Maternal Cell Phone Use and Behavioral Problems in Children

To the Editor:

Divan et al[1] found an association between behavioral difficulties in children and prenatal and postnatal mobile phone usage. They caution against assuming a causal relationship from exposure to electromagnetic fields from phones. Although this may be sensible regarding the weak fields to which the fetus would be directly exposed during maternal use of a mobile phone there are alternative mechanisms that warrant consideration.

Melatonin is a hormone that affects circadian rhythms and reproduction. Secretion of melatonin by the pineal gland is determined by exposure of the retina to light, but the neurologic pathway whereby this signal reaches the pineal gland is anatomically remarkable and potentially relevant to mobile phone exposures (Fig. 1 in Ref. 2). Nerve fibers leave the retina along the retinohypothalamic tract and reach the suprachiasmic nucleus. This nucleus does not send fibers directly to the pineal gland within the brain but stimulates the sympathetic nervous system via a pathway down the spinal cord and then to the superior cervical ganglion in the neck. Post ganglionic fibers ascend back into the brain by forming a plexus along the surface of the internal carotid artery, eventually to reach the pineal gland. The carotid artery is superficially placed near the angle of the jaw (where the pulse from it may be readily felt) and hence the sympathetic nerve fibers on it are also close to the skin. Mobile phones are commonly positioned so that the body of the phone is close to the angle of the jaw and hence to the nerve plexus. It is plausible that radiofrequency or extremely low-frequency fields from a mobile phone held close to the jaw may affect signaling in the unmyelinated nerves and in turn influence melatonin secretion.

Melatonin may affect reproduction and healthy fetal development in various ways.[2,3] Secretion of melatonin is intrinsic to regulating normal circadian rhythms for temperature and metabolism. In addition, melatonin inhibits the secretion of gonadotropin-releasing hormone and may directly affect steroid metabolism within the ovaries and progesterone synthesis. Diverse changes in maternal metabolism or the sex hormone environment may affect development of the fetal brain leading to behavioral problems.

Melatonin is also closely related to changes in puberty, possibly because of its tonic inhibition of secretion of gonadotropin-releasing hormone during childhood. Interference with this normal restraining control pathway might also lead to altered behaviors in childhood and adolescence in children who use cell phones.

Bruce Hocking
Victoria, Australia

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Women With Long Menstrual Cycles Have More Daughters

Irregular and long menstrual cycles have been linked to endocrine-related fertility problems such as reduced fecundability, pregnancy complications, and poor maternal health.[1,2] In 1 report, long follicular phase duration was associated with female births.[3] We explored the possibility that women with long menstrual cycles are more likely to have daughters than sons.

We collected data by using self-reported questionnaires on the lifetime reproductive history of 175 postreproductive Finnish women born between 1946 and 1958, who participated in a national screening program for cervical cancer in 2006. These women delivered 367 babies, of whom 185 (0.51% ± 0.39 SD) were boys. We examined whether the average duration of menstrual cycles (mean [±SD] = 27.7 [±3.8] days), the average duration of menstrual bleeding (mean [±SD] = 5.2 [±1.4] days), or self-reported menstrual irregularity (13%) was associated with lifetime offspring sex ratio. The data were analyzed with a logistic regression model, in which the number of sons was the numerator (events) and the total number of offspring was the denominator (trials). Pearson χ^2 test was used to accommodate any over-dispersion and to adjust the confidence intervals (CIs) of odds ratios (ORs).

Mothers with long menstrual cycles delivered fewer sons (OR = 0.93; 95% CI = 0.87–0.99). That is, the odds of a female birth increased by 7% for every 1-day increase in average menstrual cycle duration. Menstrual cycle irregularity (1.18; 0.62–2.26) or the duration of menstrual bleeding (1.02; 0.88–1.18) was not related to offspring sex ratio at birth. Adjustment for body mass index, birth cohort, and history of gynecologic hormone treatment did not change the association of cycle duration with sex ratio (0.92; 0.86–0.99).

If not because of chance, what might explain this association? Women with long and irregular menstrual cycles may have altered endocrine profiles because of polycystic ovarian syndrome. Androgens, and especially testosterone, may be found at high concentrations in these women. This may also hold for healthy women without a recognized diagnosis of polycystic ovary disease.[4] High maternal testosterone levels during conception have, in turn, been suggested to increase the odds of a male birth.[5,6] Therefore, the finding of more daughters among Finish women with long menstrual cycles runs counter to this hypothesis. Another possible hypothesis relates to stress. The production of testosterone is primarily regulated by the adrenal glands, which also control for the stress response. Stressed women have elevated levels of both testosterone and cortisol.[7] Maternal stress has also been reported to increase the risk of male fetal loss.[8] If stressed mothers have long menstrual cycles, this could lead to an increase in daughters born.[6] However, studies using larger data sets are needed before we can conclude that long menstrual cycles are related to offspring sex ratio.

