affective reactivity to stress in comparison to those with the Val/Met and Val/Val genotypes [9]. FK506-binding protein 5 (FKBP5) is a known glucocorticoid receptor (GR) co-chaperone, and is mainly involved in physiological processes such as binding to a nuclear receptor as a complex chaperone, modulating calcium release channels, and activating protein kinase [10,11]. FKBP5 is firmly established as a crucial factor in stress-related psychiatric diseases [12–14]. Lessard et al. discovered that FKBP5 (rs1360780) is associated with chronic stress-related disease among adults [15]. A recent Japanese study also demonstrated the effect of FKBP5 (rs1360780) on modulating HPA axis reactivity and expression of glucocorticoids, which indicated the potential association between FKBP5 (rs1360780) and chronic stress-related diseases [16]. A recent meta-analysis study reported that FKBP5 (rs3800373) and (rs1360780) are associated with depression and post-traumatic stress disorder (PTSD) [17]. Neuropeptide S (NPS), a neuropeptide discovered in 2002, was recently reported to be modulator of arousal and anxiety [18]. Furthermore, the genetic locus of heat

shock protein (HSP) and the expression of HSP are reported to be associated with stress-related diseases. In a case-control study, HSP90B1 (rs17034977) showed a significant association with bipolar disorder [19] and endoplasmic reticulum (ER) stress [20]. HSP90AA2 is a variant amino acid of HSP90, and is located at 11p14.1 of chromosome 11, which is associated with various psychological diseases [21]. In summary, these genes may be associated with many psychosocial diseases. Thus, the present study assessed the association between 11 tagged SNPs of 5 genes and psychological stress reactivity in people living in a Guangxi minority region of China.

Material and Methods

Study design and study participants

During July and August of 2015, this cross-sectional study enrolled subjects who were older than 18 years and had lived in Nandan county, Guangxi minority region, China for at least 1 year. Four villages were randomly selected. Baseline characteristics were also recorded, including sex (male/female), age, ethnicity, education (<6 years, 6–9 years, ≥9 year), monthly family income (0–499, 500–999, ≥1000 RMB), and the number of family members (1–3, 4–6, ≥7). All the participants were healthy, without any mental diseases, and could communicate. A total of 600 participants were recruited in the study, with average age of 49.3±15.3 years, of whom 227 (37.8%) were males and 373 (62.2%) were females. There are 186 Han Chinese (31.0%), 200 Zhuang Chinese (33.3%), and 193 (32.2%) BaikuYao Chinese. Nearly half of the total population had 6–9 years of education (40.8%), and the majority of them were married (86.0%), had a monthly family income of 0–499 RMB (67.0%), and 4–6 family members (68.2%) (Table 1).

Evaluation of physiological stress, coping style, and social support

All participants were personally interviewed by health personnel from the local county hospital who had received standardized training in performing face-to-face interviews. All participants were interviewed after signing written informed consent, and those who could not read the questionnaire were assisted by the interviewer. The completeness of the questionnaire was confirmed by interviewers, and questionnaires with more than 5% missing data were excluded as invalid.

The Life Event Scale (LES) questionnaire (a=0.64–0.89), which was designed specifically for Chinese, was used to evaluate the physiological stress in this study population [22]. A total of 48 common life events are measured in the LES. The participants recorded the relevant events that happened in the past year and rated each event regarding the extent of influence (5

Table 1. Baseline characteristics of 600 participants in a Chinese cross-sectional study.

No. of individuals	600	
Ethnicity		
Han	186	(32.0%)
Zhuang	200	(33.3%)
BaikuYao	193	(32.2%)
others	21	(3.5%)
Sex		
Male	227	(37.8%)
Female	373	(62.2%)
Education		
<6 years	185	(30.8%)
6–9 years	245	(40.8%)
≥9 years	170	(28.4%)
Monthly family income (RMB)		
0–499	402	(67.0%)
500–999	117	(19.5%)
≥1000	81	(13.5%)
Marital status		
Single	28	(4.8%)
Married	516	(86.0%)
Divorced or widowed	56	(9.2%)
Family member		
1–3	102	(17.0%)
4–6	409	(68.2%)
≥7	89	(14.8%)

scales, range 0–4), and the duration of influence (4 scales, range 1–4). The duration of influence was classified into 4 groups: within 3 months, 6 months, 12 months, and >12 months, with higher scores indicating more physiological stress. In China, a total score higher than or equal to 20 (≥20) was defined as having physiological stress.

