

Psychological characteristics and GoNogo research of patients with functional constipation

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Abstract

The emotional state, psychological characteristics, cognitive function, and the relevance among above factors in patients with functional constipation (FC) are complex. This study aimed to investigate whether FC symptoms might be related to implicit processing such as psychological characteristics and emotional somatization.

Thirty-five FC patients and 24 normal volunteers were recruited to collect event-related potentials (ERP) behavior and electroencephalogram data when simple digital GoNogo visual tasks were performed. Hamilton Depression Scale (HAMD-17), Hamilton Anxiety Scale (HAMA), Symptom Checklist, and Eysenck Personality Inventory (EPQ) were assessed before the ERP test.

There was significant difference in average score, positive index, somatization, obsessive-compulsive disorder, anxiety, depression and psychoticism in HAMD-17, HAMA, Symptom Checklist, and extroversion or introversion and neuroticism in EPQ between the FC patients group and the normal control group ($P < 0.05$). There was a significant difference in the amplitude of ERP-P300 at site F4, F7, and FZ ($P < 0.05$).

FC patients showed anxiety and depression. The asymmetric forebrain abnormal activities in the 2 hemispheres might initiate implicit automatic processing, such as somatization and obsessive-compulsive disorder, in order to cope with painful experience caused by anxiety and depression in patients with FC. Cognitive dysfunction of implicit processing might be involved in the abnormality of visual communication and information processing.

Abbreviations: CHPQ = Chinese translation of the Edinburgh handedness inventory, EEG = electroencephalogram, EPQ = Eysenck Personality Inventory, ERP = event-related potentials, FC = functional constipation, HAMA = Hamilton anxiety Scale, HAMD-17 = Hamilton Depression Rating Scale, IBS = irritable bowel syndrome, NC = normal control, OCD = obsessive-compulsive disorder, SCL-90 = Symptom Checklist.

Keywords: emotion, event-related potentials, functional constipation, implicit processing

1. Introduction

Functional constipation (FC) is a common functional gastrointestinal digestive disease, of which the etiology and pathogenesis are not clear yet.^[1] Studies have found that rectal power and

sensory abnormalities contributed to FC.^[2] Psychological factors were closely related to the development of functional gastrointestinal disorders, which may act through the brain-gut axis to affect gastrointestinal function.^[3,4] However, how the brain-gut axis start in patients with FC and the connection mechanism of psychological characteristics, emotional state, and cognition is unknown. Frequent urination, constipation, chest tightness, palpitation, headache, dizziness, and other symptoms were usually observed in clinical patients, but laboratory examinations of which were normal. Such a subconscious automated processing phenomenon was called implicit processing in psychology. In this study, it is envisaged that FC symptoms in FC patients might be related to implicit processing such as psychological characteristics and emotional somatization. The psychophysiological response mechanism such as somatization was initiated during implicit processing; therefore, the specific cognitive function and avoiding of emotional pain were observed in clinical patients. Most FC patients had anal sphincter dysfunction. GoNogo task can show the subconscious bowel habits of these patients. The Arabic number is used worldwide, which is simple and easy to operate. So we chose Arabic numeral “GoNogo” stimulating task in this study.

2. Methods

2.1. Subjects

Written informed consent was obtained, according to the regulation of clinical research in the correspondent country. The study has been approved by the Ethics Committee of Sir Run Run SHAW Hospital and Tongde Hospital of Zhejiang Province.

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Patients selected in the FC group matched listed criteria: (1) matched the Rome III diagnostic criteria of FC^[3]; (2) age ≥ 18 years old, male or female; (3) without cardiopulmonary, liver, kidney, and organic brain disease history; (4) without using anti-depressants, anti-anxiety, and all kinds of sedative drugs within 2 weeks before the test. The group was formed by a total of 35 cases, 15 males and 20 females, aged 18 to 70 years old.

Subjects selected in the normal control group (NC group) matched listed criteria: (1) healthy volunteers without cardiopulmonary, liver, kidney, and organic brain diseases history; (2) not taking any medication within 2 weeks before the test; (3) without constipation; (4) scores < 7 in the Hamilton anxiety Scale (HAMA) and Hamilton Depression Rating Scale (HAMD-17). The group was formed by a total of 24 cases, 12 males and 12 females, aged 18 to 68 years old.

