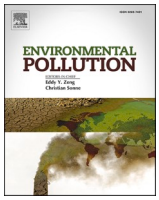
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Association between electronic device usage and sperm quality parameters in healthy men screened as potential sperm donors☆

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ABSTRACT

Cell phone use and radio-frequency electromagnetic radiation (RF-EMF) are rapidly increasing and may be associated with lower semen quality, yet results from epidemiological studies are inconclusive. Information on electronic devices use was collected through standard questionnaires from 1454 men aged 22–45 years old. Semen volume, sperm concentration, total sperm count, total motility, progressive motility, and normal morphology in repeated specimens were determined by trained clinical technicians. Percent changes [95% confidence intervals (CIs)] were estimated as $(10^{\beta}-1) \times 100$ for electronic devices use associated with repeated sperm quality parameters in the linear mixed-effect models. After adjusting for multiple confounders, we found significant inverse associations of total duration of electronic devices use with sperm progressive motility and total motility, duration of cell phone and computer use with sperm concentration, progressive motility, and total motility (all $P < 0.05$). No significant association was found between cell phone/computer use alone and sperm quality parameters. Moreover, per hour increase of time spent on cell phone talking was associated with decreased sperm concentration and total count by an average of −8.0% (95% CI: −15.2%, −0.2%) and −12.7% (95% CI: −21.3%, −3.1%), respectively. Besides, daily calling time was associated with lower sperm progressive motility and total motility among those who used headsets during a call (P for interaction <0.05). In conclusion, our study suggested that more time spent on electronic devices use had a modest reduction effect on semen quality. Daily calling time was significantly associated with lower sperm concentration and total count, and using headsets during a call appeared to aggravate the negative association between daily calling time and sperm motility. Additional studies are needed to confirm these findings.

1. Introduction

During the last two decades, there has been a significant increase in electronic device usage throughout the world. Meanwhile, there are growing concerns about the potential effects of radiofrequency electromagnetic waves (RF-EMFs) emitted by cell phones on human health

Abbreviations: BMI, body mass index; CI, confidence interval; RF-EMF, radio-frequency electromagnetic radiation; ROS, reactive oxygen species; SD, standard deviation; WHO, world health organization.

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(Deepinder et al., 2007; WHO, 2014), including cardiovascular disease, sleep quality, and cognitive function (Makker et al., 2009), as well as the possible effects on male fertility. Continuous electromagnetic radiation from cell phones can obviously lead to the development of different pathologies and can also violate spermatogenesis (De Iuliis et al., 2009; Dutta et al., 2019), potentially by disturbing oxidative stress and causing DNA fragmentation.

Around 14% of couples in high- and middle-income countries have difficulty in conceiving naturally (Evers, 2002; Thonneau et al., 1991), of which male-factor infertility accounts for approximately 40% (Sharlip et al., 2002; Thonneau et al., 1991). Unexplained declines in semen quality have been reported by many countries (Levine et al., 2017; Rolland et al., 2013; Swan et al., 2000). Sperm defects or dysfunction, mainly including decreased sperm count and motility (Agarwal et al., 2008; Sajeda and Al-Wattar, 2011) were the commonest defined cause of infertility (24%) (Hull et al., 1985). Environmental, psycho-social, and behavioral factors have certain effects on sperm quality parameters, though the underlying mechanisms are largely unknown; extensive exposure to electromagnetic radiation environments may be a contributing factor.

Animal studies indicated that radiofrequency radiation emitted by cell phones could affect the testicular function and structure, and cause histological changes that include hypospermatogenesis, and maturation arrest in the spermatozoa in the testis (Dasdag et al., 1999; Salama et al., 2010), then reduce sperm motility (Mailankot et al., 2009). Similarly, several epidemiologic studies have also reported that cell phone use may adversely affect semen quality including decreased sperm count, motility, viability, and normal morphology (Adams et al., 2014; Agarwal et al., 2008; Dama and Bhat, 2013; Fejes et al., 2005; Sajeda and Al-Wattar, 2011). Long-term exposures to computer-related repetitive radiofrequency radiation and transient scrotal hyperthermia are modern lifestyle features that may exert a negative influence on spermatogenesis (Avendano et al., 2012; Sheynkin et al., 2005). Conversely, other scientists failed to find consistent pattern or exposure-response relationship between cell phone use and semen quality (Lewis et al., 2017; Rago et al., 2013; Yu et al., 2021). The relationship between electronic device use (including cell phones, computers, or other aspects) and semen quality remains inconclusive. Given the ubiquity of electronic devices, the potential role of this environmental exposure needs to be further clarified.

