Decision-making Impairments in Primary Angle-closure Glaucoma Patients

Hui Pu1,2,3, Yong Wang4, Qiang Wei2,3, Hui-Juan Ma2,3, Pan-Pan Hu2,3, Shou-Ling Li4, Hong-Bo Pang1, Yang-Hua Tian3, Kai Wang1,2,3

1Department of Neurology, The Second People’s Hospital of Wuhu, Wuhu, Anhui 241000, China
2Department of Neurology, The First Hospital of Anhui Medical University, Hefei, Anhui 230032, China
3Anhui Province Key Laboratory of Cognition and Neuropsychiatric Disorders, Hefei, Anhui 230032, China
4Department of Ophthalmology, The First Hospital of Anhui Medical University, Hefei, Anhui 230032, China

Hui Pu and Yong Wang contributed equally to this work.

Background: Primary angle-closure glaucoma (PACG) is a common eye disease and a common cause of blindness. Inappropriate medical decisions severely affect the prognosis. This study investigated decision-making under risk in PACG patients.

Methods: Thirty patients with first acute attack of PACG before surgery and thirty healthy controls were included in the study. Decision-making under risk was evaluated with the game of dice task (GDT). The results of Eysenck Personality Questionnaire (EPQ) and GDT between PACG patients and healthy controls were compared.

Results: Risky decisions in PACG patients were more than those in healthy controls as measured by mean score of GDT (12.47 ± 5.72 vs. 4.33 ± 3.30, \( P < 0.001 \)). Higher neuroticism score in EPQ was found in PACG patients compared to healthy controls (14.97 ± 3.93 vs. 9.90 ± 4.49, \( P < 0.001 \)). Neuroticism scores in EPQ were associated with decision-making performance \( (r = 0.417, P = 0.001) \).

Conclusions: Neuroticism positively correlated with risky decisions. Decision-making might be influenced by neuroticism. Future studies will show whether therapy compliance will be improved by emotional management and psychological intervention in PACG patients.

Key words: Cognitive; Decision-making; Neuroticism; Personality; Primary Angle-closure Glaucoma

INTRODUCTION

Primary angle-closure glaucoma (PACG) is a common eye disease in Asia. This disease affects approximately 3.5 million people[1] and represents a major cause of vision loss in China. It is characterized by elevated intraocular pressure (IOP), ocular pain, and headache.[2] Treatments include pharmacology, laser therapy, and surgery. If left untreated, PACG can cause decreased vision or blind.

Beyond ocular impairments, PACG is also considered as a psychosomatic disease. Many scholars[3,4] believe that glaucoma is “a sick eye in a sick body”. Kong et al.[3] have demonstrated that PACG patients tend to have significantly higher neuroticism scores and higher level of anxiety and depression compared with normal controls.

Eysenck Personality Questionnaire (EPQ) is widely used as a classical method to evaluate personality traits. EPQ is named for its proposer, Hans J. Eysenck, a British psychologist. Eysenck proposed a theory of personality trait; extraversion/introversion, neuroticism, and psychoticism are three basic dimensions. High neurotic individuals have high response to negative events[4,5] and often present high negative affect, such as anxiety, depression, and guilt.[6] This might influence their judgment and selection of treatment. Depression has been found in relation with poor compliance of primary open-angle glaucoma (POAG) treatment.[7] The compliance...
of glaucoma patients is considered to be an important factor in vision loss prevention.\[^9\]

Selection of treatment is a part of decision-making. Decision-making is a daily important cognitive process of selection.\[^9,10\]

Neuroticism can predict some disorders, poor decision-making is also a core symptom in these disorders, such as pathological gambling and eating disorders.\[^11,12\] Two tasks are frequently used to evaluate decisions under ambiguity or decisions under risk. In Iowa Gambling Task (IGT), the gains and losses are uncertain.\[^13\] On the contrary, the game of dice task (GDT) uses explicit rules for gains and losses.\[^14\] Denburg et al.\[^15\] used IGT and found that older adults with high levels of neuroticism have poor decision-making skills.

