

Smartphone Use and Inflammation at 2-Year Follow-Up in College Students: The Mediating Role of Physical Activity

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Purpose: Smartphone use could lead to being physically inactive and a greater risk for health problems, such as inflammation. However, the associations between smartphone use, physical activity (PA), and systemic low-grade inflammation remained unclear. This study aimed to examine the potential mediating effect of PA on the association between smartphone use and inflammation.

Patients and Methods: A two-year follow-up study was conducted between April 2019 and April 2021. Duration of smartphone use, smartphone dependence and PA were assessed by a self-administered questionnaire. Laboratory analysis of blood samples was performed to evaluate the levels of TNF- α , IL-6, IL-1 β , and CRP as biomarkers of systemic inflammation. The correlations between smartphone use, PA, and inflammation were analyzed using Pearson correlation. Structural equation modelling was used to analyze the potential mediating effect of PA on the associations between smartphone use and inflammation.

Results: A total of 210 participants were included with a mean (standard deviation) age of 18.7 (1.0) years, 82 (39%) of whom were males. Smartphone dependence was negatively associated with the total PA level ($r=-0.18$, $P<0.01$). PA mediated the associations between the duration of smartphone use and smartphone dependence with inflammatory markers. Specifically, as PA decreased, the duration of smartphone use was more negatively associated with TNF- α ($ab=-0.027$; 95% CI: -0.052 , -0.007) and more positively correlated to IL-6 ($ab=0.020$; 95% CI: 0.001 , 0.046) and CRP ($ab=0.038$; 95% CI: 0.004 , 0.086); smartphone dependency was more negatively associated with TNF- α ($ab=-0.139$; 95% CI: -0.288 , -0.017) and more positively related to CRP ($ab=0.206$; 95% CI: 0.020 , 0.421).

Conclusion: Our study illustrates that there are no direct associations between smartphone use and systemic low-grade inflammation, however, PA level plays a weak but significant mediating effect on the associations between smartphone use and inflammation among college students.

Keywords: smartphone, inflammation, physical activity, mediating role, follow-up

Introduction

Over the past decade, several studies have shown that the number of smartphone users has been growing rapidly.¹⁻³ In 2019, global smartphone penetration reached approximately 41.5% of the global population.⁴ Young people (18-22 years old) are the largest and fastest-growing group of smartphone users.⁵ There is a growing body of research examining the impacts of smartphone overuse on health. Elhai et al⁶ indicated that mental health problems such as depression and anxiety were associated with excessive smartphone use. Another study showed that smartphone use was positively associated with perceived stress levels.⁷ In addition, studies have shown that media devices could negatively affect sleep quality.⁸ However, the evidence for the associations between smartphone use and physical health remains limited. A few

studies have examined the association between smartphone use and neck pain⁹ or between social media use and inflammation^{10–12} supporting the hypothesis that smartphone use hurts health.

Systemic low-grade inflammation describes the persistent production of proinflammatory factors, as opposed to an acute inflammatory state, chronic inflammation is considered integral to the development of serious systemic diseases such as type 2 diabetes mellitus, cardiovascular diseases, gastrointestinal disorders, and rheumatoid arthritis.¹³ This inflammatory state is indicated by elevated levels of circulating inflammation markers, tumor necrosis factor- α (TNF- α),¹⁴ interleukin-6 (IL-6)¹⁵ and interleukin-1 β (IL-1 β)¹⁶ are important cytokines involved in the inflammatory response. C-reactive protein (CRP) is an acute phase protein that is secreted from the liver upon IL-6 stimulation,¹⁷ which plays a crucial role in the regulation of the inflammatory process along with other inflammation cytokines. Studies suggested there was a positive association between social media use and systemic pro-inflammatory status,¹⁰ but there was no clear pattern to illustrate a specific association between the two.