Previous studies mainly recruited subjects from the fertility clinic or other specific groups which may cause a selection bias. More importantly, they collected semen samples at a single time point, which may result in measurement error due to the high within-individual variability in sperm quality parameters (Chen et al., 2020a; Chiu et al., 2017). To our knowledge, only one prospective study on this topic has been conducted with a repeated collection of semen samples from Chinese college students (Zhang et al., 2016). However, they did not consider total electronic devices exposure, certain aspects of cell phone use, and electromagnetic radiation information (including residential nearby equipment and occupational exposure). To fully consider the association between electronic devices use and semen quality, repeated-measurement studies in the general population with large sample sizes are urgently needed. Therefore, in this repeated-measurement study, we applied comprehensive questionnaires to gather information of electronic devices usage and multiple confounders, and repeatedly collect semen samples from 1454 healthy men to assess the associations between electronic devices use and semen quality.

2. Materials and methods

2.1. Study design and subjects

In this observational study, 1487 men aged 22–45 years old with a total of 6608 semen donation records were recruited at a sperm bank in Wuhan, China from April 2017 to July 2018. The details of the study design have been described previously (Chen et al., 2021; Sun et al., 2019). Participants who volunteered as potential sperm donors were first checked for eligibility if they met the following criteria: (1) aged between 22 and 45 years; (2) no less than a high school degree; (3) no sexually transmitted diseases or genetic diseases (e.g., syphilis, gonorrhea, HIV, thalassemia, and hepatitis, etc.). Donors should also meet the following criteria: fresh semen samples should have a liquefaction time <60 min, sperm concentration $\geq 60 \times 10^6$/mL, progressive motility $\geq$60%, and percentage of normal morphology $>$30%; post-thaw semen samples should have progressive motility $\geq$40%, number of motile sperm per vial $\geq 12 \times 10^6$, and frozen-thaw survival rate $\geq$60%. Participants who met the above-mentioned donation criteria were requested to provide additional semen specimens at different time points within 6 months; those who did not meet the criteria were asked to provide 1–4 samples for further screening. Semen quality was evaluated each time when the participants provided the samples regardless of whether the donation criteria were met. We conducted comprehensive questionnaires at recruitment (day 0) to collect demographic information (e.g., age, having ever fathered a child, education level, occupation, and income), lifestyle factors (e.g., smoking status, alcohol consumption, and abstinence time), and physical examination results (e.g., height, weight, and waist and hip circumstances). After ruling out 33 men with missing information on some electronic device use, a total of 1454 men were finally included in the current study. All participants were informed of the donation process and signed informed consent before enrollment. This research was approved by the Ethics Committee of Reproductive Medicine Center of Tongji Medical College, Wuhan, China.

2.2. Electronic devices use

The following information about electronic devices use over the last 3 months was collected via questionnaires by well-trained personnel, including the number of cell phones owned, duration of electronic devices (e.g., cell phone, and computer, etc.) use, position in which they carried cell phones, daily duration of switching on cell phones (within the scope of 50 cm near the body), type of networks, headsets use during a call, and daily duration of talking on cell phones. The daily duration of all electronic devices use was assessed by adding the time of cell phones, computers, and other electronic products use. In our validation analysis, 45 participants were invited to complete the same questionnaire again during the study period (time interval range: 26–339 days). The results showed high intra-class correlation coefficients (range: 0.74–0.81) for repeated measures of daily duration of electronic device use and computer use, but not in cell phone use (0.52).

