Mobile Telecommunications and Health Research Programme

Study to Evaluate the Effects of Mobile Telephone Usage on Labyrinthine Function

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RUM 11

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Study to Evaluate the Effects of Mobile Telephone Usage on Labyrinthine Function

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1. Executive summary

Low level, radio-frequency signals applied to one side of the head may produce vague symptoms of disorientation, headache and nausea as a result of stimulation of the balance receptors in the internal ear. This double blind study tested 9 case-subjects, who complained of specific symptoms, as defined by a questionnaire, after prolonged mobile telephone use (more than 15 minutes) and 20 control subjects, who reported no such complaints. Each subject underwent a series of trials, in which a dummy mobile telephone exposure system was held, in a standard position, to each ear for 30 minutes in one of three different test modes. The device was programmed to emit a pulsed or continuous radio-frequency emission or no emission. In the active pulsed and continuous modes, the same mean power, on the same GSM900 operating frequency as the output of a typical handset was delivered. Both the tester and the subject were blinded to the dummy mobile operation mode. Sensitive tests of balance and hearing were conducted at baseline, as well as either during the 25th minute of exposure (subjective visual vertical and horizontal test) or immediately after the exposure (transient evoked otoacoustic emissions and video-oculography). **Transient evoked otoacoustic emissions (TEOAEs)** measure outer hair cell function, i.e. function of the sound amplification and resolution mechanism of the inner ear, and are a sensitive test of auditory function. **Video-oculography (VOG)** enables recording of the reflex eye movement, which is generated in response to stimulation of the vestibular (balance) receptor in the inner ear. The **subjective visual vertical and horizontal tests (SVV/SVH)** assess the subject's perception of verticality /horizontality in a totally darkened room, which is also affected by stimulation of the balance organ in the inner ear. The results of the hearing and balance tests were compared between trials with and without pulsed emissions and with and without continuous emissions and between subjects complaining of symptoms and those with no complaint. There was no significant TEOAEs change from baseline recording to post-exposure recording for any of the exposures. No significant differences were found in the **TEOAEs** change from baseline to after each exposure between cases and controls. The **VOG** did not identify any effect of the exposure on the vestibular end organ (i.e., no vestibulo-ocular reflex was elicited post-exposure) in either cases or controls. The **SVV/SVH** was the only test to be recorded during the exposure. There was no significant **SVV/SVH** change from baseline recording to post-exposure recording for any of the exposures. No significant differences were found in the **SVV/SVH** change from baseline to after each exposure between cases and controls. However, there was a statistically significant difference in all subjects tested between right to left exposure for all three exposure modes for both ears. This minimal effect could reflect either the heating effects of the dummy mobile, with thermal stimulation of the labyrinth, or proprioceptive stimulation of the vestibular end organ by the weight of the dummy device, or the effect of a minor head tilt due to the weight of the dummy device, i.e. the so-called "E-effect", which results in deviation of the subjective visual vertical opposite to the head tilt. A further

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control experiment on normal subjects, on whom the SVV and SVH were measured at baseline and repeated after 25 minutes during which the switched off dummy mobile had been strapped on their heads showed similar results to the true exposure experiments, with a statistically significant difference between right to left exposure. Thus, proprioceptive stimulation of the vestibular end organ by the weight of the dummy device and/or the effect of a minor head tilt due to the weight of the dummy device rather than any effect of the functioning dummy mobile may account for the observed mild changes in the SVV/SVH in the exposure experiments.

2. Aims and objectives

The aims of this research were to assess

a) Whether low-level radio frequency stimulation from mobile phones has any effect on auditory and vestibular function. Auditory function and outer hair cell function in particular, was assessed using transient evoked otoacoustic emissions. Vestibular function was assessed by video-oculography, which enables recording of the vestibulo-ocular reflex, and by the subjective visual vertical and horizontal test, which assesses a subject's perception of verticality and horizontality in the absence of visual clues.

b) Whether some individuals who report symptoms after mobile phone use have a demonstrably greater change in outer hair cell function, as assessed by transient evoked otoacoustic emissions, and in vestibular function, as assessed by video-oculography and subjective visual vertical and horizontal test, than individuals who do not report such symptoms.

3. Participants

Professor Linda Maitland Luxon. Professor of Audiological Medicine, University College London

Dr Borka Ceranic. Consultant Audiological Physician, St George's Hospital

Dr Robin Cox. Consultant Occupational Physician Medical Advisor to Cable & Wireless

Dr Philip Chadwick. Technical Director MCL

Dr Doris-Eva Bamiou. Consultant In Neuro-otology, National Hospital for Neurology Neurosurgery

4. Achievements

4.1 Methodology

4.1.1 Subjects

Cases presenting with disorientation/ dizziness/ muzziness and/or nausea, with or without headache, from prolonged mobile telephone usage (>15 minutes) and controls without such symptoms were identified on the basis of a questionnaire by a Consultant Occupational Physician (RC) and referred blind to the tester (DEB).

