The Open Access Journal of Science and Technology
Vol. 3 (2015), Article ID 101095, 8 pages
doi:10.11131/2015/101095

AgiAl Publishing House
http://www.agialpress.com/

Research Article

Investigating the Effects of Mild Induced Hypothermia on Cognition using a Measure of Sustained Attention

Eric A. Lacey, Redmond G. O'Connell, Shane M. O'Mara, and Paul M. Dockree

Trinity College Institute of Neuroscience, Trinity College Dublin, Ireland

Corresponding Author: Eric A. Lacey; email: elacey@tcd.ie

Received 1 July 2014; Accepted 20 July 2014

Academic Editors: Laila Y. AL-Ayadhi and Dongpei Li

Abstract. Mild Induced hypothermia has come to be recognised as a successful method of providing neuro-protective treatment for patients suffering ischemic stroke, cardiac arrest and traumatic brain injury (TBI). Anti-inflammatory responses and the lowering of cerebral metabolic rates, leading to a reduction in neuronal apoptosis, are considered to be the main mechanisms by which this process benefits patients. Assessment of a new hydro based cooling device, which could potentially be used by emergency service units, provided the impetus for the current research. Neurologically normal participants underwent two treatments: a cooling procedure where the temperature of water circulating in a cooling helmet was maintained at 4˚C and a non-cooling/sham procedure where the temperature was set at 18˚C. During treatment participants were required to perform a computer-based task that measured sustained attention/vigilance via participant response times during target detection. Electroencephalographic (EEG) recordings were also acquired before and after each treatment condition. Participants' core temperature (recorded via tympanic membrane) was monitored throughout the process. The findings revealed a statistically reliable 0.62 ˚C decrease in temperature as a result of cooling after controlling for participants' body mass index (BMI). However, there were no reliable cognitive or EEG spectral changes induced by the decrease in temperature.

Keywords: induced mild hypothermia; vigilance; sustained attention

1. Introduction

Induced mild therapeutic hypothermia; where a patients core body temperature is reduced to 30–34˚C [1] has come to be recognised a major neuro-protective factor in the treatment of TBI [2, 3], ischemic stroke [4] and cardiac arrest [5]. It is thought that the main benefits include the triggering of cerebral anti-inflammatory processes and a reduction in neuronal apoptosis [6], though the precise mechanisms leading to these effects are still poorly understood [7]. The efficacy of therapeutic hypothermic care has also proved difficult to demonstrate within human studies [8].

Though there seems to be broad agreement throughout the literature that cooling procedures have led to enhanced patients outcomes [9], even after many years of research there is still an absence of consensus on the most efficacious

hypothermic induction methods, the amount of time patients should undergo treatment and the precise temperatures that bestow most benefit [10]. This situation is all the more exacerbated by the fact that physiological reactions are notably different amongst patient groups depending on age and co-morbid illnesses [11]. There are others still who question whether there is any real significant benefit resulting from induced hypothermia. In a review of the literature Alderson and colleagues concluded that therapeutic hypothermia was not beneficial in the treatment of head injury, they go on to suggest that it may in fact result in harmful side effects such as pneumonia [12]. Whilst pointing out that many trials have produced somewhat promising results the authors also note that these findings have not been replicated using larger populations.

What is of particular note when assessing the literature is the paucity of research conducted using healthy participants. This could perhaps been seen as an oversight by clinical practitioners keen to utilise a treatment which they deem potentially beneficial to patients, however, in so doing they may be missing some important details regarding normal human responses to cooling. It is hoped that the current research may go some way in addressing this issue; by testing a device designed for clinical application on a healthy population.

The ability to adapt to extreme climatic environments has bestowed enormous survival benefits on humans [13]. In healthy individuals core temperature is said to be optimal when it falls within a 36.6–38˚C range, it is our ability to maintain these temperatures that allows us to inhabit extreme locations such as the Oymyakon region of Siberia where January temperatures regularly drop below –50˚C. The main physiological process involved in this finely tuned adaptation to fluctuations in temperature is homeostasis. Homeostatic responses are designed to support a level of stability and constancy within the human thermo-regulatory system, ensuring that one does not drift into a hypo/hyper-thermic state. When hypothermia does occur the body becomes rigid and movement becomes increasingly ataxic. In an attempt to counteract these effects thermogenesis is initiated through shivering, however, as core temperature drops further (below 31˚C) pupillary responses to light slow down and consciousness may be lost [14].

