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Case Study

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# ENHANCEMENT OF COGNITIVE PROCESSING BY MULTIPLE SCLEROSIS PATIENTS USING LIQUID COOLING TECHNOLOGY: A CASE STUDY

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## ABSTRACT

**Introduction:** Cognitive dysfunction is a common symptom in patients with multiple sclerosis (MS). This can have a significant impact on the quality of life of both the patient and that of their primary care giver. This case study explores the possibility that liquid cooling therapy may be used to enhance the cognitive processing of MS patients in the same way that it provides temporary relief of some physical impairment. **Methods:** Two MS patients were presented a series of pattern discrimination tasks before and after being cooled with a liquid cooling garment for a one hour period. **Results:** The subject whose ear temperature was reduced during cooling showed greater electroencephalographic (EEG) activity and scored much better on the task after cooling. The patient whose ear temperature was unaffected by cooling showed less EEG activity and degraded performance after the one hour cooling period. **Discussion and Conclusions:** This case study indicates that "cooling therapy" may be used to temporarily improve the cognitive processing of MS patients. It also shows that the energy density analysis of topographic EEG can be used to assess the performance of cognitively impaired MS patients.

**KEYWORDS:** Multiple Sclerosis, Cooling Therapy, Cognitive Processing, Electroencephalography.

## INTRODUCTION

Recent neuropsychological studies demonstrate that cognitive dysfunction is a common symptom in patients with multiple sclerosis (Rao, 1990; Beatty, 1993). Prevalence estimates of cognitive impairment among MS patients range from 43% for a large community-based sample (Rao et. al., 1991) to 59% for a large clinic-based sample (Heaton, Nelson, Thompson, Burks, & Franklin, 1985). In many cases the presence of cognitive impairment affects the patients' daily activities to a greater extent than would be found due to their physical disability alone (Rao, Leo, Bernardin, & Unverzagt,1991). Cognitive dysfunction can have a significant impact on the quality of life of both the patient and that of their primary care giver. MS-related cognitive dysfunction most often affects short term memory recall and processing of verbal information (Fischer et. al. 1994).

Electroencephalographic multimodality evoked potential research was used (Phillips et. al., 1983; Beatty, 1993) to investigate the cognitive impairment associated with MS. These studies show that the degree of right-left asymmetry in the brain's neural activity is one measure of MS cognitive impairment. They also demonstrate that an MS patient's cognitive processing is very sensitive to hyperthermia. However, these studies were limited by the lack of indices of cortical localization and EEG activity to quantify a patient's short term neural response to evoked potential based investigations. Fischer et. al. (1994) have also stressed that more accurate methods for assessing the cognitive disturbance in MS must be developed before the effectiveness of various treatments can be validly evaluated.

## OBJECTIVES

The objectives of this research were.

a) to determine whether cooling of MS patients will enhance their cognitive function in much the same way as it has been shown to improve their physical abilities, and.

b) to demonstrate that new EEG/energy density analytical procedures, can be used to quantify the cognitive improvement of MS patients that may be produced by short term "cooling" therapy.

## METHODS

Two cognitively impared MS patients took part in this pilot study. The protocol was approved by the appropriate IRB and the subjects gave there informed consent to participate. The patients were given a visual discrimination task before and after a one hour cooling period. The subjects were presented a series of either red or blue circles or triangles. One of these combinations, or one fourth of the stimuli, was designated as the "target" presentation. The patients were asked to respond to each presented stimuli by pressing a yes or no button on a hand keypad. Patient "cooling" was accomplished using a Life Enhancement Technologies, Inc. (LET) Mark VII head and torso cooling garment.

Figure 1 shows the portable coolant thermal control and circulating cooling vest components of the LET cooling system. Figure 2 shows a patent fully instrumented for EEG measurements an wearing the LET cooling cap in addition to the vest in Figure 1.