Inclusion criteria for cases and controls were:

- age 20 to 55 years

- normal tympanometry (to ensure adequate middle ear function, which is necessary for the recording of transient evoked otoacoustic emissions)

- normal pure tone audiometric thresholds, i.e. better than 20 dBHL at 500, 1000, 2000 and 8000 Hz in both - ears (required for the presence of good transient evoked otoacoustic emissions)

We recruited 6 male and 3 female (mean age 36.7 years) cases and 12 male and 9 female (mean age 34.7 years) controls.

4.1.2 Protocol

All subjects (cases and controls) underwent **tympanometry**, to ensure adequate middle ear function and **pure tone audiometry** to establish the presence of normal audiometric thresholds, as per the inclusion criteria.

Each subject underwent two experiments, experiment I and II. For each experiment, **baseline data** were obtained on

a) **transient evoked oto-acoustic emissions (TEOAEs),** which evaluate outer hair cell function within the cochlea (experiment I).

b) vestibulo-ocular reflex as assessed by gaze testing and recorded by means of **video-oculography** (experiment II)and

c) **subjective visual vertical/horizontal test (SVV/SVH)** (experiment II)**.**

After the baseline measurement, a standardised dummy mobile exposure system was then strapped to either the right ear or the left ear, with the device's antenna positioned over the mastoid cavity. The device was operated by a letter and number code which would determine, unknown to the tester and to the subject, 1 out of 3 possible modes of operation:

a. "sham" – no radiation (heating effect from the battery only)

b continuous (cw) radiofrequency exposure or

c. pulsed radiofrequency exposure (gsm).

The choice of ear and the mode of exposure of the handset were randomly determined for each subject and control, and the relevant operating codes were given to the tester with each subject/control's name prior to their visit to the clinic. When the handset was operating in a pulsed gsm mode, the modulation regime was typical of a standard GSM mobile telephone handset used - receiving and transmitting mode (DTX mode). In continuous cw mode, the handset was radiating the same mean power as in pulsed mode on the same GSM900 operating frequency.

Experiment I: Effects on auditory function

The generic handset was kept strapped to the subject/control's head for 30 minutes, timed with a stop-watch, after which time transient evoked otoacoustic emissions measurements were repeated. TEOAEs measurement was repeated after 3 exposures per ear (6 exposures for the two ears), which were randomly presented:

(i) after 30 mins of exposure to pulsed radio-frequency signals from a simulated mobile telephone generic handset ("gsm" exposure)

(ii) after 30 mins of exposure to continuous radio-frequency signals from the handset ("cw" exposure)

(iii) after 30 mins under the same exposure protocol, but with no power applied to the handset ("sham" exposure)

At the end of each exposure, each subject was asked whether they thought the generic handset was on or off, and their response was recorded.

Experiment II: Effects on vestibular function

The stimulation paradigm was identical to experiment I. At the 25th minute of exposure, SVV/SVH were recorded, with the generic handset still strapped on. After the 30th minute of exposure, the generic handset was removed, and VOG was recorded. Thus SVV/SVH and VOG measurement was repeated during the last 5 minutes of the 30 min exposure (for the SVV/SVH) and after the 30 min of exposure for 3 exposures per ear (6 exposures for the two ears), which were randomly presented as outlined under i), ii) and iii) above.

4.1.3 Procedures

Tympanometry Single frequency tympanometry (ear canal volume, middle ear pressure and tympanic membrane compliance) was performed with a probe signal of 85dB SPL continuous tone at 226Hz (BSA Recommended Procedure, 1992) using a GSI-33 Middle Ear Analyser. Tympanograms were considered normal if middle ear pressure was > -150 mm H_2O and compliance was > 0.3 cm^3.

Pure tone audiometry at 0.25, 0.5, 1.0, 2.0, 4.0 and 8.0 kHz was conducted using the GSI 61 audiometer in a sound-treated booth, as per the recommended BSA procedure (BSA, 1981).

Otoacoustic emissions recording (Kemp, Ryan and Bray, 1990) Transient evoked otoacoustic emissions (TEOAE) are sound signals, generated by the outer hair cells in the cochlea, in response to transient acoustic stimuli and recorded in the sealed ear canal (Kemp, 1978). Click stimuli are delivered via a probe (which contains a miniature microphone and transducer) inserted in the ear canal. The peak reception level of the stimuli is 80 ± 3dB SPL. The fast fourier transform (FFT) spectrum analysis of the averaged response waveforms is automatically performed and plotted against the averaged random noise. TEOAEs were recorded using the ILO 292 DP Echoport (Otodynamics Ltd). The TEOAE responses in dBSPL (automatically displayed on the computer screen) were recorded before and after use of the generic handset.

