Electromagnetic fields and working memory

Effects of electromagnetic fields emitted by GSM phones on working memory: A meta-analysis.

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Electromagnetic fields and working memory

ABSTRACT

Background and Objective: Current treatments for Alzheimer’s Disease (AD) do not affect the course of the illness and brain stimulation techniques are increasingly promoted as potential therapeutic interventions for AD. This study reviews the effects of electromagnetic field (EMF) exposure vs. sham exposure on working memory (WM) performance of healthy human participants.

Method: Online literature databases and previous systematic reviews were searched for studies of EMF and WM in participants without reported memory problems. Two thousand eight hundred and fifty seven studies were identified and ten studies met the inclusion criteria. An assessment of study quality was completed and separate, random effects meta-analyses were conducted for each of the three WM tasks included: n-back, substitution and digit span forward.

Results: No differences were found between participants exposed to active EMF vs sham conditions in any of the three working memory tasks examined.

Conclusion: Results indicate that EMF does not affect WM during the n-back, substitution and digit-span tasks. Future studies should focus on the possible effects of chronic exposure to EMF in older adults with AD using a battery of comparable WM and attention tasks, before EMF can be seriously considered as a potential modulator of WM in AD.
Electromagnetic fields and working memory

INTRODUCTION

AD is a neurodegenerative disorder characterised by an insidious onset and progressive disturbance in cognitive function with memory being particularly affected. Symptomatic treatments including cholinesterase inhibitors provide modest relief but do not delay disease progression (AD2000, 2004). Other AD treatments are sought to reduce cognitive decline associated with AD and delay the course of disease progression.

Brain stimulation techniques are now being advocated as potential treatments for several neurodegenerative disorders. Deep Brain Stimulation (DBS) has been widely used to treat tremor, dyskinesia and motor fluctuation in Parkinson’s disease (see Honey and Ranjan, 2012 for a review) and the first clinical trial for the use of DBS on cognitive function in patients with Dementia with Lewy Bodies is now underway (NCT02263937). Transcranial direct current stimulation (tDCS) and transcranial magnetic stimulation (TMS) have both shown promise in improving cognitive function of patients suffering neurodegenerative dementias including AD (see Elder and Taylor, 2014 for a review). Recently, exposure to EMF, such as those emitted by mobile phones, has emerged as a potential modifier of cognition (see Barth et al., 2008 for a review). Phones from the Global System for Mobile communication (GSM) emit high frequency EMF in the range from 850 to 2000MHz which is partly absorbed by brain tissue (Schonborn et al., 1998). There are reports that GSM-induced EMF can increase cerebral metabolism and excitability in brain regions directly exposed to signal (for review see Valentini et al., 2007). This idea is supported by animal studies which report that exposure to EMF can enhance cognitive performance including WM in aged Alzheimer’s transgenic (Tg) mice by reversing amyloid-β (Aβ) deposition (Arendash et al., 2012; 2010) and countering neuronal hypo-activity, which occurs early in
Electromagnetic fields and working memory

AD pathogenesis (Mori et al., 2011). In human participants, Schuz et al. (2009), reported that long-term cell phone users (10 years+) had a 30–40% decreased risk of hospitalization due to AD and vascular dementia. In 2012, Ng et al. reported that in a group of older participants with age-related cognitive decline, more frequent mobile phone users showed better performance on the Mini Mental State Exam (MMSE) and neuropsychological tests including measures of memory and attention. Although these epidemiological studies could not distinguish between causal and consequence association, and the animal findings are not easily extrapolated to humans, together, these few studies show promise in the application of EMF for age-related cognitive decline. A treatment based on exposure to EMF could therefore provide an inexpensive, non-invasive, non-pharmacological therapeutic intervention for cognitive decline associated with AD.

Use of mobile phones has increased exponentially in recent years and although their impact on health and normal brain function in humans has come under intense investigation over the last decade, findings are nevertheless conflicting. The idea that EMF can benefit human cognition is supported by a number of empirical studies. Koivisto et al. (2000) reported faster reaction times during WM tasks and improved response times during simple reaction and vigilance tasks and reduced cognitive time for mental arithmetic tasks. In 2003, Smythe and Costall provided further evidence to support improvements in memory under EMF exposure but only in male participants. Keetley et al. (2006) observed faster performance on a trail making task, but that accuracy during simple and choice response times decreased. Small improvements in attention have also been reported (Lee et al., 2003).