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Samuli Helle
Department of Biology
University of Turku
Turku, Finland
sayrhe@utu.fi

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Postcards Encourage Participant Updates

To the Editor:

Participant retention is vital to the success of a longitudinal cohort study. Investigators may attempt to bolster retention rates by developing techniques to maintain up-to-date contact information, and foster participants' perception of the importance of the research and their dedication to the study.[1] Studies have used various approaches to retain cohort participants, including mailing reminders through the US Postal Service tracking programs, providing incentives for participation, maintaining open communication via a study web site or toll-free phone line, and telephone reminders.[2–4] Maintenance of reliable address information in mobile populations[3,5] may require contacting participants at regular time intervals.[4] Previous studies have shown that sending postcards to participants is an effective method of retention. Regular contact not only develops participant identification with the cohort, but also encourages participants to update any changes to their contact information.[4]

The Millennium Cohort Study was designed in the late 1990s in response to US Department of Defense, Congressional, and Institute of Medicine recommendations for coordinated epidemiologic research to determine how military service affects long-term health.[6,7] Launched in 2001, this 22-year longitudinal study surveys participants every 3 years, and a postcard and an electronic mail message are sent to cohort members on Memorial and Veterans day to honor their military service, and to thank them for their continued participation in the study. Members are reminded of the web site where they may obtain information on study progress and findings, contact the study team, and update their contact information (mailing address, e-mail address, phone number, or name). Specially designed postcards with the study logo and personal signature of the principal investigator provide study recognition and encourage a sense of membership in the cohort. The purpose of this study was to determine whether semiannual e-mails and postcards encourage participants to update their contact information.

Approximately 77% of the nearly 108,000 military service members in the current analysis have moved after enrollment in the cohort, of whom two-thirds moved to a different state or country. Of those who moved, 9% went online to change their address. Participants who updated their contact information online were more likely to be women, older, college educated, and officers. The great majority (65%) of those who updated their contact information did so within 2 weeks after receipt of the semiannual postcards (Fig. 1). Participants were much more likely to update their contact information during the 2 weeks after (average = 1.09%) receipt of the semiannual postcards than during the 2 weeks before (average = 0.03%).

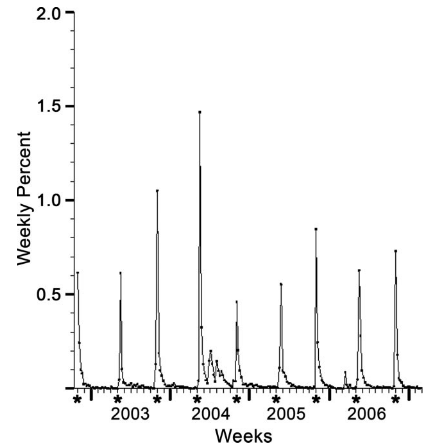

FIGURE 1. Weekly percentage of all participants who updated their contact information on the Millennium Cohort web site, November 2002 to March 2007. Asterisks (*) indicate when postcards were mailed to participants.

The results of this study quantify and confirm that semiannual postcard contact with participants produces a significant increase in the number of persons who update their contact information online compared with the baseline rate when no contact is attempted. In addition, contacting participants on a consistent basis with a personalized message seems to encourage a sense of connectivity with participants and reminds them of the value of their participation.

Kari E. Welch
Cynthia A. LeardMann
Isabel G. Jacobson
Steven J. Speigle
Besa Smith
Tyler C. Smith
Margaret A. Ryan
Department of Defense Center for
Deployment Health Research
Naval Health Research Center
San Diego, CA

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An Alternative Quality Adjustor for the Quality Effects Model For Meta-Analysis

To the Editor:

In our recently proposed quality effects model for meta-analysis, we made use of $\hat{\tau}_i$ as a quality adjustor for the ith study. Given that N is the number of studies in the analysis, w_i is the inverse variance weight and Q_i is the probability (0–1) that study i is credible, then $\hat{\tau}_i$ was defined as[1]:

$$\hat{\tau}_i = \left(\sum_{i=1}^{N} \tau_i\right) - \tau_i$$

where $\tau_i = \dfrac{w_i - (w_i \times Q_i)}{N-1}$

This adjustor redistributed the weight removed from each study equally to the remaining studies. However, we could also redistribute the weight removed to the other studies proportionate to their quality. In this case, the total value of the redistributed weight is the same, but the individual studies receive a slightly different amount based on their quality as follows:

$$\hat{\tau}_i = \left(\sum_{i=1}^{N} \tau_i \times N \times \frac{Q_i}{\sum_{i=1}^{N} Q_i}\right) - \tau_i$$

The final summary estimate is then given by the same methodology we had previously outlined.[1]

What are the implications of this update? It will not grossly alter the overall estimate in the majority of meta-analyses carried out using this model, so there is a fine line between this and the original adjustor. Nevertheless, using this update might result in less bias due to a quality-effect size discordance when there is extreme heterogeneity of both quality and effect size across the studies included in the meta-analysis. To take an example, we use the meta-analysis example studied by Verhagen et al and apply the quality effects model (QEM) to the 17 studies that report on intravenous thrombolysis.[2] Figure 1 depicts the adjusted individual effect sizes using the original (QEM) and the updated adjustor (QEM2). The pooled effect size was 0.73 (0.6–0.88) and 0.72 (0.59–0.89) using the original and updated adjustor respectively. It is clear, however, that only the Lasierra and Schreiber studies, which had the highest individual (unadjusted) effect sizes and extremes of quality (0.22 and 0.78, respectively) are handled differently by each adjustor. However, as this sort of discordance only affects low precision studies, the pooled effect size remains stable.

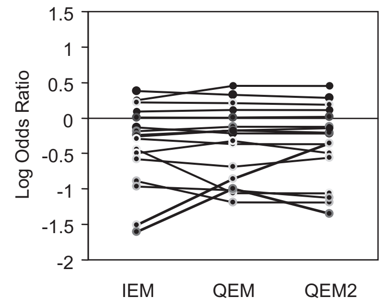

FIGURE 1. Estimation of adjusted individual effect sizes (IEM) using the QEM and QEM2 models with weight-adjusted effect sizes. The 2 discordant studies under QEM2 are those by Lasierra and Schreiber.

Suhail A. R. Doi
Lukman Thalib
Department of Medicine and Community Medicine (Biostatistics)
Kuwait University
Kuwait
sardoi@gmx.net

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