There was no statistical difference in age distribution, gender, height, weight, years of education, smoking, and drinking history of subjects in both groups ($P > 0.05$) (Table 1). All subjects signed informed consent, with their visual acuity or corrected visual acuity at 1.0 or higher.

2.2. Scale rating

Handedness inventory of all subjects was tested with Chinese translation of the Edinburgh handedness inventory (CHPQ) by professionals who were standardized trained before event-related potentials (ERP).^[5] HAMA and HAMD-17 were used to assess anxiety and depression.^[6] The Symptom Checklist (SCL-90) was used to assess the inner automatic sense experience.^[7] Eysenck Personality Inventory (EPQ) was used to assess the personality character.

2.3. GoNogo visual tasks

E-Prime, the psychology experiments development software, was used to establish the GoNogo task.^[8] The GoNogo task was composed of 36 pictures each set of number words comprised 2, 3, or 4 stimuli with the white color on black background. The stimulus (i.e., Arabic number word) presented was Arabic numbers of “2,” “3,” or “4.” The horizontal viewing angle of pictures was 4.78° , vertical viewing angle of which was 3.82° . Of the 36 pictures, the first 12 pictures were for the practice before experiment, and the other 24 were for the formal experiment. Experiment pictures were divided into the matching group and the unmatching group following the experimental requirements (12 pictures of each group). There were 4 pictures with the each stimulus (i.e., Arabic number word). Stimulation in the matching group was numbers consistent with the correct response (such as 3 Arabic words “3”), whereas that in the interference

(unmatching) group was inconsistent with the correct response (such as 3 Arabic words “2”). The size of the numbers and symbols were No.25, and the font was Arial.

The experiment was performed in a soundproof electroencephalogram (EEG) suite by specialized professionals. All subjects sat on chairs, with a cap of 10 to 20 system standard electrodes put in place. This matched the 32-channel event-related brain potentials system tester produced by the German Brain Product (Gilching, Germany). The reference electrode was placed in the left and right mastoid regions, with the forehead of the subjects in a downward position. 32-channel EEG was recorded. In the meantime, the electrodes were placed on 1.5 cm above the right eye to record EOG, and ECG electrodes were placed to record ECG. Subjects were asked to close their eyes and focus on the task. The event-related design was used to provide stimulus, which was always presented in the center of the screen at the range of 5×4 cm. Distance from eyes of all subjects to the center of the screen was 60 cm. Subjects were asked to make appropriate key response on the keyboard following the experimental requirement. Guidance language was unified before the test, and the test requirements were explained to the subjects who then did some appropriate exercises. Guidance language presented as “Please give your response to the matching number of words you see on the screen as quickly as possible and press the button 1 please if not (unmatching), please do not press any keys; if you’re ready, press any key to start.” Following the presentation of a fixation point “+,” stimulus was then presented randomly. Time of guidance language presentation was 4000 ms. The fixation point presentation time was 1200 ms or 1500 ms alternating randomly to minimize the exercise effect and the expectation effect. The stimulus presentation time was 1500 ms.

2.4. EEG recording and acquisition and processing of information from ERP detection

Data were collected and auto-analyzed by the Brian Vision Recorder and Vision Analyzer of German Brain Products Company,^[8] of which the scalp impedance was $50 \text{ k}\Omega$, and the band-pass filter was 0.01 to 70 Hz. Sampling was continuous, with the sampling rate at 1000 Hz/guide per channel. Analysis epoch was 1000 ms, including 200 ms base line. Reaction and the rates of correctness were collected at the same time, with blink, ECG, and other fake reactions automatically corrected and amplitude at $\pm 100 \mu\text{V}$ automatically removed. Latency and amplitude of P300 of each target stimulus of 32-channel were analyzed, the time window of which was 250 to 500 ms. The highest positive peak in amplitude of measurement window was analyzed. The apex point was viewed as the baseline to measure the peak amplitude of the wave.

Table 1

Scores of HAMA and HAMD-17 and comparison of assessment for each factor of EPQ (scores, $\bar{x} \pm s$).

Group	Cases	HAMA	HAMD-17	EPQ		
				Psychoticism	Extroversion or introversion	Neuroticism
FC group	35	17.00 \pm 6.58*	15.39 \pm 5.92*	48.71 \pm 8.86	51.28 \pm 9.42†	52.00 \pm 9.79*
NC group	24	6.77 \pm 3.90	5.88 \pm 3.01	50.42 \pm 9.88	56.25 \pm 7.70	43.54 \pm 9.15

EPQ = Eysenck Personality Inventory, FC = functional constipation, HAMA = Hamilton Anxiety Scale, HAMD-17 = Hamilton Depression Rating Scale, NC = normal control. Compared with the normal control group.