Cerebrally, the pre-optic anterior hypothalamic region is closely associated with directing thermo-regulation, as it is the temperature of the arterial blood passing through this site that determines brain temperature [14]. Integration of information from both core and peripheral thermo-receptors in the hypothalamus is processed and used to attain optimal core temperature [15]. One of the key elements of the homeostatic response is a change in the metabolic rates of oxygen (O_2) and glucose uptake. It has been reported that for every degree Celsius that core temperature drops there is a 5–7% decrease in the amount of cerebral O_2 uptake (e.g., 6.5%/˚C in [3]), a reduction in the permeability of the blood-brain barrier and a slowing of cerebral blood flow. However, when these processes are assessed and corrected for concurrent consideration there is thought to be a slight increase in blood flow [16]. Metabolic rates are decreased in all organ systems during mild hypothermia leading to a decrease in cardiac output of roughly 25%. Polderman also emphasizes the point that many of those studying the effects of controlled hypothermia consider this decrease in metabolic rate to be the singular process which bestows neuro-protective benefits to patients.

Contemporaneously the hemodynamic processes of vasodilation and vasoconstriction assists core thermoregulation by adjusting the transfer of heat to bodily extremities such as the hands, feet and head. At these sites the temperature is generally 2–4˚C colder than core temperature. During active cooling vasoconstriction takes place in an attempt to reduce blood flow thus limiting further heat loss.

Though the majority of research on the effects of thermal stress deals with heat stress, there does exist quite a substantial yet somewhat disjointed literature dealing with the effects of cold stress. Much of what has been written deals with healthy populations, but similar to the genesis of sustained attention research it seems to have been borne out of a post war desire to understand human responses to extreme conditions rather than examining the effects of targeted hypothermic induction. For instance, research carried out by Williams and Kitching saw participants placed in a thermo-regulated chamber for one hour of cooling, with temperatures dropping to –45˚C [17]. Interestingly the variations and decrement in participant reaction times were put down to ‘discomfort-induced distraction’ rather than any specific link between task performance and cooling. In 1947 Horvarth and Freedman found that housing 22 participants for 8-14 days at temperatures averaging –29˚C, had no effect on performance in a visual choice reaction time test [18]. Teichner [19] and Forlano et al. [20] would later report similar findings. More recently Makinen et al. found that while repeated exposure to cold did seem to have a somewhat minor impact on performance, the effect was negligible and was most likely a result of cold and task induced distraction [21], echoing Williams and Kitching’s findings sixty years previous.

Exactly what occurs physiologically that results in performance decrement due to cooling is still up for debate. For instance, it has been suggested that a slowing of synaptic transmission is perhaps one of the many reasons for the decrement in cognitive performance in hypothermic individuals [14]. Looked at separately there does seem to be at least one common factor, the decremental plateau in performance, and the homeostatic response which allows core temperatures to fall only so far in mildly hypothermic conditions at the expense of distal corporeal performance, both potentially designed to offset negative effects and stabilise performance.

The initial impetus for carrying out the current research programme was to evaluate a *head-cooling* device designed by Eurolec Instrumentation. Similar to that used by Simmons and colleagues [22], it is a prototype hydro-based cooling helmet, the long-term goal of which is the potential development of an out of hospital, first response portable cooling unit. It is hoped that such a device might to be used by emergency service units when treating victims of ischemic stroke. The benefits of early hypothermic induction for stroke have been detailed in a review Wu and Grotta [23].

The present study builds upon the work of Simmons et al. [22] whereby cognitive performance is assessed while participants undergo a head and neck-cooling treatment, using a hydro-based cooling cap. We attempted to do this whilst considering both the early theoretical underpinnings of sustained attention/vigilance, as put forward by Mackworth [24, 25], and more recent findings in relation to environmental/thermal stress by authors such as Simmons and Hoffman [14]. In a departure from current research, the inclusion of a sham condition where participants undergo a non-cooling normo-thermic treatment might go some way in addressing the conflicting and often contradictory results that have been reported in the field.

A pre-existing validated measure of sustained attention/vigilance [26] was used to test performance within a nonclinical population, thus we hoped to further elucidate on the effects of mild-induced hypothermia on cognitive processes in healthy participants and importantly on the efficacy of the device. Reaction times, thought to be a reliable indicator of speed and integrity of information processing [27] were recorded throughout the process. Tympanic membrane temperature, regarded by many to be representative of brain temperature [28], was also recorded over the course of the task.

Participants in this study represent a convenience sample of both past and present, healthy university students.

The specific research questions addressed in this project were:

(i) Is the Eurolec Instrumentation head-cooling device successful at achieving a reduction in the tympanic membrane temperature?

