The Role of Brain-gut Peptides in the Symptoms of Functional Dyspepsia and Their Predictive Value for Disease

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Abstract: Objective: To analyze the role of brain-gut peptide in the symptoms of functional dyspepsia and its predictive effect on the disease. Methods: 100 patients with functional dyspepsia were selected from the Affiliated Hospital of Shandong University of Traditional Chinese Medicine from January 2022 to August 2022. The distribution of TCM syndrome of functional dyspepsia was collected, and fasting venous blood samples were collected to detect brain-intestinal peptide levels in patients with different symptoms. Moreover, patient data were collected to analyze the influencing factors of functional dyspepsia. Results: The levels of 5-hydroxytryptamine (5-HT) and motilin (MTL) in 100 functional dyspepsia patients with early satiety and upper abdominal pain were higher than those without early satiety (P<0.05), and there was no statistically significant difference between vasoactive intestinal peptide (VIP) and no early satiety (P>0.05). There was no significant difference in 5-HT, VIP and MTL levels between patients with upper abdominal distension and upper abdominal burning sensation and those without abdominal distension (P>0.05). Early satiety and upper abdominal satiety were correlated with 5-HT (P<0.05), upper abdominal distension and upper abdominal burning, early satiety, upper abdominal distension, upper abdominal pain and upper abdominal burning were not correlated with VIP (P>0.05), early satiety, upper abdominal distension and upper abdominal burning were not correlated with MTL level (P>0.05). Epigastric pain was correlated with MTL level (P<0.05). The influencing factors of 100 patients with functional dyspepsia included gender, overeating, hot food preference, picky eating, acid products, punctual eating, late night snack, daily sleep time, drug allergy history, family history, constipation and VIP level (P<0.05). Age, drinking tea, drinking alcohol, eating spicy food, eating breakfast, and eating were not included (P>0.05). Conclusion: Brain-gut peptide has predictive effect on functional dyspepsia symptoms and diseases.

***Keywords*:** brain-intestinal peptide; Functional dyspepsia symptoms; Illness; Prediction function

1. Introduction

Functional dyspepsia is a group of clinical syndromes caused by gastric and duodenal dysfunction without organic pathology, which is relatively common worldwide and can occur at any age and in any population [1-2]. The causes of functional dyspepsia mainly include gastrointestinal dyskinesia, visceral sensory hypersensitivity, abnormal gastric acid secretion, psychosomatic factors, Helicobacter pylori infection, and so on, and the common symptoms include epigastric pain such as vague pain, flatulence, tingling and so on, epigastric distension, feeling full after eating a small amount of food, and frequent belching and so on [3-4]. The diagnosis of functional dyspepsia is mainly based on the patient's symptoms and the examination to exclude organic diseases, which usually requires gastroscopy and barium permeation of the upper gastrointestinal tract to exclude reflux esophagitis, gastric ulcer, duodenal ulcer and other organic diseases. The prognosis is mostly good, but the condition is recurrent and requires comprehensive treatment and long-term management to meet clinical needs. Brain gut peptides are those peptides that are both present in the gastrointestinal tract and distributed within the central nervous system. These substances not only widely regulate various functions of the gastrointestinal tract in the periphery, such as promoting the contraction of gastrointestinal smooth muscle and regulating gastric acid secretion, but also participate in the regulation of gastrointestinal physiological activities in the central nervous system, and their biological effects are usually realized in five ways: autocrine, paracrine, endocrine, neurotransmitter and neuroendocrine [5-6]. The aim of the present study was to analyze the role of brain gut peptides in the symptoms of functional dyspepsia and their predictive role in the disease, which is reported below.

2. Information and Methods

2.1 General information

100 cases of functional dyspepsia patients who visited the Affiliated Hospital of Shandong University of Traditional Chinese Medicine during January 2022-August 2022 were selected. Inclusion criteria: (1) clear diagnosis of functional dyspepsia in Western medicine, and diagnostic criteria in Chinese medicine's "Expert Consensus Opinions on Chinese Medicine Diagnosis and Treatment of Functional Dyspepsia" (Chinese Society of Traditional Chinese Medicine Spleen and Stomach Disease Subcommission, 2017); (2) age of 18-75 years old; (3) informed consent and voluntary participation. Exclusion criteria: (1) patients with severe mental diseases; (2) serious diseases combined with important organs; (3) women during pregnancy and lactation; (4) unable to clearly narrate their symptoms; (5) those with poor survey cooperation.

2.2 Methods

Collect the distribution of Chinese medicine symptoms of functional dyspepsia, collect fasting venous blood samples, test 5-hydroxytryptamine (5-HT), vasoactive intestinal peptide (VIP), and serum gastrin (MTL) levels; analyze the level of brain gut peptide of different symptomatic patients, and collect the patient's data to analyze the influencing factors of functional dyspepsia.

