Original Article
Relationship between peripheral blood dopamine level and internet addiction disorder in adolescents: a pilot study

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Abstract: Objectives: To explore the association between peripheral blood dopamine level and internet addiction disorder (IAD) in adolescents, this could be used to explain the neurobiological mechanism of Internet addiction disorder. Methods: 33 adolescents with IAD diagnosed by Young's Internet Addiction Test (IAT) and 33 healthy controls matched by gender and age were investigated in the present study. Peripheral blood dopamine levels of the all subjects were determined by Enzyme Linked Immunosorbent Assay (ELISA). Results: The difference of peripheral blood dopamine level between adolescents with IAD and their controls had reached significant level (t = 2.722, P < 0.05). Furthermore, the plasma dopamine level was significantly correlated with the Internet Addiction Test score (r = 0.457, P < 0.001). The result of rank correlation analysis showed a significant positive correlation between the plasma dopamine level and the weekly online time (r = 0.380, P < 0.01) and there was no significant correlation between the duration of Internet use and the plasma dopamine level (r = 0.222, P > 0.05). Binary logistic regression analysis showed that DA level and weekly online time were significant variables which contribute to internet addiction. Conclusions: The peripheral blood dopamine level is associated with adolescents' internet addiction. The present study provided new evidence in favor of the hypothesis that dopamine played an important role in IAD.

Keywords: Internet addiction disorder (IAD), adolescents, dopamine, weekly online time

Introduction

Internet has been put into use rapidly worldwide as a powerful tool for information record and diffusion. At present, there are about 2.925 billion Internet users in the world, accounting for 40.4% of the world population [1]. Out of them, a considerable proportion was adolescents under 25 years old. As the number of internet users increasing, more and more adolescents have been reported with problems such as poor academic performance, neglect of family responsibilities, and disruption of social relationships resulting from their internet overuse [2, 3]. Under such circumstances, Internet Addiction Disorder (IAD) has become an interesting research area.

The concept of addiction, though traditionally used to describe the physical dependence on a certain substance, has been applied to describe excessive use of the Internet. The

term Internet Addiction Disorder (IAD) is first brought forward by Goldberg [4] and became more and more popular since Young's [5] groundbreaking research. In recent years, a variety of terms have been used to describe this behavior, including "Internet addiction" [5, 6], "pathological Internet use" [7], "problematic Internet use" [8, 9], "Internet Addiction Disorder (IAD) [4, 10]", "Excessive Internet Use" [11], "Internet Abuse" and "Compulsive Internet Use" [12]. Though different names, they are equal to the definition "the compulsive overuse of the Internet and the irritable or moody behavior when deprived of it" [6]. Over the last decade, the acceptance of Internet addiction has grown in the mental health field.

Diagnostic criteria for IAD like other "behavioral addictions" such as pathological gambling overlapped with those for substance abuse disorder [13, 14], with specific criteria such as excessive use, tolerance, withdrawal, repeated unsuc-

Table 1. Dopamine levels and time spend in IDA and control groups

	IAD (n = 33)	Control (n = 33)	t value	p value
IAT score	65.88 ± 0.99	39.52 ± 1.34	15.81	< 0.0001
DA (pg/ml)	64.86 ± 7.98	36.79 ± 6.31	2.76	0.0076
Weekly time (h)	5.06 ± 0.28	2.97 ± 0.15	7.05	< 0.0001
Duration of internet use (y)	5.48 ± 0.22	5.42 ± 0.19	0.21	0.8400

h: hour; y: year.

Table 2. Correlation between DA levels and other parameters in all participants

	Pearson r	95% C.I.	p value
IAT score	0.4571	0.2418~0.6296	0.0001
Weekly time (h)	0.353	0.1213~0.5482	0.0036
Duration of internet use (y)	0.0255	-0.2179~0.2660	0.8388

cessful attempts to cut back or quit, and interference in major areas of life functioning. Namely, a large proportion of individuals who overuse the Internet shared the same characters with substance addicts. Therefore, it has been hypothesized that there was neurobiological similarities between IAD and substance addiction. Emerging views of addiction involved a drug or behavior-acquiring saliency via reinforcement, with subsequent transitions through reward-based learning processes into compulsive levels of engagement [15].

Extensive researches have been performed on the neurobiological underpinnings of the development and maintenance of substance addiction [16]. Previous studies revealed that addiction was based on physical dependency created by altered neurotransmitter balances, and driven by thousands of new active neurological pathways which have been established to sustain the condition in the addicts' brain [17]. The new neurological pathways were permanently established, and they would not just disappear. The reason addicts have lost control was that they have suffered permanent physical neurological changes based on their brains and nervous systems. The primary neurological disorder was the source of addiction. The root of almost all compulsive behavior was based not on free will but on neurological wiring. The overwhelming craving for drugs or alcohol that endlessly defeated addicts was not a free choice, but an electro-chemical neurological brain impulse [18]. Addiction has been identified as a neurologically based disease.

