RECORDING EEG DURING REPETITIVE TRANS-CRANIAL MAGNETIC STIMULATION

Hubert de Bruin, Mark Archambeault, Trung Trinh and Gary Hasey
Dept. of Electrical and Computer Engineering, Dept of Psychiatry and Behavioural Neurosciences
McMaster University, Hamilton, Ontario, Canada

Keywords: rTMS, Stimulus artefact, Electrode heating, Artefact reduction, EEG, Trans-cranial magnetic stimulation, Evoked potentials.

Abstract: This paper discusses several issues related to recording EEG during repetitive trans-cranial magnetic stimulation (rTMS). The objective of recording EEG is to obtain magnetically evoked and event related potentials. The issue of electrode heating is discussed and experimental results presented that show graphite as well as fully notched or "C" silver, gold or silver-silver chloride are suitable for current rTMS protocols. Standard silver or gold cup electrodes may cause excessive scalp heating. Removal or reduction of the magnetically induced stimulus artefact is also discussed. A new system is presented that uses sample and hold circuitry to block most of the artefact allowing the researcher to record ipsi- and contra-lateral evoked potentials occurring within the first few milliseconds of the magnetic stimulus.

1 INTRODUCTION

Trans-cranial magnetic stimulation (TMS) has been used during the past two decades to elicit responses in the human brain. At first this modality was suggested as a technique for studying upper motor neuron health and function. This involved placing a coil, either circular or "figure of eight" on the scalp with its centre of strongest magnetic field over an area of the motor cortex and exciting the underlying cortical tissue with 300 – 400 µsec monophasic or biphasic pulse. The response could be immediately measured by recording the M-wave from the muscle, usually the thenar, innervated by the upper motor neurons under the coil. However, in recent years, repetitive TMS has been proposed and used to treat neuro-psychiatric disorders such as depression by stimulating the medial frontal cortex (e.g. Fitzgerald et al, 2003 and Hoffman et al, 2005). Since there are no immediate recordable results such as the M-wave for these sites, stimulus amplitudes have been chosen by first determining the motor cortex threshold and using a fraction, usually from 80 to 120% of this value. As well the stimulus site and repetition frequency are chosen by convention rather than patient responses. However, There is very good evidence that the cortical responses are very dependent on the stimulus site with some sites even having no or very limited responses (Komssi et al, 2002). It has also been found that even the motor threshold varies considerably intra-subject from session to session (Wasserman, 2002) and there is considerable evidence that frontal lobe thresholds are higher than motor cortex thresholds (Kähkönen, 2005). If one could record the immediate brain evoked potentials (EP), or event related potentials (ERP), stimulus amplitude, frequency and site could be customized for each subject. This approach will also allow us to gain valuable insight and knowledge about the mechanisms of rTMS applied to the frontal lobes. However, the very large magnetic fields associated with 1 to 3 Tesla TMS pulses couple into the patient electrodes, electrode cables and input amplifiers resulting in very large voltage artefacts that can saturate the input amplifiers for up to 500 ms. This paper discusses issues related to recording EEG during rTMS and presents a new system for recording magnetically evoked EPs and ERPs

2 ELECTRODE SELECTION

Not only does the very high magnetic field induce currents in the cortex and deeper brain structures it

de Bruin H., Archambeault M., Trinh T. and Hasey G. (2009).
RECORDING EEG DURING REPETITIVE TRANS-CRANIAL MAGNETIC STIMULATION.
In *Proceedings of the International Conference on Bio-inspired Systems and Signal Processing*, pages 265-272
DOI: 10.5220/0001534102650272

also induces currents in the electrodes that are being used to record the EEG. This induced current flow will heat the electrodes. The temperature increase of an electrode per stimulus is directly related to the electrical conductivity of the electrode, the square of the radius of the electrode and the square of the stimulus strength (Roth, 1992). The conductivity of materials tested is: Silver 62.9x10^{6} S/m, Gold 41.0x10^{6} S/m, Carbon 0.029x10^{6} S/m (Serway, 2000), which suggests that silver electrodes will heat the most per stimulus, while carbon electrodes will heat the least per stimulus.