Many features of smartphone use have been reported to be associated with sedentary behaviors.¹⁸ Additional studies have shown a positive association of sedentary behavior with higher body mass index (BMI) and lower PA levels.^{19,20} Moreover, the negative impact of problematic smartphone use on PA levels was addressed.²¹ Although some studies proposed the ability of smartphones to promote PA through some apps,^{22,23} the relationships between excessive smartphone use and the symptoms of health were well-established,^{24,25} which also inevitably lead to an increase in screen-based sedentary behaviors and a decrease in PA. There are some discrepancies in the previous literature regarding the association between PA and inflammation. Concerning the anti-inflammatory effects of exercise, one study suggests that the likely mechanism is a reduction of visceral fat,²⁶ that regular exercise leads to increased circulating levels of adiponectin and decreased levels of several circulating proinflammatory adipokines, including IL-6, TNF, retinol-binding protein 4, and leptin,^{27–29} and that increased physical activity may therefore reduce systemic inflammation by decreasing proinflammatory adipokine secretion.³⁰ In addition, exercise leads to a significant increase in cellular and circulating levels of IL-6 in contracted skeletal muscle,³¹ and transient elevations in IL-6 are responsible for subsequent increases in circulating levels of the anti-inflammatory cytokine IL-10 and IL-1 receptor antagonist (IL-1RA).³² Meanwhile, IL-1RA is secreted mainly by monocytes and macrophages and inhibits the pro-inflammatory effects of IL-1 β effects.³³ However, a recent mouse study showed that intensive exercise training led to an increased response of anti-inflammatory cytokines (IL-10) to antigen exposure.³⁴ Similar findings have been reported in population experiments.³⁵ A large body of evidence from mouse and human studies suggested that IL-10 production generally imposed some limitations on the effectiveness of pathogen-specific immune responses.^{36,37} These studies suggest that high-intensity training loads induce an anti-inflammatory state that increases the risk of minor infections.

Although there were independent associations between PA or smartphone use and inflammatory status, studies illustrating a specific link between the three were limited. Based on the foregoing, we hypothesized a mediating effect of PA on the associations between smartphone use, especially the duration of smartphone use and the symptoms of dependence, and systemic low-grade inflammation. Our study was conducted in a 2-year follow-up design among healthy college students and aimed to explore the mediating role of PA in the associations between smartphone use and inflammation, which could contribute to the development of intervention strategies on PA among youth with excessive media use.

Materials and Methods

Participants and Procedure

Participants were recruited from a medical university in Hefei, Anhui Province and a comprehensive normal college in Shangrao, Jiangxi Province between April and May 2019. All first-year students from two faculties of each university were selected by cluster random sampling. A 4-wave follow-up at 6-month intervals in 2 years was conducted from October 2019 to April 2021. The baseline survey consisted of an electronic questionnaire scanned with a smartphone and a physical examination. A total of 1135 valid questionnaires were received, with a response rate of 98.6%. Blood samples were collected from 771 students at baseline. Because of the COVID-19 epidemic and the health status of students, blood samples were collected from 339 students at wave 4. Finally, 210 valid respondents who provided both

the questionnaire and blood samples at baseline and wave 4 were analyzed. The research protocol was approved by the Ethics Committee of Anhui Medical University (approval number: 20170291). All respondents signed informed consent before completing the research, and the study was conducted following the principles of the Declaration of Helsinki.

Measures

Duration of Smartphone Use and the Smartphone Dependence

Duration of smartphone use was assessed by asking “How long did you use your smartphone per day?” The answers were counted in hours and recorded as less than 2 hours (1), 2–3.99 hours (2), 4–5.99 hours (3), and greater than or equal to 6 hours (4).³⁸

Smartphone dependence was assessed by using the Self-rating Questionnaire for Adolescent Problematic Mobile Phone Use (SQAPMPU).³⁹ The questionnaire consists of 13 items containing 3 dimensions named withdrawal symptoms, craving, and physical and psychological effects, and uses a 5-point scale with scores ranging from 1 (never) to 5 (always). The total scores ranged from 13 to 65, with higher scores indicating a higher level of dependence. Smartphone dependence was defined as a total score greater than or equal to the 75th percentile of the whole group.⁴⁰ The Cronbach’s alpha coefficient was 0.92 in the present study.

