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Mobile Game Addiction Tendency and Sleep Quality among University Students: The Chain Mediating Effect of Loneliness and Negative Emotions

Yongtao Gan¹, Jing Deng², Chang Liu³, Siyi Li⁴, Jian Gao⁵

Higher Education Research Institute, University of Shantou, Shantou 515063, China

Corresponding Author: Yongtao Gan

Abstract:

This study examined the relationship between mobile game addiction tendencies (MGAT) and sleep quality among university students, using a chain mediating model. A total of 1,065 mobile phone game users participated in the study and completed a series of relevant questionnaires. The findings indicated a significant association between MGAT and poorer sleep quality. Additionally, negative emotions and feelings of loneliness were identified as mediating factors in this relationship. These findings contribute to the theoretical understanding of preventing and mitigating poor sleep quality in young individuals.

Key words: Loneliness; Mobile game addiction; Negative emotions; Mediating effect

Introduction

As of December 2021, the number of Chinese mobile internet users has surged to an astounding 1.029 billion, with an average weekly usage of 28.5 hours^[1]. This upsurge, particularly pronounced among young adults aged 18-22, mirrors a worldwide trend^[2]. Smartphones have become indispensable in the daily lives of this demographic, who are quick to adopt the latest technological advancements^[3]. However, this reliance on smartphones has been linked to adverse effects on sleep quality, social interactions, and overall well-being^[4].

Young adults who are unemployed or lack self-control are more vulnerable to smartphone addiction, especially during extended, unrestricted use^[5]. A survey conducted across eight countries revealed that two-thirds of young adults under the age of 30 play mobile games in bed^[6]. Given the psychological malleability of this age group, it is plausible that students may not fully comprehend the negative ramifications of smartphone use, particularly the impact of mobile gaming^[7]. These ramifications can include distraction, sleep disorders, and exposure to inappropriate content, all of which can detrimentally affect students' psychological health. Mobile gaming, in

particular, has been correlated with insomnia and sleep difficulties^[8]. Furthermore, a robust positive correlation exists between game addiction and mental states such as depression, anxiety, and loneliness, prompting a shift in research focus towards the origins of online gaming addiction^[9].

Smartphone game addiction has been shown to negatively impact the psychological and physical health of teenagers, with associations drawn between excessive or problematic use and poor sleep quality^[10-11]. Sleep disorders among university students are prevalent, ranging from 17.0% to 28.7%^[12]. A longitudinal study by Kwok indicated that frequent users of online gaming platforms, notably young adults, are at a higher risk of developing sleep disorders^[13]. Poor sleep quality, marked by difficulties in achieving or maintaining sleep, has been identified as a primary factor contributing to smartphone addiction^[14]. Consistent with this, previous research has demonstrated a negative association between smartphone addiction and sleep quality, characterized by prolonged sleep duration and decreased sleep latency^[11,14].

The prevalence of cellphone addiction among college students, especially in relation to the

excessive use of mobile phone games, is a pressing concern^[15]. The constraints of academic schedules often limit daytime gaming, leading students with gaming addictions to compensate by indulging in extended play sessions before bedtime or during other free periods. Such habits can erode self-control and adversely affect sleep quality. The addiction to online games can stem from various factors, including communication deficits, emotional deprivation, and family conflicts^[16-17].

Loneliness, characterized by feelings of emptiness, anxiety, boredom, and social exclusion, is another factor closely tied to excessive mobile phone use^[1]. Similar to addictions to drugs or gambling, individuals may experience irritability or loneliness when restricted from their addictive behaviors. Internet addiction has also been linked to increased irritability and loneliness when access is limited^[18]. College students experiencing negative emotions are more likely to suffer from sleep problems and reduced sleep quality, in line with research on anxiety, depression, irritability, and sleep disorders^[5,18-19].