Assessment of visual vertical and horizontal (SVV/SVH) This test was conducted during the exposure, from the 25th minute and until the end of the exposure. The SVV and SVH were obtained using the equipment from Micromedical Technologies. This consists of a LCD display unit, laser projector and a remote control. The subject was seated upright in a chair, facing a wall at a distance of 1.6 metres. The test was carried out in a dark room with no visual clues. The laser projector was used to project a luminous line1.6 metres long on the wall at a random angle to the gravitational vertical. Angles were adjusted in the clockwise and anticlockwise directions three times each for a total of 6 replicate readings for the SVV and separately for the SVH. The subjects were allowed to keep their eyes open during the offset. After each offset, the subject adjusted the orientation of this line with a remote control, in order to align it to the vertical or horizontal. Familiarisation trials were allowed and no time limits were set for the adjustments. The displacement, in degrees, from the true horizontal and vertical was noted and averaged for the 6 replicate readings for baseline and for each exposure.

Video-oculography (VOG) This test was performed using computerised, 2D video-oculography equipment (Micromedical Technologies, VisualEyes 2-channel System). The camera and infra-red light are mounted on goggles, which are held in place by an adjustable strap around the head. The eyes are illuminated by low-level infra-red light, allowing recording of eye movements regardless of lighting conditions. The infra-red image of the subject's eye is reflected by an infra-red sensitive mirror, attached to the goggles, into the camera's image sensor. The image is digitalised and input to a real-time image processing system, which identifies the pupil on the basis of light/dark contrast. The eye movements were assessed and recorded (slow component velocity in deg/sec of any spontaneous nystagmus) in the mid-position of gaze and with gaze deviation 20^o to right and left in the absence of optic fixation as well as with optic fixation. The outcome measures were

a) presence or absence of nystagmus (binary value) and

b) the slow component velocity of nystagmus in degrees per second, with a value of > 4º/sec accepted as significant.

4.1.4 {PRIVATE }Data analysis

Experiment I: Effects on auditory function

Data were analysed with the Statistical Package for the Social Sciences SPSS 11. 5. Chi-square analysis was conducted to assess the difference between cases and controls in correctly guessing whether the generic handset was on or off. Paired t-tests were used to compare the difference from baseline TEOAEs amplitude to post-exposure TEOAEs amplitude (sham, cw, gsm). The following outcome measures were computed, in order to assess differences between the case and control group:

1. The TEOAEs amplitude difference from baseline to sham exposure for each ear (R = right and L = left) (Rb-sham and Lb-sham)

2. The TEOAEs amplitude difference from baseline to cw exposure for each ear (Rb-cw and Lb-cw)

3. The TEOAE amplitude difference from baseline to gsm exposure for each ear (Rb-gsm and Lb-gsm)

The independent t-test was used to compare the means of the above outcome measures between subjects and controls.

General Linear Model Repeated Measures was also performed. This procedure provides analysis of variance when the same measurement (in this case, TEOAE amplitude) is made several times on each subject.

Experiment II: Effects on vestibular function

Data were analysed with the Statistical Package for the Social Sciences SPSS 11. 5.

For the VOG, the intention was to use chi-square tests to compare the presence or absence of nystagmus from baseline to each of the three exposures, and paired t-tests to compare the slow component velocity change from baseline to each of the three exposures. For the SVV and SVH, the following outcome measures were computed, in order to assess differences between the case and control group:

1. The SVV and SVH difference from baseline to sham exposure for each ear (Rb-sham and Lb-sham)

2. The SVVand SVH difference from baseline to cw exposure for each ear (Rb-cw and Lb-cw)

3. The SVV and SVH difference from baseline to gsm exposure for each ear (Rb-gsm and Lb-gsm)

The independent t-test was used to compare the means of the above outcome measures between subjects and controls.

In addition, paired t-tests were used to compare the difference from baseline SVV and SVH to sham-, cw-, gsm-exposure SVV and SVH in the entire group. General Linear Model Repeated Measures was also performed.

4.2 Results

There was no significant difference in correctly guessing whether the generic handset was on or off between cases and controls in either ear (Pearson chi-square or Fisher's exact test p values ranging from .331 to 1). The entire group gave a mean of 2.5 in 6 correct answers (SD 1.6, range 0-5) and a median of 3.

Experiment I: Effects on auditory function

Baseline, sham, gsm and cw TEOAEs amplitudes in the right and left ear (table 1) were not significantly different between cases and controls.

Table 1. Baseline TEOAE amplitudes in cases and controls

TEOAE	Cases mean (SD)	Controls mean (SD)	Difference in mean (95% CI)	Mann-Whitney p-value
R baseline	12.3 (7.7)	13.5 (5.3)	1.2 (-3.8 to 6.1)	.533
R sham	12.5 (6.4)	13.9 (4.3)	1.4 (-2.7 to 5.5)	.304
R cw	11.2 (6.7)	13.3 (5.3)	2.1 (-2.7 to 7.0)	.401
R gsm	12.4 (7.5)	14.4 (3.9)	2.0 (-2.2 to 6.3)	.397
L baseline	11.07 (7.3)	12.9 (5.6)	1.8 (-3.3 to 7)	.595
L sham	10.6 (7.8)	13.6 (5.5)	2.9 (-2.3 to 8)	.468
L cw	11.6 (6.8)	13.5 (5.2)	1.8 (-2.9 to 6.6)	.664
L gsm	10.7 (7.5)	12.8 (4.9)	2.1 (-2.9 to 7)	.621

There was no significant TEOAEs amplitude change from baseline to sham, from baseline to cw and from baseline to gsm exposure in either left or the right ear in the entire group (paired t test and Willcoxon test).