* $P < 0.01$.

† $P < 0.05$.

2.5. Statistical methods

SPSS 12.0 software package was applied. Mean \pm standard deviation ($\bar{x} \pm SD$) was used to assess measurement data. Student's *t* test was used to compare groups and was repeated in EPQ and SCL-90. $P < 0.05$ was considered statistically significant. The chi-square test was used to measure categorical data.

3. Results

Evaluation results of CHPQ of all subjects in 2 groups were right-handed. There was a significant difference in HAMA and HAMD-17 scores between the FC group and the normal control group ($P < 0.05$). EPQ scores showed that there was also a significant difference in extroversion or introversion, and neuroticism ($P < 0.05$), as seen in Table 1.

SCL-90 scores showed that there was a significant difference in scores of somatization, obsessive-compulsive disorder (OCD), depression, anxiety, psychoticism, and other additional projects between the 2 groups ($P < 0.05$), whereas there was no significant difference in scores of interpersonal sensitivity, hostility, terror, paranoia, or other projects ($P > 0.05$) (Table 2).

When GONO visual tasks were performed, the reaction of subjects was not significantly different between the FC group and the control group ($t = 1.699$, $P = 0.095$), and so was P300 latency ($P > 0.05$). However, the amplitude increased in site F4 and FZ and decreased in site F7. There was a significant difference in the amplitude of site F4, F7, and FZ ($P < 0.05$) ($t = -2.190$, 2.252 , -2.178 , respectively) between 2 groups (Table 3).

4. Discussion

Functional gastrointestinal disorders have common pathophysiological basis: the sensory reaction of visceral stimulation was relevant with mood changes. There is a large number of serotonin nerves distributed in regions where the nervous system is closely connected with mind and emotion, such as limbic system, hypothalamus, and brainstem. More or less serotonin in brainstem could lead to insomnia, sensory threshold change, and mental and behavioral abnormalities. The sensory reaction of visceral stimulation could affect mood and emotion regions in brain, leading to and (or) increasing depression in patients.^[3,4,9,10] Therefore, the pathogenesis of FC is not only related to intestinal motility and sensory abnormalities, but also influenced by psychological factors. Nehra et al^[4] had reported that 65% of patients with defecation disorders and constipation suffered from mental disorders, illustrating that psychological

factors also reduced the sensory thresholds of physical symptoms. This study showed that anxiety and depression were relatively obvious in patients with FC. Implicit response such as somatization and OCD as well as personality characteristics such as extroversion or introversion and neuroticism were also relatively prominent in FC patients. The results of anxiety, depression, somatization, OCD, and psychoticism of patients with FC in SCL-90 indicated that such patients had certain psychological character, demonstrating that patients with FC suffered from anxiety, depression, somatization and OCD, etc. Those symptoms were taken place to cope with implicit emotion and psychological painful experience, which may be related to neuroticism. Results of this study were consistent with previous reports.^[3,4,9,10]

ERP P300 is related to memory systems and complex cognition processes, which is the reaction process of objective things, and can be considered to be objective indicators of cognitive function to reflect the level of cognition objectively, early, and quantitatively.^[11] It is a common knowledge that the latency period of P300 reflects cognition processing speed of brain stimulation, and the P300 amplitude is relevant with attention of subjects with target stimulation,^[12] the level of which represents the intensity of brain information processing. The EPR study by Blomhoff et al^[13] showed that the prefrontal region of patients with irritable bowel syndrome (IBS) was highly activated when auditory task was performed, and cognitive function of P300 and N400 was related to the mood and personality of patients, demonstrating that the abnormal brain function may be one of the causes of IBS. Another ERP research by Blomhoff et al^[14] using emotion vocabulary auditory tasks showed that the prefrontal region of IBS patients was associated with visceral sensation, and subjective experience of illness signs could be predicted by implicit memory of brain cognition system. Those findings suggested that high activity of the prefrontal region could be viewed as the psychological and physiological mechanisms of both anxiety and IBS. The fMRI study by Andresen et al^[15] suggested brain information processing characters of nonvisceral stimulation in IBS patients and healthy controls using auditory stimulation tasks could identify different emotion features. Results showed that sensory symptoms in IBS might not be specific visceral reaction, which reflected general changes in emotional sensitivity and reaction, and might be related to abnormal psychology found in IBS patients. Dickhaus et al^[16] proved the stress-induced adjustment assumption in visceral sensation of IBS patients. Results of this study showed that P300 latency and response when performing GoNogo visual tasks in patients with FC were similar with that in the normal control

Table 2
Scores of factors in the SCL-90 scale (scores, $\bar{x} \pm s$).