Other studies, however have reported no effects on cognition including memory, attention and executive function (Haarala et al., 2007; Krause et al., 2000; Krause et al., 2007; Haarala
Electromagnetic fields and working memory

et al., 2004; Haarala et al., 2005; Haarala et al., 2003; Besset et al., 2005; Eltiti et al., 2009; Delhez et al., 2004). Despite the growing body of literature, differences in methodologies, exposure protocols and outcome measures have led to inconclusive results. Three recent meta-analyses report conflicting conclusions. In 2008, Barth et al. suggested that human attention and WM were facilitated by exposure to EMF on the subtraction and 0-back tasks, whilst Valentini et al. 2010 and Barth et al., 2012 reported no effects of exposure. These meta-analyses have several limitations in the context of assessing the effects of EMF on WM. Barth et al., 2011 and 2007 included only the n-back task as a measure of WM in their analyses, and may therefore reflect task-specific conclusions that do not generalise to WM as a whole. In addition, Barth et al’s, 2007 review was limited to studies completed by 2007, and is now nearly 10 years out of date. Whilst Valentini et al., 2011 included the subtraction task in addition to the n-back, they compared data from two distinct versions of the task: subtraction vs. the more challenging descending subtraction task, which, in addition to WM, draws on components of attention and executive function, similar to the distinctions made between digit-forward and digit-backward tasks (Hale et al., 2002) and is therefore not directly comparable to the subtraction task.

Before EMF can be seriously considered as a novel treatment for AD, consensus must be reached on its potential to modulate cognition. Although episodic memory deficits are prominent in early AD, few EMF studies measure this construct and recent reports from animal studies point explicitly to improvements in WM. To our knowledge there are currently no studies of direct EMF exposure on WM performance in patients with AD, MCI, age-related cognitive decline or even subjective cognitive complaints. Focusing on the most up-to-date literature, beyond the scope of existing meta-analyses, the current study
Electromagnetic fields and working memory

examined whether acute exposure to EMF emitted by GSM mobile phones affects WM performance in human participants without reported memory difficulties.

METHODS

Literature search and selection

Online databases (PubMed, Cochrane, Web of Science, Embase, PsychARTICLES, PsychINFO (1806-present) were searched on 21 August 2013. The following search terms were used:

‘RCT OR randomised OR randomized) AND (EMF OR electromagnetic OR RF OR radiofrequency OR radio-frequency OR "radio frequency") AND (cognition OR cognitive OR executive OR motor OR memory OR behavioural OR behavioral OR psychomotor OR performance OR attention OR "response time" OR "reaction time" OR accuracy’. All fields were searched and references of published articles were also inspected for relevant studies manually. The studies were selected on the basis of the following inclusion criteria:

1. Treatment (EMF on) and control group (EMF off/sham)
2. Within-subject and between-subject designs
3. Means and standard deviations/standard errors of dependent variables were available from article or author for both groups
4. Cognition was assessed using WM tasks defined as N-back task, Subtraction task and Digit-forward span task
5. Exposure to GSM or Universal Mobile Telecommunications System (UMTS)-like electromagnetic fields (pulsed or continuous wave)
6. Double or single blinding of study participants
Electromagnetic fields and working memory

7. Human participants

8. Studies published in peer reviewed scientific journals

Assessment of study quality

The quality of included studies was assessed using the Cochrane Collaborations Risk of Bias Tool (Cochrane Collaboration) by four independent raters (OZ, HG, HC, MC). All discrepancies were resolved by discussion.

Data extraction and calculation of effect sizes

Means and standard deviations were extracted by four independent authors (OZ, HG, HC, MC) and discrepancies were resolved through discussion. Several studies reported data separately for parameters including side of exposure and type of EMF. As there is no consensus on the precise stimulation parameters and no a-priori predictions were made for these characteristics, weighted scores were computed by averaging the responses across those trials. To work out the combined means and standard deviations, the following formulae were used:

\[
\text{Combined mean} = \frac{((n1 \times \bar{X}_1) + (n2 \times \bar{X}_2))}{\text{combined n}}
\]

\[
\text{Combined SD} = \sqrt{\frac{a+b}{\text{combined n}-1}}, \text{ with } a = \frac{(n1-1) \times (SD1 \times SD1) + (n2-1) \times (SD2 \times SD2)}{(n1 \times n2) \times \text{combined n}}
\]

\[
\text{and } b = \frac{(n1 \times n2) \times (\text{SUMSQ}(ar{X}_1, \bar{X}_2) - 2 \times (\bar{X}_1 \times \bar{X}_2))}{\text{combined n}}
\]
Electromagnetic fields and working memory

Where n = number of participants, 1 = active condition, 2 = sham condition

Averaged parameters included:

1. Left and right hemisphere exposure
2. Continuous vs pulsed wave
3. Target vs non-target: since 2/5 studies (Krause et al. 2007; Haarala et al. 2007) did not report data for target and non-target trials separately, data from these trials were averaged to compose a weighted score.
4. Finland vs Sweden
5. 20µT vs 400 µT
6. Sensitive vs control (self-reported sensitivity to EME vs no self-reported sensitivity to EME)
7. EP ‘on’ and RP ‘on’ and EP ‘off’ and RP ‘off’ conditions were averaged to analyse data from Besset et al. 2005.