Table 2. Paired samples T- test results (and Willcoxon p-values) for TEOAEs amplitude change from baseline to sham, from baseline to cw and from baseline to gsm exposure in left and right ear in the entire group

		Difference in Mean (95%CI)	SD of Differences	Paired T-test p
Pair 1	**R base - R sham**	-.32 (-0.97 to 0,34)	1.75	.331
Pair 2	**R base - R cw**	.04 (-0.82 to 0.90)	2.26	.929
Pair 3	**R base - R gsm**	-.63 (-1.46 to 0.20)	2.22	.131
Pair 4	**L base - L sham**	-.32 (-1.41 to 0.77)	2.82	.551
Pair 5	**L base - L cw**	-.55 (-1.42 to 0.33)	2.26	.211
Pair 6	**L base - L gsm**	-.07 (-0.96 to 0.81)	2.24	.865

Table 3 summarises mean amplitude change of TEOAEs from baseline to sham, cw and gsm exposure in the right and left ear in cases versus controls. No significant difference was found between cases and controls in these measures (t-tests and Mann-Whitney tests, p>.05).

Table 3. T-test results (and Mann-Whitney p-values) of TEOAEs amplitude change from baseline to sham, cw, gsm in cases versus controls.

	Cases mean (SD)	Controls mean (SD)	Difference in mean (95% CI)	Mann Whitney p-value
R baseline-sham	-.16(2.4)	-.38 (1.4)	-0.22 (-1.6 to 1.2)	.790
R baseline-CW	-.45(1.1)	.22 (2.5)	0.67 (-1.2 to 2.6)	.487
R baseline-GSM	-.03(1.09)	-.88 (2.5)	-0.85 (-2.6 to 0.90)	.349
L baseline-sham	.38 (1.6)	-.65 (3.2)	-1.03 (-3.3 to 1.3)	.357
L baseline-CW	-.55 (1.6)	-.54 (2.5)	0.01 (-1.9 to 1.9)	.595
L baseline-GSM	-.58 (.90)	.15(2.6)	0.73 (-1.2 to 2.6)	.217

GLM repeated measures analysis conducted to compare the TEOAEs amplitude at baseline, sham, CW and GSM exposure found no significant effect for type of exposure for either the right (Wilk's lambda = .939, F = .541, p=.659) or the left ear (Wilk's lambda = .912, F = .735, p= .542).

Experiment II: Effects on vestibular function

VOG results

There was no nystagmus observed on baseline recording for either cases or controls. No nystagmus was observed in cases after any of the three exposures on either ear. Minor nystagmus was observed in 3 controls only, in a single recording per control subject:

- 2 controls had 2 beats of left beating spontaneous nystagmus of 1-2º/sec slow component velocity on left gaze testing after the left sham exposure

- 1 control had 2 beats of right beating spontaneous nystagmus of 3º/sec slow component velocity on right gaze testing after the right cw exposure

SVV results

No significant differences were found in the SVV change from baseline to after each exposure between cases and controls (p>0.05). Paired T-test from baseline to sham, baseline to CW and baseline to GSM yielded non-significant differences for exposure of either the left or the right ear (paired t-tests). Willcoxon test yielded weakly significant differences for baseline to Rcw SVV and baseline to Lcw SVV (p=.025) significant difference for baseline to R gsm SVV (p= 0.005)

Table 4. Paired samples T- test results for SVV change from baseline to sham, from baseline to cw and from baseline to gsm exposure in right and left ear in the entire group

	Mean	SD	95% CI		DF	p
			lower	upper		
Baseline - R sham SVV	.229	.9537	-.127	.585	29	.199
Baseline - R cw SVV	.246	1.16	-.196	.668	29	.264
Baseline - R gsm SVV	.349	1.08	-.054	.753	29	.087

	Mean	SD	95% CI		DF	p
			lower	upper		
Baseline - L sham SVV	-.170	1.12	-.597	.257	28	.422
Baseline - L cw SVV	-.419	1.35	-.936	.097	28	.108
Baseline - L gsm SVV	-.19	1.12	-.627	.247	27	.381

Table 5. Willcoxon test results for SVV change from baseline to sham, from baseline to cw and from baseline to gsm exposure in right and left ear in the entire group

	Mean Rank		Sum of Ranks		Z	p
	negative	positive	negative	positive		
Baseline - R sham SVV	18.9	11.6	302.5	162.5	-1.44	.150
Baseline - R cw SVV	14.59	16.29	321	114	-2.23	.025
Baseline - R gsm SVV	16.09	13.57	370	95	-2.82	.005

	Mean Rank		Sum of Ranks		Z	p
	negative	positive	negative	positive		
Baseline - L sham SVV	14.29	14.66	171.5	234.5	-.717	.473
Baseline - L cw SVV	16.29	14.59	114	321	-2.23	.025
Baseline - L sham SVV	15.6	13.89	156	250	-1.07	.284

In addition, it was observed that:

- Baseline – R exposure (sham, CW, GSM) SVV yielded a positive mean difference, i.e., the right ear exposure resulted in the SVV being displaced more to the left than on baseline.

