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RESEARCH ARTICLE

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The correlation between SNPs within the gene of adrenergic receptor and neuropeptide Y and risk of cervical vertigo

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Background: The current investigation was aimed to explore the potential associations of SNPs within *ADRB2*, *ADRB1*, *NPY*, and *ADRA1A* with risk and prognosis of cervical vertigo.

Methods: Altogether 216 patients with cervical vertigo and 204 healthy controls were gathered, and their DNAs were extracted utilizing the whole-blood DNA extraction kit. Besides, the PCR reactions were conducted using the TaqMan^{R} single nucleotide polymorphism (SNP) genotyping assays, and the SNPs were detected on the 7900HT real-time fluorogenic quantitative polymerase chain reaction (PCR) instrument. Finally, the severity of cervical vertigo was classified according to the JOA scoring, and the recovery rate (RR) of cervical vertigo was calculated in light of the formula as:

$$\frac{\text{Postoperative JOA} - \text{Preoperative JOA}}{17 - \text{Preoperative JOA}} \times 100\%$$

Results: The SNPs within *ADRA1A* [rs1048101 (T>C) and rs3802241 (C>T)], *NPY* [rs16476 (A>C), rs16148 (T>C), and rs5574 (C>T)], *ADRB1* [rs28365031 (A>G)] and *ADRB2* [rs2053044 (A>G)] were all significantly associated with regulated risk of cervical vertigo (all $P < .05$). Haplotypes of *ADRA1A* [CT and TC] and *NPY* [CCT and ATT] were also suggested as the susceptible factors of cervical vertigo in comparison with other haplotypes. Furthermore, the SNPs within *ADRA1A* [rs1048101 (T>C)], *NPY* [rs16476 (A>C), rs16148 (T>C)], as well as *ADRB1* [rs28365031 (A>G)] all appeared to predict the prognosis of cervical vertigo in a relatively accurate way (all $P < .05$). Ultimately, the haplotypes of *ADRA1A* (CC) and *NPY* (CCT) tended to decrease the RR.

Conclusions: The SNPs within *ADRB2*, *ADRB1*, *NPY*, and *ADRA1A* might act as the diagnostic biomarkers and treatment targets for cervical vertigo.

KEYWORDS

ADRA1A, *ADRB1*, *ADRB2*, Cervical vertigo, *NPY*, prognosis, risk, SNP

1 | INTRODUCTION

Cervical vertigo was a disorder caused by decreased blood flow within vertebra-basilar artery and insufficient blood supply to the brain, which were facilitated by the stimulation and stress of cervical degenerative changes, degeneration of intervertebral disk, nucleus pulposus protrusion, trauma, and inflammation.[1-3] The symptoms of cervical vertigo were mainly manifested as dizziness, nausea, and vomit accompanied with discomfort and pain in the neck.[4] The golden standard for cervical vertigo was commonly recognized as multislice spiral CT angiography, although its diagnostic accuracy was limited.[5] Moreover, the pathogenesis of cervical vertigo was still far from clarification, making the diagnosis and treatment for cervical vertigo rather challenging.

The cervical sympathetic nerves have caught increasing attention as for their effects on the development of cervical vertigo. To be specific, sympathetic nerves that belonged to the automatic nervous system dominated nearly all the visceral organs.[6] Multitudes of blood vessels within human body were only subject to the control of sympathetic vasoconstrictor fibers, and the fluctuations of the discharge frequency with a certain range might alter the vessel caliber largely, thereby adjusting the blood resistance and blood flow with various organs.[7] Accordingly, stimulating cervical sympathetic nerves could contribute to reduced blood flow of the vertebra-basilar arterial (VBA) system, namely posterior circulation ischemia (PCI).[8]

