

Theory of mind deficits in patients with esophageal cancer combined with depression

Yin Cao, Quan-Di Zhao, Li-Jun Hu, Zhi-Qin Sun, Su-Ping Sun, Wen-Wei Yun, Yong-Gui Yuan

Yin Cao, Wen-Wei Yun, Department of Internal Medicine (Neurology), Changzhou Second People's Hospital Affiliated to Nanjing Medical University, Changzhou 213003, Jiangsu Province, China

Quan-Di Zhao, Li-Jun Hu, Su-Ping Sun, Department of Radiotherapy, Changzhou Second People's Hospital Affiliated to Nanjing Medical University, Changzhou 213003, Jiangsu Province, China

Zhi-Qin Sun, Department of Nursing, Changzhou Second People's Hospital Affiliated to Nanjing Medical University, Changzhou 213003, Jiangsu Province, China

Yong-Gui Yuan, Department of Psychology, Zhongda Hospital Affiliated to Southeast University, Nanjing 210009, Jiangsu Province, China

Author contributions: Zhao QD, Hu LJ and Yuan YG collected all the human material in addition to providing financial support for this work; Sun ZQ and Sun SP provided analytical tools and were also involved in editing the manuscript; Cao Y and Yun WW designed the study and wrote the manuscript.

Correspondence to: Yong-Gui Yuan, Chief Physician, Professor, Department of Psychology, Zhongda Hospital Affiliated to Southeast University, 87 Dingjiaqiao, Nanjing 210009, Jiangsu Province, China. caoyingyishi@yeah.net

Telephone: +86-25-83272111 Fax: +86-25-83272111

Received: November 10, 2012 Revised: March 5, 2013

Accepted: March 22, 2013

Published online: May 21, 2013

Abstract

AIM: To characterize the two components of theory of mind (ToM) in patients with esophageal cancer combined with depression.

METHODS: Sixty-five patients with esophageal cancer combined with depression (depressed group) and 62 normal controls (control group) were assessed using reading the mind in the eyes test, faux pas task, verbal fluency test, digit span test and WAIS IQ test. The depressed group was divided into two subgroups including psychotic depressed (PD) group (32 cases) and nonpsychotic depressed (NPD) group (33 cases).

The clinical symptoms of patients were assessed using Beck depression inventory version II and brief psychiatric reacting scale (BPRS).

RESULTS: There was a significant difference between the depressed group and the control group on tasks involving ToM social perceptual components (mind reading: $t = 7.39, P < 0.01$) and tests involving ToM social cognitive components (faux pas questions: $t = 13.75, P < 0.01$), respectively. A significant difference was also found among the PD group, the NPD group and the control group on mind reading ($F = 32.98, P < 0.01$) and faux pas questions ($\chi^2 = 78.15, P < 0.01$), respectively. The PD group and NPD group performed worse than normal group controls both on mind reading and faux pas questions ($P < 0.05$). The PD group performed significantly worse than the NPD group on tasks involving ToM (mind reading: $F = 18.99, P < 0.01$; faux pas questions: $F = 36.01, P < 0.01$). In the depressed group, there was a negative correlation between ToM performances and BPRS total score (mind reading: $r = -0.35, P < 0.01$; faux pas questions: $r = -0.51, P < 0.01$), and between ToM performances and hostile suspiciousness factor score (mind reading: $r = -0.75, P < 0.01$; faux pas questions: $r = -0.73, P < 0.01$), respectively.

CONCLUSION: The two components of ToM are both impaired in patients with esophageal cancer combined with depression. This indicates that there may be an association between ToM deficits and psychotic symptoms in clinical depression.

© 2013 Baishideng. All rights reserved.

Key words: Esophageal cancer combined with depression; Theory of mind; Social perceptual component; Social cognitive component

Core tip: In this study, the theory of mind deficits in patients with esophageal cancer combined with de-

pression was investigated, and the relation between ToM deficits and psychotic symptoms was discussed.