2.3. Semen collection and determination

Semen samples were collected into a sterile plastic container by masturbation in a room located in the laboratory. After liquefied at 37 °C, semen samples were analyzed by trained clinical technicians according to the World Health Organization (WHO, 2010). Semen volume was measured by weighing, assuming 1 g of weight equals to 1 mL of volume. After the samples underwent liquefaction in an incubator (37 °C), 10 μL of well-mixed semen sample was placed into a 10-mm-deep Makler chamber and examined by two well-trained technicians following the same methods and standards, as described previously (Chen et al., 2020b). According to WHO guidelines (WHO, 2010), semen parameters, including sperm concentration, total sperm count, and motility were analyzed within 60 min; and sperm motility was graded as progressive (PR) motility, nonprogressive (NP) motility, and immotility (IM). Total motility was defined as the sum of PR and NP, and total sperm count was the number of semen volume multiplied by sperm concentration. Sperm morphology was assessed at a high power magnification on fixed and stained smears with at least 200 sperm

evaluated per replicate. All technicians were professionally trained, and sperm quality parameters were analyzed using the same apparatus. Internal quality control was assessed every day to ensure that the within-day and between-day variations were <10%.

2.4. Statistical analysis

Descriptive analyses were conducted to describe participants' demographic characteristics, electronic devices use, and sperm quality parameters. The demographic characteristics were presented as mean ± SD or n (%), and semen parameters and the duration of electronic devices use were presented as mean ± SD or median (25%, 75%). Given that repeated within-subject semen samples were collected at different time points in this study, linear mixed-effects models in both univariable and multivariable analyses were used to explore the associations of repeated sperm quality parameters with daily duration of all electronic devices use, cell phone use, computer use, daily duration of switching on, and daily calling time. These models treat interested exposures and covariates as fixed effects while identifying random effects for the intercept to account for within-individual correlation of repeated sperm quality parameters (log_{10}-transformed). Regression coefficients (β) and the 95% confidence intervals (CIs) were converted into percent changes (95% CIs) which were estimated as $(10^{\beta}-1) \times 100$ in linear mixed-effects models.

Potential confounders were included in the multivariable models based on biological-causal and statistical considerations. Covariates with a P value < 0.2 in preliminary bivariate analyses were included in a full multivariable model; those covariates with a P value > 0.15 in a full model for all sperm quality parameters were removed from further consideration (Meeker et al., 2011). Finally, the full model included age (years), waist-hip ratio, BMI (kg/m^2), household income (≤4000, 4000–8000, or >8000 Yuan per month), education level (high school, bachelor degree, or above bachelor degree), smoking status (never, ever, or current), alcohol consumption (never, ever, or current), ever fathered a child (yes or no), sampling season (spring, summer, autumn, or winter), abstinence time (days), employed status (work, student, or others), electromagnetic radiation occupational exposure (yes or no), and electromagnetic equipment near the residence (yes or no).

Stratified analyses were performed to evaluate whether the associations of daily calling time with sperm quality parameters were consistent among different types of network categories (2/3G or 4G) and headsets use during a call (yes or no). P for interaction were estimated by including the cross-product terms between stratification variables and daily calling time in the final model (Wan et al., 2019). To test the robustness of our results, we re-analyzed the adjusted linear mixed-effects models by categorizing the daily duration of various electronic devices use based on median or tertiles of distribution, and the median values of each category of the exposures were modeled as continuous variables to test the linear trend across exposure categories associated with sperm quality parameters. Besides, we also assessed the associations of electronic devices use with within-subject average sperm quality parameters in general linear models. Data analyses were conducted by Stata version 15.0 (Stata Corp, College Station, Texas, USA).

3. Results

3.1. Population characteristics

Characteristics of the participants are presented in Table S1. The 1454 participants in the current analysis had a mean (SD) age, BMI, waist-hip ratio, and abstinence time of 28.1 (5.3) years, 22.8 (3.2) kg/m^2, 0.8 (0.1), and 6.2 (3.5) days, respectively. Approximately two-fifths of the subjects were current smokers (39.6%) and the majority were current drinkers (73.7%). The majority of participants had never fathered a child (72.3%), bachelor's or above educational level (61.9%), a stable job (79.5%), self-reported household income of >4000 Yuan per month (71.0%), and not expose to electromagnetic radiation at work (99.0%) or live near electromagnetic equipment (89.3%). Summer (34.8%) and winter (13.8%) were the most and least sampling seasons, respectively.