The safe temperature an electrode can reach without causing cutaneous damage depends on the exposure time. Figure 1 shows the time-surface temperature threshold for first degree thermal injury. Given that current rTMS treatment can include as many as 2,400 pulses at a frequency of 0.25Hz up to 20Hz, electrode heating is a concern for causing thermal skin damage. Looking at Figure 1, we see that for a 30 minute study, 46°C is the hottest temperature any scalp EEG electrode should be allowed to heat to.

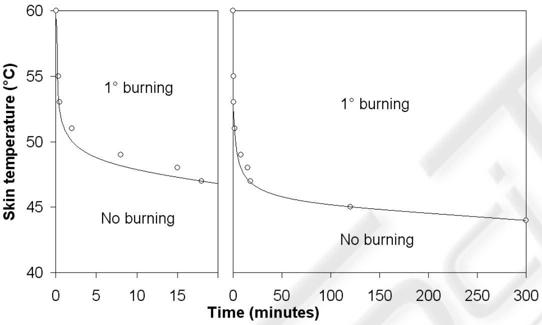

Figure 1: Time-temperature thresholds for burning of human skin. Source: Moritz et al, 1947.

2.1 Electrode Testing

We decided to test a number of common and modified EEG electrodes to determine which are suitable for recording during rTMS. Temperature was measured using a thermistor temperature probe with 0.01°C accuracy (Digi-Sense LN5775, Cole-Parmer, Illinois) calibrated to +/- 0.2°C and read to 0.1°C. The TMS machine used was a Magstim Super Rapid. The TMS coil used was a Magstim figure-of-eight air-cooled coil P/N 1640 (Inner diameter 56mm, outer diameter 87mm, 9x2 turns, 16.4µH inductance, 0.93Tesla peak magnetic field). Four commercially available EEG electrode types were tested: (i) XLTEK reusable EEG/EP electrodes Part no. #101339 (silver cup, 10mm diameter, 2mm hole); (ii) Standard gold cup electrodes (10mm diameter, 2mm hole); (iii) Ag/AgCl surface electrodes model F-E5SCH-48 (10mm diameter, 2mm hole, Grass Technologies); (iv) EL258RT reusable general purpose 8mm diameter, no hole, radio-translucent carbon electrodes with carbon leads (Biopac Systems Inc.). Several gold and silver cup electrodes were pie-notched and a gold plated silver cup electrode (10mm diameter, 2mm hole, Nicolet) was fully notched (C notched) to reduce induced current as shown in Figure 2.

All testing used a sheet of plywood that was marked with a 1cm grid pattern to help ensure accurate coil placement. Electrodes were attached using EEG paste (Ten20 conductive EEG paste). The coil was placed so that the electrode was in the area of maximum field induced heating as shown in Figure 3. This position agreed with previous findings (Roth et al 1992). The testing parameters used in this study mirrored those used in standard rTMS treatments: 10Hz stimulation for up to 8s trains and 20Hz stimulation for up to 3s trains; stimulus intensity was set at 85% of our machine's maximum to slightly exceed 110% of motor threshold (MT) of an average subject at our own and other rTMS laboratories (Thut et al, 2005).

Figure 4 shows the heating and cooling curves for the 6 different electrodes tested with 3s 20Hz trains at the maximum heating location (r = 30mm). A second test was performed to simulate a full treatment session where trains of 60 to 80 stimuli are given at 1 minute intervals for a total of up to 3000 stimuli. Figure 5 gives the test results for a gold cup electrode using only three trains of 60 stimuli at 20 Hz. As can be seen the electrode temperature would soon rise above the maximum allowable 46° C if more trains were given.

Carbon electrodes were also tested at 20Hz for 3s, 85% intensity, and 20Hz for 10s, 100% intensity and showed 0.0°C and 0.8°C temperature rise respectively. Repeating the 100% test with no electrode resulted in 0.3°C temperature rise, showing that the probe accounted for some of the increase in temperature when 200 pulses were given.

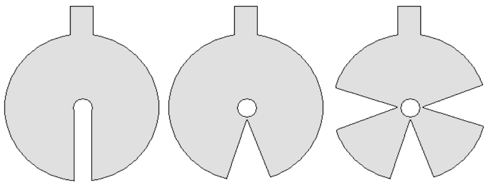

Figure 2: Notched electrodes. From left to right: C notched, pie notched, triple pie notched.