Cao Y, Zhao QD, Hu LJ, Sun ZQ, Sun SP, Yun WW, Yuan YG. Theory of mind deficits in patients with esophageal cancer combined with depression. *World J Gastroenterol* 2013; 19(19): 2969-2973 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v19/i19/2969.htm> DOI: <http://dx.doi.org/10.3748/wjg.v19.i19.2969>

INTRODUCTION

Depression exists in about 24% of patients with esophageal cancer^[1]. It is found that there are theory of mind (ToM) deficits in patients with depression^[2-4]. In cognitive neuropsychiatry, the ToM is divided into a social perceptual component and a social cognitive component^[5,6], in terms of information processing theories. In recent years, the social cognitive impairment caused by depression and its potential cognitive neuropsychological mechanisms have become a research hotspot^[2-4].

It is reported that the occurrence of esophageal cancer combined with depression is closely related with cognition in disease^[7-9]. Whether the cognitive biases include ToM deficits or not is not clear. In this study, the ToM deficits in patients with esophageal cancer combined with depression were investigated, and the relation between ToM deficits and psychotic symptoms was discussed.

MATERIALS AND METHODS

Research objects

Sixty-five patients with esophageal cancer combined with depression in Changzhou Second People's Hospital Affiliated to Nanjing Medical University (Changzhou, China) were studied from January to December in 2011. Their beck depression inventory version II (BDI-II)^[10] scores were not less than 5. All patients had an education background of junior middle school and above. They were right-handed and had normal eyesight and hearing. There was no patient with a medical history of head trauma, central nervous system disease, metastatic brain tumor, mental illness or substance dependence. No patient had been treated with chemotherapy.

The patients were divided into a psychotic depressed (PD) group (32 cases) and a nonpsychotic depressed (NPD) group (33 cases), according to whether or not patients had psychotic symptoms [the brief psychiatric reacting scale (BPRS)^[11] total score was > 35]. Psychotic symptoms were distinguished from schizophrenia. The ages of patients were 28-60 years, with an average age of 48.50 ± 4.53 years. They had obtained 9-16 years of education, with an average education duration of 12.57 ± 1.64 years. The average age of the NPD group and the PD group was 45.00 ± 5.02 and 46.28 ± 4.19 years, respectively. The average duration of education in the NPD

group and the PD group was 12.18 ± 1.06 and 11.37 ± 1.25 years, respectively.

The control group consisted of 62 cases of college students, physicians and people with normal physique. They had no medical history of neurological disease, mental illness, substance abuse, or family psychiatry. They had an education background of junior middle school and above. They were right-handed and had normal eyesight and hearing. Their ages were 27-62 years, with an average age of 47.65 ± 4.64 years. The duration of education was 9-16 years, with an average education duration of 11.59 ± 2.01 years.

All research participants had signed informed consent before enrolling in this study. The patients had obtained the agreement of guardians. There was no significant difference in gender, age, or duration of education between the depressed group and the control group ($P > 0.05$) or between the PD group, the NPD group and the control group ($P > 0.05$). The difference in disease course between the NPD group and the PD group was not statistically significant ($t = 0.69$, $P > 0.05$).

Reading the mind in the eyes test

The reading the mind in the eyes test reflected the social perceptual component of ToM. It required the participants to conduct a perceptual processing of the mental activity status of the character in the eye area, and select one word from four alternatives which could most accurately reflect the character's mental activity status. The gender recognition task was used as a control task, which required the participant to recognize the gender of the character in the eye area. It reflected the perceptual processing of general social cues. Five min of learning of alternative vocabulary annotations was performed before test. One score was obtained for each correct answer. For a total of 34 questions (17 male and 17 female), there was a total score of 34 for reading the mind in the eyes test and the gender recognition task, respectively^[12-14].

Faux pas task

The faux pas task (faux pas questions) belonged to the social cognitive component of ToM. It required the research object to plot the mental activity status of the character in the story and judge whether or not the character had said the words which should not be said or the embarrassing words, according to the storyline. The understanding of general text content in story was used as a control question. It reflected the understanding of the story content, and comprised 20 little stories (10 faux pas stories and 10 stories without faux pas). There were 2 faux pas questions and 2 control questions for each story. One score was obtained for each correct answer. The total score for faux pas questions and control questions was 20 and 40, respectively^[13-15].