3.2. Distribution of electronic devices use and sperm quality parameters

As shown in Table 1, the mean (SD) daily duration of all electronic devices use, cell phone use, computer use, having the cell phone on (near 50 cm), and daily calling time was 6.7 (4.9) h/d, 4.0 (2.5) h/d, 2.1 (2.8) h/d, 18.1 (5.1) h/d, and 20.5 (27.6) min/d for the past three months, respectively. The majority of participants had 1 cell phone (84.5%), used 4G networks (95.9%), never used headsets during a call (79.6%), and carried cell phones in pants pockets (62.2%). The median (interquartile) values for sperm concentration, total sperm count, progressive motility, total motility, and percentage of normal morphology were 60.0 (41.5, 68.0) million/mL, 156.4 (110.0, 222.0) million per ejaculate, 60.0 (50.0, 65.0) %, 63.0 (53.0, 67.0) %, and 13.0 (6.5, 18.9) %, respectively.

3.3. Association of daily duration of various electronic devices use with sperm quality parameters

In Table 2, after adjusting for multiple confounders, we found significant inverse associations of all electronic devices use with sperm progressive motility and total motility, cell phone and computer use with sperm concentration, progressive motility, and total motility (all P < 0.05), with effect sizes (i.e., percent change) ranging from −0.6% to −1.1%. No significant association was observed between single cell phone use or computer use or other electronic device use and sperm quality parameters, and between daily duration of various electronic devices use and morphologically normal spermatozoa (Table S2). The

Table 1
Distributions of electronic device use variables and semen quality parameters.

Characteristics	n (%) or mean ± SD	Median (25%, 75%)
Daily duration of usage of various electronic devices (h/d) (n = 1454)		
All electronic devices	6.7 ± 4.9	5.5 (3.5, 9.0)
Cell phone and computer	6.1 ± 3.7	5.5 (3.2, 8.0)
Daily duration of cell phones	4.0 ± 2.5	3.5 (2.0, 5.0)
Daily duration of computers	2.1 ± 2.8	0.9 (0.0, 3.0)
Other electronic devices	0.6 ± 3.0	0.0 (0.0, 0.0)
Features of cell phone use (n = 1454)		
Numbers of cell phones		
1	1229 (84.5)	-
≥2	225 (15.5)	-
Daily duration of calls (min/d)	20.5 ± 27.6	10.0 (5.0, 30.0)
Type of network		
2G/3G	60 (4.1)	-
4G	1394 (95.9)	-
Headsets use during a call		
No	1157 (79.6)	-
Yes	297 (20.4)	
Daily duration of having the cell phone on (near 50 cm; h/d)	18.1 ± 5.1	17.0 (16.0, 24.0)
Carrying cell phones in pants pockets		
No	549 (37.8)	-
Yes	905 (62.2)	-
Semen quality parameters (n = 6464)		
Concentration, million/mL	56.2 ± 23.6	60.0 (41.5, 68.0)
Total count, million per ejaculate	168.5 ± 94.5	156.4 (110.0, 222.0)
Progressive motility, %	56.9 ± 12.3	60.0 (50.0, 65.0)
Total motility, %	60.1 ± 12.2	63.0 (53.0, 67.0)
Normal morphology,[a] %	13.3 ± 7.6	13.0 (6.5, 18.9)

[a] A total of 2079 measurements of sperm morphology were conducted among 1422 men during the study period.

Table 2
Percent change (95% CIs) in sperm quality parameters associated with daily duration of various electronic devices use (h/d) based on linear mixed-effects models (n = 1454 subjects, 6464 semen samples).[a]