**Figure 1: Coolant Reservior, Thermal Control and Coolant Circulating. Vest Components of the LET Cooling System**

**Figure 2: MS Patient Fully Instrumented for EEG Recordings Wearing the Coolant Vest Illustrated in Figure 1 and the LET Cooling Cap.**

EEG was recorded from 20 scalp electrodes using a Tracor Northern 7500 EEG/ERP system at the Wadsworth VA Hospital. Subject skin and rectal temperatures were recorded using a UFI, Inc. Biolog ambulatory monitoring system. Oral and ear temperatures were obtained and recorded manually every five minutes during the one hour cooling period. The EEG ERP signatures from each series of stimuli were analyzed using energy density procedures (Montgomery, Montgomery, & Guisado, 1992; Montgomery, Montgomery, & Guisado, 1993) to determine the locus of neural activity at each EEG sampling time.

After a training period to familiarize the patient with the test conditions, each patient was instrumented for EEG, using the International 10-20 system (Homan, 1988), and seated comfortably before a computer screen. A series of visual stimuli in the form of red squares, red triangles, blue squares and blue triangles were presented on the screen using a standardized format. The patient then decided whether a given individual stimulus belonged to the designated target series and indicated his choice by pressing an appropriate key pad. The patient's response automatically triggered presentation of the next stimulus after a five second delay.

This particular pattern discrimination task, may not necessarily represent all cognitive-related processing. However, it is particularly suited to measure inter-hemisphere interaction, which is affected by multiple sclerosis. The task requires recognition of shape and color as well as the subsequent motor performance in making a response.

The patient's average performance (errors and reaction time [RT - sec]) was automatically recorded and subsequently converted into an "Error Index" which combines both aspects of performance.

Error Index = RT (1 + [stimuli misidentified/total stimuli presented])

Each patient was given two series of cognitive tests; one prior to being cooled and one following a period of body cooling using the liquid cooling garment.

As can be seen from Figure 4 the patient's post cooling ERP amplitudes are markedly increased compared to his precooling traces, especially between 100 and 200 msec. and again at approximately 300 - 350 msec. No differences were found in the similar recordings for Subject One.

A novel feature of our research will be the conversion of the voltage ERPs into "energy density ERPs" so that scalp recorded surges in electrical energy rather than the resulting voltage fluctuations can be used as a measure of localized cortical activity (Montgomery & Gleason, 1992; Montgomery, Montgomery, & Guisado, 1992; Montgomery, Montgomery, & Guisado, 1993). In addition to improving the spatial resolution of scalp EEG data, the estimate of electrical energy has another important advantage: It permits time-integration. No meaning can be attached to the time-integral of voltage (and if DC variation has been filtered out during recording, the time integral will be zero). However, electrical energy is an inherently positive quantity and its time-integral is meaningful (it is electrical power.) Time integration of cortical energy over specified periods following stimulus presentation is useful because it facilitates quantitative cross-subject comparisons and statistical analyses. The more conventional approach to ERP analysis, which emphasizes the amplitude of selected ERP peaks, may obscure cross-subject comparisons because of slight differences in ERP latency and waveform among subjects.

**RESULTS**

Figure 3. shows the mean precooling (PRE) and postcooling (PST) ear temperature (TEMP), errors (ERROR), and cortical energy density (ENERGY) for the two subjects. The first subject's ear temperature did not decrease during the cooling period. It was actually elevated approximately 0.05°C by the end of the cooling period compared to his mean ear temperature during the control period. In turn, Subject One's discrimination performance and cortical energy remained essentially the same after body cooling. In contrast, Subject Two's ear temperature decreased ~ 0.8 °C during his cooling period. Subject Two's ERROR score decreased from 12 during the precooling control period to 2 after cooling. His ENERGY value increased approximately 300%, from a precooling value of approximately 200 to a postcooling value of nearly 600.