Clinical evaluation and neuropsychological test

The clinical symptoms of patients were assessed using BDI-II and BPRS ($K = 0.83$). The WAIS-IQ test^[16], digit

Table 1 General data of patients with esophageal cancer combined with depression

Groups	<i>n</i>	BDI-II score	BPRS total score	Anxiety depression factor score	Anergia factor score	Thought disturbance factor score	Activation factor score	Hostile suspiciousness factor score
PD group	23	33.00 ± 4.62 ¹	43.72 ± 7.11 ¹	14.28 ± 2.21 ¹	6.13 ± 3.14	6.34 ± 3.35	4.99 ± 2.36	10.31 ± 2.95 ¹
NPD group	33	20.22 ± 3.28	27.13 ± 6.12	10.75 ± 2.69	5.12 ± 3.46	5.91 ± 3.29	4.97 ± 3.01	2.21 ± 1.95

PD: Psychotic depressed; NPD: Nonpsychotic depressed. ¹*t* test, $P < 0.01$ vs NPD group.

Table 2 Comparisons of neuropsychological test and theory of mind test performance

Groups	<i>n</i>	IQ score	VFT score	DST score	Mind reading score	Gender recognition score	Faux pas questions score	Control questions score
Depressed group	65	103.12 ± 5.18	32.11 ± 2.38 ¹	13.02 ± 1.08	24.12 ± 2.19 ¹	30.11 ± 1.02	15.02 ± 1.63 ¹	37.25 ± 0.68
PD group	32	103.42 ± 3.58	30.02 ± 2.16 ²	12.68 ± 1.02	22.89 ± 2.07 ^{2,3}	30.12 ± 0.99	13.16 ± 1.71 ^{2,3}	37.31 ± 0.71
NPD group	33	103.77 ± 4.30	34.21 ± 2.08	13.79 ± 1.01	25.38 ± 2.32 ²	30.22 ± 0.95	15.82 ± 1.13 ²	37.52 ± 0.62
Control group	62	104.11 ± 3.22	35.05 ± 2.01	13.88 ± 0.98	27.89 ± 2.05	30.57 ± 1.01	19.92 ± 1.01	37.51 ± 0.65

¹*t* test, $P < 0.01$ vs NPD group; ²Bonferroni test or Mann-Whitney *U* test, $P < 0.05$ vs control group; ³*t* test, $P < 0.01$ or 0.05 vs NPD group. VFT: Verbal fluency test; DST: Digit span test; PD: Psychotic depressed; NPD: Nonpsychotic depressed.

span test (DST)^[17] and verbal fluency test (VFT)^[18] were conducted on all research objects. The DST included the recitation and inverted recitation of digits. The total score was expressed as the sum of two recitation scores. The VFT required the participant to say as many names as possible of vegetables, fruits and animals. One score was obtained for each correct answer. There was no score for duplicated names.

Statistical analysis

Statistical analysis was performed using SPSS 13.0 statistical software. The χ^2 test, independent samples *t* test, single factor analysis of variance (using Bonferroni correction for multiple comparisons) and Kruskal-Wallis test (using Mann-Whitney *U* test for multiple comparisons) were used to compare data according to the different types of variables. In the depressed group, the analysis of covariance was conducted on ToM performance using the BDI-II score as a covariant, and the partial correlation analysis was conducted between ToM performance and BPRS total score, and between ToM performance and other factor scores, respectively.

RESULTS

Comparisons of general data

There was no significant difference in IQ score between the depressed group and the control group ($t = 0.52$, $P > 0.05$). It was the same with IQ score among the NPD group, PD group and control group ($F = 0.12$, $P > 0.05$). The BDI-II score ($t = 6.77$, $P < 0.01$), BPRS score ($t = 6.78$, $P < 0.01$), anxiety-depression factor score ($t = 3.56$, $P < 0.01$) and hostile suspicion factor score ($t = 10.95$, $P < 0.01$) in the PD group were significantly higher than those in the NPD group. The differences in other factors scores were not significant between the two groups ($P > 0.05$). Results were shown in Table 1.