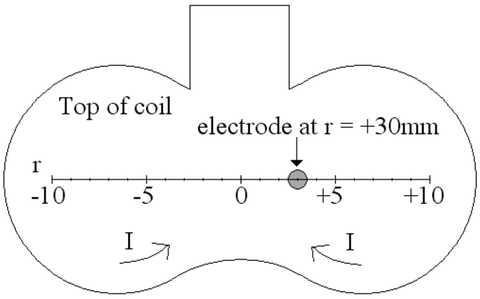

Figure 3: Stimulating coil showing how electrodes were positioned underneath with respect to the r-axis, labeled in cm.

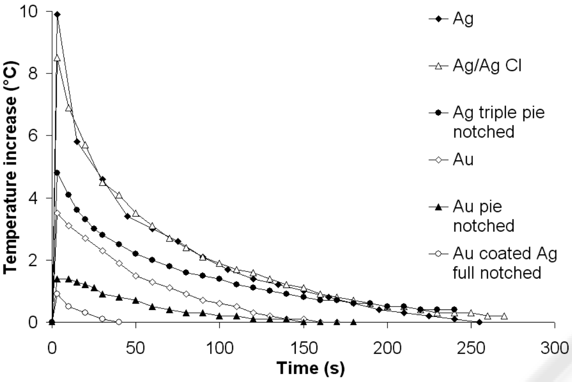

Figure 4: Temperature effects for 6 different electrodes from a single train of 3s at 20Hz at 85% intensity, r = 30 mm.

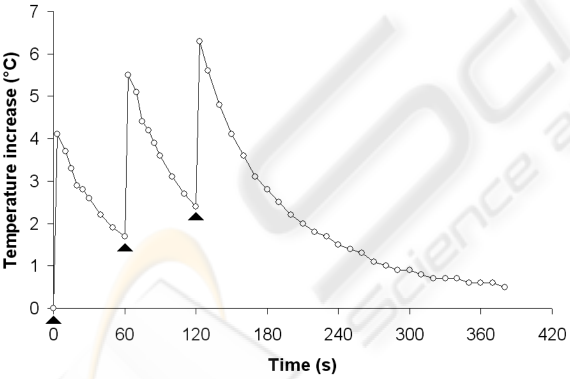

Figure 5: Temperature effects on gold cup electrodes from 3 trains of 3s at 20Hz at 85% intensity, r = 30 mm. Trains were given at 0s, 60s, and 120s.

2.2 Electrode Guidelines

Unmodified silver and silver/silver chloride electrodes appear unsuitable for standard rTMS-EEG studies when high stimulus intensities are necessary, due to the high conductivity of silver. If used at all, pulse trains should not exceed 30 pulses and electrodes should be allowed 290s to cool between trains, given the current TMS and coil parameters tested. Gold cup electrodes are suitable for rTMS-EEG studies for a Magstim cooled coil if stimulus intensity is kept below 85%, trains do not exceed 80 pulses, and electrodes are allowed to cool for 220s between stimulus trains. However, notching does work, and when notched properly (a full notch or C) electrode heating is reduced enough to make silver and gold-plated silver electrodes suitable for a standard rTMS-EEG study. The newly available carbon electrodes should be suitable for any rTMS-EEG patient study and their heating would not be the limiting factor in selecting stimulating parameters. However, they are about three times the cost of Ag/AgCl electrodes.

3 ARTEFACT REDUCTION

Most modern commercial EEG systems are protected from large voltage transients both by input protection diodes and low pass filtering of the EEG signal, typically below 70 Hz. Figure 6 shows the average EEG recorded from a standard Ag cup electrode at FP2 using a commercial EEG system (XLTEK desktop EEG, Oakville, Ontario, Canada), for six high amplitude TMS pulses delivered at the F3 position. Although the amplifier hasn't saturated the artefact lasts at least 100 ms obscuring any EPs and even some shorter latency ERPs. Several researchers (Ives et al, 2006 and Fuggetta et al 2005) have attempted to reduce this TMS stimulus artefact, recorded using commercial EEG systems, by designing low slew rate preamplifiers. Although this approach is successful if only long latency ERPs are considered, this low bandwidth is inadequate to preserve the much higher frequency EPs. Further, the sampling rate of commercial EEG systems (200 – 500 Hz) is too low to represent EPs.