Physical Activity

PA was assessed using the Chinese version of the International Physical Activity Questionnaire Short Form (IPAQ-SF).⁴¹ The questionnaire contains 7 questions covering 3 types of PA: walking, moderate PA (MPA; eg, lifting light objects, cycling at normal speed, or playing tandem tennis), and vigorous PA (VPA; eg, lifting heavy objects, digging, aerobic exercise, or fast cycling). Participants were asked to recall the frequency (days per week, d/w) and duration (minutes per day, min/d) of varying intensity of PA during the last 7 days. The amount of PA is calculated in metabolic equivalent (MET). The METs for VPA, MPA and walking are 8.0, 4.0 and 3.3, respectively. The MET-min/w scores of each activity were calculated by its METs \times frequency (d/w) \times duration (min/d). The total PA was a sum of (VPA+ MPA +walking) MET-min/w. The total PA level was classified into three groups:

High: (a) VPA on at least 3 days per week with a minimum total PA level of 1500 MET-min/w.(b) A total of VPA, MPA and walking at least 7 days per week with a minimum total PA of 3000 MET-min/w.

Medium: (a) VPA at least 20 minutes per day for a minimum total of 3 days per week. (b) MPA or walking at least 30 minutes per day for a total of 5 days or more. (c) VPA, MPA and walking for 5 days or more per week with a minimum total PA level of 600 MET-min/w.

Low: Those respondents who did not meet the high or medium criteria mentioned above were defined as at a low PA level.

Pro-Inflammatory Cytokines and C-Reactive Protein

Laboratory analysis of blood specimens was performed to evaluate TNF- α , IL-6, IL-1 β , and CRP as markers of systemic inflammation. During the physical examination, 5 mL of fasting venous blood samples were collected from 6:00 to 8:00 in the morning using a vacuum blood collection tube with anticoagulant (EDTA). The blood samples were centrifuged for 10 min at a set speed of 3000 revolutions per minute within 2 hours. The upper plasma samples were stored at -80°C . Liquid-phase protein suspension chip (Luminex) was used in the detection process. Plasma inflammatory markers were detected by multi-bead enzyme-free analyzer MILLIPLEX[®] MAP instrument (Merck Millipore). Within the analysis of variation, the intra-assay coefficient of variation of IL-1 β , IL-6, and TNF- α were all $<5\%$, and the inter-assay coefficients of variation were $<15\%$, $<20\%$, and $<15\%$, respectively. The assay had a lower detection limit of IL-1 β , IL-6, and TNF- α of 0.14 pg/mL, 0.11 pg/mL, and 0.16 pg/mL, respectively. All inflammatory markers were log-transformed to settle skewness. The level of CRP was measured by immunoturbidimetry using the serum on the day the blood samples were collected.

Socio-Demographic Information and Covariates

Baseline socio-demographic information was collected by electronic questionnaires, including age, gender (male or female), residence (rural or town), health status (poor, medium or good), socioeconomic status (SES; operationalized as the mean score derived from parental education level and self-reported family economy, each measured on a scale ranging from 1 to 5, with higher scores indicating higher SES) and body mass index (BMI). Moreover, PA levels at baseline were also assessed by IPAQ-SF; TNF- α , IL-6, IL-1 β and CRP at baseline were detected; and duration of smartphone use and smartphone dependence scores at follow-up were also collected by questionnaires and adjusted.

Statistical Analyses

IBM SPSS Statistics 26.0 was used to perform descriptive analysis and correlation analysis between variables. Total PA levels, TNF- α , IL-6, IL-1 β and CRP were all log-transformed. Normally distributed data were represented by the mean and standard deviation (SD). Categorical data were expressed as frequencies (n) and percentages (%). Additionally, to examine the differences in inflammation levels stratified by smartphone dependence or PA level groups, additional two independent samples *t*-test and one-way ANOVA were performed. Mplus version 8.3 statistical software was used for mediation analysis. To test our hypotheses, we conducted an overall structural equation model. The model can determine the total, direct and indirect effects between the duration of smartphone use and smartphone dependence and the levels of inflammation.⁴² the total effect was an unadjusted association between the duration of smartphone use, smartphone dependence and inflammation levels; The indirect effect was the associations between the duration of smartphone use, smartphone dependence and inflammation levels through PA levels; The direct effect is the association that remains after adjusting for the effects of PA level.