(ii) Does mild head cooling affect cognitive performance (measured by responses times) and produce electrophysiological changes (measured by spectral EEG)?

2. Method

2.1. Design. A repeated measures, within-subjects design was used with participants completing a task measuring sustained attention whilst undergoing two treatments: *Cooling* and *Non-Cooling*. Test sessions were one week apart (±1 day) and took place, where possible, between 8–10am. 50% of participants began with the cooling procedure while the others began with non-cooling. Participants were unaware that there was a non-cooling/sham condition, believing both testing sessions to involve the same treatment.

Participants completed a total of six blocks of the sustained attention task, each lasting between 270–305 seconds. During cooling, participants wore a cap lined with silicone rubber tubing which contained rapidly circulating water, the temperature of which was maintained at 4°C. During the non-cooling treatment the exact same procedures were applied with the exception that the water was now maintained at 18°C.

2.2. Participants. Twenty-two participants volunteered for the experiment, however data from five participants were excluded from the analysis due to due to technical problems during one of the cooling sessions ($N = 2$), or due to a failure to return for the second session ($N = 3$). In the final analysis the results from seventeen participants (7 female, 10 male (2 left-handed)) were utilised. All participants had completed or were in the process of completing third level education.

Participants were required to give written informed consent; there were no reports of current or past psychological/neurological illness, photosensitive epilepsy or past head trauma, all had normal to corrected vision.

Undergraduate psychology students from Trinity College Dublin received research credits for their participation in the study. Participants were free to withdraw from testing at anytime during the course of the experiment. Ages ranged from 18–47 years (mean, 26.6; SD, 8.1). Body mass index (BMI) was recorded for all participants and ranged from 16.2 to 31.7 (mean, 22.4; SD, 4.2). All experimental procedures were assessed and approved by the ethical review board of the School of Psychology, Trinity College Dublin in accordance with the Declaration of Helsinki.

2.3. Materials. A Braun ThermoScan PRO 4000 aural thermometer was used to measure all temperature readings. Participants performed a test of vigilance, developed by [26], which involved monitoring a black and white annulus pattern (see Figure 1) at fixation for transient contrast reductions. Participants were asked to make a right-handed mouse button press as soon as they noticed the contrast changing. The task was displayed using Presentation software (a full detailed description of the task is report by [26]). Eurolec Instrumentation designed and manufactured the cooling device used in this project. Statistical analysis for the project was carried out using SPSS Statistics (Version 20) and Matlab 2012a software.

2.4. Procedures. Participants were asked to refrain from caffeine consumption prior to testing.

Tests were performed in a quiet, dark room with participants seated 50cm from the monitor. Visual stimuli were presented on a grey background and participants were instructed to fixate on a centrally located 5 × 5–pixel white

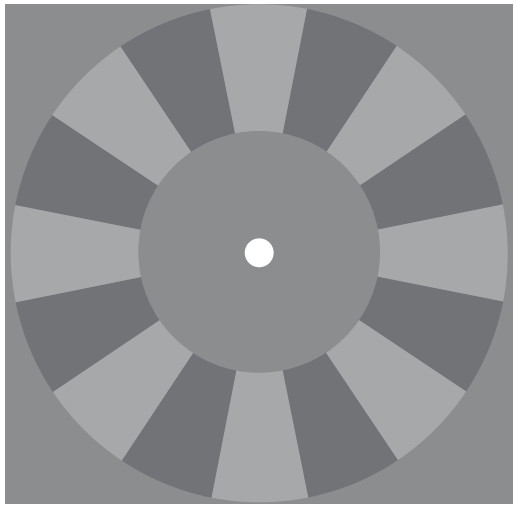

Figure 1: Annulus task.

dot. A 55-cm LCD monitor with a 120-Hz frame rate was used to display all task stimuli.

Prior to testing participants engaged in a short practice block of the vigilance task and were required to make a minimum of three consecutive correct responses in order to demonstrate that they understood the task. Participants completed one block of the task prior to cooling during which EEG was recorded. Upon completion of this first block the cooling cap was fitted (see Figure 2) and a further five blocks of the task were completed whilst undergoing the cooling/sham condition. Once the cooling cap was removed the final block was completed accompanied by EEG recording.

Temperature readings, via an aural thermometer, were recorded after each block. Testing took, on average, one hour to complete.

EEG was recorded prior to cooling/non-cooling conditions using the Biosemi Active electrode system digitized at 512Hz at baseline and again after each treatment condition. A 9-channel configuration was used which covered frontal, central, parietal and occipital scalp sites. All channels were re-referenced offline to the nasion. Data were segmented into 2-second epochs and any epochs containing absolute amplitude deviations greater than 100mV were rejected.