The theory of cognitive insomnia posits that pre-sleep worries about stressors can lead to emotional arousal and cognitive biases, resulting in a decline in subjective sleep quality and a vicious cycle of negative cognition and behavior^[11]. In the digital era, the internet and online games are increasingly used to combat loneliness^[20]. A positive relationship exists between cellphone dependence and the level of loneliness experienced by undergraduates^[21]. Factors such as personality, lifestyle, and personal circumstances contribute to feelings of loneliness among students^[22]. Those who heavily rely on mobile phones are more likely to develop cellphone addiction and face interpersonal challenges, leading to heightened loneliness^[23-25]. Additionally, excessive social media use has been linked to increased loneliness and disrupted sleep patterns^[26].

Research has consistently shown that cellphone addiction is linked to emotional, functional, and mental well-being, with consequences including depression, social distress, and solitude^[25]. Individuals experiencing higher levels of loneliness also report more negative emotions^[27].

Consequently, the academic community has focused on the interplay between interpersonal issues, smartphone addiction, anxiety disorders, and depressive states^[25,28].

In the context of mobile game addiction, studies have shown a positive correlation between negative emotions, such as depression, and the use of social networking sites^[25-26] found a positive correlation between mobile game addiction, depression, social anxiety, and loneliness, with male adolescents being more susceptible to social anxiety than females. Our research group's study on factors influencing Mobile Game Addiction Tendency (MGAT) revealed a significant inverse correlation between positive emotions and mobile game addiction, while loneliness and negative emotions had a significant positive impact^[29]. These findings suggest that positive emotions and social support can ameliorate the adverse effects of cellphone game use, whereas negative emotions and interpersonal issues can intensify them. However, further exploration of the relationships between smartphone game addiction, loneliness, negative emotions, and sleep quality is necessary.

Given the existing research, we hypothesize the following:

Hypothesis 1: University students' MGAT negatively impacts sleep quality.

Hypothesis 2: There is a positive relationship between university students' MGAT and loneliness.

Hypothesis 3: University students' MGAT is associated with negative emotions.

Hypothesis 4: Loneliness mediates the relationship between university students' MGAT and sleep quality.

Hypothesis 5: Negative emotions mediate the relationship between university students' MGAT and sleep quality.

Hypothesis 6: Loneliness and negative emotions chain mediate the relationship between university students' sleep quality and MGAT.

2. Methods

2.1. Data collection and participants

To assess the impact of MGAT on sleep quality among Chinese university students, a web-based

study was conducted. The sample included participants who met the following criteria based on their self-reports: (1) currently enrolled as college or university students, (2) completion of the questionnaire on their own computer using their own IP address (ensuring that each participant completed only one questionnaire), and (3) providing responses to all the questions in the questionnaire. To screen participants, the questionnaire included the question "Do you play mobile games?"

The final sample consisted of 1,065 university students who were mobile game users. Among them, 654 (60.7%) were women, and 423 (39.2%) were men. In terms of geographical background, 566 (53.2%) came from rural areas, and 499 (46.8%) came from cities. Regarding their academic year, 461 (54.7%) were freshmen, 165 (15.5%) were sophomores, 299 (21.5%) were juniors, and 88 (8.3%) were in their senior year. In terms of family structure, 672 (84.3%) came from two-parent families, while 106 (15.7%) came from single-parent or step-parent families.

To ensure the breadth of our research, we meticulously selected a sample that reflects a variety of genders, regions, academic levels, and family compositions. By including participants from diverse backgrounds, our study seeks to gather a wide array of experiences and viewpoints concerning MGAT and the quality of sleep.

2.2. Measures

2.2.1. Pittsburgh Sleep Quality Index (PSQI)

The Pittsburgh Sleep Quality Index (PSQI) is a recognized instrument for evaluating the quality of sleep^[30]. It encompasses 19 questions that pertain to seven distinct areas of sleep. These areas encompass: (1) Subjective sleep quality (e.g., "During the past month, how would you rate your sleep quality overall?"); (2) Sleep latency (e.g., "During the past month, how long (in minutes) has it typically taken you to fall asleep each night?"); (3) Sleep duration (e.g., "During the past month, how many hours of actual sleep did you get at night?"); (4) Habitual sleep efficiency (e.g., "Bedtime=Item 3 (get-up time) - Item 1 (go-to-bed time)"); (5) Sleep disturbances (e.g., "Did you wake up in the middle of the night or in the morning?"); (6) Use of sleeping medication (e.g., "During the past month, how often have you taken medicine to help you sleep (prescribed or over-

the-counter?"); (7) Daytime dysfunction (e.g., "During the past month, how difficult has it been to remain productive?").