The purpose of this study was to investigate decision-making under risk for PACG patients. We hypothesized that PACG patients would demonstrate impaired performance in GDT.

**METHODS**

**Ethical approval**

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Anhui Medical University. Informed written consent was obtained from all patients prior to their enrollment in this study.

**Subjects**

Thirty patients with PACG (15 women and 15 men, age range: 23–76 years) were recruited from the Department of Ophthalmology, the First Hospital of Anhui Medical University, between February 2012 and May 2016. The inclusion criteria included: (a) first attack (acute) of PACG patients without a history of surgery; (b) high IOP but good enough visual fields so that the whole computer monitor could be seen. The exclusion criteria included: (a) visual acuity worse than 0.3 in the better-seeing eye; (b) drug addition, neurological and psychiatric disorders, and other somatic diseases.

Thirty healthy controls (15 women and 15 men, age range: 24–74 years) were also recruited from the same community. The age, gender, and education years were matched to those in PACG patients. Exclusion criteria were a history of neurologic or psychiatric disorder or eye disease. All participants were right handed and had enough vision and visual field and understanding of the procedures. This is a single-blind study, the patients did not know which group they belong, but the investigator knew the grouping situation.

**Personality questionnaires**

The Chinese edition of the EPQ,\[^16\] revised by Gong\[^17\] in 1984, was used to assess the personality traits of participants. This questionnaire contains a total of 88 yes/no questions divided among four scales: the extraversion scale (E scale) consists of 21 items and is used to assess extraversion/introversion. The neuroticism scale (N scale) consists of 24 items and is used to assess the emotional neuroticism/stability of participants. The psychoticism scale (P scale) consists of 23 items and the lie scale (L scale) has 20 items designed to reflect falsified responses and social desirability, respectively.

The examiner read the questionnaire to the participants in an examination room. The participants had to answer all the 88 questions and the results were recorded for analysis.

**Game of dice task**

The GDT\[^18\] was used to assess the tendencies of participants to make risky decisions. A computerized GDT, with one virtual single die and a shaker, was used. Participants started the task with 1000 RMB yuan and had to throw the die for a total of 18 times. Participants were asked to guess the number on the die before it was thrown and to try to win as much as possible. They could choose a single number or multiple numbers. Every choice was associated with different gains or losses as follows: 1000 RMB yuan gain/loss when a single number was chosen (winning probability 1/6); 500 RMB yuan gain/loss when 2 numbers were chosen (winning probability 2/6); 200 RMB yuan gain/loss when 3 numbers were chosen (winning probability 3/6); and 100 RMB yuan when 4 numbers were chosen (winning probability 4/6). If participants guessed the correct number on the die, they won the money and their total capital increased. If they guessed incorrectly, the money subtracted from their total capital. The task was performed on a computer, and after the participants made their choices, the monetary balance and a sound were presented to warn participants of the result. Choosing 1 and 2 numbers was considered to be a risky decision since the winning probability was <50%. Choosing 3 and 4 numbers was considered to be a safe decision since the winning probability was ≥50%.

Participants who made safe decisions after losing following risky decisions were considered as using negative feedback. An index of the utilization rate of negative feedback was used in the GDT. The index refers to the frequency with which a participant made a safe decision after losing following a risky decision divided by the frequency of losing after making a risky decision. This index was used to evaluate the negative feedback from individuals' previous trials. No risky decision or always winning from risky decision was exclusion from the statistics of the rate.

**Statistical analysis**

The Statistical Package for the Social Sciences version 19.0 for Windows (SPSS Inc., Chicago, USA) was used to analyze all the data. The results of EPQ and GDT between PACG patients and healthy controls were compared by independent sample t-test for continuous variables and Chi-square test or Fisher’s exact test for categorical variables. Correlation relationships were analyzed using Pearson’s correlations. A two-sided test with $P < 0.05$ was considered statistically significant.