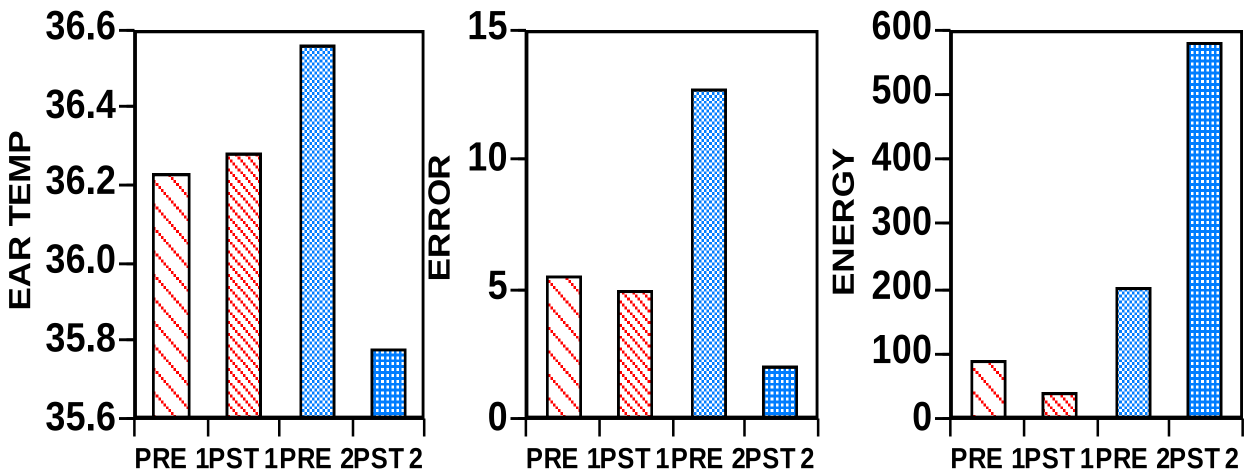


**Figure 3: Patient Performance Before and After Cooling.**

Figure 4. illustrates the individual pre (dotted traces) and postcooling (solid traces) energy density ERPs at each EEG electrode site for Subject Two. The vertical lines in Figure 4 denote every 100 msec. during the ERP. As can be seen from these traces, his post cooling ERP amplitudes are markedly increased compared to his precooling traces, especially between 100 and 200 msec. and again at approximately 300 - 350 msec. No differences were found in the similar recordings for Subject One.

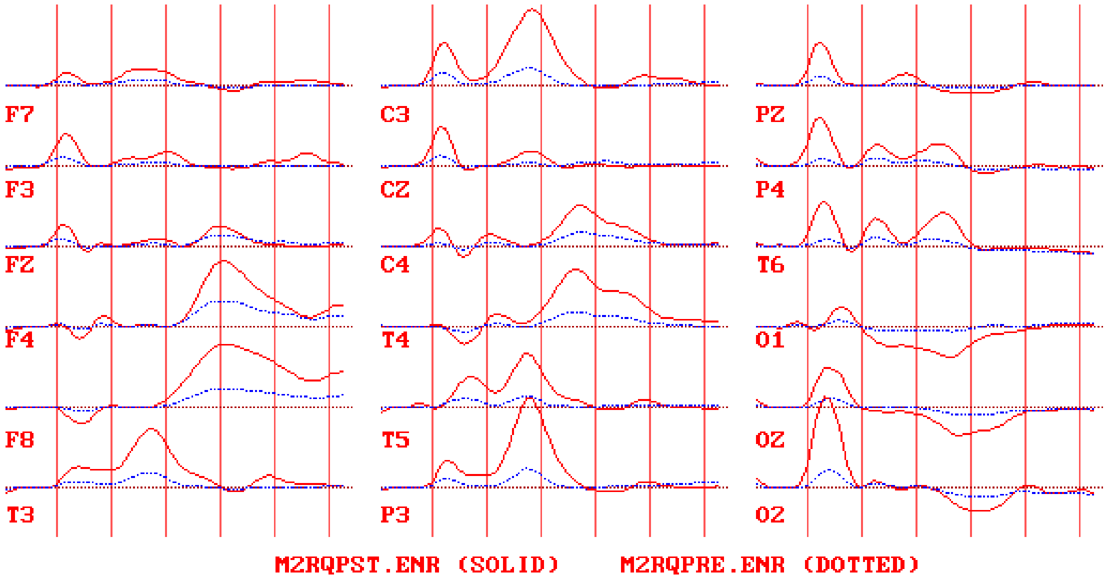


**Figure 4: Energy Density Evoked Responses for Patient Two Before (blue) and After (red) Cooling**

Figures 5 and 6 show the locus of peak energy activity throughout the duration of the 600 msec. ERP at the various electrode sites divided into 100 msec. intervals. The level of activity at each site is proportionatal to the diameter of the circle plotted in these figures. Subject Two showed a large increase in occipital activity between 100 and 200 msec. and a large increase in the left angular gyrus between 200 and 300 msec. after cooling.