Some studies reported ‘number of false answers’, ‘% error’, or ‘number of errors’. In these cases, % correct scores were calculated to allow comparison across all studies. The standardised mean difference (SMD) was used as a measure of effect size. Positive SMD values indicate faster or more accurate responses for active vs sham treatment whilst negative values indicate slower or less accurate responses for active vs sham treatment.
**Electromagnetic fields and working memory**

**Meta-analyses**

Statistical analyses were carried out using Review manager 5.3 (The Cochrane Collaboration, 2014). Only WM tasks that were present in three or more studies were included in the meta-analyses, and separate meta-analyses were conducted for each task. The meta-analyses were carried out as a comparison between EMF active and EMF sham conditions. The random effects model was used to estimate the overall SMD. The Z statistic was used to test whether the overall pooled SMD was significantly different from 0. The I² statistic was used as an indicator of variability in SMDs between included studies with I² values ranging between 25%-49% signifying low heterogeneity, 50%-74% as moderate and 75% or greater as high heterogeneity. Publication bias was assessed using funnel plots.

**RESULTS**

**Study characteristics**

Initial non-refined searches produced 2857 results which were then subjected to evaluation of title and abstract content. This selection produced 123 results. Once duplicates were removed, 76 papers were identified for full evaluation and 10 studies, published between 1999 and 2009, met the inclusion criteria (see Figure 1 for more detail).

< insert figure 1 here>

In total, 553 participants were tested: 524 under active GSM exposure and 525 under sham conditions (one between-subjects study was included with 28 participants in the active condition and 29 in sham and 9 between-subjects design studies). Research characteristics
Electromagnetic fields and working memory

of eligible studies are summarized in Table 1. All studies examined effects of EMF on WM using the n-back, subtraction or digit-span tasks. Participants in the Haarala et al., 2007 study completed both the n-back and the subtraction tasks but since separate analyses were performed for each task, no double-counting of participants occurred. 9 of 10 studies were of a within-subjects crossover design with participants performing both the active and sham exposures in a counterbalanced order. Besset et al., 2005 used a between-subjects design with one group performing the active and another group performing the sham exposure. Participants were exposed to EMF via a GSM phone or a signal generator connected to a GSM phone in 9 of 10 studies. Eltiti et al., 2009 combined GSM and UMTS signal. Exposure duration for each session lasted between 30-120mins. In 9 studies, participants were exposed for 1-2 sessions completed within a fortnight and one study (Besset et al., 2005) exposed participants for 2 hrs daily for 4 weeks. 7 studies reported EMF exposure to the right side of the head, one reported exposure to both sides (Haarala et al., 2007) and two provided no details on side of exposure (Besset et al., 2005 and Eltiti et al., 2009). All except two studies (Koivisto et al., 2000; 1999) used a double blind design.

< insert table 1 here>

Quality of studies

Table 2 provides a summary of potential sources of bias for included studies. No studies were excluded on the basis of inadequate ratings and only 1 of 10 studies was rated inadequate on 3 of 6 parameters. The remaining studies were all rated as adequate on 4 or more parameters. The randomisation of sequence generation and allocation concealment
Electromagnetic fields and working memory

were least adequately addressed whilst blinding of participants and outcome measures, dealing with incomplete outcome data and selective outcome reporting were most adequate.

< insert table 2 here>

Meta-analyses

Three WM tasks were identified as being present in three or more studies: the N-back task, subtraction and digit span. Six studies were initially identified for the n-back task but one study reported log-transformed data so had to be excluded from the analyses (Krause et al., 2000), leaving 5 suitable studies (see Table 1). Separate meta-analyses were performed for each level of the n-back task and for the reaction time (RT) and accuracy (ACC) measures. Three studies were identified for the subtraction task (see Table 1). RT was used as the dependent variable as accuracy data was not available for Koivisto et al., 1999. Three studies with digit span forward task were identified (see Table 1). In Besset et al., 2005, only data from the exposure period (EP) and recovery period (RP) stages were used and data from the baseline period (BLP) were excluded as there was no exposure to EMF/sham during this period. Similarly, in Keetley et al., 2006 only data in ‘real field’ exposure and ‘sham field’ exposure were used and ‘pre exposure’ data were excluded as performance in this condition was not subject to EMF/sham exposure.