2.3 Observation indexes

Observation indexes: (1) Comparison of brain and intestinal peptide levels in patients with different symptoms, and comparison of 5-HT, VIP and MTL levels in patients with or without early satiety, epigastric pain, epigastric distension and epigastric burning sensation. (2) Correlation between different symptoms and brain gut peptide index levels, analyzing the correlation between early satiety, epigastric pain, epigastric distension, epigastric burning sensation and 5-HT, VIP and MTL levels. (3) Distribution of general data of functional dyspepsia, analyzing gender, age, dietary habits (overeating, hot food, picky eating, drinking tea, eating acidic products, eating spicy food, eating cold food, eating breakfast, eating on time, eating late-night snacks, daily sleep, history of drug allergy, past family history, constipation, normal value of VIP), and bad hobbies (smoking, drinking alcohol); of which, the normal reference value range of VIP is ≤60 ppi, the normal reference value range is ≤60 ppi. normal reference value range ≤60pg/ml.

2.4 Statistical analysis

SPSS 17.0 was adopted to analyze the data, and the count data were expressed as [n (%)] with the t-test, and the measurement data were expressed as ( ) with the t-test, and the difference of data was statistically significant at $P<0.05$.

3. Results

3.1 Comparison of brain gut peptide levels in patients with different symptoms

In 100 cases of functional dyspepsia with early satiety and epigastric pain, 5-hydroxytryptamine (5-HT) and serum motrin (MTL) were higher than those without early satiety ($P<0.05$), and the difference between vasoactive intestinal peptide (VIP) and those without early satiety was not statistically significant ($P>0.05$); in patients with epigastric bloating and epigastric burning, the differences between the levels of 5-HT, VIP and MTL and those without epigastric bloating were not statistically significant ($P>0.05$); details are shown in Table 1; in patients with epigastric swelling, epigastric burning and epigastric burning, the differences were statistically significant. The difference was not statistically significant ($P>0.05$); see Table 1 for details.

Table 1. Comparison of brain-gut axis levels in patients with different symptoms ($\bar{x} \pm s$)

Symptoms	Number of cases (n)	5-HT (pg/ml)	VIP (pg/ml)	MTL (ng/L)	
Early satiety	Have	35	180.44±35.98	42.34±7.95	245.18±50.23
	Without	65	155.68±37.36	39.21±8.49	220.24±44.45
	t		3.202	1.797	2.556
	P		0.002	0.075	0.012
Epigastric pain sensation	Have	72	174.37±35.62	38.90±11.15	240.18±39.62
	Without	28	135.48±31.16	40.45±10.94	203.77±40.15
	t		5.067	0.627	4.111
	P		0.000	0.532	0.000
Epigastric distension	Have	68	170.50±35.23	40.46±11.98	238.65±50.65

Symptoms	Number of cases (n)	5-HT (pg/ml)	VIP (pg/ml)	MTL (ng/L)	
Burning sensation in epigastric abdomen	Without	32	167.28±33.45	37.24±10.75	220.41±42.48
	t		0.433	1.294	1.765
	P		0.666	0.199	0.08
	Have	38	168.46±37.59	38.24±11.92	231.23±45.68
	Without	62	160.74±41.28	39.01±11.53	225.70±46.35
	t		0.939	0.320	0.582
	P		0.350	0.750	0.562

3.2 Correlation between different symptoms and brain gut peptide index levels

Early satiety and epigastric fullness had correlation with 5-HT (P<0.05), epigastric bloating and epigastric burning scores had no correlation with 5-HT (P>0.05), early satiety, epigastric bloating, epigastric pain and epigastric burning sensation did not have any correlation with VIP (P>0.05), early satiety, epigastric bloating, and epigastric burning scores did not have any correlation with MTL levels (P>0.05), and epigastric pain sensation was correlated with MTL levels (P<0.05); see Table 2 for details.

Table 2. Correlation between different symptoms and brain gut peptide index levels

Symptoms	5-HT (pg/ml)	VIP (pg/ml)	MTL (ng/L)
Early satiety			
r	0.259	0.115	0.252
P	0.044	0.320	0.080
Epigastric pain sensation			
r	0.188	0.219	0.186
P	0.108	0.115	0.131
Epigastric distension			
r	0.283	0.173	0.284
P	0.018	0.180	0.035
Burning sensation in epigastric abdomen			
r	0.155	0.086	0.110
P	0.216	0.515	0.416

3.3 Distribution of general data of functional dyspepsia patients

The factors affecting the prevalence of 100 patients with functional dyspepsia included patients' gender, overeating, liking hot food, picking food, acid products, eating on time, eating late-night snacks, daily sleep time, history of drug allergy, family history, constipation, and VIP level (P<0.05), excluding age, tea drinking, alcohol consumption, eating spicy food, eating breakfast, and eating raw and cold foods (P>0.05); for details, see Table 3.