The adjustment of vessel caliber was indicated as a major regulatory factor engendering PCI, and the vasoconstrictive effects of sympathetic nerves were realized through the neurotransmitters released from postganglionic fibers, including noradrenaline (NA) and neuropeptide Y (NPY).[9,10] Taking NA for example, when sympathetic nerves were activated, the combining capacity of NA and α adrenergic receptor [eg, adrenoceptor alpha 1A (ADRA1A)] within smooth muscles around vessel walls outperformed that of NA and β adrenergic receptor [eg, adrenoceptor beta 2 (ADRB2) and adrenoceptor beta 1 (ADRB1)], rendering the occurrence of vasomotor reaction. Furthermore, NPY could directly act on vascular smooth muscle cells to contract vessels and also reinforced the vasoconstrictive effects of other vasoconstrictive substances. All in all, NPY and NA could corelease to induce arterial reflex spasm.[11]

As the functions of NA and NPY might be subject to the regulation of genetic polymorphisms, for instance, the adrenoceptor alpha 2B (*ADRA2B*) del301-303 variants were associated with remarkably dropped de-sensitization that was mediated by G protein-coupled receptor kinase.[12] Furthermore, certain single nucleotide polymorphisms (SNPs) within NA and NPY also modified the susceptibility to vasoconstriction-relevant disorders, such as hypertension and obesity.[13,14] Consequently, it was hypothesized that the SNPs located within NA and NPY might also play a regulating role in the development of cervical vertigo, for that it was PCI-induced.

Thus, the current investigation was aimed to explore the potential associations of SNPs within *ADRB2*, *ADRB1*, *NPY*, and *ADRA1A* with risk and prognosis of cervical vertigo, which might provide assistance regarding the search for the corresponding diagnostic biomarkers and treatment targets.

2 | MATERIALS AND METHODS

2.1 | Subjects

There were totally 216 patients with cervical vertigo and 204 healthy controls collected from the Second Hospital of Shandong University and the Fourth Hospital of Jinan during the period from January 2016 to February 2017. All the patients were mainly accompanied with symptoms of long-term (> 3 months) and repeated (> 3 times) dizziness and vertigo. They were diagnosed as cervical vertigo after systematic registration of medical history, physical examination, as well as checking with ordinary X-ray film, computed tomography (CT), magnetic resonance imaging (MRI), magnetic resonance angiography (MRA), and transcranial Doppler (TCD). Moreover, the subjects would be excluded from this investigation if their dizziness were derived from heart, hypertension, brain, ears, eyes, poisoning, and so on. All the subjects have signed informed consents, and the protocols within this investigation have been approved by the Second Hospital of Shandong University and the Fourth Hospital of Jinan and the ethics committee of the Second Hospital of Shandong University and the Fourth Hospital of Jinan.

2.2 | Genotyping

The whole-blood DNA extraction kit (Model Number: D3184-02™, OMEGA corporation, Doraville, GA, USA) was employed to extract DNA following the method of centrifugal column. The SNPs were detected on the 7900HT real-time fluorogenic quantitative polymerase chain reaction (PCR) instrument (Model Number: 7900 Realtime PCR System™, Applied Biosystems, Foster City, CA, USA), and PCR reactions were conducted using the TaqMan® SNP genotyping assays (ID: 4351379, ABI corporation, Carlsbad, CA, USA). The primers for selected SNPs are shown in Table S1. The PCR reaction abided by the conditions of (1) pre-degeneration at 95°C for 10 minutes; and (2) 40 cycles of 92°C for 15 seconds and 60°C for 1 minutes. The genotypes were automatically interpreted through the attached Sequence Detection System v2.3 (SDS 2.3).

2.3 | Clinical manifestation and physical examination

The subjects were clinically manifested as swirling and/or vertigo, along with symptoms of nausea, vomiting, tinnitus, and hearing loss. The severe ones might suffer from cataplexy, and the most commonly associated neck symptoms were shown as neck and shoulder pain. Of note, the clinical performance of cervical vertigo included swirling and vertigo. Swirling was the misconception of motion and included senses of rotation, roll, topple, swing, and sink. Vertigo only possessed senses of head heaviness, head lightness, dim eyesight, and blackout, without any feeling of sports. In addition, the subjects with cervical vertigo were checked with mainly tenderness of cervical muscles, positiveness of the neck-spinning experiment, and hyperextension of the neck.