3. Results

3.1. Temperature Analysis. The average temperature for participants in each condition and at each time point is plotted in Figure 3 (Error bars represent the standard error of the mean). A 2×5 within-subjects Analysis of Covariance (ANCOVA) was conducted with Condition (Cooling, non-cooling) as one factor and Time bin as a second factor (5 levels subtracted from baseline) controlling for Body Mass Index (BMI) as a covariate in the analysis. The tympanic membrane temperature (˚C) was the dependent variable in this analysis.

There was a main effect of Condition, $F(1, 15) = 7.43$, $P = 0.016$, showing greater overall temperature reduction in the cooling condition compared to the non-cooling condition. In addition, there was a main effect of Time bin, $F(4, 60) = 2.6$, $P = 0.045$, indicating that temperature decreased over time. Importantly, there was also a Condition × Time bin interaction, $F(4, 60) = 3.59$, $P = 0.011$. Simple effects demonstrated that in the cooling condition there was a reliable linear decline in temperature relative to baseline ($P = 0.006$). By contrast, in the non-cooling condition there was no reliable linear decline ($P = 0.404$).

3.2. Cognitive Analysis. The average response times for participants in each condition and at each time point is plotted in Figure 4 (Error bars represent the standard error of the mean). A further 2×5 within-subjects Analysis of Covariance (ANCOVA) was conducted with Condition (cooling, non-cooling) as one factor and Time bin (5 levels subtracted from baseline) and controlling for Body Mass Index (BMI).

There was no main effect of condition, $F < 1$, indicating that response times did not vary across the cooling and non-cooling condition. Additionally, there was no main effect of Time bin, $F(4, 52) = 2.05$, $P > 1$, indicating that RTs did not reliably change over time. A significant interaction between Condition and Time bin, $F(4, 52) = 3.22$, $P = 0.022$, did not lead to further significant simple effects that could demonstrate a greater lengthening of response time (i.e., reduced cognitive performance) in the cooling condition compared to the non-cooling condition at each time point recorded (all $P > 0.05$).

3.3. EEG Analysis. We examined different oscillatory EEG activity expressed as a measure of power (microvolts squared; μV^2) before and after cooling (theta band: 4–8Hz; alpha band: 8–14hz; beta band: 14–30Hz). The average EEG spectral power for each of the three spectral bands, before and after each condition, is presented in Figure 5. For each oscillatory band, a 2 × 2 repeated measures ANCOVA was conducted with Condition (cooling, non-cooling) as one factor and Time (baseline, post-treatment) as the second factor, controlling for Body Mass Index (BMI) as a covariate in the analysis.

Theta band activity did not vary as a function of Condition, $F < 1$, or Time, $F(1, 12) = 1.82$, $P > 0.05$, and there was no significant interaction between the Condition and Time, $F < 1$.

Alpha band activity did not vary as a function of Condition or Time and there was no interaction between these factors (all $F < 1$).

Beta band activity did not vary as a function of Condition, $F < 1$, or Time, $F(1, 12) = 1.91$, $P > 0.05$, and there was

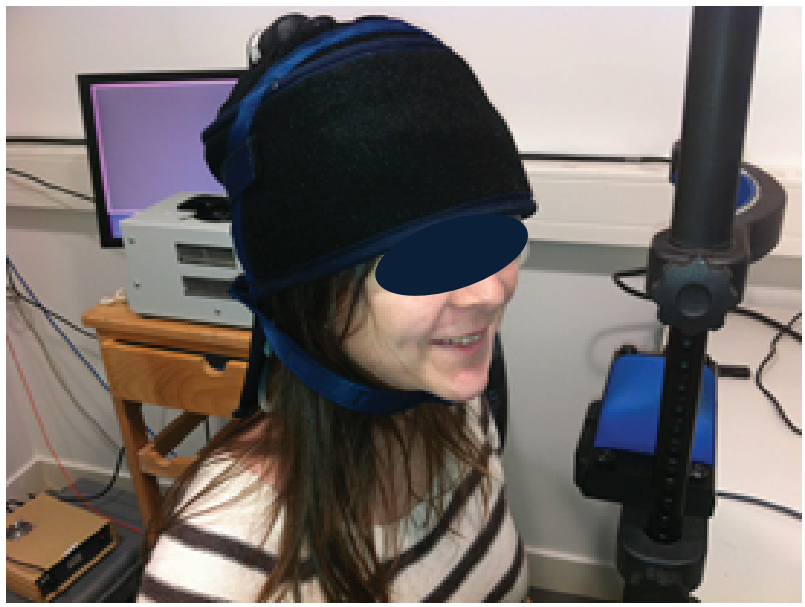

Figure 2: Eurolec cooling device.