Table 3. Comparison of general information on the prevalence of functional dyspepsia

Factor	Number of cases (n)	Symptom score (points)	t/F	P
Gender			7.863	0.000
Male	38	30.01±2.10		
Female	62	34.58±3.18		
Age			1.909	0.155
< 30 years old	38	29.56±3.40		
31-45 years old	25	30.45±4.50		
Aged 46-60	23	31.50±3.49		
> 60 years old	14	32.23±3.17		
Overeating			10.659	0.000
Yes	59	34.14±2.01		
No	41	29.63±2.18		
Eating hot food				

Factor	Number of cases (n)	Symptom score (points)	t/F	P
Yes	62	35.10±1.72	20.140	0.000
No	38	28.01±1.69		
Piddle				
Yes	58	32.36±1.31	16.434	0.000
No	42	27.35±1.73		
Drink tea			1.104	0.272
Yes	53	33.10±2.87		
No	47	32.46±2.92		
Smoking			9.940	0.000
Yes	54	32.52±2.64		
No	46	27.46±2.41		
Drinking			11.169	0.000
Yes	48	33.10±2.01		
No	52	27.93±2.56		
Eating acid products			8.520	0.000
Average or more	72	34.10±2.46		
Less or none	18	28.24±3.16		
Eat spicy food			1.481	0.142
Average or more	46	33.12±2.40		
Less or none	54	32.41±2.38		
Eating raw and cold food			0.758	0.450
Average or more	54	34.14±2.48		
Less or none	46	33.68±3.56		
Eat breakfast			1.607	0.111
Average or more	55	33.18±2.52		
Less or none	45	34.01±2.63		
Eat on time			14.260	0.000
Average or more	88	21.34±3.56		
Less or none	12	36.20±1.39		
Eat a midnight snack			13.870	0.000
Average or more	79	34.48±1.45		
Less or none	21	29.59±1.38		
Daily sleep			23.399	0.000
< 6h	48	34.21±1.63		
6-8h	34	33.84±1.25		
> 8h	18	31.37±2.67		
Drug allergy history			19.054	0.000
Yes	40	34.64±1.68		
No	60	28.54±1.49		
Past Family History			17.023	0.000
Yes	35	33.65±1.80		
No	65	27.66±1.61		
Constipation			15.405	0.000
Yes	34	34.40±1.66		
No	66	29.32±1.51		
VIP Normal Value			7.355	0.000
Yes	49	28.14±3.50		
No	51	33.38±3.62		

3.4 Logistic regression analysis of factors affecting the prevalence of functional dyspepsia

Logistic regression analysis showed that the factors influencing the prevalence of functional dyspepsia in 100 patients included patients' gender, poor dietary habits, bad hobbies, daily sleep time <6h, drug allergy history, family history, constipation and abnormally elevated VIP levels (P<0.05); see Tables 4 and 5 for details.

Table 4. Assignment of factors influencing the prevalence of functional dyspepsia

Factor	Assignment
Gender	Enter at original value
Poor eating habits	Enter at original value
Bad habits	Enter at original value
Daily sleep time<6h	Enter at original value
Drug allergy history	Enter at original value
Family history	Enter at original value
Constipation	Enter at original value
VIP level abnormally elevated	Enter at original value

Table 5. Logistic regression analysis of factors influencing the prevalence of functional dyspepsia

Factor	β	Standard error	Wald X^2 Value	*OR* Value	95% *CI*	*P* Value
Gender	0.495	0.423	13.480	1.543	1.044-2.043	0.001
Poor eating habits	0.504	0.486	11.316	1.568	1.239-2.115	0.004
Bad habits	0.598	0.516	11.668	1.608	1.247-2.229	0.002
Daily sleep time<6h	0.539	0.551	12.148	1.674	1.259-2.231	0.001
Drug allergy history	0.640	0.320	13.385	1.429	1.089-1.876	0.003
Family history	0.687	0.364	11.456	1.558	0.897-2.135	0.001
Constipation	0.722	0.335	12.140	1.438	0.953-2.385	0.001
VIP level abnormally elevated	0.716	0.283	12.439	1.427	1.016-1.976	0.001

3.5 ROC curve for the predictive value of VIP for functional dyspepsia

The AUC for VIP was 0.564; the ROC curve for the predictive value of VIP for functional dyspepsia is shown in Figure 1.