Groups	Cases	SCL-90				
		Somatization	OCD	Interpersonal sensitivity	Depression	Anxiety
FC group	35	1.65 \pm 0.34*	1.84 \pm 0.65 [†]	1.59 \pm 0.52	2.18 \pm 2.62*	1.46 \pm 0.41*
NC group	24	1.25 \pm 0.32	1.48 \pm 0.44	1.72 \pm 1.81	1.31 \pm 0.32	1.17 \pm 0.26

Groups	Cases	SCL-90				
		Hostility	Terror	Paranoia	Psychoticism	Additional projects
FC group	35	1.43 \pm 0.62	1.37 \pm 0.44	1.39 \pm 0.54	1.66 \pm 1.68 [†]	1.55 \pm 0.51 [†]
NC group	24	1.22 \pm 0.24	1.22 \pm 0.28	1.22 \pm 0.24	1.15 \pm 0.14	1.27 \pm 0.30

FC=functional constipation, NC=normal control, OCD=obsessive-compulsive disorder, SCL-90=Symptom Checklist. Compared with the normal control group.

* $P < 0.01$.

[†] $P < 0.05$.

Table 3**Latency and amplitude results of GoNogo visual tasks in the functional constipation (FC) group and the normal control (NC) group.**

Electrode location	FC group ($\bar{x} \pm SD$, n=35)		NC group ($\bar{x} \pm SD$, n=24)		t_{Latency}	P_{Latency}	$t_{\text{Amplitude}}$	$P_{\text{Amplitude}}$
	Latency (ms)	Amplitude (μV)	Latency (ms)	Amplitude (μV)				
F3	364.40 ± 129.15	3.24 ± 1.77	332.57 ± 81.27	2.55 ± 0.98	0.607	0.549	0.968	0.343
F4	398.35 ± 102.73	2.47 ± 1.01	367.33 ± 107.42	3.43 ± 1.39	0.786	0.439	-2.190	0.037*
C3	469.12 ± 154.78	3.19 ± 1.32	468.75 ± 149.60	3.13 ± 2.19	0.008	0.994	0.110	0.913
C4	408.92 ± 95.21	3.28 ± 1.96	449.27 ± 110.33	2.99 ± 2.18	-1.360	0.180	0.474	0.638
P3	461.16 ± 140.85	4.69 ± 3.12	478.09 ± 123.61	4.93 ± 3.29	-0.446	0.657	-0.269	0.789
P4	435.61 ± 112.61	5.15 ± 3.78	471.30 ± 116.32	4.52 ± 3.50	-1.136	0.261	0.627	0.534
O1	438.29 ± 105.22	7.06 ± 3.88	474.86 ± 122.31	5.34 ± 3.56	-1.039	0.305	1.515	0.137
O2	428.80 ± 112.36	6.38 ± 3.86	473.91 ± 130.01	5.41 ± 3.81	-1.289	0.204	0.880	0.383
F7	438.10 ± 156.70	4.68 ± 1.89	451.00 ± 108.87	3.42 ± 1.05	-0.212	0.834	2.252	0.034*
F8	478.18 ± 146.94	4.53 ± 1.89	454.86 ± 97.24	4.49 ± 2.48	0.524	0.604	0.045	0.964
T7	467.50 ± 158.83	5.14 ± 2.70	515.64 ± 99.28	5.21 ± 3.18	-0.922	0.363	-0.067	0.947
T8	499.70 ± 113.93	4.57 ± 2.12	483.60 ± 109.87	4.38 ± 2.40	0.486	0.629	0.273	0.786
P7	472.00 ± 141.98	5.25 ± 2.59	513.26 ± 113.70	5.68 ± 3.40	-1.016	0.316	-0.451	0.655
P8	457.22 ± 108.51	5.28 ± 2.77	482.18 ± 110.38	4.86 ± 3.20	-0.795	0.431	0.502	0.618
FZ	450.00 ± 120.99	1.58 ± 0.46	420.00 ± 35.02	3.27 ± 2.85	0.476	0.651	-2.178	0.038*
CZ	467.43 ± 122.15	2.54 ± 1.71	450.67 ± 123.06	2.73 ± 1.60	0.271	0.790	-0.231	0.821
PZ	437.86 ± 127.84	5.64 ± 3.74	477.09 ± 129.58	4.75 ± 3.48	-1.071	0.290	0.870	0.389
OZ	430.61 ± 117.23	6.67 ± 4.14	476.00 ± 114.91	5.15 ± 3.52	-1.326	0.192	1.344	0.186
FC1	402.40 ± 128.46	2.29 ± 0.52	341.00 ± 88.69	1.67 ± 0.92	0.941	0.378	1.289	0.238
FC2	478.80 ± 118.57	1.78 ± 0.70	406.29 ± 69.32	2.49 ± 0.63	1.446	0.169	-2.177	0.047
CP1	463.10 ± 144.81	3.54 ± 2.61	490.55 ± 134.74	3.29 ± 2.44	-0.700	0.487	0.339	0.736
CP2	427.27 ± 106.27	3.43 ± 2.54	461.20 ± 122.51	3.72 ± 2.97	-1.063	0.293	-0.379	0.706
FC5	428.73 ± 152.71	3.92 ± 1.37	453.20 ± 132.98	2.66 ± 1.09	-0.436	0.666	2.545	0.017
FC6	451.09 ± 117.25	3.88 ± 2.33	455.50 ± 114.46	3.87 ± 2.10	-0.116	0.909	0.007	0.994
CP5	475.08 ± 156.74	4.72 ± 2.19	476.75 ± 119.73	4.73 ± 3.50	-0.037	0.971	-0.020	0.984
CP6	344.03 ± 109.32	4.84 ± 2.28	479.27 ± 112.43	4.39 ± 3.27	-1.246	0.219	0.573	0.569
TP9	485.04 ± 151.12	5.89 ± 2.07	487.11 ± 103.58	6.30 ± 6.18	-0.050	0.961	-0.294	0.770
TP10	469.71 ± 123.23	5.45 ± 2.65	469.89 ± 107.68	4.81 ± 3.29	-0.005	0.996	0.686	0.497