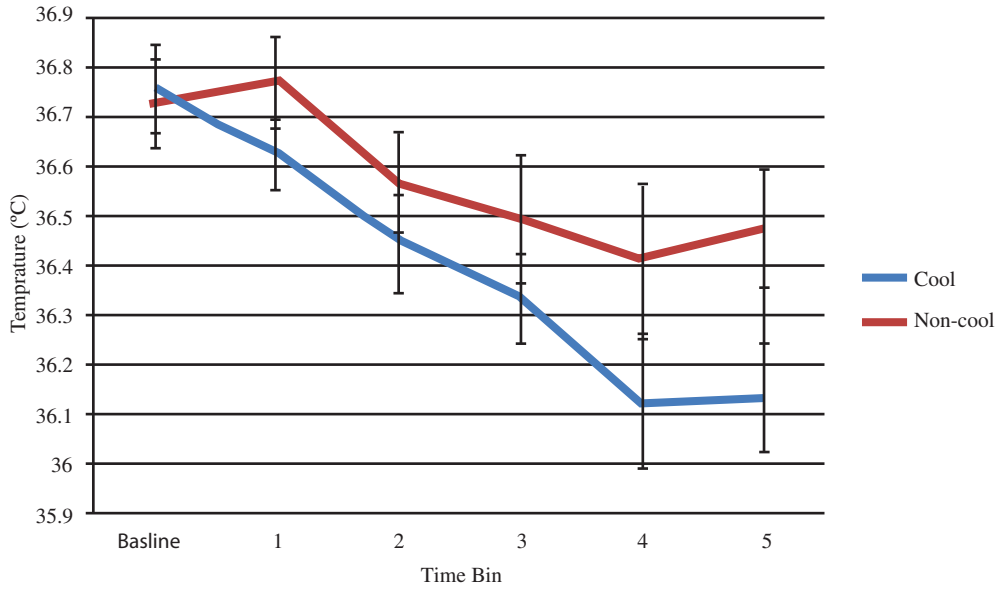

Figure 3: Temperature change from baseline across five time bins as a function of codition.

no significant interaction between the Condition and Time, $F < 1$.

4. Summary of Results

This investigation revealed a statistically reliable change of –0.62 ˚C in tympanic membrane temperature induced by the Eurolec brain cooling device over a one hour period. It is important to note that this cooling effect is only reliable when body mass index (BMI) is controlled for in the analysis. Previous research has demonstrated that mean body temperature is inversely related to BMI [29]. The effects of cooling did not alter the cognitive measures as there was no slowing of response times to the experimental stimuli over the course of the cooling period. Moreover, the EEG measures were also not altered by the effects of cooling. Specifically, we examined different oscillatory EEG activity expressed as a measure of power (microvolts squared) before and after cooling (theta band: 4–8Hz; alpha band: 8–14hz; beta band: 14–30Hz). For each of these bands there was no reliable statistical change from baseline to after the treatment conditions.

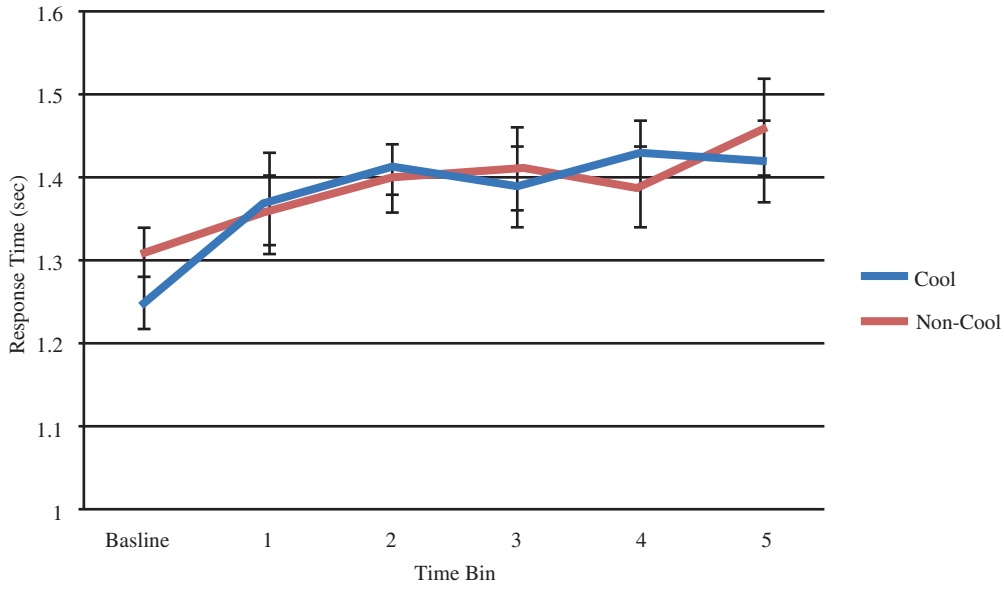

Figure 4: Response times from baseline across five time bins as a function of condition.