Variables (h)	Sperm concentration, million/mL	Total sperm count, million per ejaculate	Progressive motility, %	Total motility, %
All the electronic devices				
Crude model	−0.4 (−1.2, 0.3)	0.2 (−0.8, 1.2)	−0.3 (−0.7, 0.1)	−0.3 (−0.7, 0.1)
Adjusted model[b]	−0.4 (−1.2, 0.4)	−0.02 (−1.0, 1.0)	−0.4 (−0.8, −0.02)*	−0.4 (−0.8, −0.02)*
Cell phone and computer				
Crude model	−1.3 (−2.3, −0.3)*	−0.7 (−1.9, 0.6)	−0.4 (−0.9, 0.2)	−0.4 (−0.9, 0.1)
Adjusted model[b]	−1.1 (−2.2, −0.1)*	−0.8 (−2.1, 0.5)	−0.6 (−1.1, −0.03)*	−0.6 (−1.1, −0.1)*
Cell phone				
Crude model	−2.0 (−3.4, −0.5)*	−2.2 (−4.0, −0.3)*	−0.5 (−1.3, 0.3)	−0.5 (−1.3, 0.2)
Adjusted model[b]	−1.3 (−2.7, 0.2)	−1.4 (−3.3, 0.4)	−0.6 (−1.4, 0.2)	−0.6 (−1.4, 0.1)
Computer				
Crude model	−0.7 (−1.9, 0.7)	0.6 (−1.1, 2.3)	−0.2 (−0.9, 0.5)	−0.2 (−0.9, 0.4)
Adjusted model[b]	−0.8 (−2.2, 0.6)	−0.2 (−1.9, 1.6)	−0.5 (−1.2, 0.2)	−0.5 (−1.2, 0.2)
Other electronic devices				
Crude model	0.8 (−0.4, 2.1)	1.5 (−0.1, 3.1)	−0.2 (−0.9, 0.4)	−0.1 (−0.8, 0.5)
Adjusted model[b]	0.5 (−0.7, 1.7)	1.0 (−0.5, 2.6)	−0.3 (−0.9, 0.4)	−0.2 (−0.8, 0.4)

[a] Effect values transformed by the logarithm and back-transformed [100 × (10^{β}-1)] to obtain the percent change.

[b] All models were adjusted for age (years), waist-hip ratio, BMI (kg/m^2), household income (≤4000, 4000–8000, or >8000 Yuan per month), education level (high school, bachelor degree, or above bachelor degree), smoking status (never, ever, or current), alcohol consumption (never, ever, or current), ever fathered a child (yes or no), sampling season (spring, summer, autumn, or winter), abstinence time (days), employed status (work, student, or others), electromagnetic radiation occupational exposure (yes or no), and electromagnetic equipment near the residence (yes or no). Abbreviations: CI, confidence interval. BMI, body mass index. *$P < 0.05$.

above-mentioned relationships were largely unchanged when we re-analyzed the associations between categories of the daily duration of various electronic devices use and repeated sperm quality parameters (Table 3), and our results remained consistent when we used the within-individual average sperm quality parameters as the outcome in the adjusted general linear models (Table S3).

3.4. Associations of characteristics of cell phone use with sperm quality parameters

In Table 4, after adjusting for potential confounders, daily talking time on the cell phone was negatively associated with sperm concentration [percent change (95% CI): −8.0% (−15.2%, −0.2%)] and total count [percent change (95% CI): −12.7% (95% CI: −21.3%, −3.1%)], respectively; while there were no significant associations between other characteristics of cell phone use (including position for carrying cell phones, and daily duration of having the cell phones on) and sperm quality parameters. In the stratified analyses, significant decreasing trends were observed in the associations of daily calling time with sperm concentration, total sperm count, progressive motility, and total motility among men who used 4G devices during a call (all $P < 0.05$), although there was no evidence of effect modification (P for interaction > 0.05); and negative associations of daily calling time with sperm concentration and total motility were only found among men who used headsets during a call (all $P < 0.05$). Especially, increased daily calling time might

Table 3
Percent change (95% CIs) in sperm quality parameters in relation to categories of the daily duration of various electronic devices use based on linear mixed-effects models (n = 1454 subjects, 6464 semen samples).[a]