2.4 | JOA scoring

The JOA score included scoring of 6 domains, including motor dysfunction in the upper extremities (scoring: 0-4), motor dysfunction in the lower extremities (scoring: 0-4), sensory function in the upper extremities (scoring: 0-2), sensory function in the trunk (scoring: 0-2), sensory function in the lower extremities (scoring: 0-2), and bladder function (scoring: 0-3). The severity of cervical vertigo would be classified as (1) mild if JOA > 13; (2) moderate if JOA ranged between 9 and 13; (3) severe if JOA < 9.[15] Based on the JOA scoring, the recovery rate (RR) of cervical vertigo was figured out as the following formula (Hirabayashi method):

$$\frac{\text{Postoperative JOA} - \text{Preoperative JOA}}{17 - \text{Preoperative JOA}} \times 100\% \quad (16)$$

2.5 | Statistical analysis

All the statistical analyses were carried out with usage of the SPSS software. The enumeration data were managed with chi-square test. The measurement data were analyzed with independent *t* test if they accorded with normal distribution; otherwise, they would be dealt with using Kruskal-Wallis H test. Besides, the intergroup comparisons on the distribution of allele frequencies were carried out through chi-square test. The significance of all tests was set as *P* value < .05.

3 | RESULTS

3.1 | Baseline features of the subjects

There exhibited few distinctions between patients with cervical vertigo and healthy controls in the aspects of sex ratio and age (*P* > .05) (Table 1). Nevertheless, the TCD results of patients with cervical vertigo were far beyond those of healthy controls, regardless of left vertebral artery, right vertebral artery and basilar artery (all *P* < .05). Furthermore, the cervical vertigo cases investigated could be classified as 156 ones with superior cervical vertigo and 60 ones with inferior cervical vertigo. The sequence of probabilities among the concomitant symptoms was enlisted as nausea (n = 209) > headache (n = 195) > sweating (n = 182) > aural fullness (n = 171) > tinnitus (n = 164) > impaired hearing (n = 123).

TABLE 1 Baseline characteristics of recruited patients and healthy people

Characteristics	Case group	Healthy group	*P* value
Number	216	204	
Gender			
Male	118	114	.796
Female	98	90	
Age	42.08 ± 5.13	45.67 ± 4.26	.111
Period (year)	5.62 ± 3.11	-	
Classification			
Superior cervical vertigo	156	-	
Inferior cervical vertigo	60	-	
TCD			
Left vertebral artery	37.26 ± 5.46	52.35 ± 4.27	**<.001**
Right vertebral artery	36.42 ± 3.88	50.08 ± 6.39	**<.001**
Basilar artery	38.52 ± 6.04	42.68 ± 5.25	**.044**
Concomitant symptoms			
Nausea	209	-	
Sweating	182	-	
Tinnitus	164	-	
Impaired hearing	123	-	
Aural fullness	171	-	
Headache	195	-	

TCD, transcranial Doppler.
Bold numbers denote a statistical significance at .05 level.

3.2 | Association of genetic polymorphisms with the incidence of cervical vertigo

According to Table 2, *ADRA1A* rs1048101 (T>C) and rs3802241 (C>T), *NPY* rs16476 (A>C), rs16148 (T>C), and rs5574 (C>T) and *ADRB1* rs28365031 (A>G) all could significantly raise the risk of cervical vertigo in the allelic models (OR = 1.65, 95%CI: 1.20-2.27, *P* < .05; OR = 2.07, 95%CI: 1.47-2.92, *P* < .05; OR = 1.61, 95%CI: 1.20-2.16, *P* < .05; OR = 1.84, 95%CI: 1.37-2.47, *P* < .05; OR = 1.39, 95%CI: 1.03-1.89, *P* < .05; OR = 1.38, 95%CI: 1.02-1.88, *P* < .05), yet *ADRB2* rs2053044 (A>G) was associated with reduced susceptibility to cervical vertigo (OR = 0.62, 95%CI: 0.46-0.83, *P* < .05).