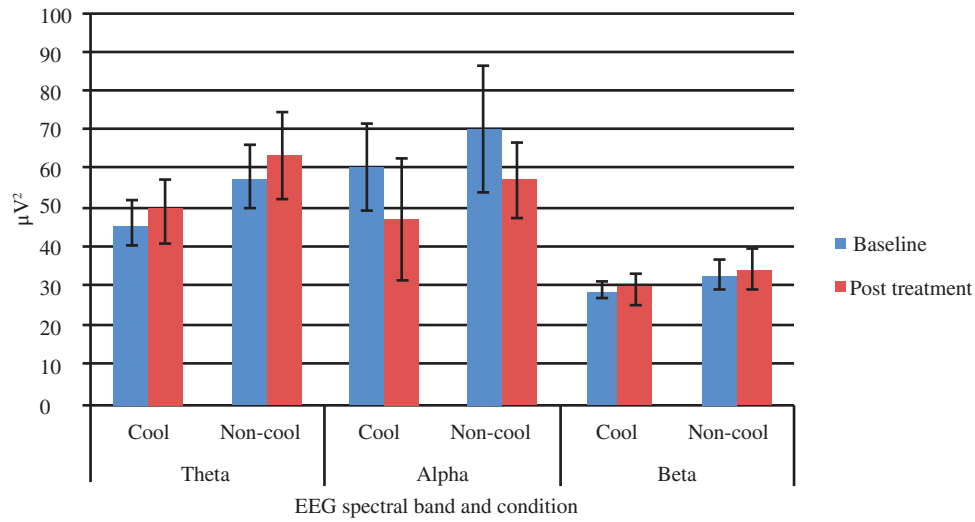

Figure 5: EEG spectral power in theta, alpha, and beta bands as a function of condition and treatment.

5. Discussion

It seems that the Eurolec cooling device is successful in reducing tympanic membrane temperature, however, the effects are rather modest. No reliable impact of head cooling was observed on either electrophysiological or cognitive markers of brain function and this appears consistent with several previous studies. As was stated earlier, the main impetus for carrying out this research was to assess the efficacy of the cooling device in achieving mildly hypothermic temperatures, unfortunately a reduction of –0.62˚C does not achieve the desired target temperatures required to bestow any potential clinical benefits.

It is still possible however to consider the effect that the minor reduction in temperature had on the reaction times of participants during the gradual detection sustained attention task. Reaction times recorded throughout the procedure did not differ significantly from one treatment to the other, though this does not necessarily suggest that cooling does not have an effect on cognitive processes. It would seem more likely that the failure to identify any difference in the current research is due to the inability of the cooling device to achieve temperatures that would allow for a true comparison of conditions and the potential effect they may have on performance during the task.

Potential support for two phenomena described earlier in the report, one cognitive the other physiological, may exist. Mackworth's theory of vigilance decrement does seem to be supported by the fact that in both conditions participant's performance deteriorated before reaching what might be described as a plateau. Physiologically, what one might term a homeostatic rebound seems to occur after the fourth trial during both the cooling and non-cooling treatment, with temperatures rising slightly. It is not possible within the confines of the current analysis to accurately assess these results concurrently. Possible links between vigilance and arousal [30], and arousal reduction as a result of cooling (as measured by pupillary responses), could perhaps mean that the topics of attention and cooling may in the future be capable of informing one another. For this to happen, outstanding issues on the precise nature of iatrogenically created vigilance/attention [31] and a standardising of cooling methods used in psychological experiments need to be addressed.

Enander has highlighted a recurring theme of claim and counter claim pervading the literature on hypothermia [32]. Perhaps one of the reasons that an abundance of conflicting evidence exists is that the relevant research has been carried out almost exclusively in clinical settings. New induction methods and devices are tested on the targeted clinical populations, without knowing the effects on healthy individuals. There seems to exist two disparate fields of study; those who wish to understand the effects of hypothermia on cognitive function with a view to better understanding cognition in general, and those who wish to use hypothermia as a clinical tool without giving consideration to the generalised effects of cooling. As has so often been pointed out in the past, a pooling of resources through a synthesis of methods and theories may bestow mutual benefit on both disciplines. Importantly it might also influence the direction of future studies.

