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SHORT REPORT

The effect of a 2 week ketogenic diet, versus a carbohydrate-based diet, on cognitive performance, mood and subjective sleepiness during 36 h of extended wakefulness in military personnel: An exploratory study

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Summary

Extended wakefulness, or sleep deprivation, impairs cognitive performance and brain glucose metabolism. A ketogenic diet (KD) provides an alternative fuel source, ketone bodies, that could elicit a metabolic benefit during sleep deprivation. A randomised, cross-over trial was conducted with seven male military personnel. Participants ingested an iso-energetic ketogenic diet or carbohydrate-based diet for 14 days, immediately followed by 36 h of extended wakefulness and separated by a 12 day washout. Cognitive performance, mood, subjective sleepiness, capillary blood glucose, and D-β-hydroxybutyrate concentrations were measured every 2 h during extended wakefulness. Linear mixed models were used to analyse data. D-β-hydroxybutyrate was higher ($p < 0.001$) and glucose was lower ($p < 0.01$) on the KD compared with the carbohydrate-based diet. The KD improved psychomotor vigilance task performance (number of lapses, mean reciprocal response time, mean fastest 10% response time (RT), and mean slowest 10% RT; all $p < 0.05$), running memory continuous performance test performance (RT and number of correct responses per minute; both $p < 0.01$), and vigour, fatigue, and sleepiness (all, $p \leq 0.001$) compared with the carbohydrate-based diet. In conclusion, a KD demonstrated beneficial effects on cognitive performance, mood, and sleepiness during 36 h of extended wakefulness compared with a carbohydrate-based diet.

KEYWORDS
fatigue management, keto-adaptation, ketosis, psychomotor vigilance task, randomised controlled trial, sleep deprivation

1 | INTRODUCTION

Sleep deprivation (SD) is prevalent in the military despite the implementation of fatigue management strategies. Sleep deprivation-related cognitive impairments increase the risk of incidents, accidents and, in some circumstances, loss of life (Caldwell et al., 2019). Cerebral carbohydrate (CHO) metabolism appears to decline during SD (Thomas et al., 2000), which coincides with reduced cognitive performance (Wu et al., 1991). As CHO is the primary energy source for the brain (Mergenthaler et al., 2013), the supply of alternative oxidisable

energetic substrates, such as ketone bodies (KBs), could ameliorate cognitive impairments following SD.

A very-low CHO, ketogenic diet (KD) increases blood KBs, particularly D-β-hydroxybutyrate (D-βHB) (Shaw et al., 2019). This can increase the contribution of KBs to brain energy production and reduce the contribution of glucose (i.e., CHO) (Courchesne-Loyer et al., 2017). We recently demonstrated no effect of a KD on cognitive performance in military personnel after 1 and 2 weeks of adherence to a KD in a non-SD state (Shaw et al., 2022), which corroborated earlier research demonstrating that cognitive performance was unaltered after ~29 days of a KD (Iacovides et al., 2019). Therefore, the cognitive benefit of a KD is potentially more likely to be observed following SD when the brain CHO metabolism is impaired and this remains to be investigated.

The aim of our study was to examine the effect of a 2-week KD, versus a CHO-based diet, on cognitive performance, mood, and subjective sleepiness during 36 h of extended wakefulness in military personnel. We hypothesised that SD-related impairments in cognitive performance, mood, and sleepiness would be mitigated by the KD compared with the CHO-based diet.

2 | METHODS

This randomised, controlled, cross-over trial was conducted with male military personnel. Written consent was obtained prior to commencement and participation was voluntary. Ethical approval was provided by the New Zealand Defence Force and Massey University Ethics Committees (SOA 20/47).