With new imaging techniques [19], researchers have observed that addictive drugs caused the activation of a specific set of neural circuits called the brain reward system. Research showed that almost all normal activities we found pleasurable can activate the reward system. When those activities happened, the circuits enabled our brains to encode and remember the circumstances that led to the pleasure, so that we would repeat the behavior and go back to the reward in the future [20]. This was the underlying mechanism of addiction. A critical component was the chemical dopamine, which was released from neurons in the reward system circuits and functioned as neurotransmitter. Through a combination of biochemical, electrophysiological, and imaging experiments, scientists have learned that all addictive drugs increased the release of dopamine in the brain. When dopamine is released in certain areas of the brain it gives the feeling of pleasure or satisfaction. The person will grow a desire for the satisfaction. To satisfy the desire, the person will repeat behaviors that cause the release of dopamine, which conduce the feeling of satisfaction as reward. The feeling of euphoria that dopamine lead to is so strong that one can always loses his mind to achieve it [21]. That is why addiction emerges.

Other researchers have observed that both a chemical such as cocaine and a behavior such as gambling can have the similar neurobiological processes [22]. Behavioral addictions were thought to show dopaminergic system disorders. A typical example was that pathological gamblers have long been shown to demonstrate the same patterns of cortical arousal as substance abusers, and dosing with naltrexone has mitigated problematic gambling behavior in some individuals [23]. It has been suggested that these same pathways may make the Internet rewarding and addictive in the same way as other behaviors.

There were very few studies using control groups and randomization in the etiological area of IAD, especially in the neurophysiological

Table 3. Binary logistic regression of the DA level and the weekly online time with the diagnosis of IDA as dependent variable

	B	Exp (B)	Exp (B) 95% C.I.	p value
DA level	0.020	1.020	1.003~1.038	0.0200
Weekly time	1.157	3.180	1.917~5.276	0.0000
Duration of internet use	0.044	1.045	0.691~1.580	0.8330

mechanism. The existence of the relationship between substance addiction and behavior dependence has caused us to postulate a role of dopamine in Internet addiction. Based on the existing research findings, it must be meaningful to make a pilot study about the effect of dopamine on IAD. That is the purpose of the present study.

Materials and methods

Diagnosis criteria

Young's Internet Addiction Test (IAT) was used as diagnosis criteria for IAD in this study. It was a diagnostic scale adapted by Young to assess Internet addiction. Based on the DSM-IV [24] criteria for pathological gambling, Young [25] developed the Diagnostic Questionnaire for diagnosing Internet addition. In a later study, Young [26] expanded her Diagnostic Questionnaire and constructed an assessing scale called Internet Addiction Test (IAT). The IAT was a Liket-type scale consisted of 20 items, covering factors such as tolerance, withdrawal, craving, and negative impacts of internet use. For each item, a graded response (1 = "not at all" to 5 = "always") can be chose. The subjects with total scores higher than 60 were diagnosed as IAD addicts and the higher test scores represent higher levels of internet addition. The IAT have been identified as an eligible scale [27] and it was widely used in researches.

Subjects

The study was carried out on 33 adolescents with IAD diagnosed according to Young's IAT. The ages of the participants ranged between 12 and 22 years old. The average age of the patients was 16.58 ± 2.29 y. 28 were males and 5 were females. 33 healthy adolescents served as controls. Adolescents in control group were matched with adolescents in case group by gender and age (± 6 months), and the match ratio was 1:1. All participants had no diagnosis for other psychological disorder and

no history of brain damages and psychoactive substance abuse. Each subject or his/her guardian signed the informed consent before the experiments. The study was undertaken in accordance with the Declaration of Helsinki.

Research instrument

The research instrument was a questionnaire designed based on the review of literature, which was filled out by each subject collectively. It was to investigate the participant's information including age, gender, educational background, weekly Internet usage, Internet experience, and online activities.

Laboratory analysis

Blood samples collection: All subjects avoided high tyramine diet for 3 d and rested for 15 min prior to blood samples collection. The fasting blood samples for measurement were drawn into 5ml vacuum glass tubes pre-filled with anticoagulant Ethylene Diamine Tetra Acetic (EDTA) at 7:00 AM. All blood samples were taken from the left arm vein in a sitting position and were sent to laboratory at a temperature under 10°C immediately after collection.

Blood samples pretreatment: The whole blood samples were fractionated by centrifuging at 3000 r/min for 15 min at room temperature as soon as they were delivered to laboratory. After centrifugation, the plasma was separated into the upper layer and then was transferred to a clean tube one by one. All the plasma samples were stored at -80°C right away.

Experimental methods

After thawing, 200 μl plasma was taken to assay. Peripheral blood plasma dopamine levels of all subjects were tested by Enzyme Linked Immunosorbent Assay (ELISA). The Thermo MK-3 ELISA Reader was used for dopamine determination in this step. Elisa Kit was purchased from Transhold Navigation Technology Ltd and the repacking reagent was from RapidBio Lab of Calabsas, California USA.

Quality control

All investigators were received strict unified training before the study. The phlebotomist and

the lab technician were qualified and experienced.