It is indicated in Table 3 that haplotype CT of *ADRA1A* and haplotype CCT of *NPY* both might serve as the risk factors of cervical vertigo when compared with other haplotypes (OR = 2.30, 95%CI: 1.33-3.98, *P* < .05; OR = 2.24, 95%CI: 1.29-3.88, *P* < .05). In contrast, haplotype TC of *ADRA1A* and haplotype ATT of *NPY* could function to protect people against cervical vertigo (OR = 0.54, 95%CI: 0.33-0.88, *P* < .05; OR = 0.59, 95%CI: 0.35-1.00, *P* < .05).

3.3 | Association of genetic polymorphisms with the prognosis of patients with cervical vertigo (ie, JOA score)

The homozygote TT of *ADRA1A* rs3802241 and homozygote GG of *ADRB1* rs28365041 were remarkably associated with aberrantly higher JOA score (≥ 9), respectively, in comparison with genotypes CC and AA (OR = 0.25, 95%CI: 0.08-0.78, *P* < .05; OR = 0.28, 95%CI: 0.08-0.99, *P* < .05) (Table 4). Nevertheless, regarding *NPY*, the heterozygote AC of rs16476 and heterozygote CT of rs5574 were both probably the hazard parameters contributing to cervical vertigo (OR = 4.43, 95%CI: 1.40-13.99, *P* < .05; OR = 8.41, 95%CI: 1.95-36.20, *P* < .05). Besides, the haplotype CC of *ADRA1A* appeared to produce less favorable prognosis (OR = 1.85, 95%CI: 1.05-3.25, *P* < .05), yet haplotype CTT was more able to cause the more ideal JOA score than other haplotypes (OR = 0.29, 95%CI: 0.15-0.53, *P* < .05) (Table 5).

3.4 | Association of genetic polymorphisms with the RR of patients with cervical vertigo

In light of Table 6, the heterozygote TC of *ADRA1A* rs1048101 seemed to promote the RR of cervical vertigo up to more than 46.32%

TABLE 2 Association of genetic polymorphisms within *ADRA1A*, *NPY*, *ADRB2*, and *ADRB1* with the incidence of cervical vertigo