5.1. Limitations & Future Research. In many ways it is difficult to suggest changes to the overall design of the current project. Most, if not all, are practical measures with the obvious one being the need for a cooling device capable of achieving the desired temperatures in a safe and effective manner. In redesigning the cooling device it should be of paramount importance that engineers take into account the fact that a wide range of participants/patients would be tested and that the device should be as adjustable as possible in order to facilitate the many potential users. At the same time it is necessary to maintain as much contact as possible with the outer surface area of the head and the nape of the neck. While the helmet used during the experimental protocol did not provide as much coverage to the neck and surrounding areas as the one used in a later pilot trial session, at all times during testing every attempt was made to maximize the level of contact between the cooling cap and the surface of the participants head.

It was hoped that a modified second helmet, which aimed to provide increased coverage and contact between the cooling cap and the head, would increase the effect of cooling; however, the temperature reduction was marginal. Throughout the main research programme a mean temperature drop of 0.62°C was recorded, yet using the modified helmet in the pilot test session a reduction of only 0.5°C was observed. Interestingly, this was despite the fact that the second procedure aimed to further reduce core temperature with the inclusion of nasopharyngeal cooling (via a nasal cannula).

Mild induced hypothermia is effective at 32–34°C, throughout the course of this research a 0.62°C reduction from participant normo-thermic states was recorded. Unfortunately the current rate of cooling is insufficient for clinically relevant research.

Acknowledgement

We are grateful to Eurolec Instrumentation (http://eurolec-instruments.com/) as partners in the research with Trinity College Institute of Neuroscience, Trinity College Dublin, Ireland.

References

[1] K. W. Cheung, R. S. Green, and K. D. Magee, Systematic review of randomized controlled trials of therapeutic hypothermia as a neuroprotectant in post cardiac arrest patients, *Cjem*, **8**, no. 05, 329–337, (2006).

[2] L. A. Urbano and M. Oddo, Therapeutic hypothermia for traumatic brain injury, *Current Neurology and Neuroscience Reports*, **12**, no. 5, 580–591, (2012).

[3] M. Schreckinger and D. W. Marion, Contemporary management of traumatic intracranial hypertension: Is there a role for therapeutic hypothermia? *Neurocritical Care*, **11**, no. 3, 427–436, (2009).

[4] H. B. Van Der Worp, M. R. MacLeod, and R. Kollmar, Therapeutic hypothermia for acute ischemic stroke: Ready to start large randomized trials, *Journal of Cerebral Blood Flow and Metabolism*, **30**, no. 6, 1079–1093, (2010).

[5] J. Arrich, M. Holzer, C. Havel, M. Müllner, and H. Herkner, Hypothermia for neuroprotection in adults after cardiopulmonary resuscitation, *Cochrane database of systematic reviews (Online)*, **9**, p. CD004128, (2012).

[6] H. Deng, H. S. Han, D. Cheng, G. H. Sun, and M. A. Yenari, Mild hypothermia inhibits inflammation after experimental stroke and brain inflammation, *Stroke*, **34**, no. 10, 2495–2501, (2003).

[7] X. Liu, M. Wang, H. Chen, Y. Guo, F. Ma, F. Shi, Y. Bi, and Y. Li, Hypothermia Protects the Brain from Transient Global Ischemia/Reperfusion by Attenuating Endoplasmic Reticulum Response-Induced Apoptosis through CHOP, *PLoS ONE*, **8**, no. 1, p. e53431, (2013).

[8] H. J. Nathan, G. A. Wells, J. L. Munson, and D. Wozny, Neuroprotective effect of mild hypothermia in patients undergoing coronary artery surgery with cardiopulmonary bypass: A randomized trial, *Circulation*, **104**, no. 1, i85–i91, (2001).

[9] W. G. Liu, W. S. Qiu, Y. Zhang, W. M. Wang, F. Lu, and X. F. Yang, Effects of selective brain cooling in patients with severe traumatic brain injury: A preliminary study, *Journal of International Medical Research*, **34**, no. 1, 58–64, (2006).

[10] L. I. Groysman, B. A. Emanuel, M. A. Kim-Tenser, G. Y. Sung, and W. J. Mack, Therapeutic hypothermia in acute ischemic stroke, *Neurosurgical Focus*, **30**, no. 6, p. E17, (2011).