**RESULTS**

**Demographic data**

There were no significant differences between PACG patients and healthy controls in terms of age, gender, and years of education ($P > 0.05$; Table 1). All individuals without cardiovascular disease and dementia were participated in this study.
Performance on the Eysenck Personality Questionnaire

The mean score of the N scale in PACG patients (14.97 ± 3.93) was significantly higher than that in healthy controls (9.90 ± 4.49, \(P < 0.001\)). The mean score of the E scale in PACG patients (9.70 ± 3.21) was significantly lower than that in healthy controls (11.70 ± 4.28, \(P = 0.045\)). No significant difference was found in P and L scores between two groups (\(P > 0.05\); Figure 1).

The game of dice task results

Independent sample t-test was used to evaluate risky decision of GDT as measured by mean score of GDT. Risky decisions in PACG patients (12.47 ± 5.72) were more than that in healthy controls (4.33 ± 3.30, \(P < 0.001\)). Safe decisions in healthy controls (5.53 ± 5.72) were more than that in PACG patients (13.67 ± 3.30, \(P < 0.001\); Figure 2).

Utilization rate of negative feedback

Three patients and four healthy controls either did not make a risky decision for any of the 18 dice throws or always won after making risky decisions were excluded from the study. Results from 27 PACG patients and 26 healthy controls were analyzed. There were no significant differences between the two groups in age, gender, and years of education. PACG patients (0.14 ± 0.15) had a significantly lower utilization rate of negative feedback compared to healthy controls (0.56 ± 0.38; \(P < 0.001\)).

Table 1: Demographic characteristic of patients with primary angle-closure glaucoma and healthy controls

| Characteristics | Patients (\(n = 30\)) | Controls (\(n = 30\)) | \(t\) | \(P\) |
|-----------------|------------------------|------------------------|------|------|
| Age (years)     | 60.73 ± 8.88           | 60.70 ± 9.97           | −0.19| 0.99 |
| Education (years) | 6.57 ± 4.73           | 8.60 ± 3.92           | 1.91 | 0.08 |
| Male/female, \(n\) | 15/15                 | 15/15                 | –    | –    |

Data are shown as mean ± SD or \(n\). SD: Standard deviation; –: Not applicable.

Association between personality and decision-making

There was a positive correlation between the N score and risky decision-making (\(r = 0.417, P = 0.001\); Figure 3) in all patients. However, there were no significant correlations found between any of the other three scores and risky decision-making in all patients (E score and risky decision: \(r = −0.210, P = 0.108\); P score and risky decision: \(r = 0.129, P = 0.328\); L score and risky decision: \(r = −0.226, P = 0.082\)).

There was also a significant correlation between utilization rate of negative feedback and risky decision-making in 53 patients (\(r = −0.703, P < 0.001\); 27 PACG patients and 26 healthy controls, see utilization rate of negative feedback; Figure 4).

Discussion

To our knowledge, there are few studies about decision-making in PACG patients. In the current study, personality traits, decision-making under risk, and the relationship between them were investigated in PACG patients. The GDT was used to test decision-making under risky conditions and the EPQ was used to test the personality traits of participants. The results showed that PACG patients made risky decisions more often compared to healthy controls. PACG patients also scored significantly higher on the N scale and lower on the E scale. A correlation between decision-making under risk and neuroticism scores was found, and a correlation between risky decision and utilization rate of negative feedback was also found.

PACG patients showed high neuroticism score, indicating that they are prone to suffer from negative affect and they also showed high levels of neuroticism, reflecting emotional instability which may result in overresponsiveness to different
daily life events. Neuroticism has been found to be an important predictor for poststroke depression. It has also been reported that anxiety and depression are more prevalent in PACG patients than in POAG patients and controls.