The Simplified Coping Style Questionnaire (SCSQ) [23], consisted of positive and negative coping dimensions, was designed by Yaning Xie to evaluate coping style in Chinese; it is a self-rating scale in which a total of 20 items are measured, including positive coping (range 1–12, a=0.89) and negative coping (range 13–20, a=0.78). Multilevel scoring was used for each coping (range 0–3), and the results of the SCSQ are the overall positive and negative coping scores. Higher scores indicate higher frequencies of relevant coping.

The Social Support Rating Scale (SSRS) [24] was designed by Shuiyuan Xiao based on the Interview Schedule for Social Interaction (ISSI) [25] and the Social Support Questionnaire (SSQ) [26]. Designed for use in China, the SSRS measures 3

domains of social support: objective support (3 items), subjective support (4 items), and social support utilization (3 items). A higher total SSRS score shows stronger social support. The internal consistency of the total scale and subscales is over 0.825 [27].

Genotypes analysis

Fasting blood samples were collected in the morning. About 5 ml of venous blood was drawn from each patient, of which 2 ml was stored at −80°C with anticoagulation EDTA for DNA extraction. The serum of the rest of the 3-ml venous blood samples was separated by centrifuging at 3500 rpm for 5 min and used for biochemical profile measurement.

Single-nucleotide polymorphisms (SNPs) of COMT, NPSR1, HSP90B1, HSP90AA, and FKBP5 genes were selected using the linkage disequilibrium structure of the gene in HapMap database (*http//www.hapmap.org*) and the parameters r^2 >0.80 and MAF >0.10 [28]. The algorithm of de Bakker implemented in HaploView 4.0 software (Daly Lab, Broad Institute, Cambridge, MA) was then used to select tagged SNPs for the target block in each gene [29]. The population was set as CHB (Han Chinese in Beijing, China). Eleven tagged SNPs were selected and genotyped using the improved multiplex ligase detection reaction (iMLDR). The 11 tagged SNPs were: rs6267, rs769224, and rs4680 of COMT; rs12673132, rs6947841, rs324981, and rs6972158 of NPSR1; rs17034977 of HSP90B1; rs2726836 of HSP90AA2; and rs1360780 and rs3800373 of FKBP5.

Statistical analysis

The distribution of genotypes was compared between positive and negative psychological stress (Table 2) using goodness-of-fit to the Hardy-Weinberg equilibrium (HWE). Genotype distributions of the SNPs COMT (rs769224) and NPSR1 (rs12673132) were not in agreement with HWE (P<0.05). Bonferroni correction was applied to make the adjustment to reach agreement. Other genotype distributions were all in agreement with HWE (P>0.05). In the second step, univariate logistic regression and hierarchical regression were used in binary logistic regression analysis. We used univariate logistic regression in SPSS 17.0 (SPSS Inc; Chicago, IL) to assess the additive genetic model, recessive genetic model, dominant genetic model, and codominant genetic model. The strength of the association between SNPs and the risk of having psychological stress events was estimated with the odds ratio (OR) with 95% confidence intervals (CIs) (P<0.05). We then used hierarchical regression analysis to assess the association between psychological stress and genes (P<0.05), total score of support and coping, and the gene-environment interaction, with gender and race included as a covariate. The study was approved by the Regional Ethics Committee of Guangxi Medical University in China.

Table 2. Genotype analyses for polymorphisms in eleven genes in psychological stress in Southern China.

Gene	Marker	Genotype		
COMT	rs4680	GG	GA	AA
	Positive	185 (63.4)	97 (33.2)	10 (3.4)
	Negative	200 (65.2)	94 (30.6)	13 (4.2)
COMT	rs6267	GG	GT	TT
	Positive	260 (88.8)	32 (10.9)	1 (0.3)
	Negative	260 (84.7)	45 (14.7)	2 (0.6)
COMT	rs769224	GG	GA	AA
	Positive	269 (91.8)	24 (8.2)	0 (0.0)
	Negative	287 (93.5)	206.5)	0 (0.0)
NPSR1	rs12673132	GG	GA	AA
	Positive	145 (49.5)	118 (40.3)	30 (10.2)
	Negative	160 (52.1)	108 (35.2)	39 (12.7)
NPSR1	rs6947841	CC	CT	TT
	Positive	203 (69.3)	76 (25.9)	14 (4.8)
	Negative	200 (65.1)	94 (30.6)	13 (42.3)
NPSR1	rs324981	AA	AT	TT
	Positive	79 (27.0)	160 (54.6)	54 (18.4)
	Negative	84 (27.4)	140 (45.6)	83 (27.0)
NPSR1	rs6972158	GG	GA	AA
	Positive	14 (4.8)	78 (26.6)	201 (68.6)
	Negative	12 (3.9)	102 (33.2)	193 (62.9)
HSP90B1	rs17034977	AA	CA	CC
	Positive	181 (57.6)	109 (34.7)	24 (7.7)
	Negative	181 (63.3)	88 (30.8)	17 (5.9)
HSP90AA2	rs2726836	CC	CT	TT
	Positive	36 (12.3)	117 (39.9)	140 (47.8)
	Negative	41 (13.4)	141 (45.9)	125 (40.7)
FKBP5	rs1360780	TT	CT	CC
	Positive	30 (10.2)	121 (41.3)	142 (48.5)
	Negative	18 (58.6)	133 (43.3)	156 (50.8)
FKBP5	(rs3800373)	CC	CA	AA
	Positive	32 (10.9)	119 (40.6)	142 (48.5)
	Negative	21 (6.8)	131 (42.7)	155 (50.5)