The PSQI operates as a self-administered survey that delivers a comprehensive evaluation of one's sleep quality within the past month. Each of the components is rated on a scale from 0 to 3, with the composite scores ranging between 0 and 21. In clinical practice, a Pittsburgh Sleep Quality Index (PSQI) score that surpasses the threshold of 5 points is indicative of potential sleep disturbances. Furthermore, a score reaching 8 or above is frequently recognized as a significant marker, suggesting the likelihood of a more profound sleep disorder. In the current study, Cronbach's α for PSQI is calculated to be 0.82.

2.2.2. Chinese Mobile Phone Game Addiction Scale (CMPGAS)

The CMPGAS was utilized to examine the participants' level of MGAT^[29]. It is an adapted version of the Mobile Phone Addiction Index^[15], and consists of 17 items that measure four dimensions of mobile game addiction: (1) Control craving (four items; e.g., "During the past month, how difficult has it been to remain productive?"); (2) Feeling lost and anxious (seven items; e.g., "Playing mobile games is consuming valuable sleep time"); (3) Escape and withdrawal (three items; e.g., "You have played mobile games to alleviate feelings of loss"); (4) Loss of productivity, (three items; e.g., "Your time spent on mobile games is the direct cause of decreased productivity"). Respondents evaluate their level of agreement with each statement using a 5-point Likert-type scale, where 1 signifies 'strongly disagree' and 5 denotes 'strongly agree'. For the present research, the Cronbach's alpha, a measure of internal consistency, for the CMPGAS yielded a value of 0.85.

2.2.3. UCLA Loneliness Scale

UCLA Loneliness Scale (Version 3) was employed to examine feelings of loneliness^[31]. This scale comprised of 20 items, consisting of nine positively worded (indicating not feeling lonely) terms and eleven negatively worded (indicating feeling lonely) terms. The scale's reliability, as indicated by Cronbach's alpha, was determined to be 0.88.

2.2.4. Negative Affect Scale

To assess negative emotions, the study utilized the Negative Affect Scale, which includes items of anger, anxiety, disgust, restlessness, hostility, irritability, nervousness, fidgeting, fearfulness, and sadness [32]. Participants were instructed to indicate how profoundly they felt each of these emotions on a 4-point Likert-type scale, where '1' represented 'never' and '4' signified 'to a high degree'. The Negative Affect Scale demonstrated strong internal consistency with a Cronbach's alpha value of 0.86.

2.3. Design and procedure

The study was conducted between January 2022 and April 2022, with the aim of recruiting university students from China through social networking websites that were developed using Wen Juanxing (<https://www.wjx.cn/>). Participants were assured of the voluntary nature of their participation and the strict confidentiality of their responses. They were also informed of their right to withdraw from the study at any time. Informed consent forms were obtained from all participants prior to proceeding with the survey. The survey had an estimated completion time of 20-25 minutes. The research protocol received approval from the ethics committee at the first author's

university.

2.4 Analysis strategy

All analyses were conducted using MPLUS (V8.3) and SPSS (V24). Initially, Spearman's RHO and descriptive correlation were used for measurement purposes. Subsequently, a chi-squared test was employed to assess demographic differences in sleep quality. Finally, Mplus was utilized to assess the significance and magnitude of the hypothesized relationship between the endogenous and exogenous variables. Confidence intervals were calculated using bootstrap sampling, with a total of 5,000 bootstrap samples. Maximum Likelihood Estimation (MLE) was employed to determine the path/regression coefficients.

3. Results

3.1. Descriptive statistics and correlations

In Table 1, the means, standard deviations, and correlations among the main variables are displayed. Significant correlations ($p < 0.01$) were found between loneliness, negative emotions, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and MGAT.