Table 3 summarises the results of the meta-analyses. All WM measures examined in this review were homogenous, with the exception of the digit span task which showed
Electromagnetic fields and working memory

heterogeneity. No significant differences between active EMF and EMF off/sham conditions were found for any of the three working memory tasks investigated.

No evidence of publication bias was found as indicated by the funnel plots for each task (see Figure 2).

DISCUSSION

Our analysis does not support the hypothesis that exposure to EMF has any impact on WM of healthy human participants. This result is consistent with earlier meta-analyses (Barth et al., 2011; Valentini et al., 2011). In contrast to previous reports, we examined whether EMF affects performance during three separate WM tasks and compared only identical task conditions. Despite these methodological refinements, and examination of a larger pool of potentially eligible studies, no significant effects of EMF on WM were observed. It is possible that the WM tasks chosen were not sensitive to the effects of EMF and that other tasks measuring memory capacity and attention, which are most compromised in AD, might have indicated significant effects.

Closer inspection of the data suggests that heterogeneity observed in the digit span analysis is driven entirely by the Eltiti et al., 2009 study, which combined signal from the 900 and 1800MHz frequency bands and counterbalanced participants to an additional UMTS signal exposure with a frequency of 2020MHz. This combination of frequencies is much higher
Electromagnetic fields and working memory

than that used in the other three studies and may account for the drop in accuracy in the exposure condition. Removing this study achieves 100% homogeneity between tasks and does not produce any significant effects: -0.04 [-0.25, 0.17]; P=0.69, X²=0.16, Z=0.36.

Precise parameters of EMF exposure for most potential benefit are not understood and it is possible that characteristics including ‘side of exposure’ and ‘type of wave’ (pulsed vs. continuous) may interact with task performance. There is some, limited evidence that ‘left-sided’ exposure to EMF slowed response times during a spatial memory task (Eliyahu et al., 2006 and Luria et al., 2009). It is therefore possible that averaging across trials with left and right sided exposure has masked underlying effects on WM. Two studies included in the analysis of the n-back tasks reported data separately for ‘left vs. right’ and ‘continuous vs. pulsed’ stimulation. In a separate, post-hoc analysis we therefore compared whether ‘left-sided’ exposure under pulsed stimulation (as GSM devises typically emit a pulsed wave) revealed any differences that may have been masked during combined analyses. No significant differences were found and all n-back tasks remained homogenous (see Table 4).

<insert table 4 here>

Current literature is limited to examining short-term EMF effects, where participants are exposed for brief durations, across few sessions, typically no more than a few days apart. Benefits from such exposure protocols may therefore be transient, an idea supported by findings that EMF-induced physiological changes, including cerebral metabolism and brain electrical activity, return to baseline levels as quickly as one hour following cessation of exposure (Valentini et al., 2007; Hamlin and Wood, 2002). Other types of brain stimulation techniques rely on repeated application to induce longer lasting effects (Wilkinson et al., 2014; Garin et al., 2011) and allow for long-term plastic change following repeated stimulus
Electromagnetic fields and working memory

exposure (Hoffman and Cavus, 2002). Effects of EMF may therefore be observed following longer exposure and follow-up protocols which allow potential treatment carry-over effects to emerge. A number of recent reports suggest that long-term exposure to EMF provides cognitive benefits in mice. Arendash et al., 2010 found that daily EMF exposure during a 7-month period improved cognitive performance of AD Tg mice on a battery of cognitive tests compared to controls and reduced brain Aβ deposition. In 2012 these findings were extended to show that advanced Aβ deposition in the brains of very old AD Tg mice was reversed following daily EMF exposure over a 2-month period. These findings are encouraging and similar protocols now need to be applied to human participants.