The full information maximum likelihood method was used to deal with missing data.⁴³ The goodness of fit was assessed with the following fitting indexes: comparative fit index (CFI), Tucker-Lewis index (TLI), and root mean square error of approximation (RMSEA). Thresholds were considered as follows: for CFI and TLI excellent fit >0.95 and moderate fit >0.90; for RMSEA excellent fit <0.05 and moderate fit <0.08.⁴⁴

Results

Descriptive Analyses

Table 1 presents demographic information for 210 college students (39.0% males and 61.0% females) aged 16–26 years old ($M=18.7$, $SD=1.0$). There were 182 (86.7%) college students from rural areas and 28 (13.3%) from urban areas. One hundred and eighteen (56.2%) college students described their health as good, 88 (41.9%) as medium, and 4 (1.9%) as poor. The mean SES scores were 8.27 ± 2.14 . The mean BMI was 21.00 ± 2.51 kg/m². The mean duration of smartphone use at baseline was 3.07 ± 0.80 hours and 2.22 ± 1.19 hours at the 2-year follow-up. The total scores of smartphone dependence at baseline were 23.91 ± 8.30 and 21.95 ± 8.95 at the two-year follow-up. The prevalence of smartphone dependence among college students was 30.5% at baseline and 21.4% at the two-year follow-up. The IPAQ-SF scores (log-transformed) were 3.34 ± 0.37 at baseline and 3.29 ± 0.45 at the two-year follow-up. At the follow-up after 2 years, 39%, 43.3%, and 17.6% of participants reported high, medium, and low PA levels, respectively. The log-transformed mean levels of TNF- α , IL-6, IL-1 β , and CRP at baseline were 0.83 ± 0.21 pg/mL, 0.76 ± 0.35 pg/mL, 0.41 ± 0.28 pg/mL, -0.39 ± 0.58 pg/mL, respectively; and were 0.37 ± 0.21 pg/mL, -0.40 ± 0.75 pg/mL, 0.34 ± 0.22 pg/mL, -0.06 ± 0.36 pg/mL at the two-year follow-up. Demographic differences between the final included and excluded samples for the analysis are shown in [Table S1](#).

Correlation Analysis

Table 2 demonstrates the correlations between smartphone use, PA, and inflammation. The duration of smartphone use was significantly and positively correlated with smartphone dependence at baseline. Smartphone dependence at baseline was negatively correlated with PA measured at follow-up. Total PA levels were positively correlated with TNF- α and negatively correlated with IL-6 at the 2-year follow-up. The correlations between the duration of smartphone use and smartphone dependence measured both at baseline and follow-up were displayed in [Table S2](#). There were significant correlations among inflammatory factors measured both at baseline and follow-up, shown in [Table S3](#).

Table 1 Descriptive Statistics of the Study Samples (n=210)

Variables	Baseline	2-Year Follow-Up
Age (years, M±SD)	18.7±1.0	
Males (n, %)	82 (39.0)	
Residence		
Rural (n,%)	182 (86.7)	
Urban (n,%)	28 (13.3)	
Health status		
Good (n,%)	118 (56.2)	
Medium (n,%)	88 (41.9)	
Poor (n,%)	4 (1.9)	
SES scores (M±SD)	8.27±2.14	
BMI (kg/m ² , M±SD)	21.00±2.51	
Duration of smartphone use (hours, M±SD)	3.07±0.80	2.22±1.19
Total scores of smartphone dependence (M±SD)	23.91±8.30	21.95±8.95
Smartphone dependence (n,%)	64 (30.5)	45 (21.4)
Total PA levels (MET-min/w, M±SD)	3.34±0.37	3.29±0.45
Physical activity levels		
High group (n,%)	79 (37.6)	82 (39.0)
Medium group (n,%)	116 (55.2)	91 (43.3)
Low group (n,%)	15 (7.1)	37 (17.6)
TNF- α (M±SD)	0.83±0.21	0.37±0.21
IL-6 (M±SD)	0.76±0.35	-0.40±0.75
IL-1 β (M±SD)	0.41±0.28	0.34±0.22
CRP (M±SD)	-0.39±0.58	-0.06±0.36

Notes: Total PA levels, TNF- α , IL-6, IL-1 β and CRP were all log-transformed.

