Towards therapeutic application of non-invasive whole-head cooling without sedation

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1. Introduction

Despite the best medical and surgical therapy, a significant number of epilepsy patients do not attain adequate seizure control, let alone a seizure-free state. New therapeutic options are necessary for those who are not eligible for or have failed surgery, and especially for patients with neocortical epilepsy who do not respond well to epilepsy surgery[1].

Clinical and experimental evidence suggests that hyperthermia decreases seizure threshold[2,3] and experimental data demonstrate that cooling of the cortex changes its electrical behavior[3-7] and may stop seizures[2, 3, 6, 7]. Cooling of the human brain has typically been performed under sedation or general anesthesia with or without the brain exposed [2-4, 8]. In this setting, the application of cold saline stops after-discharges induced by electrical stimulation, and intraoperative focal cooling of the cortex stops spontaneous interictal epileptiform discharges[8].

Hence, adequate cooling of the cortex may have therapeutic potential for epilepsy, but finding a feasible and safe approach is a requisite first step. Non-invasive whole head cooling without sedation[9] is an appealing choice, but its feasibility and safety have not been established.

2. Methods

Ten normal volunteers (5 females, 21-47 years old) underwent two cooling sessions (30 and 60 minutes) three days apart.

The subjects were comfortably seated in a reclining chair and covered with blankets to keep the body warm during cooling (Figure 1 D & E).

Figure 1: Cooling helmet on a model (A, B, C) and study participant before (D) and during (E) cooling. The temperature pill is shown in the insert of panel E.

Cooling was performed using a head-neck cooling system (CoolSystems Inc., **Figure 1 A, B & C**) consisting of a head/neck liner and conditioning unit.

Intestinal temperature, as an indicator of central core temperature (CT), was measured using a capsular probe (HQT Inc.; **Insert, Figure 1E**), and external temperature was measured from multiple sites on the head (scalp, ears, face and mouth) and elsewhere (forearm, abdomen and leg). Pulse and O2 saturation were monitored continuously.

3. Results

Thirty minutes of cooling produced a mean scalp temperature reduction of 12.4 °C (**Table 1**) and a mean ear temperature reduction of 1.09 °C (Data not shown, DNS). At the end of cooling, the mean CT was decreased by 0.06 °C. At the end of 60 minutes of cooling, scalp temperature fell an average of 12.2 °C, and ear temperature 1.67 °C (DNS). The mean CT was decreased by 0.12 °C.

Table 1: Scalp and CT changes from baseline in 10 studied volunteers (°C). "-"indicates decrease, and no "-" indicates increase. Data from the patient shown on the **Figure 2** are in bold.

Subject	30 minutes		60 minutes	
	Scalp	CT	Scalp	CT
Males				
47 y/o	-12.2	0.12	-11.6	-0.24
25 y/o	-16.8	-0.09	-11.7	0.26
35 y/o	-15.6	-0.27	-14.0	-0.37
34 y/o	-13.6	-0.08	-15.9	0.05
27 y/o	**-12.0**	**-0.21**	**-13.8**	**-0.47**
Mean	**-14.0**	**-0.11**	**-13.4**	**-0.15**
Females				
21 y/o	-10.2	0.02	-10.0	0.2
22 y/o	-13.8	0.09	-11.4	0.08
21 y/o	-5.8	0.06	-9.8	-0.16
44 y/o	-11.0	-0.09	-12.5	-0.48
27 y/o	-12.7	-0.15	-11.1	-0.06
Mean	**-10.7**	**-0.01**	**-11.0**	**-0.08**
Overall mean	**-12.4**	**-0.06**	**-12.2**	**-0.12**

Figure 2 A. Scalp and CT changes before, during and after 60-minute cooling in a 27-year old male. Arrows indicate start (↑) and end (↓) of cooling.

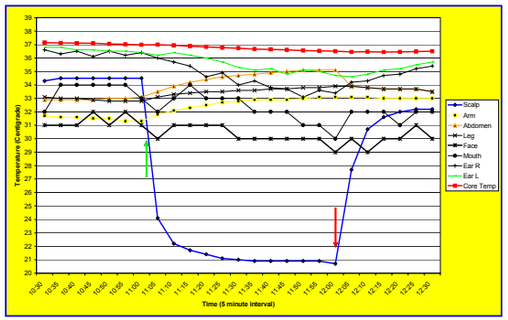
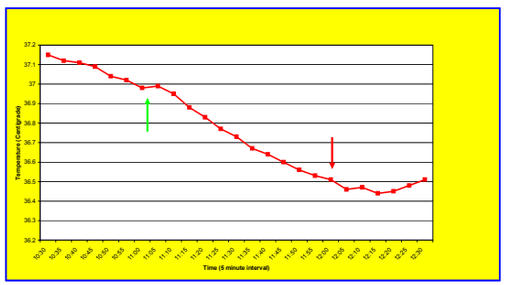


Figure 2 B. CT changes before, during, and after 60-minute cooling in the same subject. Arrows indicate start (↑) and end (↓) of cooling.



The difference between the beginning and end of cooling was statistically significant for scalp temperature ($p < 0.0001$) and tympanic temperature (right $p<0.0001$, left $p<0.0003$; DNS), but not for CT ($p=0.2166$). There was no statistical difference in degrees of temperature changes between males and females except for a scalp temperature change at the end of 60 minutes of cooling ($p=0.0235$).

During both cooling sessions, temperatures from the arm, abdomen, and leg remained unchanged, as did pulse and O2 saturation (DNS).

There were no changes in subjects' physical examination after cooling, and the subjects reported no complaints that necessitated interruption of cooling.

4. Discussion

This is the first study to show that 60 minutes of head-neck cooling can be performed safely without sedation or shivering. The critical element was to keep the torso warm using layers of blankets during the cooling period in order to prevent shivering. Cooling efficacy appears to depend on the fitness of the head harness and amount of hair[9].

There is the possibility that the CT may not reflect actual brain temperature, which may be lower than the CT indicated[10*]. The question remains as to what degree of brain temperature change is necessary to achieve a therapeutic effect[10, 11].

Further study in patients is necessary to optimize the procedure for attaining a possible therapeutic effect. Since this study attests to the feasibility and safety of whole head cooling, the next natural step would be to apply this approach to patients with epilepsy. [* Personal communication]

5. Conclusions

1. Whole-head cooling in normal volunteers for 60 minutes proved feasible and safe.
2. This treatment can easily be applied to patients with epilepsy, MS, stroke, etc.
3. Further study in patients is necessary to optimize the procedure for attaining a possible therapeutic effect.

6. Future directions

Our NINDS IRB approved a pilot study of 5 patients with epilepsy (03-N-0272), with the first participant recently recruited.

7. References

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7. Acknowledgements

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