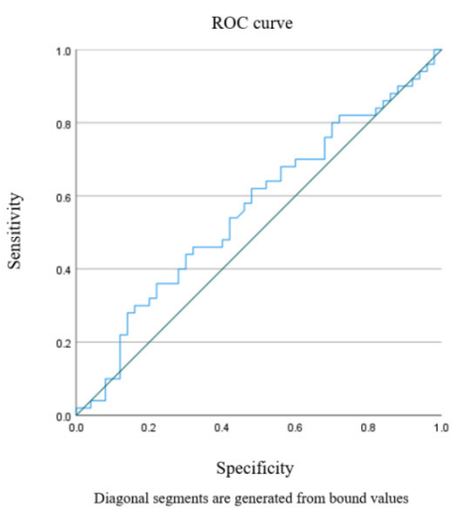

Figure 1. ROC curve of the predictive value of VIP for functional dyspepsia

4. Discussion

4.1 Correlation between functional dyspepsia symptoms and brain gut peptide indexes

Functional dyspepsia is one of the most common functional gastrointestinal diseases in the clinic [7-9]. Functional dyspepsia patients are often accompanied by postprandial discomfort, epigastric pain and other symptoms, which seriously affect the quality of life of patients. Brain gut peptides can play an important regulatory role in the gastrointestinal system,

including gastrointestinal peristalsis, secretion and absorption and other physiological activities [10-12]. In patients with functional dyspepsia, abnormal secretion of brain gut peptides may lead to slowed or enhanced intestinal peristalsis, which may exacerbate the patient's symptoms. Brain gut peptides may also affect visceral sensitivity, resulting in enhanced or diminished perception of gastrointestinal stimuli in patients[13-14]. The results of the present study showed that 5-HT and MTL were higher in patients with functional dyspepsia symptoms of early satiety and epigastric pain than in those without early satiety ($P<0.05$), and there was a correlation between the epigastric pain sensation score and the MTL level ($P<0.05$). 5-HT, an important neurotransmitter and a vasoactive substance, is widely present in the gastrointestinal tract, and it has a modulating effect on the motility, secretion, and sensory functions of the gastrointestinal tract in patients with functional dyspepsia, abnormal levels of 5-HT may be closely related to patients' symptoms. MTL is a hormone secreted by the gastrointestinal tract, whose main function is to promote gastrointestinal motility and emptying; in patients with functional dyspepsia, the levels of MTL may also be abnormal.5-HT and MTL may not be isolated in the pathogenesis of functional dyspepsia, and there may be an interaction between them, such as 5-HT and MTL[15-17]. The present study confirmed that there is a significant correlation between brain gut peptide indexes and functional dyspepsia symptoms, which provides a new idea for the study of the pathogenesis of functional dyspepsia. In the future, the specific mechanism of 5-HT and MTL in the pathogenesis of functional dyspepsia, as well as their interactions with other neurotransmitters and hormones can be further investigated in depth to provide a theoretical basis for the development of more effective therapeutic programs.

4.2 Functional dyspepsia influencing factors and predictive role of VIPs

Functional dyspepsia is a common digestive disease with numerous influencing factors [18-20]. In the present study, 100 patients with functional dyspepsia suffered from influencing factors including patients' gender, binge eating, preference for hot food, picky eating, acidic products, eating on time, eating late night snacks, daily sleep time, history of drug allergy, family history, constipation, and VIP level ($P<0.05$), excluding age, drinking tea, drinking alcohol, eating spicy food, eating breakfast, and eating ($P>0.05$). Among them, most functional gastrointestinal disorders were more prevalent in women than in men. Binge eating is an unhealthy eating habit that increases the burden on the gastrointestinal tract and leads to functional dyspepsia. Although excessive alcohol consumption may be harmful to the gastrointestinal tract, moderate alcohol consumption usually does not lead to functional dyspepsia, but individual differences may lead to different tolerance of alcohol in different people. Not only that, the stimulation of the gastrointestinal tract by spicy foods varies from person to person, and not everyone will experience functional indigestion as a result of eating spicy foods. In addition, eating breakfast is generally considered to be good for health and is not directly related to functional dyspepsia.

Logistic regression analysis showed that the factors influencing the prevalence of functional dyspepsia in 100 patients included patients' gender, poor dietary habits, bad hobbies, daily sleep time <6h, history of drug allergy, family history, constipation, and abnormally high VIP levels ($P<0.05$); the AUC of the ROC curve of the predictive value of VIP for functional dyspepsia was 0.564, which suggests that VIP has good predictive value for functional dyspepsia.

5. Conclusion

In conclusion, functional dyspepsia is a common disease, and brain peptide and functional dyspepsia symptoms and the existence of a certain predictive effect on the disease can be used to study the relevant targeted therapeutic programs.

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