Virtanen et al (1999) developed a multi-channel EEG system with artefact blocking hardware to record both EPs and ERPs following TMS. However, this system cannot record EPs occurring during the first 4 ms following stimulation and the sampling rate of 1000 Hz is too low to fully capture the shape of very short duration EPs. We have also developed an artefact blocking system based on sample and hold circuitry similar to Virtanen et al's approach. An earlier version (Archambeault and de Bruin, 2007) was designed as a blocking preamplifier for commercial EEG systems. However, the sampling rates possible for these systems are inadequate for multichannel EP recording.

3.1 A New System

We decided to implement a 16 channel EEG system with the previous artefact blocking amplifiers using the virtual instrument language Labview running on a standard PC equipped with a National Instruments DAQ interface. As shown in Figure 7, the DAQ analog outputs are used to control the sample and hold circuit for each channel and trigger the magnetic stimulator. The system has selectable hold time window duration and the stimulator trigger time within this window. The user can also select the channel sample rate, total signal period, stimulus rate and the number of stimuli given. During rTMS the channel recordings are continually displayed for analysis and verification, and synchronously averaged for background EEG and instrumentation noise reduction. Following completion of the stimulus train the averge signal for each channel is stored in an EXCEL format file for further signal processing and analysis using programs such as Matlab. This gives us a very flexible clinically friendly system with aggregate sampling rates up to 200 KHz (at least 10 KHz per channel). This system can easily be upgraded to 32 channels with different DAQ hardware.

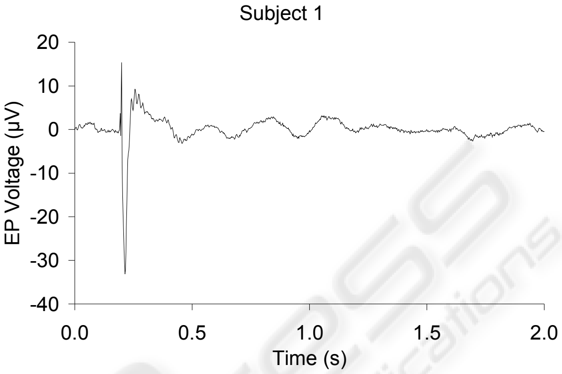

Figure 6: Averaged ERP, created from six ERPs recorded with XLTEK EEG machine. TMS over left hemisphere frontal cortex. EEG recorded from right hemisphere frontal cortex.