- Baseline – L exposure (sham, CW, GSM) SVV yielded a negative mean difference, i.e., the left ear exposure resulted in the SVV being displaced more to the right than on baseline.

We thus conducted paired T-tests to compare the difference between right to left sham, right to left cw and right to left gsm SVV, reasoning that because of the "push-pull" arrangement of the right and left side vestibular end-organ, a right exposure would result in a comparable in size but opposite side SVV deviation than the left ear exposure. This comparison yielded significant results in both parametric and non-parametric tests:

Table 6. Paired T-test results and Willcoxon p-values of right to left exposure (sham, CW, gsm) SVV differences.

	Paired T-tests			Willcoxon
	Mean	**T**	**P value**	**P value**
RshamSVV -LshamSVV	-.3883	-2.364	.025	.033
RcwSVV - LcwSVV	-.6471	-2.829	.009	.009
RgsmSVV - LgsmSVV	-.5529	-2.728	.011	.014

GLM repeated measures analysis conducted to compare the SVV at baseline, sham, CW and GSM exposure found a significant effect (Wilk's lambda = .558, F = 2.586, p=.047 eta squared = .414).

SVH results

No significant differences were found in the SVH change from baseline to after each exposure between cases and controls (p>0.05). Paired T-tests from baseline to sham, baseline to cw and baseline to gsm SVH yielded non-significant differences for exposure of either the left or the right ear, with the exception of the baseline – Lcw SVH (p=.035). Willcoxon test yielded weakly significant differences for the baseline – Lcw SVH (p=.040) only.

Table 7. Paired samples T- test results for SVH change from baseline to sham, from baseline to cw and from baseline to gsm exposure in right and left ear in the entire group

	Mean	**SD**	**95% CI**		**DF**	**p**
			lower	**upper**		
Baseline - R sham SVH	.190	1.05	-.202.	.583	29	.330
Baseline - R cw SVH	.040	1.25	-.438	.518	28	.865
Baseline - R gsm SHV	.180	1.11	-.237	.597	29	.385

	Mean	**SD**	**95% CI**		**DF**	**p**
			lower	**upper**		
Baseline - L sham SVH	-.330	1.27	-.814	.153	28	.173
Baseline - L cw SVH	-.575	1.4	-1.11	-.031	28	.039
Baseline - L gsm SVH	-.432	1.1	-.878	.013	27	.057

Table 8. Willcoxon test results for SVH change from baseline to sham, from baseline to cw and from baseline to gsm exposure in right and left ear in the entire group

	Mean Rank		Sum of Ranks		Z	p
	negative	positive	negative	positive		
Baseline - R sham SVH	16.66	12.96	266.5	168.5	-1.06	.289
Baseline – R cw SVH	14.96	12.96	209.5	168.5	-.493	.622
Baseline – R sham SVH	18.33	12.67	275	190	-.874	.382

	Mean Rank		Sum of Ranks		Z	p
	negative	positive	negative	positive		
Baseline - L sham SVH	16	14.47	160	275	-1.243	.214
Baseline – L cw SVH	10.27	17.24	113	293	-2.05	.040
Baseline – L sham SVH	11.75	16.03	117.5	288.5	-1.947	.052

However, it was observed that:

- Baseline – R exposure (sham or cw or gsm) SVH yielded a positive mean difference i.e., the right ear exposure resulted in the SVV being displaced more to the left than on baseline.

- Baseline – L exposure (sham or cw or gsm) SVH yielded a negative mean difference, i.e., the left ear exposure resulted in the SVV being displaced more to the right than on baseline.

We thus conducted paired T-tests to compare the difference between right to left sham, right to left cw and right to left gsm SVV reasoning that because of the "push-pull" arrangement of the right and left side vestibular end-organ, a right exposure might result in a change of comparable size but opposite side SVV deviation than the left ear exposure. This comparison yielded significant results:

Table 9. Paired T-test results (and Willcoxon p-values) of right to left exposure (sham, CW, gsm) SVH differences.

	Paired T-tests			Willcoxon
	Mean	T	P value	P value
RshamSVH -LshamSVH	-.5462	-2.643	.013	.031
RcwSVH - LcwSVH	-.6514	-3.482	.002	.003
RgsmSVH - LgsmSVH	-.5971	-2.737	.011	.012

GLM repeated measures analysis conducted to compare the SVH at baseline, sham, CW and GSM exposure found significant effect (Wilk's lambda = .368, F = 6.311, p=.001, eta squared = .632).