By pooling results from different studies, this meta-analysis allowed us to provide a summary of current findings with more accurate estimation of effect size and without the difficulties of small sample size and low statistical power. This study is nevertheless limited by the number and the quality of studies included. One difficulty is that there is a shortage of studies which fulfil the minimum requirements for inclusion. Many studies were excluded due to unreported means and/or standard deviations required for analysis. Another shortcoming is the vastly different outcome measures across studies which could not be compared in the meta-analysis. In total, only 10 studies fulfilled our minimum inclusion criteria, so clearly these findings must be interpreted with caution. Given the large amount of conflicting data in the field, and the likelihood of future meta-analyses, establishing a minimum agreed standard for reporting methodological and statistical details, together with a standard battery of cognitive tests, would help advance this line of research. Given the wider context of AD-related cognitive decline that this study is set in, the average age of participants (28.5yrs) is also a noticeable limitation, particularly given that differential
Electromagnetic fields and working memory

effects of EMF have been reported on physiological brain changes of old and young participants (Croft et al., 2010; Veccio et al., 2010). There is now a handful of animal (Arendash et al., 2012, 2010) and epidemiological human studies (Shuz et al., 2009; Ng et al., 2012) which show promise for EMF as a cognitive enhancer in older brains but clearly there is a gap in current research and a need for similar, empirical studies to be conducted in older human populations with memory difficulties. The tolerability and incidence of adverse events will also be an important factor in determining suitability of using EMF amongst the older population who are more likely to suffer from ill health and a multitude of comorbidities.

In conclusion, the current analysis provides no evidence that short-term exposure to EMF has an effect on WM and its potential for relieving cognitive decline associated with AD remains unconfirmed. Given the lack of current treatments for AD, there is an urgent need to explore other possible interventions such as EMF. Future studies should focus on long-term exposure to EMF and assess potential treatment carry-over effects on WM and attention, particularly in older participants with memory problems. More detailed reporting of methodological details and study results will enable a larger pool of comparable studies to be generated for future analyses. Finally, study designs which focus on specific stimulation parameters including side of exposure and type of wave with a focus on tolerability will greatly inform this field of research.
Electromagnetic fields and working memory

Figure 1: PRISMA flow diagram detailing the number of records identified, included and excluded with reasons for exclusions. Adapted from Moher et al. (2009).
## Electromagnetic fields and working memory