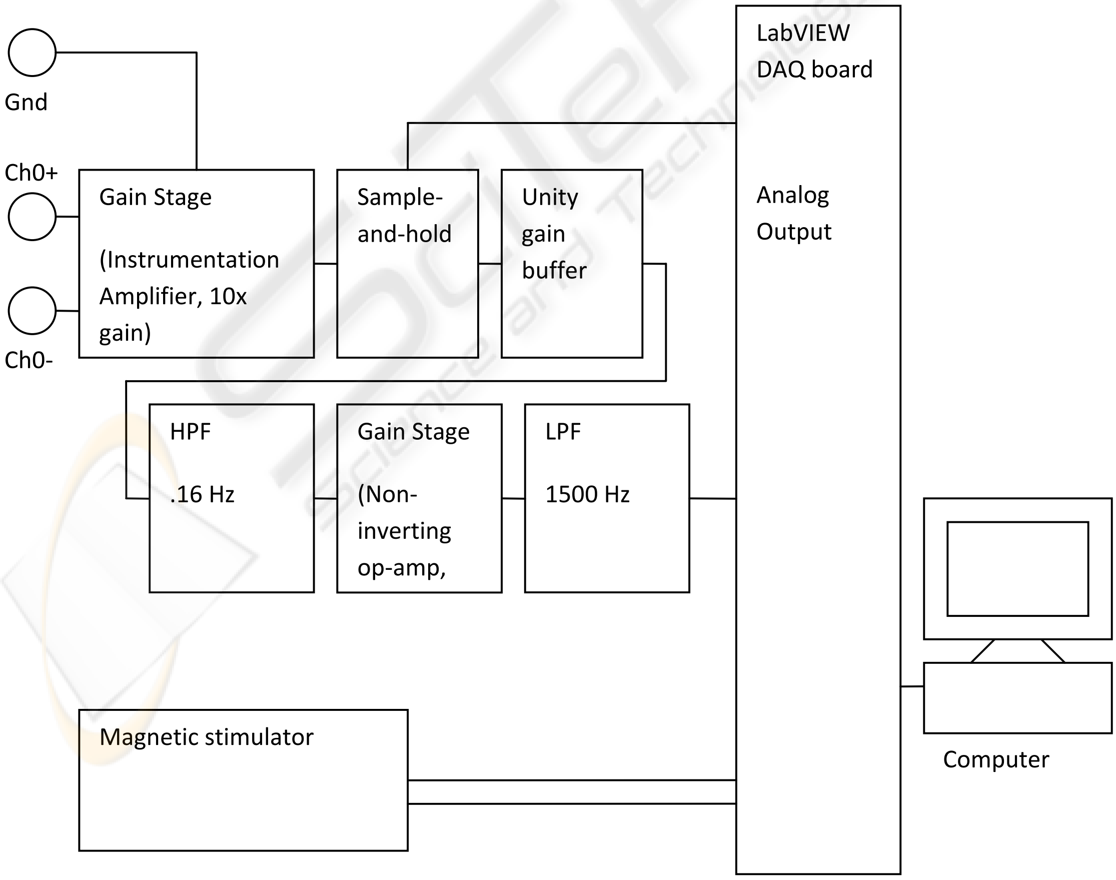

Figure 7: Artefact blocking EEG machine design using the sample-and-hold (blocking) approach (one channel shown).

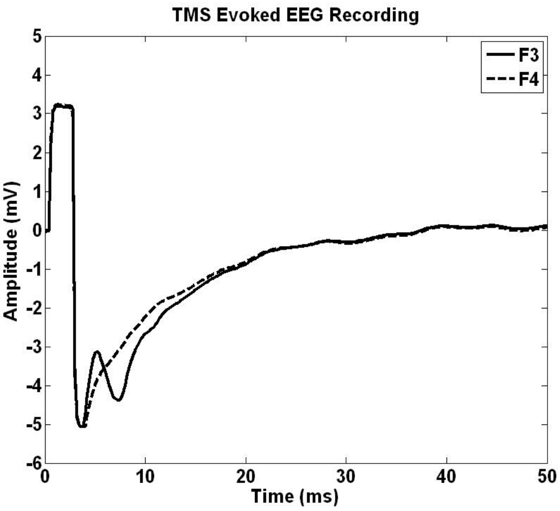

Figure 8: EEG responses for medial left frontal lobe stimulation at F3 at 66% maximum amplitude.

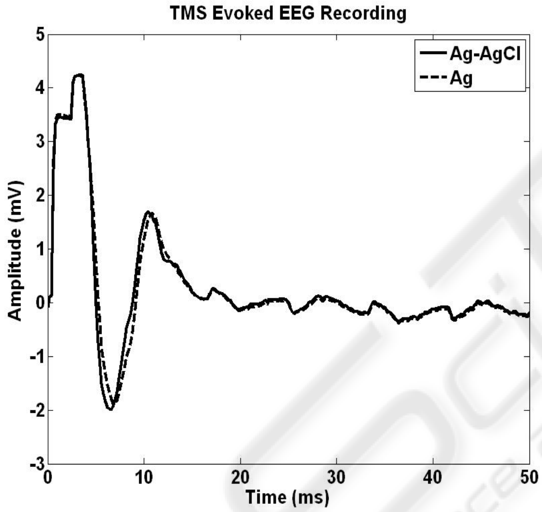

Figure 9: EMG responses for left thenar muscle for two recording electrodes, Ag and AgCl for wrist stimulation at 90% maximum amplitude.

3.2 System Tests

The system was tested to determine whether the blocking circuit could manage large magnetic artefacts and which hold window durations were suitable. A 24 year old subject was instrumented with Grass 10 mm Ag/AgCl electrodes at F3 and F4, the right mastoid (reference) and the neck (ground). 60 magnetic pulses at a rate of 2 Hz were given near F3 in the medial frontal lobe at 66% of the maximum amplitude of a Magstim Super Rapid stimulator. The hold time duration was set to 2.6 msec with the stimulus trigger command given at 0.3 msec after the start of the sample and hold command. The signals were collected for 100 msec at 5 KHz sample rate. Figure 8 shows the average EEG signals for both locations.