Post-study control experiment

There was a significant difference on both SVV and SVH between left and right exposure for all modes of exposure. This could be due to:

a) The thermal effect of the dummy phone

b) The radiofrequency effect of the dummy phone

c) The weight of the mobile phone, via changes of somatosensory perception

d) A combination of any of the above.

In order to assess how the weight of the phone affects the SVV/SVH results, we conducted a further experiment, which will be referred to as "Control experiment", after the end of the study.

Control experiment methods

Inclusion criteria for subjects for this experiment were, as for the main study, age 20 to 55 years, normal tympanometry and normal pure tone audiometric thresholds. We recruited 20 normal volunteers (8 male, 12 female, age range 27-57 years, mean age 39).

e.

Control experiment protocol

All subjects underwent **tympanometry** and pure tone **audiometry** as per the inclusion criteria. In addition, baseline data were obtained on **subjective visual vertical/horizontal test (SVV/SVH).**

After the baseline measurement, the standardised dummy mobile exposure system was strapped to either the right ear or the left ear, with the device's antenna positioned over the mastoid cavity. The device was left switched off. The SVV and SVH were then repeated 25 minutes later. The dummy mobile exposure system was then strapped on the opposite side, and the SVV/SVH were again repeated 25 min later.

Control experiment data analysis

Data were analysed with the Statistical Package for the Social Sciences SPSS 11. 5.

PairedPa Paired t-tests were used to compare the means of baseline versus left SVV/SVH, baseline versus right SVV/SVH, and right versus left SVV/SVH.

Control experiment results

SVV results

Paired T-test and Willcoxon signed ranks tests from baseline SVV to right or left ear positioning of the dummy mobile SVV yielded non-significant differences ($p>.05$) for either ear. However, it was observed that:

- Baseline SVV – R positioning of the dummy mobile SVV yielded a positive mean difference i.e., the right ear exposure resulted in the SVV being displaced more to the left than on baseline.

- Baseline SVV – L positioning of the dummy mobile SVV yielded a negative mean difference, i.e., the left ear exposure resulted in the SVV being displaced more to the right than on baseline.

We conducted paired T-tests and Willcoxon signed ranks test to compare the difference between right to left positioning of the mobile SVV. This comparison yielded significant results.

Paired samples T-test

	Mean	SD	95% CI		DF	p
			lower	upper		
Baseline SVV- R SVV	.305	.979	-.140	.751	20	.168
Baseline SVV- L SVV	-.114	.808	-.492	.264	20	.535
R SVV-L SVV	-.551	.989	-1.01	.088	20	.022

Wilcoxon Signed Ranks Test

	Mean Rank		Sum of Ranks		Z	p
	negative	positive	negative	positive		
Baseline SVV- R SVV	13.63	7.5	163.5	67.5	-1.669	.095
Baseline SVV- L SVV	8.45	11.72	84.5	105.5	-.423	.673
R SVV-L SVV	8.42	11.39	50.50	159.50	-2.035	.042

GLM repeated measures analysis conducted to compare the SVV at baseline, right and left positioning of the dummy mobile found a significant effect (Wilk's lambda = .713, F = 3.62, p=.048, eta squared = .287).

SVH results

Paired T-test and Willcoxon signed ranks tests from baseline SVH to right or left ear positioning of the dummy mobile SVH yielded non-significant differences (p>.05) for either ear. However, it was observed that:

- Baseline SVH – R positioning of the dummy mobile SVH yielded a positive mean difference i.e., the right ear exposure resulted in the SVH being displaced more to the left than on baseline.

- Baseline SVH – L positioning of the dummy mobile SVH yielded a negative mean difference, i.e., the left ear exposure resulted in the SVH being displaced more to the right than on baseline.

We conducted paired T-tests and Willcoxon signed ranks test to compare the difference between right to left positioning of the mobile SVH. The paired T-test comparison yielded non significant results at p=.088, while the Willcoxon signed ranks test yielded just significant results at p=.050 .

Paired T-tests

	Mean	SD	95% CI		DF	p
			lower	upper		
Baseline SVH- R SVH	.119	.898	-.289	.528	20	.550
Baseline SVH- L SVH	-.103	.868	-.509	.303	20	.601
R SVH-L SVH	-.345	.859	-.748	-.056	20	.088

Wilcoxon Signed Ranks Test

	Mean Rank		Sum of Ranks		Z	p
	negative	positive	negative	positive		
Baseline SVH- R SVH	11.5	10.33	138	93	-.782	.434
Baseline SVH- L SVH	8.68	12.72	95.5	114.5	-.355	.723
R SVH-L SVH	10.5	10.5	52.5	157.5	-1.960	.050

GLM repeated measures analysis conducted to compare the SVV at baseline, right and left positioning of the dummy mobile found a non-significant effect (Wilk's lambda = .827, F = 1.883, p=.181, eta squared = .173).