[11] K. H. Polderman, Application of therapeutic hypothermia in the ICU: Opportunities and pitfalls of a promising treatment modality. Part 1: Indications and evidence, *Intensive Care Medicine*, **30**, no. 4, 556–575, (2004).

[12] P. Alderson, C. Gadkary, and D. F. Signorini, Therapeutic hypothermia for head injury, *Cochrane database of systematic reviews (Online)*, no. 4, p. CD001048, (2004).

[13] P. A. Bell and T. C. Greene, *Thermal Stress: Physiological, Comfort, Performance, and Social Effects of Hot and Cold Environments. Environmental Stress*, **G. W. Evans**, Cambridge university press, London, 1982.

[14] R. G. Hoffman, Human psychological performance in cold environments, *Medical Aspects of Harsh Environments*, **1**, no. 24, 383–410, (2001).

[15] D. J. Buggy and A. W. A. Crossley, Thermoregulation, mild perioperative hypothermia and post-anaesthetic shivering, *British Journal of Anaesthesia*, **84**, no. 5, 615–628, (2000).

[16] K. H. Polderman, Application of therapeutic hypothermia in the intensive care unit: Opportunities and pitfalls of a promising treatment modality - Part 2: Practical aspects and side effects, *Intensive Care Medicine*, **30**, no. 5, 757–769, (2004).

[17] C. Williams and J. Kitching, The effects of cold on human performance, I: Reaction time, *Misc Canad Aviat Rep*, (1942).

[18] S. M. Horvath and A. Freedman, The influence of cold upon the efficiency of man, *The Journal of Aviation Medicine*, **18**, no. 2, p. 158, (1947).

[19] W. H. Teichner, Recent studies of simple reaction time, *Psychological Bulletin*, **51**, no. 2, 128–149, (1954).

[20] G. Forlano, J. Barmack, and J. Coakley, The effect of ambient and body temperature upon reaction time: SDC Report (1948).

[21] T. M. Mäkinen, L. A. Palinkas, D. L. Reeves, T. Pääkkönen, H. Rintamäki, J. Leppäluoto, and J. Hassi, Effect of repeated exposures to cold on cognitive performance in humans, *Physiology and Behavior*, **87**, no. 1, 166–176, (2006).

[22] S. E. Simmons, T. Mündel, and D. A. Jones, The effects of passive heating and head-cooling on perception of exercise in the heat, *European Journal of Applied Physiology*, **104**, no. 2, 281–288, (2008).

[23] T. Wu and J. C. Grotta, Hypothermia for acute ischaemic stroke, *Lancet neurology*, **12**, no. 3, 275–284, (2013).

[24] N. Mackworth, Researches on the measurement of human performance, *Med. Res Council Spec Rep Ser (268)*, (1950).

[25] N. Mackworth, The breakdown of vigilance during prolonged visual search, *Quarterly Journal of Experimental Psychology*, **1**, no. 1, 6–12, (1948).

[26] R. G. O'Connell, P. M. Dockree, and S. P. Kelly, A supramodal accumulation-to-bound signal that determines perceptual decisions in humans, *Nature Neuroscience*, **15**, no. 12, 1729–1735, (2012).

[27] T. H. Rammsayer, E. Bahner, and P. Netter, Effects of cold on human information processing: Application of a reaction time paradigm, *Integrative Physiological and Behavioral Science*, **30**, no. 1, 34–45, (1995).

[28] Z. Mariak, M. D. White, T. Lyson, and J. Lewko, Tympanic temperature reflects intracranial temperature changes in humans, *Pflugers Archiv European Journal of Physiology*, **446**, no. 2, 279–284, (2003).

[29] K. Adam, Human body temperature is inversely correlated with body mass, *European Journal of Applied Physiology and Occupational Physiology*, **58**, no. 5, 471–475, (1989).

[30] J. S. Warm, R. Parasuraman, and G. Matthews, Vigilance requires hard mental work and is stressful, *Human Factors*, **50**, no. 3, 433–441, (2008).

[31] P. A. Hancock, The problem of iatrogenically created psychological phenomena, *American Psychologist*, **68**, no. 2, 97–109, (2013).

[32] A. E. Enander, Effects of thermal stress on human performance, *Scandinavian Journal of Work, Environment and Health*, **15**, no. 1, 27–33, (1989).

[33] N. J. Robertson, G. S. Kendall, and S. Thayyil, Techniques for therapeutic hypothermia during transport and in hospital for perinatal asphyxial encephalopathy, *Seminars in Fetal and Neonatal Medicine*, **15**, no. 5, 276–286, (2010).