Positive: psychological stress (+); Negative: psychological stress (–);

Results

Univariate logistic regression analysis

Among COMT (rs6267), COMT (rs769224), COMT (rs4680), and NPSR1 (rs12673132) genes, GG and GA were the most common genotypes. The outcome of univariate logistic regression indicated a significant association of NPSR1 (rs324981) A allele with psychological stress risk: A allele carriers *vs.* TT genotype (OR 1.64, 95% CI 1.11, 2.42), and AT genotype *vs.* TT genotype (OR 1.76, 95% CI 1.17, 2.65) (Table 3). However, no statistically significant associations between other SNPs and psychological stress were found.

Hierarchical regression analysis

Results of hierarchical regression of NPSR1 (rs324981) and gender, race, the overall coping score and the overall social support score predicting psychological stress, are shown in Table 3. In the first model, we found that NPSR1 (rs324981) positively predicted psychological stress after taking into account sex and race. In the second model (the overall coping score and the overall social support score were into the existing model one), the main effect of NPSR1 (rs324981) and the overall coping score was found. In the third model (NPSR1 (rs324981)* the overall coping scores were entered into the existing model). The interaction between LES and rs324981 remained, with no association with psychological stress risk (Table 4).

Table 3. Univariate logistic regression analysis between genotypes and psychological stress, expressed as odd ratio (OR) with 95% confidence interval (CI), in a Chinese cross-sectional study.