Abbreviations: M, mean; SD, standard deviation; SES, socioeconomic status; BMI, body mass index; PA, physical activity; TNF- α , tumor necrosis factor- α ; IL-6, interleukin-6; IL-1 β , interleukin-1 β ; CRP, C-reactive protein.

Table 2 Bivariate Correlations Between Smartphone Use, Physical Activity and Inflammation

Variables	1	2	3	4	5	6
1. Duration of smartphone use ^a						
2. Total scores of smartphone dependence ^a	0.33**					
3. Total PA levels (MET-min/w) ^b	-0.11	-0.18**				
4. TNF- α ^b	-0.12	-0.09	0.21**			
5. IL-6 ^b	0.08	0.03	-0.26**	0.04		
6. IL-1 β ^b	-0.12	-0.06	0.08	0.47**	0.36**	
7. CRP ^b	0.01	0.07	0.06	0.13	-0.16*	-0.01

Notes: * $P<0.05$, ** $P<0.01$; Total PA levels, TNF- α , IL-6, IL-1 β and CRP were all log-transformed. ^aBaseline; ^bFollow-up.

Abbreviations: PA, physical activity; TNF- α , tumor necrosis factor- α ; IL-6, interleukin-6; IL-1 β , interleukin-1 β ; CRP, C-reactive protein.

The Inflammation Levels in Different Groups of Smartphone Dependence and PA

The inflammation levels at 2-year follow-up in different groups of smartphone dependence at baseline are shown in [Figure 1](#). The results showed that there were no significant differences in TNF- α ($P=0.59$), IL-6 ($P=0.93$), IL-1 β ($P=0.41$), and CRP ($P=0.92$) at follow-up between the college students with smartphone dependence and those without smartphone dependence at baseline. The differences in inflammation levels at follow-up between different levels of PA at follow-up are shown in [Figure 2](#). TNF- α was significantly higher in the high PA level group than that of the medium PA level group ($P=0.005$). IL-6 was significantly higher in the high PA level group than in the medium PA level group ($P<0.001$) or the low PA level group ($P<0.001$). CRP levels were higher in the high PA level group than in the medium

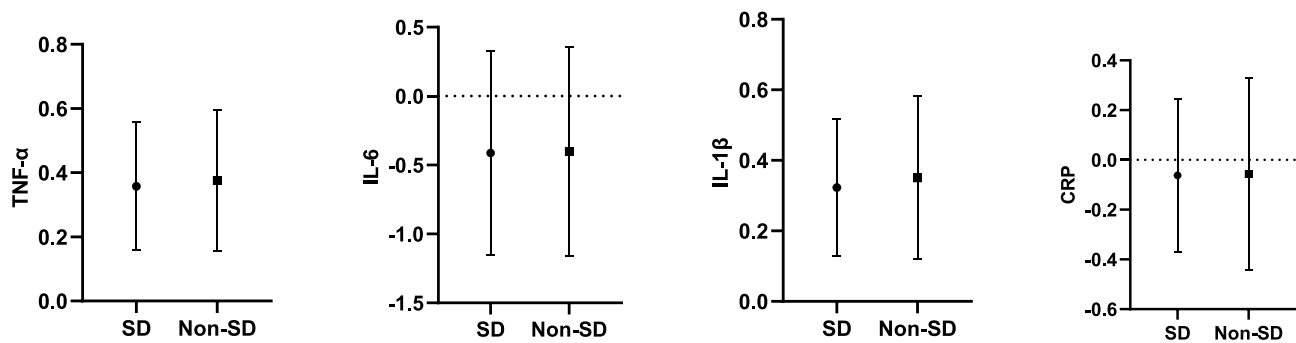


Figure 1 Comparison of the inflammation levels in different groups of smartphone dependence.

Notes: TNF- α , IL-6, IL-1 β and CRP were all log-transformed.

Abbreviations: TNF- α , tumor necrosis factor- α ; IL-6, interleukin-6; IL-1 β , interleukin-1 β ; CRP, C-reactive protein; SD, smartphone dependence; Non-SD, non-smartphone dependence.