Variables (h)	N	Sperm concentration, million/mL	Total sperm count, million per ejaculate	Progressive motility, %	Total motility, %
All the electronic devices					
Tertile1 (≤4.0 h/d)	2325	0 (ref)	0 (ref)	0 (ref)	0 (ref)
Tertile2 (4.1–7.5 h/d)	2049	3.7 (−5.4, 13.7)	1.5 (−9.8, 14.1)	−2.3 (−7.0, 2.5)	−2.2 (−6.7, 2.5)
Tertile3 (>7.5 h/d)	2090	−7.6 (−15.9, 1.5)	−4.3 (−15.0, 7.9)	−5.0 (−9.5, −0.1)	−4.9 (−9.4, −0.3)
P for trend		0.048	0.402	0.045	0.037
Cell phone and computer					
Tertile1 (≤4.0 h/d)	2536	0 (ref)	0 (ref)	0 (ref)	0 (ref)
Tertile2 (4.1–7.0 h/d)	1884	1.5 (−7.4, 11.3)	−2.8 (−13.6, 9.3)	−0.5 (−5.2, 4.5)	−0.5 (−5.1, 4.3)
Tertile3 (>7.0 h/d)	2044	−7.7 (−15.9, 1.3)	−4.9 (−15.5, 7.1)	−3.8 (−8.4, 1.1)	−3.9 (−8.4, 0.7)
P for trend		0.060	0.418	0.105	0.080
Cell phone					
Tertile1 (≤3.0 h/d)	3231	0 (ref)	0 (ref)	0 (ref)	0 (ref)
Tertile2 (3.1–4.5 h/d)	1374	−1.2 (−10.2, 8.7)	−7.6 (−18.2, 4.3)	1.2 (−3.8, 6.4)	1.7 (−3.1, 6.8)
Tertile3 (>4.5 h/d)	1859	−2.5 (−10.5, 6.2)	−5.6 (−15.4, 5.2)	−0.9 (−5.3, 3.7)	−0.9 (−5.2, 3.5)
P for trend		0.556	0.258	0.740	0.735
Computer					
0 h/d	2801	0 (ref)	0 (ref)	0 (ref)	0 (ref)
0.1–2.0 h/d	1424	−0.01 (−9.3, 10.2)	3.5 (−8.6, 17.1)	−0.9 (−5.9, 4.3)	−0.9 (−5.7, 4.1)
>2.0 h/d	2239	−1.3 (−10.0, 8.3)	1.1 (−10.1, 13.7)	−3.0 (−7.6, 1.8)	−3.2 (−7.6, 1.5)
P for trend		0.757	0.964	0.214	0.176
Other electronic devices					
0 h/d	5428	0 (ref)	0 (ref)	0 (ref)	0 (ref)
>0 h/d	1036	1.3 (−8.5, 12.1)	2.4 (−10.0, 16.5)	0.8 (−4.4, 6.3)	0.8 (−4.2, 6.2)

[a] Effect values transformed by the logarithm and back-transformed [100 × (10^{β}-1)] to obtain the percent change. Test for linear trend across electronics devices use time was evaluated by modeling median values within each category as a continuous variable in models. All models were adjusted for age (years), waist-hip ratio, BMI (kg/m^2), household income (≤4000, 4000–8000, or >8000 Yuan per month), education level (high school, bachelor degree, or above bachelor degree), smoking status (never, ever, or current), alcohol consumption (never, ever, or current), ever fathered a child (yes or no), sampling season (spring, summer, autumn, or winter), abstinence time (days), employed status (work, student, or others), electromagnetic radiation occupational exposure (yes or no), and electromagnetic equipment near the residence (yes or no).

Table 4
Percent change (95% CIs) in sperm quality parameters associated with characteristics of cell phone use (n = 1454 subjects, 6464 semen samples).[a]

Variables	N	Sperm concentration, million/mL	Total sperm count, million per ejaculate	Progressive motility, %	Total motility, %
Carrying cell phones in pants					
No	2401	0 (ref)	0 (ref)	0 (ref)	0 (ref)
Yes	4063	−0.3 (−7.6, 7.7)	3.9 (−5.7, 14.6)	1.7 (−2.3, 5.9)	1.4 (−2.5, 5.4)
Daily duration of having the cell phone on (near 50 cm, h/d)	6464	−0.1 (−0.9, 0.6)	0.1 (−0.8, 1.0)	−0.1 (−0.5, 0.3)	−0.2 (−0.5, 0.2)
Daily duration of calls (h/d)	6464	−8.0 (−15.2, −0.2) *	−12.7 (−21.3, −3.1)*	−4.0 (−8.1, 0.3)	−4.1 (−8.0, 0.1)
Type of networks[b]					
2G/3G	346	−21.8 (−70.1, 104.0)	−18.9 (−71.1, 128.2)	6.6 (−35.8, 77.0)	4.8 (−33.6, 65.3)
4G	6118	−8.4 (−15.6, −0.6)*	−13.2 (−21.9, −3.6)*	−4.7 (−8.8, −0.5)*	−4.8 (−8.8, −0.6)*
P for interaction		0.169	0.276	0.065	0.070
Headsets use during a call[b]					
No	5092	−5.0 (−14.3, 5.4)	−10.1 (−21.3, 2.6)	0.9 (−3.5, 5.5)	0.8 (−3.4, 5.1)
Yes	1372	−12.4 (−24.4, 1.5)	−17.1 (−31.1, −0.2)*	−10.3 (−19.7, 0.1)	−10.4 (−19.7, −0.1)*
P for interaction		0.426	0.539	0.005	0.004