### Table 1: Characteristics of included studies for all three memory tasks

<table>
<thead>
<tr>
<th>Study reference</th>
<th>Working memory task</th>
<th>Outcome Measure</th>
<th>Design</th>
<th>Exposure: gsm, frequency, continuous etc</th>
<th>Exposure duration</th>
<th>Blinding</th>
<th>Randomisation</th>
<th>Active sample</th>
<th>Control sample</th>
<th>Participant age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haarala et al 2004</td>
<td>0-back, 1-back, 2-back, 3back</td>
<td>RT, ACC</td>
<td>Within-subject</td>
<td>Gsm phone mounted to left side of head with antenna, 902MHz, mean power 0.25W, pulsed</td>
<td>65mins</td>
<td>Double</td>
<td>Order of exposure counterbalanced</td>
<td>32</td>
<td>32</td>
<td>24.2yrs</td>
</tr>
<tr>
<td>Koivisto et al 2000</td>
<td>0-back, 1-back, 2-back, 3back</td>
<td>RT, ACC</td>
<td>Within-subject</td>
<td>Gsm phone mounted on head with antenna over left temporal lobe, 902MHz, mean power 0.25W, pulsed</td>
<td>30mins</td>
<td>Single</td>
<td>Order of task counterbalanced</td>
<td>48</td>
<td>48</td>
<td>23.2yrs</td>
</tr>
<tr>
<td>Krause et al 2007</td>
<td>0-back, 1-back, 2-back, 3back</td>
<td>RT, ACC</td>
<td>Within-subject</td>
<td>Signal generator connected to Nokia 6110 MP antenna, 902MHz, 0.25W, exposure to left and right under continuous and pulsed wave</td>
<td>40 mins for each exposure side</td>
<td>Double</td>
<td>Order of task counterbalanced</td>
<td>36</td>
<td>36</td>
<td>23.6yrs</td>
</tr>
<tr>
<td>Haarala et al 2007</td>
<td>0-back, 1-back, 2-back, 3back</td>
<td>RT, ACC</td>
<td>Within-subject</td>
<td>EMF generator connected to GSM Nokia 6110 MP antenna over left posterior temporal lobe, and over right posterior temporal lobe, 902MHz, 0.25W, continuous and pulsed wave</td>
<td>90mins</td>
<td>Double</td>
<td>Order of hemisphere, EMF and task were counterbalanced</td>
<td>36</td>
<td>36</td>
<td>23.8yrs</td>
</tr>
<tr>
<td>Haarala et al 2005</td>
<td>0-back, 1-back, 2-back, 3back</td>
<td>RT, ACC</td>
<td>Within-subject</td>
<td>GSM phone mounted on left side of head with antenna over left posterior temporal lobe, 902MHz, mean power 0.25W, pulsed</td>
<td>50mins on each of two successive days</td>
<td>Double</td>
<td>Order of task and exposure counterbalanced</td>
<td>32</td>
<td>32</td>
<td>12.1yrs</td>
</tr>
<tr>
<td>Koivisto et al 1999</td>
<td>Subtraction</td>
<td>RT</td>
<td>Within-subject</td>
<td>GSM phone mounted on left side of head with antenna over left posterior temporal lobe, 902MHz, mean power 0.25W, pulsed</td>
<td>1hr on each of two successive days</td>
<td>Single</td>
<td>Order of exposure counterbalanced</td>
<td>48</td>
<td>48</td>
<td>26.0yrs</td>
</tr>
<tr>
<td>Haarala 2007</td>
<td>Subtraction</td>
<td>RT, ACC</td>
<td>Within-subject</td>
<td>Signal generator connected to Nokia 6110 MP antenna, 902MHz, 0.25W, exposure to left and right under continuous and pulsed wave</td>
<td>3 sessions 90mins each separated by 1 week</td>
<td>Double</td>
<td>Order of exposure, task and hemisphere counterbalanced</td>
<td>36</td>
<td>36</td>
<td>23.8yrs</td>
</tr>
<tr>
<td>Haarala et al 2003</td>
<td>Subtraction</td>
<td>RT, ACC</td>
<td>Within-subject</td>
<td>GSM phone mounted to left side of head with antenna, 902MHz, mean power 0.25W, pulsed</td>
<td>2 sessions of 65mins 24hrs apart</td>
<td>Double</td>
<td>Order of task and exposure counterbalanced</td>
<td>64</td>
<td>64</td>
<td>24.2yrs</td>
</tr>
<tr>
<td>Besset et al 2005</td>
<td>Digit span forward</td>
<td>ACC</td>
<td>Between-subject</td>
<td>GSM phone held against preferred ear with preferred hand, 900MHz, mean power 0.54W, pulsed</td>
<td>2hrs/day for 4 weeks (EP stage)</td>
<td>Double</td>
<td>Unknown</td>
<td>28</td>
<td>29</td>
<td>24.3yrs</td>
</tr>
<tr>
<td>Keetley et al 2006</td>
<td>Digit Span forward</td>
<td>ACC</td>
<td>Within-subject</td>
<td>GSM (Nokia 6110) headset with antenna clipped onto head against left ear, mean power 0.25W, pulsed</td>
<td>2 x 30min sessions 1 week apart</td>
<td>Double</td>
<td>Order of testing session and exposure counterbalanced</td>
<td>120</td>
<td>120</td>
<td>33yrs</td>
</tr>
<tr>
<td>Eltiti et al 2009</td>
<td>Digit Span forward</td>
<td>ACC</td>
<td>Within-subject</td>
<td>GSM signal combined 900 and 1800MHz; UMTS – 2020MHz</td>
<td>50mins</td>
<td>Double</td>
<td>Order of task and exposure counterbalanced</td>
<td>44</td>
<td>44</td>
<td>46.1yrs</td>
</tr>
</tbody>
</table>
### Electromagnetic fields and working memory