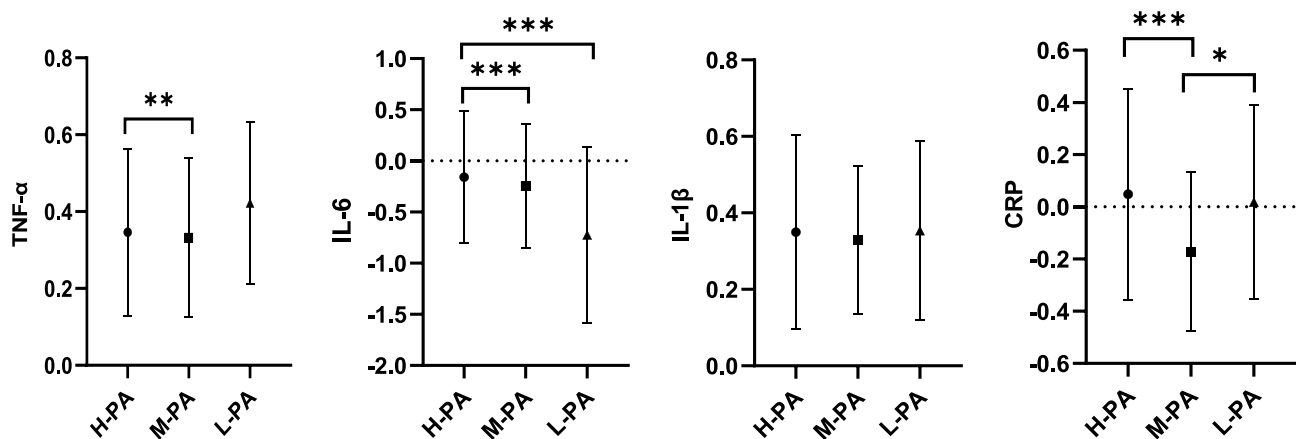


Figure 2 Comparison of the inflammation levels in different groups of physical activity.

Notes: TNF- α , IL-6, IL-1 β and CRP were all log-transformed. * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

Abbreviations: TNF- α , tumor necrosis factor- α ; IL-6, interleukin-6; IL-1 β , interleukin-1 β ; CRP, C-reactive protein; H-PA, high physical activity group; M-PA, medium physical activity group; L-PA, low physical activity group.

PA level group ($P < 0.001$), but were lower in the medium PA level group than in the low PA level groups ($P = 0.001$). IL-1 β was not significantly different between high, medium and low PA level groups ($P = 0.74$). We additionally explored the differences in the total PA levels at follow-up between students with and without smartphone dependence at baseline, which indicated the total PA levels at follow-up were significantly lower in the smartphone dependence group at baseline, as seen in [Figure S1](#) ($P = 0.018$).

The Mediating Effect of Follow-Up PA on the Associations Between Baseline Smartphone Use and Follow-Up Inflammation in College Students

[Table 3](#) exhibits the mediating effect of PA at follow-up between smartphone use at baseline and inflammation levels at follow-up in college students. After adjusting for gender, total PA levels at baseline, inflammatory indicators at baseline, duration of smartphone use at follow-up, and symptoms of smartphone dependence at follow-up, the results showed a negative mediating effect of total PA level on the association between the duration of smartphone use and TNF- α ($ab = -0.027$, 95% CI: $-0.052, -0.007$), but the direct and total effects were not significant. Furthermore, there was a positive mediating effect of total PA level on the association between duration of smartphone use and IL-6 ($ab = 0.020$, 95% CI: $0.001, 0.046$) and CRP ($ab = 0.038$, 95% CI: $0.004, 0.086$), but the direct and total effects were not significant. The mediating effect of total PA level on the association between the duration of smartphone use and IL-1 β was not significant, but there was a total effect ($c = -0.049$, $P < 0.05$). When smartphone dependence was used as a predictor,

Table 3 The Mediating Effect of Physical Activity on the Associations Between Smartphone Use and Inflammation Among College Students