High neuroticism has been related to lower threshold of stressors, thus causing higher reaction of the brain. Neuroticism can influence stress assessment and impact the ability to judge which situations are stressful and which are not. Previous studies have found that individuals with high neuroticism scores have enhanced reactivity to daily stressors, cannot cope with situations using effective efforts, and have improper responses to stress. Hyperactivity of the amygdale has been found in high neuroticism individuals in the face of negative stimuli. Stress response is thought to be related to cognition and affect the areas of the brain in decision-making. Poor decision-making performance has been found under risky conditions. When in a stressful situation, the adrenal cortex releases the stress hormones, glucocorticoids, and adrenaline, through the hypothalamic-pituitary-adrenal axis. Glucocorticoids can cross the blood–brain barrier and bind to the receptors in hippocampus, amygdala, and frontal lobes. Adrenaline also plays a regulatory role in the frontal cortex. Frontal and temporal activation has been found in association with neuroticism using a functional magnetic resonance imaging (fMRI). The frontal lobe region is the most important brain area for decision-making. The elevated glucocorticoids and adrenaline, caused by stress, can act on frontal cortex and influence decision-making under risk. It has been confirmed that GDT performance is negatively associated with glucocorticoids. PACG patients who had high N scores may not have properly responded to stress. This may be due to elevated level of stress hormones that act on the frontal cortex, such as glucocorticoids and adrenaline, leading to poor GDT performance.

In this study, we have also found that PACG patients scored significantly lower in utilization rate of negative feedback compared with healthy controls, indicating that PACG patients cannot cope with negative emotion processing. Utilization rate of negative feedback is also associated with risky decision-making. This might be due to the fact that glaucoma patients cannot or do not use the negative feedback to change their choices and thus keep making risky decisions. Camille et al. found that the orbitofrontal cortex is important for processing negative feedback. As mentioned above, the frontal lobe is one of the brain regions affected by stress hormones, and improper stress responses are often seen in PACG patients with high levels of neuroticism. It could be that a high neuroticism level leads to stress responses, causing the release of stress hormones that bind with the receptors in frontal lobe, which then influences the processing of negative feedback.

Patients with glaucoma often show poor compliance to medical therapies. The tendency to make risky decisions has a serious impact on PACG patients’ medical decision-making and may interfere with the therapy. The reasons for this might be the high level of neuroticism, the tendency to make risky decisions, and deficits in the ability to use negative feedback. It may be more likely that PACG patients will choose harmful options, stop medication, not go to the clinic on time, and not use negative feedback as glaucoma worsens. Therefore, we believe that improvements in decision-making performance may also improve therapeutic dependence. Personality traits (neuroticism) may play an important part in decision-making, thus PACG patients need psychometric tests before surgery or medication, and emotional management, psychotherapy, and stress intervention are also necessary for PACG patients.

Overall, the current study demonstrates that PACG patients appear to have poor decision-making skills under risky conditions and those neuroticism traits may play a role in this risk-taking behavior. Negative feedback processing, which

![Figure 3: Correlation between neuroticism score and risky decision in all participants (n = 60). There was a positive correlation between neuroticism score and risky decision in all participants (r = 0.417, P < 0.05).](image1)

![Figure 4: The correlation between risky decision and utilization rate of negative feedback rate in primary angle-closure glaucoma patients (n = 27) and healthy controls (n = 26). There was a negative correlation between risky decision and utilization rate of negative feedback rate in 53 patients (r = -0.702, P < 0.001).](image2)
is related to risk-taking decision-making, is also impaired in PACG patients.

However, there are some limitations in our study. First, our study population was relatively small and from single center, and we will enlarge the sample size in further study. Second, we need some imaging evidence (fMRI or event-related potential research) to find the relationship between neuroticism and decision-making in PACG patients. Brain activity with neuroticism could be analyzed during decision-making. Third, as groups of high neuroticism, glaucoma patients have visual deficit, they cannot tolerate long-time study. Further research could adopt similar approach to investigate associations between neuroticism and decision-making in other psychosomatic disorders and high neuroticism adults. We could also investigate which emotion would influence decision-making in PACG patients.