Table: 1 Descriptive statistics and correlations

Variable	1	2	3	4	5	6	7	8	9	10	11
1. Mobile phone game addiction tendency	1										
2. Loneliness	.197**	1									
3. Negative emotions	.313**	.313**	1								
4. Subjective sleep quality	-0.042	-0.02	0.047	1							
5. Sleep latency	.206**	0.05	.104**	-0.031	1						
6. Sleep duration	.128**	.118**	.134**	.062*	.104**	1					
7. Habitual sleep efficiency	-0.044	0.009	-0.02	-0.049	-0.027	.201**	1				
8. Sleep disturbances	.228**	.175**	.247**	-0.056	.400**	.235**	0.025	1			

9. Use of sleeping medication	.140**	0.054	.176**	.319**	.080**	.130**	.083**	.252**	1		
10. Daytime dysfunction	.313**	.313**	.324**	0.047	.104**	.134**	-0.02	.247**	.176**	1	
11. Sleep quality(total)	.389**	.134**	.341**	-.067*	.144**	.153**	-0.003	.225**	.112**	.341**	1
M	33.68	43.71	24.23	0.93	1.11	0.43	0.92	1.36	0.18	0.84	5.77
SD	13.38	10.576	7.972	0.73	0.79	0.70	1.17	1.31	0.43	0.72	2.72

Note. **p<0.01.

Significant differences in demographic characteristics were found between university students in the normal and abnormal sleep groups. Specifically, family structure, region, and grade level were found to have significant associations ($p < 0.05$). Having a two-parent family, living in

an urban area, and being in a lower college year were significantly associated with having normal sleep. Conversely, not having a two-parent family, living in a rural area, and being in a higher college year were significantly associated with having abnormal sleep.

Table: 2 Differences in demographic characteristics between college students with normal sleep and college students with abnormal sleep [n(%)]

<i>Characteristic</i>	<i>Normal group(778)</i>	<i>SleepAbnormal Sleep group(287)</i>	<i>X²</i>	<i>Sig.</i>
<i>Gender</i>				
Women (n=654)	458(71.30)	184(28.70)	2.207	0.121
Men (n=423)	320(75.7)	103(24.3)		
<i>One-child</i>				
yes (n=635)	458(72.10)	177(27.90)	0.685	0.408
no (n=430)	320(74.40)	110(27.60)		
<i>Family structure</i>				
Two-parental family (n=898)	672(74.80)	226(25.20)	9.231**	0.002
others (n=167)	106(63.50)	61(36.50)		
<i>Region of students</i>				
Rural (n=566)	397(70.10)	169(29.90)	5.197*	0.023
City (n=499)	381(76.40)	118(23.60)		
<i>Grades</i>				
freshmen (n=583)	461(79.07)	122(20.93)	27.077***	0.000
sophomore (n=165)	111(67.27)	54(32.73)		

junior (n=299)	155(51.84)	74(48.16)
senior (n=88)	51(57.95)	37(42.05)

Note. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

3.2. Path analysis

In order to investigate the chain mediating effect of loneliness and negative emotions in the association between MGAT and sleep quality, path analysis was conducted. The model fit indices, as shown in Table 3 and Figure 1, indicated an excellent fit. MGAT was found to have a significant positive predictive effect on sleep quality, loneliness, and negative emotions ($\beta = 0.16$, $p < 0.001$; $\beta = 0.20$, $p < 0.001$; $\beta = 0.26$, $p < 0.001$). Therefore, H1–H3 were supported, suggesting that mobile game addiction in university students can lead to loneliness and negative emotions, which in turn can decrease sleep quality.

Using a 95% confidence interval and a sample

size of 5000, H6 was tested with two mediators, loneliness and negative emotions. Sleep quality was considered the dependent variable (Y), while loneliness (W1) and negative emotions (W2) served as mediators, and MGAT was the independent variable (X). Two chain mediating models were examined, resulting in three indirect effects:

Ind1: $X \rightarrow W1 \rightarrow Y$; Ind2: $X \rightarrow W2 \rightarrow Y$; Ind3: $X \rightarrow W1 \rightarrow W2 \rightarrow Y$.