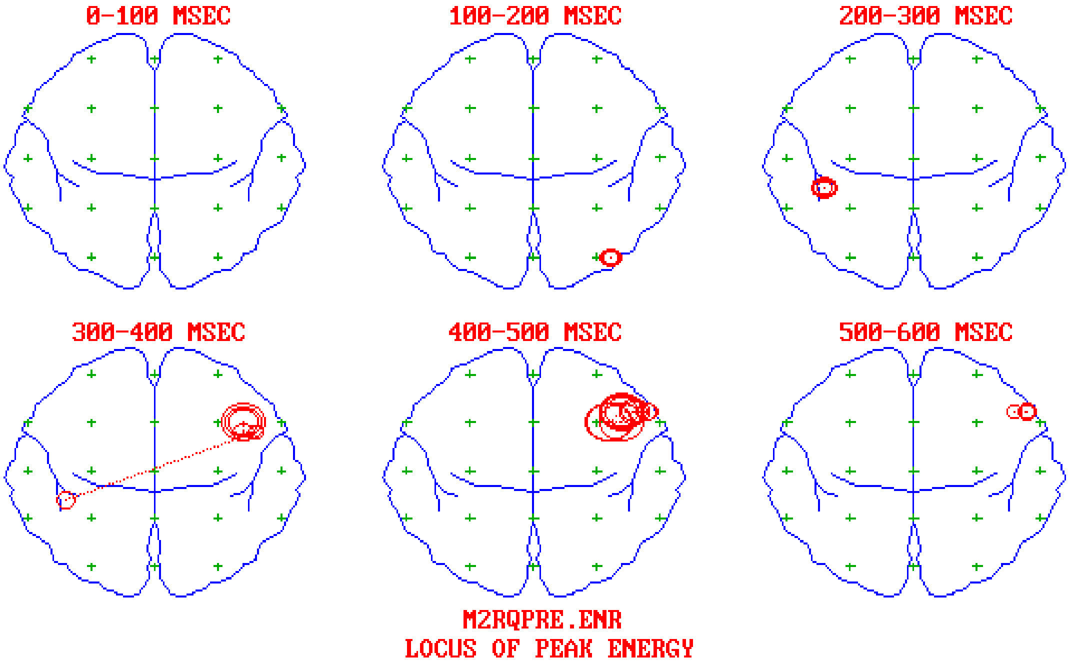


**Figure 5: Locus of Peak Energy for Patient Two Before Cooling.**

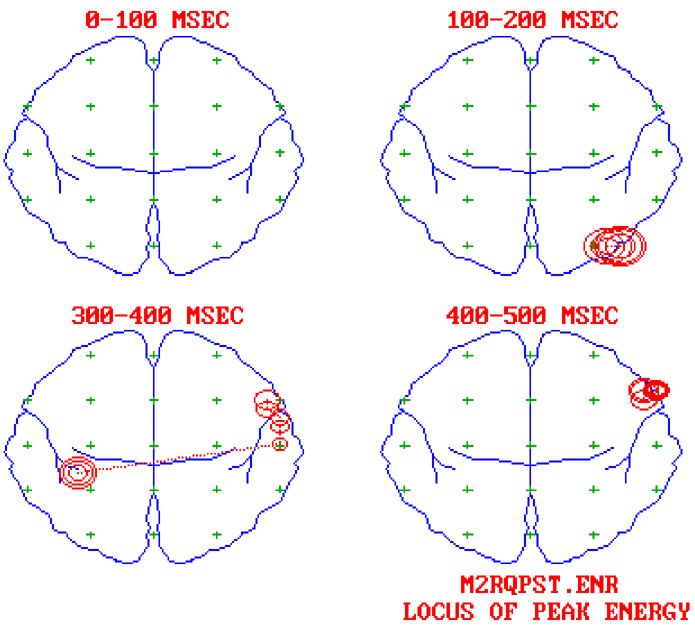


**Figure 6: Locus of Peak Energy for Patient Two After Cooling.**

## DISCUSSION

This case study indicates that "cooling therapy" may be used to temporarily improve the cognitive processing of MS patients. It also shows that the energy density analysis of topographic EEG can be used to assess the performance of cognitively impaired MS patients.