	Estimate (S.E.)				Indirect (S.E.)	
	a	b	c'	c	ab	95% CI
Duration of smartphone use						
TNF- α	-0.177 (0.064)**	0.154 (0.048)**	-0.016 (0.030)	-0.043 (0.028)	-0.027 (0.012)*	-0.052, -0.007
IL-6	-0.177 (0.064)**	-0.115 (0.059)	-0.040 (0.072)	-0.020 (0.071)	0.020 (0.012)	0.001, 0.046
IL-1 β	-0.177 (0.064)**	0.014 (0.021)	-0.047 (0.024)	-0.049 (0.023)*	-0.002 (0.004)	-0.011, 0.004
CRP	-0.177 (0.064)**	-0.213 (0.081)**	-0.028 (0.039)	0.010 (0.044)	0.038 (0.021)	0.004, 0.086
Smartphone dependence						
TNF- α	-0.898 (0.354)*	0.155 (0.047)**	-0.075 (0.163)	-0.214 (0.167)	-0.139 (0.070)	-0.288, -0.017
IL-6	-0.898 (0.354)*	-0.107 (0.061)	-0.044 (0.393)	0.053 (0.383)	0.096 (0.075)	-0.004, 0.289
IL-1 β	-0.898 (0.354)*	0.021 (0.021)	-0.076 (0.115)	-0.095 (0.115)	-0.019 (0.021)	-0.068, 0.013
CRP	-0.898 (0.354)*	-0.229 (0.084)**	-0.565 (0.247)*	-0.359 (0.238)	0.206 (0.109)	0.020, 0.421

Notes: Total PA levels, TNF- α , IL-6, IL-1 β and CRP were all log-transformed. * $P < 0.05$, ** $P < 0.01$; ab=indirect effect; c'=direct effect; c=total effect.

Abbreviations: TNF- α , tumor necrosis factor- α ; IL-6, interleukin-6; IL-1 β , interleukin-1 β ; CRP, C-reactive protein; CI, confidence interval; S.E., standard error.

the total PA levels showed a negative mediating effect on the association between smartphone dependence scores and TNF- α (ab=-0.139, 95% CI: -0.288, -0.017), and the direct and total effects were not significant. There was a positive mediating effect of total PA level on the association between smartphone dependence and CRP (ab=0.206, 95% CI: 0.020, 0.421), with a significant direct effect (c'=-0.565, $P < 0.05$) and a non-significant total effect; The mediating, direct, and total effects of total PA level on the associations between smartphone dependence and IL-6 and IL-1 β were not significant.

Discussion

To our knowledge, most previous studies have focused on the associations between problematic smartphone use and depression, anxiety, chronic stress, or low self-esteem.⁶ This is the first study to examine the relationships between smartphone use and inflammation among healthy college students. We also found a weak but significant mediating role of PA in the associations between smartphone use and inflammatory status.

Our results reported the percentage of smartphone dependence was 30.5% at baseline and 21.4% at the 2-year follow-up, which differed from that of college students in Spain (12.8%),⁴⁵ Serbia (22.7%)⁴⁶ and another city of China (29.8%).⁴⁷ Moreover, our findings indicated smartphone dependence inevitably led to increasing screen time and decreasing the time spent on PA. A large number of studies have shown that increased media-based screen time can lead to sedentary behavior.⁴⁸⁻⁵⁰ Macias et al⁵¹ noted that television viewing, computer use, and other screen-based activities were associated with sedentary time spent in front of a screen. A Finnish study showed that a large amount of sedentary behavior was associated with lower PA.²⁰ A systematic review identified that a surge in screen time was a major risk factor for sedentary behavior.⁵²

To date, there are no studies that have specifically tested the association between smartphone dependence and inflammation. There was also no direct associations between smartphone dependence and inflammation observed in our study. However, significant differences in inflammation between groups of PA were found. The potential beneficial effects of exercise on inflammation are well-established anteriorly.⁵³ Previous studies have shown that PA can prevent clinical conditions associated with systemic low-grade inflammation in adults.^{26,54} Otherwise, some evidence was consistent with our findings. A study showed that TNF- α levels were significantly lower in the moderate PA group compared to the low PA group, while IL-6 levels were significantly higher in the high PA group than in the moderate and low PA groups.⁵⁵ This suggests that moderate PA may be the optimal intensity to reduce the pro-inflammatory state. In addition, some studies have shown that IL-1 β may not be as sensitive as IL-6 and TNF- α ,^{55,56} which confirmed that why did not find a mediating role of PA on the relationship between smartphone use and IL-1 β .