In this figure the first rectangular pulse is the offset voltage applied by the sample and hold circuit and can be viewed as the total hold window. Unfortunately both Labview and the Magstim control program are Windows based and there is some uncertainty that the magnetic stimulus is given at the precise time (0.3 msec after the start of hold). The maximum artefact block in this case is 2.3 msec but it could be less. The negative excursion is due to the residual stimulus artifact, which decays exponentially toward the baseline. The F3 signal shows the evoked muscle M-wave resulting from magnetic stimulation of the temporalis muscle under the coil. This usually occurs within 1 msec of the magnetic motor point stimulation. F4, as expected shows no muscle response and only the decaying artefact, which is almost the same size as the F3 artefact. Both signals were heavily contaminated by 60 Hz and other environmental noise and, although not synchronized to the stimuli, were still not entirely removed by averaging. The laboratory contained a number of high power instruments with large transformers resulting in very large 60 Hz ambient noise. Because of the residual noise in the signal we cannot be sure the small μvolt excursions were brain evoked potentials.

The duration and amplitude of the artefact are determined by stimulus amplitude and shape, as well as the impedances of the electrodes, electrode wires and input amplifier. If these impedances were purely resistive, the artefact would last no longer than the stimulating pulse (400μsec). We wanted to address the issue whether polarisable or non-polarisable electrodes would result in less artefact. The hypothesis was that a non-polarisable electrode such as Ag-AgCl would store less artefact energy because of their low capacitance. Ag or Au commercial polarisable electrodes, on the other hand would store more energy resulting in a larger residual artefact when the sample and hold circuit reconnected the electrodes to the amplifier.

The left thenar muscle of a 24 year old male was instrumented with two electrodes, Ag-AgCl and Ag, in close proximity. A reference Ag-AgCl electrode distal to the second joint of the thumb and a ground Ag-AgCl electrode on the dorsum of the hand. The Magstim figure-of-eight coil was placed at the wrist, 5 cm equidistance from the two thenar electrodes. The sample and hold circuitry was set to block the artefact a maximum of 1.7 msec after the stimulus was given . A single 90% maximum amplitude stimulus pulse was given by the Magstim and 100 msec of signal recorded from both electrodes at 5 KHz sample rate. Figure 9 shows the first 50 msec of the unprocessed signals.

As for Figure 8, the hold window of 2.0 msec appears first, followed by a rise to approximately 4.25 mV (amplifier saturation) due to the residual stimulus artefact. The resulting signal excursion is due to the evoked muscle M-wave and the decaying stimulus artefact. The signals after 15 msec are due to 60 Hz and other environmental noise. The M-waves and decaying stimulus artefacts are very similar with the Ag-AgCl signal decaying slightly faster. This could also be due to the slightly different M-waves recorded by the two electrodes. Lower levels of stimulation that resulted in much smaller M-waves showed the same similarities. At this point it must be concluded that the type of electrode has little effect on the residual stimulus artefact and our early hypothesis that non-polarisable electrodes would have lower magnetically induced artefacts was wrong.

3.3 Multi-Channel Tests

The multi-channel system was tested for 16 channels of evoked potentials recorded from a male subject instrumented using the standard 10-20 electrode configuration. The human tests were approved by the Research Ethics Board of St. Joseph's Health Care, Hamilton, Ontario, Canada. Figure 10 shows the averaged responses for 80 stimuli given at 8 Hz at 69% of the Magstim maximum amplitude (110% of the motor threshold) with the coil placed over Brodmann area 46. The signals were sampled at 5 KHz and bandpass filtered from 15 Hz to 2.5 KHz. At the scale shown all that can be seen are the very large amplitude muscle responses or M-waves from the underlying temporalis and occipitofrontalis muscles. The null response for F3 is a result of amplifier saturation since the coil was placed over F3 and the amplifier hold time was only 2 msec.
Figure 11 shows the same response starting at 15 msec with increased resolution. Fp1 shows EPs at 18 msec, while other EPs can also be seen at 47 and 85 msec in all channels. These synchronous EPs may be a result of using linked reference electrodes over the mastoid bone.

