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Use of wireless telephones and serum S100B levels: A descriptive cross-sectional study among healthy Swedish adults aged 18–65 years

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ABSTRACT

Background: Since the late 1970s, experimental animal studies have been carried out on the possible effects of low-intensive radiofrequency fields on the blood–brain barrier (BBB), but no epidemiological study has been published to date.
Objective: Using serum S100B as a putative marker of BBB dysfunction we performed a descriptive cross-sectional study to investigate whether protein levels were higher among frequent than non-frequent users of mobile and cordless desktop phones.
Method: One thousand subjects, 500 of each sex aged 18–65 years, were randomly recruited using the population registry. Data on wireless phone use were assessed by a postal questionnaire and blood samples were analyzed for S100B.
Results: The response rate was 31.4%. The results from logistic and linear regression analyses were statistically insignificant, with one exception: the linear regression analysis of latency for UMTS use, which after stratifying on gender remained significant only for men ($p = 0.01$; $n = 31$). A low p-value (0.052) was obtained for use of cordless phone ($n = 98$) prior to giving the blood samples indicating a weak negative association. Total use of mobile and cordless phones over time yielded odds ratio (OR) 0.8 and 95% confidence interval (CI) 0.3–2.0 and use on the same day as giving blood yielded OR = 1.1, CI = 0.4–2.8.
Conclusions: This study failed to show that long- or short-term use of wireless telephones was associated with elevated levels of serum S100B as a marker of BBB integrity. The finding regarding latency of UMTS use may be interesting but it is based on small numbers. Generally, S100B levels were low and to determine whether this association – if causal – is clinically relevant, larger studies with sufficient follow-up are needed.

1. Introduction

Recent years have seen a rapid increase in the use of wireless telephones and public concerns about the safety of these devices have intensified concomitantly. Usage is now becoming highly prevalent also among younger groups in the population (Söderqvist et al., 2007, 2008), who compared to adults may be more sensitive to radiofrequency fields (Kheifets et al., 2005). In particular, debate has focused on whether the so-called non-thermal effects of radiofrequency fields (RF) may have adverse health consequences. Biological effects of RF have been reported both in vitro and in experimental animal studies, some well below the safety limits (Hardell and Sage, 2008). The latter have been obtained only from a minority of studies (Barnes and Greenebaum, 2007) but they do contribute to scientific uncertainty.

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There has long been uncertainty about the possible effects of RF on the blood–brain barrier (BBB). This special feature of brain blood vessels, made up of endothelial tight junctions in the astrocytic end-feet, controls the traffic of molecules between the blood and brain tissue. Thus, the BBB is a functional as well as an anatomical barrier of importance for the maintenance of a constant environment for optimal CNS function. Alteration of the BBB is a marker/symptom of different conditions such as some neurological diseases and traumas to the head, but is also considered potentially harmful in itself. The first reports on alterations of the blood–brain barrier in rats after exposure to RF came in the late 1970s (Frey et al., 1975; Oscar and Hawkins, 1977; Merritt et al., 1978). Since then, and despite the availability of well-established vascular tracers to detect impairments, findings have been contradictory. A number of studies have shown pathologically significant increases in permeability – some reversible – while others have reported no effect. Possible explanations for these discrepancies may lie both in variations in factors relating to exposure systems and in biological endpoints. For a review see Nittby et al. (2008) and Orendacova et al. (2007). To date no study has been carried out on humans.

Over the last three decades, however, the search for specific peripheral biochemical markers of brain tissue activity and injury has been extensive, especially concerning the calcium-binding protein S100B. This protein is mainly synthesized by the end-feet of the astrocytes, and is found in both cytoplasm and nucleus where along with other members of the S100 family it regulates cytoskeleton and cell proliferation. Several characteristics of this protein make it a suitable marker of BBB integrity: it is (1) usually very low in serum in normal subjects, (2) normally present in cerebrospinal fluid (CSF), (3) found in far higher concentration in CSF than serum, (4) normally prevented from passage to blood by the BBB and (5) quickly released from the brain into blood serum in response to insult leading to functional and/or morphological disruption of the BBB (Buccoliero et al., 2002; Dyck et al., 1993; Kapural et al., 2002; Marchi et al., 2003).

Using S100B as a putative marker of BBB-dysfunction, we performed a descriptive cross-sectional study to investigate whether protein levels were higher among frequent than non-frequent users of mobile phones and cordless desktop phones (DECT). Besides assessing descriptive information on S100B, the aim of this study was to test two hypotheses, namely (1) that long-term wireless phone use is associated with permanently elevated levels of S100B and/or (2) that short-term wireless phone use is associated with temporarily elevated levels of S100B. We further expected that if use of wireless phones was to be associated with elevated levels of serum S100B these would be of a moderate degree indicating BBB dysfunction as discussed for example in Marchi et al. (2003). The study was approved by the local ethics committee.

2. Materials and methods

2.1. Study design

Since we used a cross-sectional study design, one challenge in preparing the study was to assess as much information as possible about agents and diseases with the potential to alter the integrity of the BBB in our participants. An extensive literature search was therefore carried out on research studies reporting on agents, conditions or activities known or suspected to alter the integrity of the BBB in humans. The result of this search was then used in designing the questionnaire for data collection.

2.2. Recruitment of subjects and collection of questionnaire data

One thousand subjects, 500 of each sex, aged 18–65 years and living in the municipality of Örebro, Sweden, were randomly recruited using the population registry. Invitations started to go out at the end of March 2007 and the last questionnaire was returned in November 2007. Single reminders, and supplementary questions if necessary, were sent to improve data quality. All persons invited to participate in the study first received a letter of information and were asked to give informed consent to leave blood and have it stored in a so-called Biobank. Respondents who chose to take part then received further information on the procedure for blood sampling and were asked to complete a postal questionnaire. Those who had not answered the questionnaire after one reminder were regarded as non-responders. Questions covered four topics; employment history, use of wireless phones (mobile phone and DECT), various other exposures such as X-rays, chemicals or radiation therapy and finally health- and lifestyle related questions such as physical exercise and various conditions known or suspected to have an effect on the integrity of the BBB (Grant et al., 1998; Hawkins and Egleton, 2008). These conditions included meningitis, hypertension, head trauma, epilepsy, cancer, syncope, psoriasis, neurological diseases, serious infectious disease, head- or neck operation, stroke, memory deficit (as a sign of dementia) and stress-related conditions.

Regarding use of mobile phones, respondents were asked to state which type of phones they had been or were presently using e.g. NMT, GSM or 3G. Average use in minutes per day for each phone type was assessed both with regard to a longer time period e.g. year of first use, but also with regard to the week before leaving a blood sample. The same types of questions were used to assess information on DECT phones. For all phone types information on average use of hands-free equipment was also assessed. On the day blood was left, questions were asked about total use that day and time since last use of any wireless phone. All questions regarding use of wireless telephones were coded independently by two persons. Any lack of agreement was followed by consulting the original questionnaire.

2.3. Blood sampling and S-100B

Participants were asked if possible to leave blood at our hospital in the afternoon at the end of a working week. All samples were centrifuged and frozen immediately thereafter. A commercially available non-competitive sandwich ECLIA (electrochemiluminescence immunoassay) from Roche Diagnostics GmbH (Mannheim, FRG) on an Elecsys 2010 instrument was then used to measure S100B in the serum. The coefficient