**Table 2: Potential source of bias for included studies based on the Cochrane Collaboration Risk of Bias Tool**

<table>
<thead>
<tr>
<th>Study reference</th>
<th>Type of study</th>
<th>Randomisation: Sequence generation</th>
<th>Randomisation: allocation concealment</th>
<th>Blinding of participants</th>
<th>Blinding of outcome assessors</th>
<th>Incomplete outcome data</th>
<th>Selective outcome reporting</th>
<th>No. of adequate ratings</th>
<th>Further details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haarala et al. 2004</td>
<td>Within subjects CO design</td>
<td>Inadequate</td>
<td>Inadequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>4/6</td>
<td>No information about sequence generation or allocation concealment</td>
</tr>
<tr>
<td>Koivisto et al. 2000</td>
<td>Within subjects CO design</td>
<td>Inadequate</td>
<td>Inadequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>4/6</td>
<td>No information about sequence generation or allocation concealment</td>
</tr>
<tr>
<td>Krause et al. 2007</td>
<td>Within subjects CO design</td>
<td>Inadequate</td>
<td>Inadequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>4/6</td>
<td>No information about sequence generation or allocation concealment</td>
</tr>
<tr>
<td>Haarala et al. 2007</td>
<td>Within subjects CO design</td>
<td>Inadequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>5/6</td>
<td>No information about sequence generation provided</td>
</tr>
<tr>
<td>Haarala et al. 2005</td>
<td>Within subjects CO design</td>
<td>Inadequate</td>
<td>Inadequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>4/6</td>
<td>No information about sequence generation or allocation concealment</td>
</tr>
<tr>
<td>Koivisto et al. 1999</td>
<td>Within subjects CO design</td>
<td>Inadequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>5/6</td>
<td>No information about sequence generation provided</td>
</tr>
<tr>
<td>Haarala et al. 2003</td>
<td>Within subjects CO design</td>
<td>Inadequate</td>
<td>Inadequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>4/6</td>
<td>No information about sequence generation or allocation concealment</td>
</tr>
<tr>
<td>Besset et al. 2005</td>
<td>Between subjects design</td>
<td>Inadequate</td>
<td>Inadequate</td>
<td>Inadequate</td>
<td>Inadequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>4/6</td>
<td>No mention of randomisation, sequence generation, allocation of concealment, blinding of participants or outcome assessors</td>
</tr>
<tr>
<td>Keetley et al. 2006</td>
<td>Within subjects CO design</td>
<td>Inadequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>5/6</td>
<td>No information about sequence generation provided</td>
</tr>
<tr>
<td>Eltiti et al. 2009</td>
<td>Within subjects CO design</td>
<td>Adequate</td>
<td>Inadequate</td>
<td>Inadequate</td>
<td>Inadequate</td>
<td>Adequate</td>
<td>Adequate</td>
<td>3/6</td>
<td>No information about allocation of concealment or blinding of participants or outcome assessors</td>
</tr>
</tbody>
</table>
Electromagnetic fields and working memory

Table 3: Homogeneity Measures, P-Values, SMD and 95% Confidence Intervals for Working Memory Tasks under the pulse/continuous and left/right conditions averaged

<table>
<thead>
<tr>
<th>Task</th>
<th>No. of studies/participants</th>
<th>RE pooled estimate (SMD)</th>
<th>95% CI</th>
<th>X²</th>
<th>Heterogeneity (p-value)</th>
<th>Overall effect: Z</th>
<th>Overall effect: P</th>
<th>I²</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-back RT a</td>
<td>5/216</td>
<td>0.01</td>
<td>-0.18, 0.20</td>
<td>1.25</td>
<td>0.87</td>
<td>0.11</td>
<td>0.91</td>
<td>0%</td>
</tr>
<tr>
<td>1-back RT a</td>
<td>5/216</td>
<td>0.09</td>
<td>-0.10, 0.28</td>
<td>1.63</td>
<td>0.80</td>
<td>0.96</td>
<td>0.34</td>
<td>0%</td>
</tr>
<tr>
<td>2-back RT a</td>
<td>5/216</td>
<td>0.05</td>
<td>-0.14, 0.24</td>
<td>0.69</td>
<td>0.95</td>
<td>0.87</td>
<td>0.39</td>
<td>0%</td>
</tr>
<tr>
<td>N-back 3 RT a</td>
<td>5/216</td>
<td>-0.12</td>
<td>-0.31, 0.07</td>
<td>1.67</td>
<td>0.80</td>
<td>1.22</td>
<td>0.22</td>
<td>0%</td>
</tr>
<tr>
<td>0-back ACC a</td>
<td>5/216</td>
<td>0.05</td>
<td>-0.13, 0.24</td>
<td>0.40</td>
<td>0.98</td>
<td>0.56</td>
<td>0.58</td>
<td>0%</td>
</tr>
<tr>
<td>1-back ACC a</td>
<td>5/216</td>
<td>0.03</td>
<td>-0.16, 0.22</td>
<td>0.97</td>
<td>0.92</td>
<td>0.31</td>
<td>0.76</td>
<td>0%</td>
</tr>
<tr>
<td>2-back ACC a</td>
<td>5/216</td>
<td>-0.03</td>
<td>-0.22, 0.16</td>
<td>0.72</td>
<td>0.95</td>
<td>0.34</td>
<td>0.73</td>
<td>0%</td>
</tr>
<tr>
<td>3-back ACC a</td>
<td>5/216</td>
<td>-0.02</td>
<td>-1.30, 1.26</td>
<td>0.56</td>
<td>0.97</td>
<td>0.03</td>
<td>0.98</td>
<td>0%</td>
</tr>
<tr>
<td>Subtraction RT b</td>
<td>3/112</td>
<td>-0.06</td>
<td>-0.32, 0.21</td>
<td>0.04</td>
<td>0.98</td>
<td>0.41</td>
<td>0.68</td>
<td>0%</td>
</tr>
<tr>
<td>Digit span ACC c</td>
<td>3/219</td>
<td>-0.13</td>
<td>-0.32, 0.06</td>
<td>4.05</td>
<td>0.17</td>
<td>1.37</td>
<td>0.72</td>
<td>51%</td>
</tr>
</tbody>
</table>