		Case group			Control group			Allelic test		Homozygote test		Recessive test	
Gene	Rs number	Wild allele	Mutant allele	MAF	Wild allele	Mutant allele	MAF	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
ADRA1A	rs2229126	242	190	0.44	208	200	0.49	0.82 (0.62-1.07)	.143	0.76 (0.5-1.17)	.213	0.76 (0.48-1.22)	.255
	rs1048101	87	345	0.80	120	288	0.71	**1.65 (1.20-2.27)**	**.002**	**2.83 (1.22-6.57)**	**.012**	**1.67 (1.13-2.46)**	**.010**
	rs3802241	315	117	0.27	346	62	0.15	**2.07 (1.47-2.92)**	**<.001**	**2.26 (1.51-3.4)**	**<.001**	**3.18 (1.14-8.86)**	**.020**
	rs574584	102	330	0.76	110	298	0.73	1.19 (0.87-1.63)	.264	1.35 (0.62-2.96)	.453	1.22 (0.83-1.79)	.312
	rs3739216	199	233	0.54	171	237	0.58	0.84 (0.64-1.11)	.226	0.79 (0.49-1.29)	.346	0.81 (0.53-1.22)	.304
NPY	rs16147	346	86	0.20	320	88	0.22	0.90 (0.65-1.26)	.553	0.86 (0.58-1.28)	.455	1.04 (0.43-2.51)	.929
	rs16476	119	313	0.72	155	253	0.62	**1.61 (1.20-2.16)**	**.001**	**1.91 (1.00-3.65)**	**.049**	**1.85 (1.25-2.73)**	**.002**
	rs16148	265	167	0.39	304	104	0.25	**1.84 (1.37-2.47)**	**<.001**	**3.02 (2.02-4.51)**	**<.001**	1.02 (0.47-2.22)	.964
	rs16135	334	98	0.23	304	104	0.25	0.86 (0.62-1.18)	.342	0.84 (0.57-1.24)	.372	0.8 (0.36-1.77)	.578
	rs5574	103	329	0.76	124	284	0.70	**1.39 (1.03-1.89)**	**.033**	2.09 (0.91-4.8)	.077	1.43 (0.97-2.1)	.067
ADRB2	rs1042713	117	315	0.73	102	306	0.75	0.90 (0.66-1.22)	.492	0.85 (0.4-1.82)	.676	0.88 (0.6-1.29)	.519
	rs1042714	251	181	0.42	244	164	0.40	1.07 (0.81-1.41)	.616	1.09 (0.73-1.63)	.669	1.11 (0.66-1.84)	.699
	rs2053044	315	117	0.27	255	153	0.38	**0.62 (0.46-0.83)**	**.001**	**0.56 (0.38-0.82)**	**.003**	**0.5 (0.26-0.96)**	**.035**
	rs1042711	306	126	0.29	302	106	0.26	1.17 (0.87-1.59)	.302	1.2 (0.82-1.76)	.359	1.29 (0.64-2.59)	.480
ADRB1	rs2229169	370	62	0.14	337	71	0.17	0.80 (0.55-1.15)	.226	0.78 (0.51-1.2)	.260	0.67 (0.21-2.14)	.492
	rs61767072	271	161	0.37	265	143	0.35	1.10 (0.83-1.46)	.503	1.12 (0.76-1.66)	.559	1.15 (0.65-2.04)	.620
	rs7434630	284	148	0.34	281	127	0.31	1.15 (0.86-1.54)	.334	1.18 (0.8-1.73)	.407	1.26 (0.68-2.33)	.464
	rs28365031	302	130	0.30	311	97	0.24	**1.38 (1.02-1.88)**	**.039**	**1.79 (1.22-2.64)**	**.003**	0.74 (0.34-1.62)	.453

ADRA1A, adrenoceptor alpha 1A; ADRB2, adrenoceptor beta 2; ADRB1, adrenoceptor beta 1; CI, confidence interval; MAF, mutant allele frequency; NPY, neuropeptide Y; OR, odds ratio.
Bold numbers denote a statistical significance at .05 level.

TABLE 3 Association of haplotypes of *ADRA1A* and *NPY* with the risk of cervical vertigo

			Case		Control			
Gene	Rs number	Haplotype	Frequency	Number	Frequency	Number	OR (95% CI)	*P* value
ADRA1A	rs1048101_rs3802241	TC	0.146	32	0.247	50	**0.54 (0.33-0.88)**	**.012**
		TT	0.054	12	0.044	9	1.27 (0.53-3.09)	.591
		CC	0.584	126	0.604	123	0.92 (0.62-1.36)	.683
		CT	0.216	47	0.107	22	**2.3 (1.33-3.98)**	**.002**
NPY	rs16476_rs16148_rs5574	ATC	0.041	9	0.086	17	0.48 (0.21-1.10)	.077
		ATT	0.130	28	0.200	41	**0.59 (0.35-1.00)**	**.049**
		ACT	0.083	18	0.067	14	1.23 (0.60-2.55)	.570
		CTC	0.105	23	0.140	28	0.75 (0.42-1.35)	.335
		CTT	0.334	72	0.326	66	1.05 (0.70-1.57)	.831
		CCC	0.067	15	0.047	9	1.62 (0.69-3.78)	.264
		CCT	0.213	46	0.109	22	**2.24 (1.29-3.88)**	**.003**

ADRA1A, adrenoceptor alpha 1A; CI, confidence interval; NPY, neuropeptide Y; OR, odds ratio.
Bold numbers denote a statistical significance at .05 level.