Genetic loci	Genotypes	OR (95% CI)			
		Additive model	Dominant model	Condiment model	Recessive model
		GA/AA/GG	(GA+AA)/GG	GA/AA	(GG+GA)/AA
COMT (rs4680)	GG	1.00 (ref)	1.00 (ref)		1.25 (0.54, 2.90)
	GA	1.12 (0.78, 1.58)	1.08 (0.77, 1.51)	1.34 (0.56, 3.21)	1.00 (ref)
	AA	0.83 (0.36, 1.94)		1.00 (ref)	
		GT/TT/GG	(GT+TT)/GG	GT/TT	(GG+GT)/TT
COMT (rs6267)	GG	1.00 (ref)	1.00 (ref)		
	GT	0.71 (0.44, 1.16)	0.70 (0.44, 1.13)	1.42 (0.12, 16.36)	1.91 (0.17, 21.23)
	TT	0.50 (0.45, 5.55)		1.00 (ref)	1.00 (ref)
		GA/AA/GG	(GA+AA)/GG	GA/AA	(GG+GA)/AA
COMT (rs769224)	GG	1.00 (ref)	1.00 (ref)	—	—
	GA	1.28 (0.69, 2.37)	128 (0.69, 2.37)		
	AA				
		GA/AA/GG	(GA+AA)/GG	GA/AA	(GG+GA)/AA
NPSR1 (rs12673132)	GG	1.00 (ref)	1.00 (ref)		
	GA	1.21 (0.85, 1.70)	1.11 (0.81, 1.53)	1.42 (0.83, 2.44)	1.28 (0.77, 2.12)
	AA	0.85 (0.50, 1.44)		1.00 (ref)	1.00 (ref)
		CT/TT/CC	(CT+TT)/CC	CT/TT	(CC+CT)/TT
NPSR1 (rs6947841)	CC	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
	CT	0.80 (0.56, 1.14)	0.83 (0.59, 1.17)	0.75 (0.33, 1, 70)	0.88 (0.41, 1.91)
	TT	1.06 (0.49, 2.31)			
		AT/TT/AA	(AT+TT)/AA	**AT/TT**	**(AA+AT)/TT**
NPSR1 (rs324981)	AA	1.00 (ref)	1.00 (ref)		
	AT	1.22 (0.83, 1.78)	1.02 (0.71, 1.46)	**1.76 (1.17, 2.65)**	**1.64 (1.11, 2.42)**
	TT	0.69 (0.44, 1.10)		**1.00 (ref)**	**1.00 (ref)**
		GA/GG/AA	(GA+GG)/AA	GA/GG	(AA+GA)/GG
NPSR1 (rs6972158)	AA	1.00 (ref)	1.00 (ref)		
	GA	0.73 (0.53, 1.05)	0.78 (0.55, 1.09)	0.66 (0.29, 1.50)	0.81 (0.37, 1.78)
	GG	1.12 (0.51, 2.48)		1.00 (ref)	1.00 (ref)
		CA/CC/AA	(CA+CC)/AA	CA/CC	(AA+CA)/CC
HSP90B1 (rs17034977)	AA	1.00 (ref)	1.00 (ref)		
	CA	0.81 (0.57, 1.14)	0.89 (0.64, 1.23)	0.57 (0.30, 1.13)	0.66 (0.35, 1.25)
	CC	1.41 (0.73, 2.72)		1.00 (ref)	1.00 (ref)
		CT/TT/CC	(CT+TT)/CC	CT/TT	(CC+CT)/TT
HSP90AA2 (rs2726836)	CC	1.00 (ref)	1.00 (ref)		
	CT	0.95 (0.57, 1.57)	1.10 (0.68, 1.78)	0.74 (0.53, 1.05)	0.75 (0.54, 1.04)
	TT	1.28 (0.78, 2.12)		1.00 (ref)	1.00 (ref)
		CT/CC/TT	(CT+CC)/TT	CT/TT	(TT+CT)/CC
FKBP5 (rs1360780)	TT	1.00 (ref)	1.00 (ref)		
	CT	0.55 (0.29, 1.03)	0.55 (0.30, 1.00)	1.00 (0.72, 1.40)	1.10 (0.80, 1.51)
	CC	0.55 (0.29, 1.02)		1.00 (ref)	1.00 (ref)
		CA/AA/CC	(CA+AA)/CC	CA/AA	(CC+CA)/AA
FKBP5 (rs3800373)	CC	1.00 (ref)	1.00 (ref)		
	CA	0.60 (0.33, 1.09)	0.60 (0.34, 1.07)	0.99 (0.71, 1.39)	1.08 (0.79, 1.49)
	AA	0.60 (0.33, 1.09)		1.00 (ref)	1.00 (ref)

Table 4. MultiplerRegression of NPSR1rs324981 and total score of coping and support predicting psychological stress in Chinese sample.

Genetic *loci*	Model	Psychological stress		
		Factors	OR (95% CI)	*P* value
rs324981 TT/AT+AA	Model 1	rs324981	**1.64** **(1.11, 2.43)**	**0.01**
		Sex	1.36 (0.97, 1.90)	0.07
		Race	1.08 (0.90, 1.30)	0.40
	Model 2	rs324981	**1.55** **(1.04, 2.30)**	**0.03**
		Sex	**1.42** **(1.02, 2.00)**	**0.04**
		Race	1.10 (0.92, 1.33)	0.31
		The overall coping score	**1.03** **(1.01, 1.04)**	**0.00**
		The overall social support score	0.99 (0.96, 1.02)	0.63
	Model 3	rs324981	.830 (0.19, 3.62)	0.81
		Sex	**1.42** **(1.01, 2.00)**	**0.04**
		Race	1.10 (0.91, 1.32)	0.32
		The overall coping score	1.00 (0.94, 1.07)	0.95
		The overall social support score	0.99 (0.96, 1.02)	0.60
		rs324981* the overall coping score	1.02 (0.98, 1.05)	0.39
rs324981 TT/AT	Model 1	rs324981	**1.77** **(1.17, 2.67)**	**0.01**
		Sex	1.33 (1.00, 1.96)	0.16
		Race	1.20 (0.96, 1.50)	0.11
	Model 2	rs324981	**1.67** **(1.10, 2.52)**	**0.02**
		Sex	1.45 (0.97, 2.16)	0.07
		Race	1.25 (0.99, 1.57)	0.06
		The overall coping score	**1.03** **(1.01, 1.05)**	**0.00**
		The overall social support score	1.00 (0.96, 1.03)	0.76
	Model 3	rs324981	.062 (0.13, 3.02)	0.56
		Sex	1.45 (0.97, 2.17)	0.07
		Race	1.25 (0.99, 1.57)	0.06
		The overall coping score	1.00 (0.93, 1.06)	0.77
		The overall social support score	0.99 (0.96, 1.03)	0.72
		rs324981* the overall coping score	1.03 (0.99, 1.07)	0.21

Discussion

Using iMLDR, we detected 11 tagged SNPs of 5 genes in China subjects, which has not been reported previously. Psychological stress was defined by having a total score above 20. We found that only NPSR1 (rs324981) TT genotype was associated with decreased risk of psychological stress in healthy Chinese subjects. Hierarchical regression demonstrated that the overall coping score was associated with psychological stress risk.