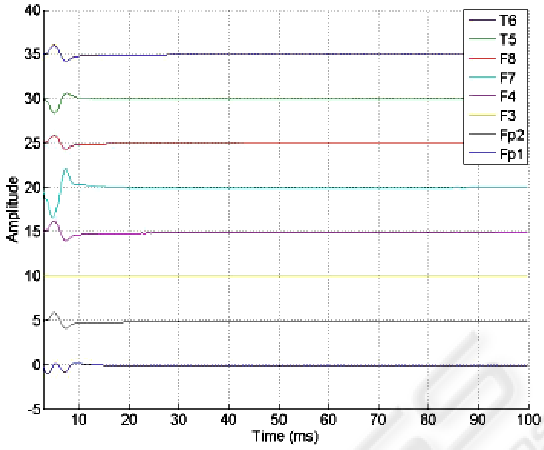

Figure 10: EEG averaged responses for 80 stimuli at 8 Hz, 69% max, Brodmann area 46. One unit = 1 mV, channels spaced by 5 mV.

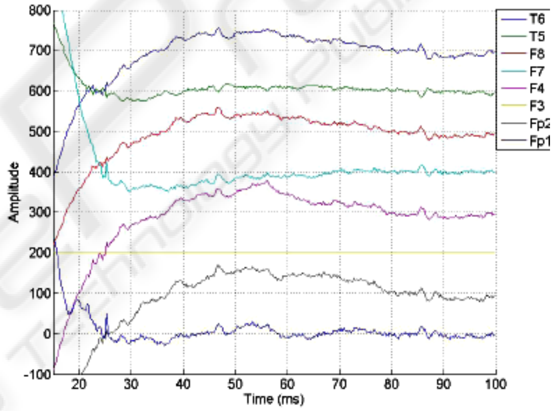

Figure 11: EEG averaged response of Fig. 10 One unit = 0.25 µV, channels spaced by 25 µV.

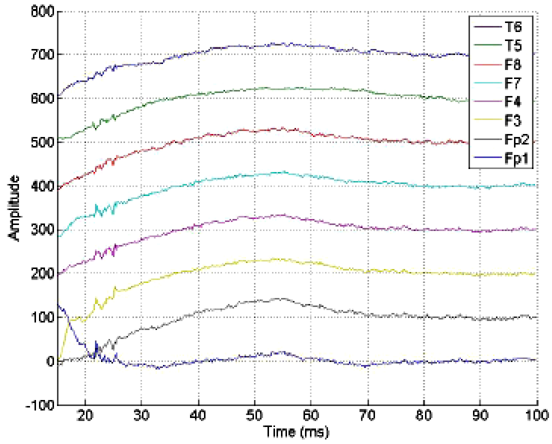

Figure 12: EEG averaged responses for 80 stimuli at 8 Hz, 69 % max, Brodmann area 9. One unit = 0.25 µV with channels spaced by 25 µV.

Figure 12 shows the results for the same stimulus train but with the coil placed over Brodmann area 9. Two features can be noted: (i) the F3 channel is not saturated since the coil was not immediately over the F3 electrode position and the pattern of EPs is different for that shown in Figure 11.

4 CONCLUSIONS

Our research has shown that standard commercial Au and Ag or Ag-AgCl EEG electrodes cannot be used for general rTMS applications, due to excessive skin heating. However, these electrodes can be used if fully or "C" notched. Further the choice among these electrodes does not seem to affect the amplitude or duration of the stimulus artefact. Although our heating results are in general agreement with the conclusions of previous researchers, the lack of dependency of the stimulus artefact amplitude on electrode material does not (Virtanen et al, 1999). Their results show that the amplitude depends mostly on electrode size and that Ag-AgCl electrodes had very low artefacts compared to Ag, although this could be a result of the very small Ag-AgCl pellet size. Further, their fully notched Ag standard electrodes had much lower artefact than the intact ones. The principle contributors to the stimulus artefact are not well understood, and electrode, wire and input amplifier capacitances all play a part. Even in a multichannel recording situation, where the magnetic field orientation and amplitude is very different for each electrode, the residual stimulus artefacts can be very similar as shown in Figure 8. Further research will be conducted to investigate the determining factors for magnetically induced artefacts and how common these are for all stimulating and recording conditions.