Financial support and sponsorship
This study was supported by grants from the National Basic Research Program of China (973 Program; No. 2015CB856405) and the National Natural Science Foundation of China (No. 81471117 and No. 81671354).

Conflicts of interest
There are no conflicts of interest.

References
1. Aung T, Friedman DS, Chew PT, Ang LP, Gazzard G, Lai YF, et al. Long-term outcomes in asias after acute primary angle closure. Ophthalmology 2004;111:1464-9. doi: 10.1016/j.ophtha.2003.12.061.
2. Ang LP, Aung T, Chua WH, Yip LW, Chew PT. Visual field loss from primary angle-closure glaucoma: A comparative study of symptomatic and asymptomatic disease. Ophthalmology 2004;111:1636-40. doi: 10.1016/j.ophtha.2004.01.032.
3. Kong X, Yan M, Sun X, Xiao Z. Anxiety and depression are more prevalent in primary angle closure glaucoma than in primary open-angle glaucoma. J Glaucoma 2015;24:127-63. doi: 10.1097/IJO.0000000000000225.
4. Canli T. Toward a neurogenetic theory of neuroticism. Ann N Y Acad Sci 2005;1091:159-74. doi: 10.1196/annals.1417.022.
5. Canli T. Functional brain mapping of extraversion and neuroticism: A neurogenetic study. Ann N Y Acad Sci 2005;1091:267-77. doi: 10.1196/annals.1417.022.
6. Watson D, Clark LA. Health, well-being, and performance. Health Psychol 2001;17:159-74. doi: 10.1002/smi.897.
7. Ramos BP, Arnsten AF. Adrenergic pharmacology and cognition: Learning from individual differences in emotion processing. J Pers 2001;72:1105-32. doi: 10.1111/j.1467-6494.2001.00292.x.
8. Watson D, Clark LA, Harkness AR. Structures of personality and their relevance to psychopathology. J Abnorm Psychol 1994;103:18-31. doi: 10.1037/0021-843X.103.1.18.
9. Pappas C, Hyphantis T, Pappa S, Aspiotis M, Stefaniotou M, Kitisos G, et al. Psychiatric manifestations and personality traits associated with compliance with glaucoma treatment. J Psychosom Res 2006;61:609-17. doi: 10.1016/j.jpsychres.2006.03.050.
10. Konstas AG, Markaleris G, Gratosidis S, Sardelli C. Compliance and viewpoint of glaucoma patients in Greece. Eye (Lond) 2000;14(Pt 5):752-6. doi: 10.1038/sj.eye.2000.197.
11. Doya K, Shadlen MN. Decision making. Curr Opin Neurobiol 2012;22:911-3. doi: 10.1016/j.conb.2012.10.003.
12. ChurchillAK, Ditterich J. New advances in understanding decision-making among multiple alternatives. Curr Opin Neurobiol 2012;22:920-6. doi: 10.1016/j.conb.2012.04.009.
13. Brand M, Kalbe E, Labudda K, Fujiwara E, Kessler J, Markowitz HJ. Decision-making impairments in patients with pathological gambling. Psychiatry Res 2005;133:91-9. doi: 10.1016/j.psychres.2004.10.003.
14. Vaidyanathan S, Brand M, Tuschen-Cafler B. Decision-making impairments in women with binge eating disorder. Appetite 2010;54:84-92. doi: 10.1016/j.appet.2009.09.010.
15. Chen X, Zhu C, Li J, Qiu L, Zhang L, YU F, et al. Dissociation of decision making under ambiguity and decision making under risk in breast cancer patients receiving adjuvant chemotherapy: A neuropsychological study. Brain Res 2013;1553:63-72. doi: 10.1016/j.brainres.2013.08.015.
16. Ma H, Lv X, Han Y, Zhang F, Ye R, Yu F, et al. Decision-making impairments in patients with Wilson’s disease. J Clin Exp Neuropsychol 2013;35:472-9. doi: 10.1080/13803395.2013.789486.