POWER OF THE STUDY

The power of the study was >80% to detect TEOAE changes > 2.5 dB (i.e. the 75% percentile of TEOAE change in repeated TEOAE recordings in normal subjects) and SVV/SVH change > 1º .

Power to detect differences between means, according to size of difference we wish to detect (at 5% significance level) (based on observed SD's in this study, averaged across all comparisons in tables referred to)

Difference in means	TEOAE comparing changes between cases and controls[1]	TEOAE Finding changes from baseline[2]	SVV Comparing Difference in means[3]
0.25	6	9	24
0.5	10	22	70
0.75	17	43	96
1	27	66	99.9
1.5	53	95	>99.9
2	77	99.8	>99.9
2.5	92	>99.9	>99.9
3	98	>99.9	>99.9

1 from table 3. Based on unpaired t-test, with 9 patients (SD=1.5) and 21 controls (SD=2.5).

2 from table 2. Based on paired t-test, in 30 people (combined group of patients and controls), SD of differences=2.3.

3 from table 4. Based on paired t-test in 30 people (combined group of patients and controls), SD of differences=1.1.

5. Analysis of objectives met

The objective of this project for stage I, as stated on the original proposal, was to determine any effect of pulsed or continuous radio signals from a generic handset on the labyrinth, in subjects with and without symptoms related to mobile phone usage.

Experience with the initially proposed protocol resulted in the need for review of the experimental techniques (SVV/SVH). However, more importantly, and similar to other groups, we encountered problems with identifying enough symptomatic subjects that would be willing to participate in our research as unpaid volunteers. Despite the fact we made every effort to recruit more symptomatic subjects to this study, we were unsuccessful in recruiting the originally proposed 20 symptomatic cases and we completed investigations on a total of 30, 9 cases and 21 controls.

Efforts to identify and recruit subjects included:

1. Advertisement on MTHR website.
2. Subjects shared with Professor Wessley's group.
3. Advertisements put on hospital boards and libraries.
4. Advertisement sent by email to UCLH cascade email list and to ICH email list
5. Ongoing contact with Occupational Physicians in the City to identify subjects
6. Short film which was shown on the BBC six and ten o'clock news with details of the project and research team on the BBC website.

And while the objective of the project was met, to some extent, by demonstrating negative effects for the two tests that were conducted post-exposure (TEOAEs and VOG) and a minor effect for the test that was conducted during the exposure (SVV/SVH),

and no differences between cases and controls, the small size of the symptomatic case sample has to be taken into consideration when considering the results.

6. Interpretation

The main findings of our study are as follows:

1. There were no differences between subjects and controls in any of the tests employed (TEOAEs, VOG and SVV/SVH). However, the symptomatic cases sample was small.

2. There was no significant difference in correctly guessing whether the generic handset was on or off between cases and controls, with a median score of 50% correct answers (3:6) in the entire group. Our results are in agreement with other reports. While Johansson (1995) reported that one in 7 tested individuals who report symptoms after mobile phone usage could detect whether a mobile phone was 'on' or 'off' nine times out of nine, this finding was not replicated in a larger study of about 70 such individuals, and no individual was identified who could consistently detect whether the mobile phone was on or off (Johansson, personal communication, as reported in Rubin et al., 2004).

3. We found no significant baseline to exposure changes in the TEOAEs amplitude for any of the 3 exposures in either ear, similarly to other reports. Aran et al (2005) assessed distortion product otoacoustic emissions of guinea pigs, who were exposed to either sham or to GSM mobile phone microwaves for 1 hour per day, 5 days a week, at a specific absorption rate (SAR) of 1, 2 and 4 W/kg. DPOAES were recorded and compared at baseline before the exposure, immediately after the exposure period of 2 months and 2 months later. No dose-response relationship was found between SAR and DPOAEs for either exposed or non-exposed ears.

These results were in agreement with the results of Marino et al (2000), who measured DPOAEs in guinea pigs after a 4 week 900 MHz microwave exposure, Kizilay et al (2003) who measured the DPOAEs of both adult and newborn rats after a 4 week 900 MHz microwave exposure, and the results of Ozturan et al (2002) on human volunteers. Ozturan et al (2002) measured both TEOAEs and DPOAEs on 17 normal hearing individuals twice before exposure, immediately after a 10-minute exposure to an activated mobile phone held over the mastoid for 10 minutes, and 10 minutes after the exposure, and they found no significant difference between any of the sessions.

4. We found no significant changes in the VOG recording from baseline to after each of the three exposures. We are not aware of any similar experiments conducted in either humans or animal. However, it must be noted that due to the time necessary to take off the generic handset and put on the subject's head the VOG goggles, as well as to the need to calibrate the VOG equipment before conducting the actual recording, the VOG was recorded between 1 min and 2 min after exposure, thus a small vestibular effect may well have dissipated in that time frame.