Comparisons of neuropsychological test performance

As shown in Table 2, the VFT score in the depressed group was significantly lower than that in the control group ($t = 4.34$, $P < 0.01$), but there was no significant difference in DST score between the two groups ($t = 0.75$, $P > 0.05$). The differences in VFT score among the NPD group, PD group and control group were statistically significant ($F = 15.56$, $P < 0.01$). The VFT score in the PD group was significantly lower than that in the control group and the NPD group ($P < 0.05$), respectively, and there was no significant difference between the NPD group and the control group ($P > 0.05$).

Comparisons of ToM test performances

There was a significant difference between the depressed group and control group on tasks involving a ToM social perceptual component (mind reading: $t = 7.39$, $P < 0.01$) and tests involving a ToM social cognitive component (faux pas questions: $t = 13.75$, $P < 0.01$), respectively. But there was no significant difference for the gender recognition score and control questions score ($t = 0.47$, $P > 0.05$; $t = 0.52$, $P > 0.05$), respectively. A significant difference was also found among PD group, NPD group and control group on mind reading ($F = 32.98$, $P < 0.01$) and faux pas questions ($\chi^2 = 78.15$, $P < 0.01$). Results of multiple comparisons showed that the PD group was worse than the NPD group and the NPD group was worse than the control group on mind reading ($P < 0.05$ for both). In addition, on faux pas questions, the PD group performed worse than the control group and the NPD group, respectively, (Mann-Whitney *U* = 153.08, $Z = -7.38$, $P < 0.05$; Mann-Whitney *U* = 127.95, $Z = -4.26$, $P < 0.05$), and the NPD group performed worse than the control group (Mann-Whitney *U* = 153.13, $Z = -6.81$, $P < 0.05$). In addition, the PD group performed significantly worse than the NPD group on tasks involving ToM (mind reading: $F = 18.99$, $P < 0.01$; faux pas questions: $F = 36.01$, $P < 0.01$).

Partial correlation analysis between ToM performance and BPRS score

In the depressed group, the faux pas questions score was positively correlated with the mind reading score ($r = 0.56$, $P < 0.01$). There was a negative correlation between ToM performances and BPRS total score (mind reading: $r = -0.35$, $P < 0.01$; faux pas questions: $r = -0.51$, $P < 0.01$), and between ToM performances and hostile suspiciousness factor scores (mind reading: $r = -0.75$, $P < 0.01$; faux pas questions: $r = -0.73$, $P < 0.01$), respectively. There was no correlation between ToM performances and other factors score related to BPRS ($P > 0.05$).

DISCUSSION

This study aims to investigate the components of ToM in patients with esophageal cancer combined with depression. Results show that the depressed group performed worse than the control group on tasks involving ToM social perceptual components and test involving ToM social cognitive components, respectively. This suggests that the ToM deficits exist in patients with esophageal cancer combined with depression. These results are in accordance with the studies of Inoue *et al.*^[3,4] and Lee *et al.*^[19], in which ToM deficits are found in patients with depression in ToM tests.

In this study, there are impairments in the social perceptual component and social cognitive component of ToM. The social perceptual component of ToM occurs mainly in the right cerebral hemisphere, and the left cerebral hemisphere is mainly responsible for the social cognitive component^[6,12]. This indicates that there are bilateral brain impairments in patients with esophageal cancer combined with depression. These results are similar to those of the study by Rotenberg^[20] which suggests that depression is related not only to right hemisphere dysfunction, but also to left hemisphere prefrontal hypo-function. This indicates that there is a cognitive neuropsychology mechanism of bilateral brain impairments for depression.