17. Denburg NL, Weller JA, Yamada TH, Shivapour DM, Kaup AR, LaLoggia A, et al. Poor decision making among older adults is related to elevated levels of neuroticism. Ann Behav Med 2009;37:164-72. doi: 10.1007/s12160-009-9094-7.
18. Eysenck H, Eysenck S. Manual of the Eysenck Personality Questionnaire. London: Hodder and Stoughton; 1975.
19. Gong Y. Eysenck Personality Questionnaire revised in China. Psychol Sci 1984;4:11-8.
20. Brand M, Fujiwara E, Borsutzky S, Kalbe E, Kessler J, Markowitz HJ. Decision-making deficits of korsakoff patients in a new gambling task with explicit rules: Associations with executive functions. Neuropsychology 2005;19:267-77. doi: 10.1073/pnas.0409919.13.3.267.
21. Aben I, Denollet J, Lousberg R, Verhey F, Wojciechowski F, Honig A. Personality and vulnerability to depression in stroke patients: A 1-year prospective follow-up study. Stroke 2002;33:2391-5. doi: 10.1161/01.STR.0000092826.41672.2E.
22. Code S, Langan-Fox J. Motivation, cognitions and traits: Predicting occupational health, well-being and performance. Stress Health 2001;17:159-74. doi: 10.1002/smi.897.
23. Nolte N, Schilling EA. Personality and the problems of everyday life: The role of neuroticism in exposure and reactivity to daily stressors. J Pers 1991;59:355-86. doi: 10.1111/j.1467-6494.1991.tb00253.x.
24. Klein K, Boals A. The relationship of life event stress and working memory capacity. Appl Cogn Psychol 2001;15:565-79. doi: 10.1002/acp.727.
25. Baradell JG, Klein K. Relationship of life stress and body consciousness to hypervigilant decision making. J Pers Soc Psychol 1993;64:267-73. doi: 10.1037/0022-3514.64.2.267.
26. Starcke K, Wolf OT, Markowitz HJ, Brand M. Anticipatory stress influences decision making under explicit risk conditions. Behav Neurosci 2008;122:1352-60. doi: 10.1037/a0013281.
27. Labuda K, Woermann FG, Mertens M, Pohlmann-Eden B, Markowitz HJ, Brand M. Neural correlates of decision making with explicit information about probabilities and incentives in elderly healthy subjects. Exp Brain Res 2008;187:641-50. doi: 10.1007/s00220-008-1332-x.
28. Lupien SJ, Maheu F, Tu M, Fiocco A, Schramek TE. The effects of stress and stress hormones on human cognition: Implications for the field of brain and cognition. Brain Cogn 2007;65:209-37. doi: 10.1016/j.bandc.2007.02.007.
29. Ramos BP, Arnsten AF. Adrenergic pharmacology and cognition: Focus on the prefrontal cortex. Pharmacol Ther 2007;113:523-36. doi: 10.1016/j.pharmthera.2006.11.006.
30. Canli T, Zhao Z, Desmond JE, Kang E, Gross J, Gabrieli JD. An fMRI study of personality influences on brain reactivity to emotional stimuli. Behav Neurosci 2001;115:33-42. doi: 10.1037/0735-7044.115.1.33.
31. Camille N, Coricelli G, Sallet J, Pradat-Diehl P, Duhamel JR, Sirigu A. The involvement of the orbitofrontal cortex in the experience of regret. Science 2004;304:1167-70. doi: 10.1126/science.1094550.
32. Friedman DS, Okeke CO, Jampel HD, Ying GS, Pfyler RJ, Jo J, et al. Risk factors for poor adherence to eyedrops in electronically monitored patients with glaucoma. Ophthalmology 2009;116:1097-105. doi: 10.1016/j.ophtha.2009.01.021.