*aHaarala et al. (2007); Krause et al. (2007); Haarala et al. (2005); Haarala et al. (2004); Koivisto et al. (2000).  
bHaarala et al. (2007); Haarala et al. (2003); Koivisto et al. (2000).  
cEltiti et al. (2009); Keetley et al. (2006); Besset et al. (2005).
### Table 4: Homogeneity Measures, P-Values, SMD and 95% Confidence Intervals for Working Memory Tasks under the pulsed, left exposure condition

<table>
<thead>
<tr>
<th>Task</th>
<th>No. of studies /participants</th>
<th>RE pooled estimate (SMD)</th>
<th>95% CI</th>
<th>$X^2$</th>
<th>Heterogeneity (p-value)</th>
<th>Overall effect: Z</th>
<th>Overall effect: P</th>
<th>$I^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-back RT a</td>
<td>5/216</td>
<td>0.00</td>
<td>-0.19, 0.19</td>
<td>1.40</td>
<td>0.84</td>
<td>0.01</td>
<td>0.9999</td>
<td>0%</td>
</tr>
<tr>
<td>1-back RT a</td>
<td>5/216</td>
<td>0.03</td>
<td>-0.16, 0.23</td>
<td>0.52</td>
<td>0.97</td>
<td>0.35</td>
<td>0.72</td>
<td>0%</td>
</tr>
<tr>
<td>2-back RT a</td>
<td>5/216</td>
<td>0.06</td>
<td>-0.13, 0.25</td>
<td>0.74</td>
<td>0.95</td>
<td>0.44</td>
<td>0.66</td>
<td>0%</td>
</tr>
<tr>
<td>N-back 3 RT a</td>
<td>5/216</td>
<td>-0.15</td>
<td>-0.34, 0.04</td>
<td>1.08</td>
<td>0.90</td>
<td>1.55</td>
<td>0.12</td>
<td>0%</td>
</tr>
<tr>
<td>0-back ACC a</td>
<td>5/216</td>
<td>0.10</td>
<td>-0.09, 0.29</td>
<td>0.57</td>
<td>0.97</td>
<td>1.07</td>
<td>0.28</td>
<td>0%</td>
</tr>
<tr>
<td>1-back ACC a</td>
<td>5/216</td>
<td>0.04</td>
<td>-0.15, 0.23</td>
<td>1.23</td>
<td>0.87</td>
<td>0.38</td>
<td>0.71</td>
<td>0%</td>
</tr>
<tr>
<td>2-back ACC a</td>
<td>5/216</td>
<td>-0.02</td>
<td>-0.21, 0.17</td>
<td>0.77</td>
<td>0.94</td>
<td>0.21</td>
<td>0.84</td>
<td>0%</td>
</tr>
<tr>
<td>3-back ACC a</td>
<td>5/216</td>
<td>0.03</td>
<td>-0.17, 0.22</td>
<td>0.64</td>
<td>0.96</td>
<td>0.25</td>
<td>0.80</td>
<td>0%</td>
</tr>
<tr>
<td>Subtraction RT b</td>
<td>3/112</td>
<td>-0.06</td>
<td>-0.32, 0.21</td>
<td>0.04</td>
<td>0.98</td>
<td>0.41</td>
<td>0.68</td>
<td>0%</td>
</tr>
<tr>
<td>Digit span ACC c</td>
<td>3/219</td>
<td>-0.13</td>
<td>-0.32, 0.06</td>
<td>4.05</td>
<td>0.13</td>
<td>1.37</td>
<td>0.17</td>
<td>51%</td>
</tr>
</tbody>
</table>

[a] Haarala et al. (2007); Krause et al. (2007); Haarala et al. (2005); Haarala et al. (2004); Koivisto et al. (2000).
[b] Haarala et al. (2007); Haarala et al. (2003); Koivisto et al. (2000).
[c] Eltiti et al. (2009); Keetley et al. (2006); Besset et al. (2005).
Electromagnetic fields and working memory

Figure 2: Funnel plots for all three tasks included, under each task condition.
Electromagnetic fields and working memory

REFERENCES


Cochrane Collaboration (online). Available at: [http://www.cochrane.org](http://www.cochrane.org)


Electromagnetic fields and working memory


Electromagnetic fields and working memory