In this study, the ToM performances in the PD group are significantly worse than those in the NPD group. Results of partial correlation analysis show that there was a negative correlation between ToM performances and BPRS total score, and between ToM performances and hostile suspiciousness factor score, respectively. This indicates that there is a positive correlation between ToM deficits and psychiatric symptoms in clinical depression. Therefore, early detection and intervention of ToM deficits and psychiatric symptoms in patients with esophageal cancer combined with depression is helpful for reducing the perniciousness of disease.

There is no metastatic brain tumor or chemotherapy in these patients, which has purified the samples to a certain extent. But the remote effects of tumors on neuropsychiatric function can not be excluded. Therefore, the follow up is very important for enriching and improving the final results.

COMMENTS

Background

Twenty-four percent of esophageal cancer patients also have depression, which may aggravate the disease condition and affect the treatment and rehabilitation. Previous studies suggest that there are a variety of cognitive disorders including theory of mind (ToM) deficits in patients with depression. The occurrence of esophageal cancer complicated with depression is closely related to cognition on disease. Whether cognitive biases include ToM deficits is not clear.

Research frontiers

ToM deficits are social cognitive disorders. In this study, ToM deficits in esophageal cancer patients complicated with depression are observed using "Reading the Mind in the Eyes" test and Faux pas Task.

Innovations and breakthroughs

Previous studies on cognitive impairment in esophageal cancer patients complicated with depression mainly focus on episodic memory impairment, executive function decline, psychomotor slowing and attention deficits, except ToM deficits. In this study, ToM deficits in esophageal cancer patients complicated with depression have been investigated. This contributes to prevention and treatment of esophageal cancer with depression, and improvement of patient's social adaptability.

Applications

Results of this study can be applied to preventing and treating esophageal cancer with depression, and improving the rehabilitation level and social adaptability of patients.

Terminology

ToM refers to the knowledge system on speculation of psychological state, namely the cognitive system on judgment of psychological state such as belief, intention, wish, need, motive and emotion. It is one of the most basic abilities of an individual for adapting into society. In cognitive neuropsychiatry, ToM is divided into a social perceptual component and social cognitive component, in terms of information processing theory.

Peer review

This is good research. It finds ToM deficits in esophagus cancer patients complicated with depression, and has analyzed the damage characteristics of two subcomponents. This study is helpful for clinical assessment of cognitive disorders in esophageal cancer patients complicated with depression, and prevention and treatment of disease. In addition, it can provide new approaches for improving the social adaptabilities of patients.

REFERENCES

- 1 Jia L, Jiang SM, Shang YY, Huang YX, Li YJ, Xie DR, Huang KH, Zhi FC. Investigation of the incidence of pancreatic cancer-related depression and its relationship with the quality of life of patients. *Digestion* 2010; **82**: 4-9 [PMID: 20145402]
- 2 Kerr N, Dunbar RI, Bental RP. Theory of mind deficits in bipolar affective disorder. *J Affect Disord* 2003; **73**: 253-259 [PMID: 12547294 DOI: 10.1016/S0165-0327(02)00008-3]
- 3 Inoue Y, Tonooka Y, Yamada K, Kanba S. Deficiency of theory of mind in patients with remitted mood disorder. *J Affect Disord* 2004; **82**: 403-409 [PMID: 15555691]
- 4 Inoue Y, Yamada K, Kanba S. Deficit in theory of mind is a risk for relapse of major depression. *J Affect Disord* 2006; **95**: 125-127 [PMID: 16797082 DOI: 10.1016/j.jad.2006.04.018]
- 5 Sabbagh MA, Moulson MC, Harkness KL. Neural correlates of mental state decoding in human adults: an event-related potential study. *J Cogn Neurosci* 2004; **16**: 415-426 [PMID: 15072677 DOI: 10.1162/089892904322926755]
- 6 Sabbagh MA. Understanding orbitofrontal contributions to theory-of-mind reasoning: implications for autism. *Brain Cogn* 2004; **55**: 209-219 [PMID: 15134854]
- 7 Dempster M, McCorry NK, Brennan E, Donnelly M, Murray LJ, Johnston BT. Illness perceptions among carer-survivor dyads are related to psychological distress among Oesophageal cancer survivors. *J Psychosom Res* 2011; **70**: 432-439 [PMID: 21511073 DOI: 10.1016/j.jpsychores.2010.07.007]