Moderate physical activity plays a positive role in reducing anxiety, depression and complicated anxiety and depression symptoms.⁵⁷ At the same time, the level of biomarkers of peripheral inflammation increased in patients with depression.⁵⁸ Studies on animal models have also shown that the release of pro-inflammatory factors and the activation of microglia in the animal brain show signs of anxiety and depression.^{59,60} Therefore, anxiety and depression may be important factors leading to the development of inflammation due to the decrease in physical activity. In addition, TNF- α and IL-6 are usually overexpressed in adipose tissue cells and macrophages in the physically inactive and obese population, which could cause an inflammatory response.^{61,62} However, exercise-induced intramuscular IL-6 mRNA, which increases circulating IL-6, then acts as a trigger to activate hepatic glycogenolysis and lipolysis, providing additional energy to exercising muscles.⁶³ This is consistent with the results observed in this study where IL-6 levels were higher in the high PA group than in the moderate and low PA groups, suggesting that high-intensity PA appear to play a pro-inflammatory role.⁶⁴ A systematic review and meta-analysis of 83 randomized controlled trials involving 3769 participants suggested that exercise for more than 2 weeks can reduce CRP.⁶⁵ In our study, the moderate PA group also showed a significant decrease in CRP levels compared to the low PA group. Thus, the mediating role of PA may be an important pathway for the associations between screen-based sedentary behaviors and inflammation. It is worth noting that PA played a negative mediating effect between smartphone use and TNF- α levels, which suggested that while smartphone use can certainly lead to altered PA, the level of PA intensity may be associated with inflammatory status. Paolucci et al⁵⁵ showed that high-intensity intermittent exercise increased the concentration of TNF- α , which in turn leads to an increase in inflammatory levels. In addition, we found a positive mediating effect of PA on the association between the duration of smartphone use and IL-6 or CRP, and PA played a fully mediated role between smartphone use and inflammation. Preacher et al⁶⁶ explained that fully mediated results are easily obtained when the total effect and sample size are small. Therefore, the sample population should be appropriately increased in future studies.

Several strengths of the present study should be addressed. First, a longitudinal design was used to examine the associations between smartphone use, PA, and inflammation over two years, and controlled for PA and inflammation at baseline, duration of smartphone use and smartphone dependence at follow-up in the study. Second, the combined measurement of several inflammatory biomarkers provided a more comprehensive picture of the systemic pro-inflammatory state. Otherwise, some limitations of this study should be acknowledged. First, self-report instruments were used to assess smartphone use and PA levels, which may introduce potential reporting bias, but they were well-verified with good reliability worldwide.^{39,67} Second, although smartphone use represents prior exposure, no clear conclusions can be drawn regarding the timing of the occurrence of elevated PA levels and inflammation. The temporal sequence of changes in PA levels and inflammation should be further clarified in future studies to establish potential pathways of associations between smartphone use, PA, and inflammation. Third, because of the impact of COVID-19, students devoted more time to taking courses online, which resulted in increased access to digital media devices and decreased physical activity time.^{68,69} The extrapolation of our results is limited and future studies should further track observations in a broader population. Finally, although our study has controlled for several confounding factors, there are still some confounders which are difficult to measure (eg, physical and chemical environment, immunization) that may interfere with the results, and future studies should set up better-designed protocols.

Conclusion

Our study illustrates that there are no direct associations between smartphone use and inflammation among college students, PA level plays a weak but significant mediating effect on the associations between smartphone use and inflammatory status among college students. These findings suggest that an appropriate increase in PA level has positive implications for reducing screen-based sedentary behaviors and systemic pro-inflammatory status.

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Disclosure

The authors declared no potential conflicts of interest concerning the research, authorship, and/or publication of this article.

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