[a] Effect values transformed by the logarithm and back-transformed [100 × (10^{β}-1)] to obtain the percent change. All models were adjusted for age (years), waist-hip ratio, BMI (kg/m^2), household income (≤4000, 4000–8000, or >8000 Yuan per month), education level (high school, bachelor degree, or above bachelor degree), smoking status (never, ever, or current), alcohol consumption (never, ever, or current), ever fathered a child (yes or no), sampling season (spring, summer, autumn, or winter), abstinence time (days), employed status (work, student, or others), electromagnetic radiation occupational exposure (yes or no), and electromagnetic equipment near the residence (yes or no). *$P < 0.05$.

[b] Percent change (95% CIs) in sperm quality parameters associated with daily duration of calls stratified by type of networks or headsets use during a call.

interact synergistically with headsets use during a call to further decrease sperm progressive motility and total motility (*P* for interaction = 0.005 and 0.004, respectively). However, no significant association was found between characteristics of cell phone use and morphologically normal spermatozoa (Table S4). Similar results were observed in the adjusted general linear models using the within-individual average sperm quality parameters as the outcome (Table S5).

4. Discussion

Among 1454 healthy men recruited from a sperm bank located in Wuhan, China, we found the duration of various electronic device use was adversely associated with lower semen quality in modest effect size. Daily calling time was negatively associated with sperm concentration and total count, and headsets use during a call appeared to aggravate the negative associations of daily calling time with sperm progressive motility and total motility.

Electronic devices have become an indispensable part of our lives, and their potentially detrimental effects on male reproduction have also caused growing concerns, but the evidence from epidemiological studies is still equivocal. Two observational studies suggested that daily duration of cell phone use was associated with decreased sperm counts, percentage motility, viability, and normal morphology among 361 men (Agarwal et al., 2008) and 2110 men attending infertility clinics (Gutschi et al., 2011), respectively. Fejes et al. (2005) revealed that the duration of possessing cell phones was negatively correlated with the rapid progressive motility among 371 infertile males at a clinic. These results indicate that cumulative exposure to electronic devices should be sufficiently taken into account in daily life concerning the potential detrimental effects on semen quality. However, a previous longitudinal study reported no significant exposure-response relationships between cell phone use patterns and semen quality among 153 men from a fertility clinic (Lewis et al., 2017). Although the negative associations were observed in the present study, the decline trend in semen quality for per unit increase in electronic devices use was relatively small, which indicates no immediate practical or clinical implications. In addition, no significant association was observed between electronic device use and sperm morphology. Discrepancies between the studies could be explained by variability in the morphologic assessment of human sperm (Wang et al., 2014), and the differences in study design, sample size, and slection of the study population, which was somewhat healthier in our current study than those recruited from infertility centers and therefore had a better semen quality.

Calling has been traditionally considered as a type of cell phone use that affects semen quality. Animal studies found that long-term exposure to cell phone radiation reduced the percentage of motile sperm (Mailankot et al., 2009), even causing a significantly higher incidence of sperm cell death (Yan et al., 2007). It should be noted that the degree of exposure in animal studies is 100 times greater than daily exposure to human spermatozoa (Suzuki et al., 2017), and electromagnetic radiation exposure emitted from cell phones tends to be much smaller than in animal studies. Nevertheless, our current study suggested that increasing daily calling time was significantly associated with decreased sperm concentration and total count. In supporting our findings, Zhang et al. (2016) reported significant negative associations of internet use via cellular networks and daily calling time with sperm concentration and total count among 794 Chinese male college students. Zilberlicht et al. (2015) revealed that talking through cell phone for more than 1 h per day was associated with an elevated rate of abnormal sperm concentration among 106 men referred for semen analysis. Furthermore, our findings revealed that the negative associations of daily calling time with progressive and total sperm motility were significantly modified by headsets use during a call. It is possible that cell phones may be put closer to the reproductive organs for those using headsets during a call, while the intensity of RF-EMFs exposure at the target tissue was inversely associated with the distance from the cell phone (Cleveland and Ulcek, 1999). 4G devices were also found to aggravate the negative effects of daily calling time on semen quality in the present study, though there was no evidence of an interaction. Our results are inconsistent with those reported by Zhang et al. (2016), which found that college students who used 3G or more advanced telecommunication devices seemed to have a better sperm concentration than those who utilized 2G devices. The observed differences may be due to most of the participants in our study using 4G or more advanced communication devices, which need more signal towers and may also increase electromagnetic radiation exposure. The synergistic effect between different calling patterns and the duration may also explain some of the deviations, but all these need to be clarified in future studies.