The new EEG system works very well, and depending on the stimulus strength, the amplifier can be reconnected to the recording electrodes with delays from 1 to 4 msec, allowing us to record EPs as well as ERPs. The initial voltage offset introduced by sample and hold circuitry, shown as the square pulse in Figures 8 and 9, can be ignored and does not affect the signal when the block is terminated. Tests with the stimulating coil at some distance from the electrodes resulting in very low short duration artefacts have shown that the amplitude returns to baseline within µsec. The test results shown in this paper were for worst case scenario experiments with large stimulus amplitudes and the coil either directly over the recording electrodes or in close proximity. However, the system must be made more immune to environmental noise by better shielding and cabling.

Future work will include postprocessing to estimate and remove the exponentially decaying residual artefact and periodic environmental noise. Although synchronous averaging can remove asynchronous environmental noise if enough stimuli are given, the technique is inefficient. The number of stimuli presented to the brain should be determined by clinical efficacy rather than noise reduction.

The multi-channel results show that even when stimulus artefact is removed new signal processing techniques will have to be developed to model and remove the muscle M-waves.

ACKNOWLEDGEMENTS

Support for this research from the Natural Sciences and Engineerung Research Council of Canada is gratefully acknowledged.

REFERENCES

Archambeault, M., de Bruin, H. 2007, Development of an electroencephalography data acquisition system for clinical research into transcranial magnetic stimultion evoked potentials, *Proc. IEEE Cdn. Conf. ECE*, Vancouver, pp 202 – 205.

Fitzgerald P.B., Brown, T.L., Marston, N.A., Daskalakis, Z.J., De Castella, A., Kulkarni, J. 2003, Transcranial magnetic stimulation in the treatment of depression: a double-blind, placebo-controlled trial. *Arch Gen Psychiatry* 60(10): 1002-1008.

Fuggetta, G., Fiaschi, A., Manganotti, P. 2005, A direct demonstration of cortical oscillatory activities induced by varying single-pulse transcranial magnetic stimulation intensity over the left primary motor area: a combined EEG and TMS study. *Neuroimage* 27(4): 896-908

Hoffman, R.E., Gueorguieva, R., Hawkins, K.A., Varanko, M., Boutros, N.N., Wu, Y.T., Carroll, K., Krystal, J.H. 2005, Temporoparietal transcranial magnetic stimulation for auditory hallucinations: safety, efficacy and moderators in a fifty patient sample. *Biol Psychiatry* 58(2): 97-104.

Ives, J.R., Rotenburg, A., Poma, R., Thut, G., Pascual-Leone, A. 2006, Electroencephalographic recording during transcranial magnetic stimulation in humans and animals. *Clin Neurophysiol* 117:1870-1875.

Kähkönen, S., Komssi, S., Wilenius, J., Ilmoniemi, R.J. 2005, Prefrontal TMS produces smaller EEG responses than motor-cortex TMS: implications for rTMS treatment in depression. *Psychopharmacology* 181:16-20

Komssi, S., Aronen, H.J., Huttunen, J., Kesäniemi, M., Soinne, L., Nikouline, V.V., Ollikainen, M., Roine, R.O., Karhu, J., Savolainen, S., Ilmoniemi, R.J. 2002, Ipsi- and contralateral EEG reactions to transcranial magnetic stimulation. *Clin Neurophysiol* 113:175-184.

Roth, B.J., Pascual-Leone, A., Cohen, L.G., Hallett, M., 1992, The heating of metal electrodes during rapid-rate magnetic stimulation: a possible safety hazard. *Electroencephalography and Clinical Neurophysiol* 85: 116-123.

Serway, R. A., Beichner, R. J. 2000, *Physics For Scientists and Engineers*. Orlando: Saunders College Publishing,.

Thut, G., Ives, J.R., Kampmann, F., Pastor, M.A., Pascual-Leone, A. 2005, A new device and protocol for combining TMS and online recordings of EEG and evoked potentials. *Journal of Neuroscience Methods* 141: 207-217.Virtanen, J., Ruohonen, J., Näätänen, R., Ilmoniemi, R.J. 1999, Instrumentation for the measurement of electric brain responses to transcranial magnetic stimulation. *Med Biol Eng Comput* 37:322-6.

Wassermann, E.M. 2002, Variation in the response to transcranial magnetic brain stimulation in the general population. *Clin Neurophysiol* 113:1165-1171