Consistent with the hypotheses, the chain-mediated effect measured by MGAT and sleep quality (Table 3) showed a significant correlation with the joint significance test.

Table: 3 Results from hypothesis testing using path analysis parameter estimates

<i>Hypothese</i>	<i>Path</i>	b	β	SE	95%CI
H1	Mobile game addiction tendency(X) \rightarrow sleep quality(Y)	1.00***	0.16***	0.19	[0.62, 1.39]
H2	Mobile game addiction tendency(X) \rightarrow Loneliness(W1)	0.36***	0.20***	0.06	[0.25, 0.47]
H3	Mobile game addiction tendency(X) \rightarrow negative emotions(W2)	0.30***	0.26***	0.03	[0.23, 0.36]
-	Loneliness \rightarrow negative emotions	0.16***	0.26***	0.02	[0.13, 0.20]
-	Negative emotions \rightarrow sleep quality	0.94***	0.17***	0.18	[0.59, 1.29]
-	Loneliness \rightarrow sleep quality	0.32***	0.09***	0.11	[0.11, 0.53]

Note. n = 1,065. Bootstrap resample = 5,000. b, nonstandard regression coefficient; β , completely standard regression coefficient; SE, standard error; CI, confidence interval. *** $p < 0.001$.

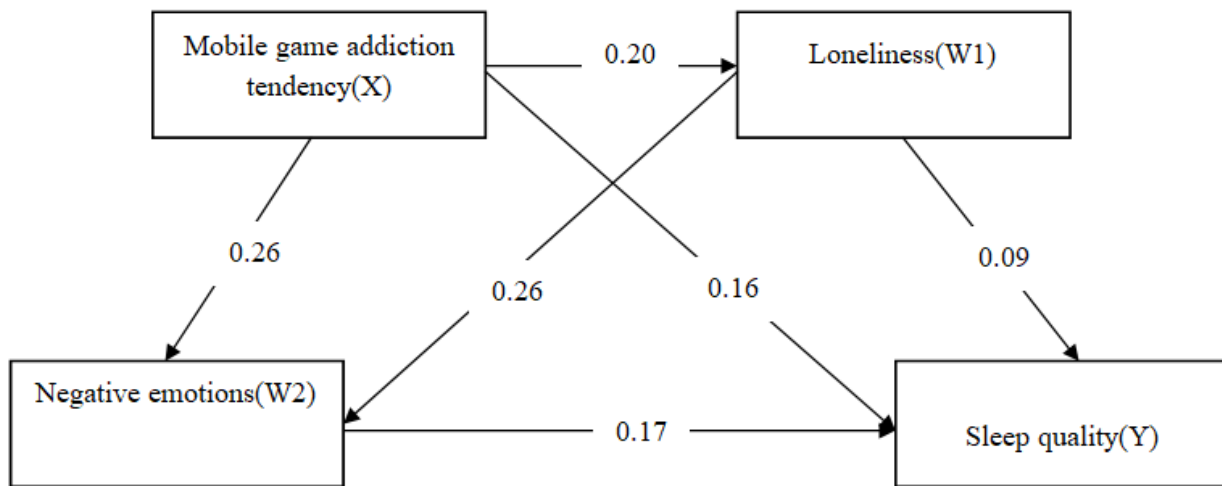


Figure 1. The path model illustrates the direct and indirect effects and causal paths linking variables with sleep quality.

The summary of indirect effects can be found in Table 4, where a significant indirect effect was observed ($\beta = 0.07$, 95% CI [0.04, 0.10]), accounting for 30.43% of the total effect. Ind1 ($\beta = 0.02$, 95% CI [0.01, 0.03]) and Ind2 ($\beta = 0.04$, 95% CI [0.02, 0.07]) also showed statistically significant indirect effects, accounting for 8.70% and 17.39% of the overall effect, respectively. The

positive relationship between MGAT and loneliness and negative emotions (Table 4) further supported H4 and H5, predicting sleep quality. The indirect effect of Ind3 was also statistically significant ($\beta = 0.01$, 95% CI [0.004, 0.01]), accounting for 4.35% of the total effect. These results confirmed H6.