FC=functional constipation, NC=normal control, SD = standard deviation.

* $P < 0.05$.

group, indicating there was no significant difference in response time of visual stimulation in patients with FC and normal control group ($P > 0.05$). But the P300 amplitude increased in site F4 and FZ of FC patients, of which the activity in the right anterior region was higher, whereas the P300 amplitude in site F7 was lower, suggesting that attention and processing of visual channels and implicit cognition processing which was related to emotions were abnormal in FC patients.

Implicit processing reflects the subconscious, automatic process of stimulation. Some researchers^[17] found that the implicit processing of face words was mainly presented in the central and top region at 300 to 500 ms after stimulation. It had been suggested that the ERP-P300 could better reflect cognitive function in patients with somatization disorder,^[14] which could be viewed as an objective electrophysiological reference index in clinical use. The results of this study showed that the visual channel P300 presented abnormal processing activities and increased amplitude in site F4 and FZ while decreased brain activity in site F7, suggesting that patients with FC suffered from forebrain region dysfunction and asymmetric cognitive processing abnormality caused by activity change in the 2 hemispheres, presumably that was associated with implicit processing. The forebrain abnormal activity of asymmetry in the 2 hemispheres initiated implicit automatic processing such as somatization and OCD to avoid or reduce psychological painful experience caused by anxiety and depression in FC patients.

The limitation of this study was that the sample size was relatively small. We, therefore, recommend to expand the sample size in future studies to explore the differences between the

2 groups in depth using the standard 32-channel electrode EEG. Age-related factors such as the function changes of local muscle power involved in FC, therefore needs to be included in future research design. In addition, implicit processing of emotion and cognitive function is complex; thus, a variety of designs will be needed for further study.

In summary, this study found that patients with FC suffered from anxiety and depression and had the tendency of somatization, OCD, psychoticism, and neuroticism. The forebrain abnormal activity of asymmetry in the 2 hemispheres might initiate implicit automatic processing such as somatization and OCD in patients with FC in order to cope with painful experience caused by anxiety and depression. The P300 cognitive function involved in implicit processing in visual communication and information processing in patients with FC, presumably that was associated with emotional implicit cognition processing dysfunction.

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