in comparison with homozygote TT (OR = 4.92, 95%CI: 1.08-22.46, $P < .05$). Conversely, homozygotes CC of *NPY* rs16476 and rs16148 could avoid the cervical vertigo from recurring when, respectively, compared with homozygote AA and TT (OR = 0.26, 95%CI: 0.08-0.87, $P < .05$; OR = 0.20, 95%CI: 0.06-0.71, $P < .05$). The genotype GG of *ADRB1* rs28365031 also acted in an inhibitory manner with regard to cervical vertigo (GG vs AA, OR = 0.24, 95%CI: 0.07-0.87, $P < .05$). The haplotype CC of *ADRA1A* and haplotype CCT of NPV followed the

TABLE 4 Association of genetic polymorphisms with the JOA score of patients with cervical vertigo

Gene	Rs number	Genotype	JOA Score≥9	JOA Score<9	OR	95% CI	χ^2	*P* value
ADRA1A	rs1048101	TT	5	3	Reference			
		TC	31	40	0.47	0.10-2.10	1.03	.311
		CC	102	35	1.75	0.40-7.70	0.56	.455
	rs3802241	CC	74	41	Reference			
		CT	59	26	1.26	0.69-2.29	0.56	.453
		TT	5	11	**0.25**	**0.08-0.78**	**6.43**	**.011**
NPY	rs16476	AA	9	7	Reference			
		AC	74	13	**4.43**	**1.40-13.99**	**7.17**	**.007**
		CC	55	58	0.74	0.26-2.12	0.32	.571
	rs16148	TT	42	21	Reference			
		TC	87	52	0.84	0.45-1.57	0.31	.576
		CC	9	5	0.90	0.27-3.03	0.03	.865
	rs5574	CC	4	5	Reference			
		CT	74	11	**8.41**	**1.95-36.20**	**10.46**	**.001**
		TT	60	62	1.21	0.31-4.72	0.08	.784
ADRB2	rs2053044	AA	73	42	Reference			
		AG	56	29	1.11	0.62-2.00	0.12	.725
		GG	9	7	0.74	0.26-2.13	0.31	.576
ADRB1	rs28365031	AA	63	35	Reference			
		AG	71	35	1.13	0.63-2.01	0.16	.685
		GG	4	8	**0.28**	**0.08-0.99**	**4.30**	**.038**

ADRA1A, adrenoceptor alpha 1A; ADRB2, adrenoceptor beta 2; ADRB1, adrenoceptor beta 1; CI, confidence interval; JOA score, Japanese Orthopaedic Association score; NPY, neuropeptide Y; OR, odds ratio.
Bold numbers denote a statistical significance at .05 level.

TABLE 5 Association of haplotypes of *ADRA1A* and *NPY* with the JOA score of patients with cervical vertigo

Gene	Rs number	Haplotype	JOA Score≥9		JOA Score<9		OR (95% CI)	*P* value
			Frequency	Number	Frequency	Number		
ADRA1A	rs1048101_rs3802241	TC	0.113	16	0.200	16	0.51 (0.24-1.08)	.076
		TT	0.038	5	0.090	7	0.38 (0.12-1.24)	.099
		CC	0.638	88	0.490	38	1.85 (1.05-3.25)	**.031**
		CT	0.213	29	0.220	17	0.95 (0.49-1.88)	.893
NPY	rs16476_rs16148_rs5574	ATT	0.143	20	0.090	7	1.72 (0.69-4.27)	.239
		ACT	0.088	12	0.058	4	1.76 (0.55-5.66)	.336
		CTC	0.125	17	0.066	5	2.05 (0.73-5.80)	.168
		CTT	0.178	25	0.440	34	0.29 (0.15-0.53)	**<.001**
		CCC	0.076	11	0.042	3	2.17 (0.59-8.01)	.237
		CCT	0.178	25	0.282	22	0.56 (0.29-1.09)	.084

ADRA1A, adrenoceptor alpha 1A; CI, confidence interval; JOA score, Japanese Orthopaedic Association score; NPY, neuropeptide Y; OR, odds ratio.
Bold numbers denote a statistical significance at .05 level.