These findings might be interpreted by the following three-part hypothesis: 1) the general cognitive impairment of MS patients may be a result of low or unfocused metabolic energy conversion in the cortex; 2) such differences show up most strongly in reduced energy in the occipital region during the initial processing of the precooling period visual stimulus, which may indicate impaired early visual processing; 3) increased post cooling activation in the left angular gyrus, as evidenced by the higher P3/C3 energy peaks at 300 ms in Figures 4 and 6 may result in enhanced higher-level processing of information. By this hypothesis the superior performance of Subject Two following body cooling may be a result of increased neural activation in his early visual recognition and processing centers.

The application "cool suit" technology to cognitive enhancement of neurologic patients needs to be studied further. An enlarged study, such as the one described herein, is needed to conclusively establish the efficacy of cognitive enhancement due to cooling therapy.

## ACKNOWLEDGEMENT

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## REFERENCES

1. Beatty, W. W. (1993). Cognitive and emotional disturbances in multiple sclerosis. Neurol. Clin, 11: 189-204.
2. Fischer, J. S., Foley, F. W., Aikens, J. E., Ericson, G. W., Rao, S. M., & Shindell, S. (1994). What do we really know about cognitive dysfunction, affective disorders, and stress in multiple sclerosis? A practitioner's guide. J. Neuro. Rehab, 8(3): 151-164.
3. Guisado, R., Montgomery, L. D., & Montgomery, R. W. (1992). Electroencephalographic monitoring of complex mental tasks. Final Report NASA Contract NAS1-18847. NASA Langley Research Center, Hampton, VA.
4. Heaton, R. K., Nelson, L. M., Thompson, D. S., Burks, J. S., & Franklin, G. M. (1985). Neuropsychological findings in relapsing-remitting and chronic-progressive multiple sclerosis. J. Consult. Clin. Psychol, 53: 103-110.
5. Homan, R. (1988). The 10-20 system and cerebral location. Am. J. EEG Tech. 28: 269-279.
6. Montgomery, L. D., & Gleason, C. R. (1992). Simultaneous use of rheoencephalography and electroencephalography for the monitoring of cerebral function. Aviat. Space Environ. Med, 63: 314-321.
7. Montgomery, R. W., Montgomery, L. D., & Guisado, R. (1992). Cortical localization of cognitive function by regression of performance on event related potentials. Aviat. Space Environ. Med. 63, 919-924.

8. Montgomery, R. W., Montgomery, L. D., & Guisado, R. (1993). Electroencephalographic scalp energy analysis as a tool for investigation of cognitive performance. Journal of Biomedical Instrumentation and Technology, 27(2): 137-142.
9. Phillips, K. R., Potvin, A. R., Syndulko, K., Cohen, S. N., Tourtellotte, W. W., & Potvin, J. H. (1983). Multimodality evoked potentials and neurophysiological tests in multiple sclerosis: Effects of hyperthermia on test results. Arch. Neurology, 40: 159-164.
10. Rao, S. M. (1990). Neurobehavioral aspects of multiple sclerosis. New York: Oxford University Press.
11. Rao, S. M. (1994). The cognitive effects of multiple sclerosis. Multiple Sclerosis, 2(1): 2-5.
12. Rao, S. M., Leo, G. J., Bernardin, L., & Unverzagt, F. (1991). Cognitive dysfunction in multiple sclerosis, I: Frequency, patterns, and prediction. Neurology, 41: 685-691.
13. Rao, S. M., Leo, G. J., Ellington, L., Nauertz, T., Bernardin, L., & Unverzagt, F. (1991). Cognitive dysfunction in multiple sclerosis, II: Impact on social functioning. Neurology, 41: 692-696.