5. The SVV/SVH was the only test to be recorded during the exposure. No significant differences were found in the SVV/SVH change from baseline to after each exposure between cases and controls. There was no significant SVV/SVH change from baseline recording to post-exposure recording for any of the exposures. However, it was observed that all right ear exposures resulted in the SVV and SVH being displaced more to the left than on baseline, and all left ear exposures resulted in the SVV and SVH being displaced more to the right than on baseline. This effect would suggest that any exposure of either ear resulted in excitation of the otolithic organ on that side.

We thus conducted paired T-tests to compare the difference between right to left sham, right to left cw and right to left gsm SVV/SVH, reasoning that because of the "push-pull" arrangement of the right and left side vestibular end-organ, a right exposure would result in a comparable in size but opposite side SVV deviation than the left ear exposure. This comparison yielded a statistically significant difference in the entire group between right to left exposure for all three exposure modes for both ears.

This minimal effect could reflect either the heating effects of the dummy mobile, with thermal stimulation of the labyrinth, proprioceptive stimulation of the vestibular end organ by the weight of the dummy device, or the effect of a minor head tilt due to the weight of the dummy device. We thus conducted a further experiment to investigate this phenomenon, in which after obtaining baseline measurements of the SVV and SVH in 20 normal subjects, the SVV/SVH were repeated 25 minutes after strapping the dummy mobile (switched off) over the left or right ear, and comparing the values obtained to the baseline. As in the true exposure experiments, baseline SVV – R positioning of the dummy mobile SVV yielded a positive mean difference i.e., the right ear exposure resulted in the SVV being displaced more to the left than on baseline, while baseline SVV – L positioning of the dummy mobile SVV yielded a negative mean difference, i.e., the left ear exposure resulted in the SVV being displaced more to the right than on baseline, with similar results for the SVH. The difference between R-L SVV and SVH were significant, albeit at a lower level of significance than in the true exposure experiments, possibly due to the smaller numbers of subjects (20 in this experiment versus 30 in the original study). Thus, the effect on the SVV/SVH observed in the true exposure experiments could reflect proprioceptive stimulation of the vestibular end organ by the weight of the dummy device, or the effect of a minor head tilt due to the weight of the dummy device, ie the so-called "E-effect" (Hoppenbrouwers et al., 2003), which results in deviation of the subjective visual vertical opposite to the head tilt. However, a potential additional effect of the switched on device cannot be entirely outruled.

7. Future priorities

A. Similar to other groups, we encountered problems with identifying enough symptomatic subjects that would be willing to participate in our research as unpaid volunteers. It is not clear whether this was due to the unwillingness of symptomatic subjects to be exposed to what they regard as "dangerous" radiation exposure for the sole purposes of a scientific experiment, or whether the number of symptomatic subjects has actually decreased over time, due to either technical improvement of the new generation handsets, or to the public perception of mobiles changing over time. In either case, it would be essential to create a national programme of identifying people who complain of symptoms after mobile phone usage and to recruit these people in future studies.

B. The SVV/SVH was the only test to be recorded during the exposure, and the only test that demonstrated a small, but consistent, change from baseline to exposure. A further experiment which was conducted in order to assess the effect of other potential confounders, such as the weight of the dummy phone, indicated that the observed effects were probably due to the weight of the dummy mobile. However, the change observed in the exposure group was statistically more significant than in the post-study experiment. This could be due to the fact that the numbers in the exposure experiment were bigger than in the post-study experiment (30 versus 20), however, there is also a possibility that there was an additional small effect from the switched on device. A further study should be conducted, in order for these findings to be replicated, on healthy volunteers, since the observed effects were seen across cases and controls. In this further study, the SVV/SVH will be conducted at baseline with the dummy mobile in situ but in non-operating mode, to be followed by measurements on the 25th minute post exposure, as per the original study experiment. In addition, the SVV/SVH recording protocol should be slightly changed, with more readings taken, and with the angle of initial deviation of the SVV/SVH recorded.

8. Publications

1. Effects of mobile phones on hearing. B Ceranic, Deafness Genetics Workshop, Institute of Child Health, London, June 2002.

2. Effects of mobile phone stimulation on labyrinthine function. L. Luxon, B. Ceranic, R. Cox, P. Chadwick. 6th European BioElectromagnetic Association Meeting Budapest, November 2003.

3. Electrical hypersensitivity - human studies in the UK. Robin Cox, WHO International Seminar and Working Group meeting on EMF Hypersensitivity, Prague, Czech Republic, October 2004.

In preparation:

1. Effects of low-level radiofrequency mobile phone stimulation on outer hair cell function: a double-blind, case-control study. DE Bamiou, B. Ceranic, P. Chadwick, R. Cox, L. Luxon.

2. Effects of low-level radiofrequency mobile phone stimulation on vestibular function: a double-blind, case-control study. DE Bamiou, B. Ceranic, P. Chadwick, R. Cox, L. Luxon.

9. Financial summary

Pay	£74,431
Overheads	£29,772
Non-Pay	£71,537

Total	£175,740

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