The rs324981 T allele (107Ile) appears to increase NPSR expression and NPS efficacy more than A allele [30]. NPS binding to its cognate receptor (NPSR) can lead to anxiety in rodents [31], whereas NPS is involved in HPA axis regulation in mice and activates the NPS brain nuclear gene when mice are exposed to stress [32]. Recent studies showed that the rs324981 T allele increased cortisol stress responses in healthy young European participants [33] and modulated acute stress response [34]. Similarly, a previous study showed that the

NPSR1 (rs324981) T allele increased stress reactivity in 196 healthy European males [35]. Participants underwent the Trier Social Stress Test for Groups (TSST-G), a standardized laboratory protocol for stress exposure in a group format. A significant genotype-by-time interaction and a main effect of genotype were shown, with T allele carriers displaying larger cortisol and subjective stress responses. This is the first report to show involvement of the NPS system in the regulation of the neuroendocrine stress response in humans. NPSR1 (rs324981) was also found to be associated with brain activation patterns under acute psychosocial stress and it modulates the link between living in an urban area and central stress processing [36]. The rs324981 T allele also associated with sleep disorder [37], anxiety disorders [38], panic disorder [39], and impulsivity and ADHD-related traits [40]. These findings suggest that rs324981 T allele is a potential risk factor for psychological stress and other mental diseases. However, the present study is the first to confirm that T/T genotype is a protective factor for psychological stress in healthy Chinese

subjects. Similarly, animal studies showed an association between less active NPS-ergic neurotransmission and anxiety-related behavior risk [41]. Other studies also suggested that *NPSR1* rs324981 AA genotype (the least active genotype) carriers had higher anxiety, depression, and suicidal behavior in females [42], as well as maladaptive impulsivity and neuroticism [43]. Indeed, AA carriers had a high activity in the prefrontal cortex (PFC), while T allele carriers had less cortical activation activity when subjected to emotional stimuli [44]. In additional, the function of PFC was more active in generalized anxiety disorder subjects [45], indicating the association of A alleles with anxiety disorder risk. The use of different research methods and samples may have contributed to differences in research results among studies. rs324981 T allele was reported to be a risk factor in most previous studies of participants taking the TSST-G, while the present study was a cross-sectional study in Chinese healthy subjects. Our study is the first to detect an association of *NPSR1* rs324981 gene polymorphisms with psychological stress in the Guangxi minority region of China. Further research using standardized laboratory protocols is needed to confirm the association.

We also found an association between the overall coping score and psychological stress, and there was no interaction between NPSR1 rs324981 polymorphisms and the overall coping score in inducing psychological stress. Previous studies found that coping style is a mediator between life stressors and health [46]. Researcher have found that subjects with a negative coping style have high risk of chronic PTSD [47]. In contrast, a review study suggested that higher stress reactivity perpetuates insomnia [48]; similarly, people who used a more negative religious coping style to adapt to high levels of acculturative stress had higher rates of alcohol use [49]. These studies show that excessively positive or negative coping styles can lead to psychological stress. However, our study of overall coping style reported a weak effect for psychological stress; thus, further research with larger samples is needed.

Strengths of our study include the population-based design, the high participation rates, the complete response in the questionnaire, the use of an evaluation questionnaire specially designed for the Chinese population, and the face-to-face personal interviews with all study participants. Despite some strengths, our study has some limitations that should be described. First, although all participants were randomly selected from their local village, the selection bias and information bias could not be completely eliminated. Second, samples were small, which may have caused false negatives in some genes. Third, data on psychological stress were collected through self-report questionnaires, which can cause recall bias. Moreover, we were unable to detect causality due to our cross-sectional study design; thus, we need conduct a large-cohort study. Lastly, various populations have different minor allele frequencies, which can lead to inconsistent effects.

Conclusions

We found that the NPSR1 (rs324981) T/T genotype carriers had significantly lower psychological stress, and that overall coping style affects psychological stress. However, there was no interactive effect of genes and environment on psychological stress. Our results will contribute to understanding of the biological basis underlying psychological stress if the findings can be replicated in further research.

Acknowledgements

Conflict of interest

None.

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