Table: 4 Mediation model: Indirect effect between mobile game addiction tendency and sleep quality through loneliness and negative emotions

Effect	b[95%CI]	β [95%CI]	SE	Relative mediating effect
Total Effect	1.46**[1.08, 1.82]	0.23**[0.11, 0.45]	0.19	-
Direct Effect	1.00**[0.62, 1.39]	0.16**[0.09, 0.22]	0.16	-
Indirect Effect	0.3**5[0.27, 0.67]	0.07**[0.04,0.10]	0.10	30.43%
Ind1: X→W1→Y(H4)	0.12**[0.04, 0.20]	0.02**[0.01, 0.03]	0.04	8.70%
Ind2: X→W2→Y(H5)	0.28**[0.12,0.47]	0.04**[0.02, 0.07]	0.09	17.39%
Ind3:X→W1→W2→Y(H6)	0.06**[0.02, 0.09]	0.01**[0.004, 0.01]	0.02	4.35%

Note. n =1,065; Bootstrap resample = 5,000. b, nonstandard regression coefficient; β , completely standard regression coefficient; SE, standard error; CI, confidence interval. **p<0.01.

4. Discussion

4.1 Evaluation of conclusions

The present study has revealed a significant correlation between mobile game addiction

tendencies (MGAT) in university students and poorer sleep quality, which is consistent with previous research conducted by Leung and Zhang [15,33]. Sleep, being a fundamental physiological process, plays a critical role in maintaining overall

health by combating fatigue, preserving the cerebral cortex, boosting immune capacity, enhancing metabolism, and regulating mood^[34]. Moreover, it is worth noting that a staggering 45.6% of students reported using mobile phones to play games during class time^[35]. Consequently, it is imperative for educational institutions to implement measures that address the negative emotions arising from students' addiction to mobile games, such as prohibiting the use of mobile phones in classrooms^[7]. This issue is pervasive in Chinese university classrooms.

Individuals with mobile game addiction seek psychological solace in the virtual world of games as a means to escape from annoyance, depression, or loneliness^[32,36-37]. Numerous studies have confirmed the association between mobile game addiction and loneliness among college students^[38-39]. Extended periods of mobile game usage leading to high addiction levels have been observed to significantly reduce social opportunities^[30,40]. Mobile games have become a refuge for those experiencing loneliness, and over time, mobile game addiction tends to intensify, perpetuating a vicious cycle.

Most sleep quality factors, as well as the overall sleep quality scores, were found to be significantly associated with tendencies towards internet game addiction and negative emotions, which aligns with previous research on the relationship between online game addiction and sleep quality^[41-42]. Furthermore, this study revealed that negative emotions partially mediate the relationship between loneliness and mobile game addiction. Consistent with prior research, the immediate access to the internet, the anonymity it provides, and the availability of a virtual environment can lead college students to believe that they are effectively avoiding or mitigating negative emotions stemming from social interactions or life events^[9].

The phenomenon of mobile game addiction reflects the problems and challenges faced by users in their real lives to a considerable extent, particularly among college students who often seek an escape from negative situations related to their academic, familial, and interpersonal experiences. However, the excessive time spent in this virtual space ultimately plunges them into unprecedented loneliness^[43]. Therefore, negative

emotions serve as a conduit for the indirect impact of loneliness on internet game addiction.

Excessive mobile phone use was found to have no direct impact on sleep quality ($p=0.705$); however, it was associated with feelings of anxiety and depression, which in turn affected sleep quality^[14]. Therefore, excessive mobile phone use can lead to the development of depression, anxiety, or both, ultimately resulting in sleep problems.