TABLE 6 Association of genetic polymorphisms within *ADRA1A*, *NPY*, *ADRB2*, and *ADRB1* with the recovery rate of patients with cervical vertigo

Gene	Rs number	Genotype	RR≥46.32%	RR<46.32%	OR	95% CI	χ^2	*P* value
ADRA1A	rs1048101	TT	4	4	Reference			
		TC	59	12	**4.92**	**1.08-22.46**	**4.877**	**.027**
		CC	71	66	1.08	0.26-4.48	0.010	.920
	rs3802241	CC	68	47	Reference			
		CT	60	25	1.66	0.91-3.01	2.785	.095
		TT	6	10	0.41	0.14-1.22	2.674	.102
NPY	rs16476	AA	12	4	Reference			
		AC	72	15	1.60	0.45-5.65	0.541	.462
		CC	50	63	**0.26**	**0.08-0.87**	**5.310**	**.021**
	rs16148	TT	42	21	Reference			
		TC	88	51	0.86	0.46-1.62	0.213	.644
		CC	4	10	**0.20**	**0.06-0.71**	**6.912**	**.009**
	rs5574	CC	5	4	Reference			
		CT	60	25	1.92	0.48-7.75	0.862	.353
		TT	69	53	1.04	0.27-4.07	0.003	.953
ADRB2	rs2053044	AA	69	46	Reference			
		AG	53	32	1.10	0.62-1.96	0.114	.736
		GG	12	4	2.00	0.61-6.59	1.339	.247
ADRB1	rs28365031	AA	66	32	Reference			
		AG	64	42	0.74	0.42-1.31	1.070	.301
		GG	4	8	**0.24**	**0.07-0.87**	**5.345**	**.021**

ADRA1A, adrenoceptor alpha 1A; ADRB2, adrenoceptor beta 2; ADRB1, adrenoceptor beta 1; CI, confidence interval; NPY, neuropeptide Y; OR, odds ratio; RR, recovery rate.
Bold numbers denote a statistical significance at .05 level.

similar tendency to decrease the RR (OR = 0.53, 95%CI: 0.30-0.95, $P < .05$; (OR = 0.43, 95%CI: 0.22-0.83, $P < .05$), whereas haplotype ATT of NPV played an opposite role (OR = 2.92, 95%CI: 1.06-8.02, $P < .05$)(Table 7).

4 | DISCUSSION

NPY and NA coexisted within the same vesicle, and they were, respectively, secreted in the manners of adjustable and direct secretions.

TABLE 7 Association of haplotype within *ADRA1A* and *NPY* with the recovery rate of patients with cervical vertigo

			RR≥46.32%		RR<46.32%			
Gene	Rs number	Haplotype	Frequency	Number	Frequency	Number	OR (95% CI)	*P* value
ADRA1A	rs1048101_rs3802241	TC	0.183	24	0.088	7	2.14 (0.87-5.21)	.090
		TT	0.068	9	0.032	3	1.74 (0.46-6.64)	.410
		CC	0.548	73	0.642	53	0.53 (0.30-0.95)	**.031**
		CT	0.203	27	0.238	19	0.76 (0.39-1.47)	.408
NPY	rs16476_rs16148_rs5574	ATC	0.061	8	0.016	1	4.74 (0.58-38.61)	.111
		ATT	0.173	23	0.064	5	2.92 (1.06-8.02)	**.031**
		ACT	0.093	12	0.048	4	1.76 (0.55-5.66)	.336
		CTC	0.108	14	0.098	8	0.99 (0.39-2.47)	.979
		CTT	0.308	41	0.392	32	0.61 (0.34-1.09)	.091
		CCC	0.058	8	0.074	6	0.74 (0.25-2.21)	.587
		CCT	0.166	22	0.296	24	0.43 (0.22-0.83)	**.011**

ADRA1A, adrenoceptor alpha 1A; CI, confidence interval; NPY, neuropeptide Y; OR, odds ratio; RR, recovery rate.
Bold numbers denote a statistical significance at .05 level.