Statistical analysis

All data were entered into a standard statistical database for analysis. The statistical analysis was done with the Statistical Product for Service Solutions (SPSS, 14.0). Statistical analysis of the data was made with Student's paired *t*-test and correlation analysis. The significance level of $\alpha = 0.05$ or less was considered significant.

Results

Comparison of plasma dopamine levels

The plasma dopamine level in IDA group was significantly higher than that of the control group ($t = 2.722$, *P* < 0.05, **Table 1**). Results also indicated that time spent online weekly in IDA group was longer when compared with the healthy adolescents. However, there is no significant difference in duration of the internet use between two groups (**Table 1**).

Correlation between plasma dopamine level and weekly online time

Pearson correlation analyses (**Table 2**) revealed that the plasma dopamine level was positively correlated with the Internet Addiction Test score($r = 0.457$, *P* < 0.001). For the time the subjects spent in using computer every week, a graded response (1 = never, 2 = less than 3 hrs, 3 = less than 7 hrs, 4 = less than 14 hrs, 5 = less than 21 hrs, 6 = more than 21 hrs) can be chose. The result of rank correlation analysis showed a significant positive correlation between the plasma dopamine level and the weekly online time ($r = 0.380$, *P* < 0.01). Namely, the more the time subjects spent on using Internet, the higher plasma levels they had. The duration of Internet use among the participants ranged from 0 to 5 years. For this item, a graded response (1 = never, 2 = less than 3 m, 3 = less than 6 m, 4 = less than 12 m, 5 = less than 24 m, 6 = more than 24 m) can be chose. There was no significant correlation between the duration of Internet use and the plasma dopamine level ($r = 0.222$, *P* > 0.05).

Logistic regression analysis

In the binary regression analysis (**Table 3**), the independent variable was IDA or not and DA level, weekly online time and duration of the internet use were set as independent variables. The results showed that DA level (OR = 1.02, 95% CI 1.003-1.038) was independent predictor of IDA after adjusting weekly online time spent.

Discussion

At present, IAD is mostly managed with cognitive-behavioral therapy because researchers have asserted that Internet addiction is primarily related with cognitive disorder. In fact, the effect is not obvious. Some pharmacological treatments of excessive Internet users have been thought to be more effective [28]. However, they are not widespread used because of lacking in theoretical basis. With more work to be done in the area of the neurochemistry of IAD, it is possible that IAD can be ameliorated using drugs in combination with other strategies.

To our knowledge, there are few empirical researches to evaluate quantitatively the association between dopamine level and Internet addiction among adolescents. The results showed that peripheral blood plasma dopamine level of IAD group was significantly higher than that of control group. Furthermore, the plasma dopamine level was significantly correlated with the Internet Addiction Test score. It has been suggested that there was a link between peripheral blood plasma dopamine level and IAD. These results were consistent with previous research findings on substance addiction that dopamine played a vital role in IAD as a neurotransmitter in the brain. Numerous studies have confirmed that dopamine was an essential component of the basal ganglia motor loop, as well as the neurotransmitter responsible for controlling brain function including decision making, impulsiveness [29]. Like addictive substance, the activities on the Internet, such as online gambling, interactive games, or chatting, would stimulates the reward systems to increase the release of dopamine giving the person a state of euphoria.

A significant positive correlation was found between participants' weekly online time and their peripheral blood plasma dopamine levels. It was indicated that the more the time subjects spend on using Internet, the higher peripheral plasma level they had. Precious studies

revealed that addictive substance could increase the release of dopamine [20, 30]. Our results conformed to this theory. However, this positive correlation was not continued, an opposite effect would occur after over stimulation that decreases the number of receptors and the remaining receptors become less sensitive to dopamine [31]. This phenomenon is called tolerance. In alcoholics, using neuroimaging, researchers have actually seen decreases of dopamine in the brain. Thus, the user needs to take greater amounts of the drug to produce the same increase in dopamine or the same heightened response of the dopamine nerves [32]. According to this theory, we can conclude that the more subjects use Internet, the lower plasma level they will have at this stage. Obviously, our result in this study is opposite to this conclusion. At present, we can't find more logical explanation. The results in this study could be explained by the fact that the Internet addicts we observed were not yet in the stage of tolerance for the time being.

In conclusion, these results of the present study provided evidence in favor of the hypothesis that dopamine played an important role in the development and maintenance of Internet addiction. This study preliminary affirmed the effect of dopamine in IAD, though the details about dopamine's action are still unclear. Moreover, the present study prompted that dopamine in peripheral blood plasma might be easily accessible candidate as biological markers for future research into the mechanisms of Internet addiction.

This study has some limitations that should be considered. In respect that cross-sectional research design could not confirm the causal relationship, prospective study should be applied to make more reliable conclusions about the association between peripheral blood dopamine level and IAD in future researches. Furthermore, peripheral blood plasma dopamine level was only one of the indicators to demonstrate dopamine's role in IAD, future research should pay attention to more biochemical index.

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Disclosure of conflict of interest

None.

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