- 8 **Dempster M**, McCorry NK, Brennan E, Donnelly M, Murray L, Johnston BT. Psychological distress among survivors of esophageal cancer: the role of illness cognitions and coping. *Dis Esophagus* 2012; **25**: 222-227 [PMID: 21819485 DOI: 10.1111/j.1442-2050.2011.01233.x]
- 9 **Kataria K**, Verma GR, Malhotra A, Yadav R. Comparison of quality of life in patients undergoing transhiatal esophagectomy with or without chemotherapy. *Saudi J Gastroenterol* 2012; **18**: 195-200 [PMID: 22626799 DOI: 10.4103/1319-3767.96454]
- 10 **Novy DM**, Stanley MA, Averill P, Daza P. Psychometric comparability of English- and Spanish-language measures of anxiety and related affective symptoms. *Psychol Assess* 2001; **13**: 347-355 [PMID: 11556271 DOI: 10.1037/1040-3590.13.3.347]
- 11 **Overall JE**, Gorham DR. The brief psychiatric rating scale. *Psychological Reports* 1962; **10**: 799-812
- 12 **Byom LJ**, Turkstra L. Effects of social cognitive demand on Theory of Mind in conversations of adults with traumatic brain injury. *Int J Lang Commun Disord* 2012; **47**: 310-321 [PMID: 22512516 DOI: 10.1111/j.1460-6984.2011.00102.x]
- 13 **Inoue Y**, Yamada K, Hirano M, Shinohara M, Tamaoki T, Iguchi H, Tonooka Y, Kanba S. Impairment of theory of mind in patients in remission following first episode of schizophrenia. *Eur Arch Psychiatry Clin Neurosci* 2006; **256**: 326-328 [PMID: 16927040]
- 14 **Baron-Cohen S**, Wheelwright S, Hill J, Raste Y, Plumb I. The "Reading the Mind in the Eyes" Test revised version: a study with normal adults, and adults with Asperger syndrome or high-functioning autism. *J Child Psychol Psychiatry* 2001; **42**: 241-251 [PMID: 11280420]
- 15 **Stone VE**, Baron-Cohen S, Knight RT. Frontal lobe contributions to theory of mind. *J Cogn Neurosci* 1998; **10**: 640-656 [PMID: 9802997]
- 16 **Miller LJ**, Myers A, Prinzi L, Mittenberg W. Changes in intellectual functioning associated with normal aging. *Arch Clin Neuropsychol* 2009; **24**: 681-688 [PMID: 19783531 DOI: 10.1093/arclin/acp072]
- 17 **Wykes T**, Reeder C, Huddy V, Taylor R, Wood H, Ghirasim N, Kontis D, Landau S. Developing models of how cognitive improvements change functioning: mediation, moderation and moderated mediation. *Schizophr Res* 2012; **138**: 88-93 [PMID: 22503640 DOI: 10.1016/j.schres.2012.03.020]
- 18 **Amaral-Carvalho V**, Caramelli P. Normative data for healthy middle-aged and elderly performance on the Addenbrooke Cognitive Examination-Revised. *Cogn Behav Neurol* 2012; **25**: 72-76 [PMID: 22596112 DOI: 10.1097/WNN.0b013e318259594b]
- 19 **Lee L**, Harkness KL, Sabbagh MA, Jacobson JA. Mental state decoding abilities in clinical depression. *J Affect Disord* 2005; **86**: 247-258 [PMID: 15935244 DOI: 10.1016/j.jad.2005.02.007]
- 20 **Rotenberg VS**. The peculiarity of the right-hemisphere function in depression: solving the paradoxes. *Prog Neuropsychopharmacol Biol Psychiatry* 2004; **28**: 1-13 [PMID: 14687851 DOI: 10.1016/S0278-5846(03)00163-5]

P- Reviewers Inoue Y, Kataria K **S- Editor** Wen LL
L- Editor O'Neill M **E- Editor** Li JY