Intriguingly, after the release of NPY, NPY combined with NPY-Y1 receptors directly or indirectly heightened the NA-caused vasoconstrictive affects.[17] Moreover, NPY also could inhibit the vascularization led to by such molecules as acetylcholine and P substance. As vasoconstriction contributed much to the risk of cervical vertigo, this study investigated the effects of SNPs within *NPY* and *NA* on the susceptibility to and prognosis of cervical vertigo.

In particular, ADRA1A worked in such aspects as contraction of smooth muscles, variable time and force of myocardium, as well as adjustment of blood pressure.[18] Moreover, the ADRA1A antibody could be found within the serum of essential hypertension (EH), malignant hypertension, and refractory hypertension.[19-21] Among the investigated SNPs of *ADRA1A*, rs1048101 was located in the 4th exon of *ADRA1A*, and the mutation of C to T belonged to nonsynonymous mutation, suggesting that the mutation of bases could alter the sequences of the translated proteins and thereby to affect the function of proteins. Previously, a Brazilian study covering 1500 subjects of multiple ethnicities drawn a conclusion that rs1048101 could participate in altering the blood pressure of physically active populations.[22] More than that, rs1048101 was also documented to display associations with the effects of antihypertensive drugs on the blood pressure.[23-25] Thus, the correlation between rs1048101 and susceptibility to cervical vertigo was quite acceptable. In addition, rs3802241 (G>A), situated in the 5th exon of *ADRA1A*, was a tag SNP among the Chinese population according to HapMap database, which might render rs3802241 as a crucial factor in deciding the status of vasoconstriction.

Besides, ADRB2, which was expressed differently within cardiomyocytes, vascular endothelial cells, and bronchial smooth muscle cells, was documented to be involved with modifying heart rate, blood pressure, and breath.[26-28] For example, ADRB2 could induce the relaxed microcirculatory vessels of human coronary artery, implying the potential relations between its SNPs with vasoconstriction, which was a critical factor in regulating the development of cervical vertigo.[29] For another, rs28365031 of *ADRB1* has been reported as a biomarker predicting the unfavorable cardiovascular prognosis in certain populations, which also corresponded to our study result that rs28365031 could be associated with the prognosis of cervical vertigo in this investigation.[30-32]

In addition, NPY levels were found to be significantly elevated under the circumstances of sympathetic hyperactivity, which included hypertension, renal failure, and congestive heart.[33] Interestingly, males and females largely differed in NPY release and the vasoconstriction mediated by NPY for that testosterone would participate in upregulating the NPY expressions.[34,35] As was demonstrated, NPY could contribute to forming the neointimal lesion that blocked the vessels within rats, which was partly representative of the occurrence of human advanced atherosclerotic plaques and neovascularization.[36] The molecule also stimulated restoration of blood flow and vascularization of local ischemia, indicating that NPY and its relevant genetic polymorphisms might modify the degree of vasoconstriction, one cause of cervical vertigo.[33,37]

Above all, although this study preliminarily introduced the effects of sympathetic nerves on the development of cervical vertigo, it still remained at n the clinical level and in-depth inquiry was in demand. For example, the bioinformatic information during the process of spondylopathy was in demand with respect to the functions of receptors, release of neurotransmitters, and mediation of proteins within or around the pathway of sympathetic nerves. Besides, exploring the specific mechanisms about the pathological changes in nerve microcirculation, as well as the modulation of cerebral blood supply and compensatory balance that caused PCI still needed additional researches of basic subjects, including nerve physiology, molecular biochemistry, neuro-morphological anatomy, neuropathology, and so on. Finally, as cervical vertigo was an edge discipline that was related to ear-nose-throat department, ophthalmology

department, orthopedics department, cardiology department, and gynecology department, the clinical and basic studies based on multidisciplines should be carried out to clarify the mechanisms underlying cervical vertigo.

In conclusion, this study provided proof that SNPs within NPY and NA were significantly associated with the susceptibility to and the prognosis of cervical vertigo, so that NPY and NA might serve as the precise diagnostic marker and treatment target of cervical vertigo. Nonetheless, further researches in a large scale were in need to confirm the results of this study.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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