The path analysis conducted in this study revealed that both MGAT and negative emotions have a direct impact on sleep quality. In other words, higher levels of MGAT and negative emotions were associated with poorer sleep quality. Loneliness was also found to indirectly affect sleep quality through its influence on negative emotions. University students who experience negative emotions, such as depression and anxiety, often turn to mobile game usage as a means of seeking comfort. Consequently, their sleep duration and efficiency are reduced, leading to daytime fatigue, sleepiness, and a lack of energy, all of which negatively impact learning efficiency and exacerbate sleep disorders^[43].

4.2 Theoretical and practical contributions of the study

In this research, we initially explored the impact of negative emotions and loneliness on sleep quality and mobile phone game addiction. The study has contributed to the existing literature by enriching our understanding of the relationship between MGAT and sleep quality, and offers theoretical guidance for preventing and addressing poor sleep quality among younger individuals. The findings shed light on how mobile game addiction affects sleep quality and underscore the mediating role of loneliness and negative emotions. The research results confirm that loneliness directly and indirectly influences MGAT and sleep quality, while negative emotions exacerbate the direct and indirect impact of MGAT on sleep quality.

In terms of implications for clinical practice, the ability to modify mobile phone habits relies on developing awareness of one's problematic usage and its underlying causes^[44]. By cultivating awareness, university students can learn to suppress their desire for mobile games and reduce the intensity of their mobile phone use.

Furthermore, health education campaigns focusing on sleep hygiene and the implementation of effective, targeted interventions can help prevent the adverse effects of excessive mobile game addiction on adolescent mental health ^[14].

Mobile phone game addiction has the potential to disrupt the emotional balance of university students, leading to negative emotions and impacting their sleep quality. Therefore, parents and teachers should assist young adults in acquiring emotion regulation strategies and improving their ability to regulate emotions, in order to weaken the influence of negative emotions on addictive behaviour and sleep quality. Individuals should exercise caution in recreational and transactional mobile phone usage, as models of human interaction can mitigate the direct link between alcoholism and cell phone dependence ^[45]. Intervention training, such as mindfulness-based stress reduction and cognitive therapy with meditation as a core component, as well as daily practice, can significantly enhance individuals' sleep quality ^[46-48].

4.3 Limitations and future directions

Despite the significant practical and theoretical implications of our study, it does have some limitations. Firstly, the method of sampling, which involved recruiting participants over social media, cannot be considered a truly random sample. This may limit the generalizability of the findings. Secondly, self-report measures were used to assess the dimensions of this study, which may introduce self-report bias. To mitigate this, future research should consider incorporating different methods, such as peer and clinician ratings. Additionally, future research could explore the impact of students' specializations (degree enrolled in) as a potential factor influencing mobile gaming addiction tendencies. Thirdly, the research uses the cross-sectional design approach to the investigation of the questionnaire. While hypotheses are analysed and discussed on the basis of current studies, the findings do not identify causality among the variables or their effects on time. In order to overcome this limitation, further studies will need to take into account the longitudinal design.

5. Conclusions

The study revealed a significant association between MGAT and poor sleep quality,

underscoring the importance of addressing gaming habits in the context of overall well-being. Furthermore, loneliness emerged as a noteworthy mediator; individuals with higher levels of mobile game addiction tended to experience increased feelings of loneliness, subsequently affecting their sleep quality. The chain mediating effect of loneliness and negative emotions elucidates a potential pathway through which mobile game addiction influences sleep quality.

In summary, we have provided a valuable contribution to the increasing amount of research on MGAT and its impact on university students' wellbeing. Understanding the intricate interplay of these factors is crucial for developing targeted interventions and support systems to enhance the overall mental health and sleep hygiene of this demographic.

Declarations:

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Ethics approval

Approval was obtained from the ethics committee of Shantou University. The procedures used in this study adhere to the tenets of the Declaration of Helsinki. Informed consent was obtained from all participants and their legal guardians.

Data availability statement

Data can be made available on request.

Informed Consent

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5). Informed consent was obtained from all patients for being included in the study.

Author contribution statement.

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Jing Deng, Chang Liu, Siyi Li, and Jian Gao. The first draft of the

manuscript was written by Yongtao Gan and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Data Availability Statement

Data can be made available on request.

Declaration of Competing Interest

Authors declare that they have no conflict of interest.

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