The biological mechanisms underlying the negative associations between cell phone use and semen quality remain unclear. Previous studies revealed that RF-EMFs could induce the production of mitochondrial reactive oxygen species (ROS) through extensive electron leakage from the mitochondrial electron transport chain (Oktem et al., 2005; Santini et al., 2018). The ROS, probably produced by complex III

of the electron transport chain (Houston et al., 2018), may lead to the increase of DNA fragmentation and apoptosis in sperm (De Iuliis et al., 2009; Kesari et al., 2010), eventually damaging male fertility characterized by the decrease of sperm motility and viability. Besides, dehydrogenase (NAD(+)-IDH) in human seminal plasma could be one of the seminal plasma biomarkers reflecting the mitochondrial function of spermatozoa, and alteration of its level could reflect the defective motility of sperms in some cases of cellular phone users (Hagras et al., 2016).

A major strength of this study is that repeated within-subject semen samples were collected at different time points, thus taking into account within-individual variability in sperm quality parameters (Chiu et al., 2017). Moreover, our study recruited healthy men screened as potential sperm donors, who were more representative of the general population compared to previous studies recruited from infertility clinics or other specific populations. The present study also had several limitations. First, self-reported information about electronic devices use may introduce misclassification bias, but we asked study subjects to recall electronic devices use over the past 3 months, which may result in less recall bias (Lewis et al., 2017), and our validation analysis of 45 participants showed no significant difference for the repeated measures of electronic devices use. Second, we couldn't assess the specific absorption rate which may evaluate RF-EMF exposure emitting from cell phones more accurately. Third, we tried to adjust the source of RF-EMFs exposure except for interested exposures, such as occupational exposure and electromagnetic base station, but they were still incomprehensive, such as Wi-Fi routers. Fourth, the lack of measurement of reproductive hormones (e.g., testosterone and estriol) was a limitation of our analysis and we cannot test whether electronic device usage affected reproductive hormones, which in turn could be reasons for poor sperm quality. Finally, we cannot prove causal relationships since this was an observational study, and caution is still needed when generalizing our findings.

5. Conclusions

In conclusion, more time spent on electronic devices use was associated with decreased semen quality in modest effect size. Daily calling time was significantly associated with lower sperm concentration and total count, and it might interact synergistically with headset use during a call to further decrease sperm progressive motility and total motility. Although our research suggests that electronic devices exert no obvious reproductive hazards to healthy men with good fertility, we still advise men with a pregnancy plan to avoid excessive electronic devices use, especially avoid using headsets during a call. Additional well-designed prospective population studies are required to identify the effects of electronic devices use on semen quality more precisely, and to evaluate the clinical importance of the risk to both sub-fertile men and the general population.

Author statement

All authors fulfill the criteria for authorship. Heng-Gui Chen and Ping Wu analyzed the data. Heng-Gui Chen and Ping Wu drafted the original manuscript. An Pn and Weimin Ye lead the study conception, study design, analysis plan, and interpretation of findings. Bin Sun, Jun-Xiang Chen, Cheng-Liang Xiong, Tian-Qing Meng, and Yi-Xin Wang contributed to the acquisition of data. Xiao-Yin Huang and Qing-Ling Su validated the accuracy of data analysis with a technical review. Huiliang Zhou and Yi-Xin Wang reviewed and edited the manuscript. All authors read and approved the final manuscript and approved the final submitted version.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available upon reasonable request with the approval from the Institutional Review Board.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envpol.2022.120089.

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