Participants ingested their habitual diet for 7 days during a baseline phase (data not reported here), then in the 14-day dietary adaptation phase the participants were randomised to either a KD (<5% energy intake [EI; <40 g·day^{-1}] from CHO, 15%–20% energy intake from protein and > 75% energy intake from fat) or CHO-based diet (>45% energy intake from CHO, 15%–20% energy intake from protein and < 40% energy intake from fat). Dietary compliance during dietary adaptation was measured using weight, image assisted diet records on three non-consecutive days each week, and verified using daily measures of waking, fasted capillary whole-blood D-βHB concentration (Shaw et al., 2022). Sleep was monitored using actigraphy (Micro Motionlogger Watch; Ambulatory Monitoring Inc., Ardsley, New York, USA) and sleep logs.

On the last night of the dietary adaptation, the participants were required to attempt 8 h sleep and were woken by a phone call at 0630 the following morning. They presented to the Aviation Medicine Unit, Royal New Zealand Air Force Base Auckland, at 0700 to commence 36 h of extended wakefulness from 0730, which comprised six 6 h periods, each commencing with a meal (Figure 1). Cognitive performance, subjective sleepiness, mood, capillary blood glucose, and D-βHB were measured at 1, 3, and 5 h following each meal. Physical exertion, interaction with people external to the study, or the use of technology for work purposes was not permitted. Lighting (500–600 lux) and ambient temperature (20–22°C) were kept constant. A 12 day washout period separated the two trial arms.

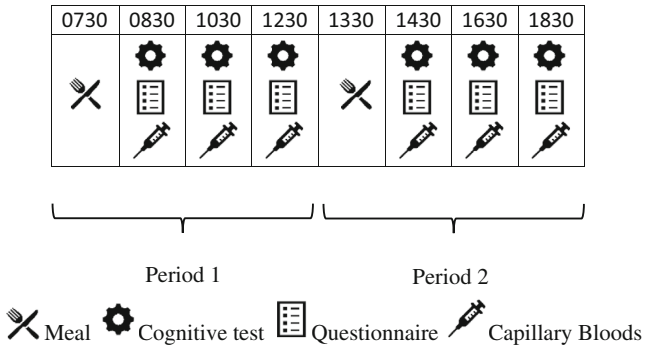

FIGURE 1 Schematic of the first two 6 h periods of extended wakefulness protocol

Meals were provided in accordance with the participants' dietary allocation (i.e., CHO-based diet or KD) at 0730 (breakfast), 1330 (lunch), 1930 (dinner), and 0130 (night meal). Example meal plans can be viewed in Supporting Information, Tables S1 and S2.

Cognitive performance was assessed with the 10 minute psychomotor vigilance task (Dinges & Powell, 1985), and analysed for the number of lapses, the mean reciprocal response time (RRT; 1/mean response time (RT) × 1000), the mean fastest 10% RT, and the mean slowest 10% RT. From the ANAM test battery, the 2-choice reaction time test and running memory continuous performance test (RMCPT) were analysed for the RT and the number of correct responses per minute (Reeves et al., 2007). The Stanford Sleepiness Scale (Hoddes et al., 1973) from the ANAM test battery was used to quantify changes in subjective sleepiness. Fatigue and vigour were measured using the ANAM mood scale, which is validated against the Profile of Mood Scores (Johnson et al., 2008).

All statistical analyses were performed using linear mixed effects models with the restricted maximum likelihood in R version 3.6.0 with RStudio version 1.1463 (R Core Team, 2013). Fixed effects factors included diet (2 levels; KD and CHO-based diet), period (6 levels), and test (3 levels), diet order (2 levels), and a random intercept for participant. Significance was inferred when $p \leq 0.05$. See Supporting Information, Statistical Analyses, for further details.

3 | RESULTS

Ten participants were recruited for the study; three withdrew due to operational demands, giving a total sample size of $n = 7$ men: age, 34.7 ± 7.0 years (range, 26–45 years); body mass, 84.1 ± 10.2 kg; height, 1.79 ± 0.03 m; body mass index, 26.2 ± 2.5 kg·m^2.

A detailed summary of dietary intake for each dietary condition during the adaptation phase is reported in Supporting Information, Table S3. Briefly, participants adhered to all dietary requirements and there were no differences between dietary conditions for EI; however, the KD was slightly (~21 g) higher in protein ($p = 0.049$). Blood D-βHB

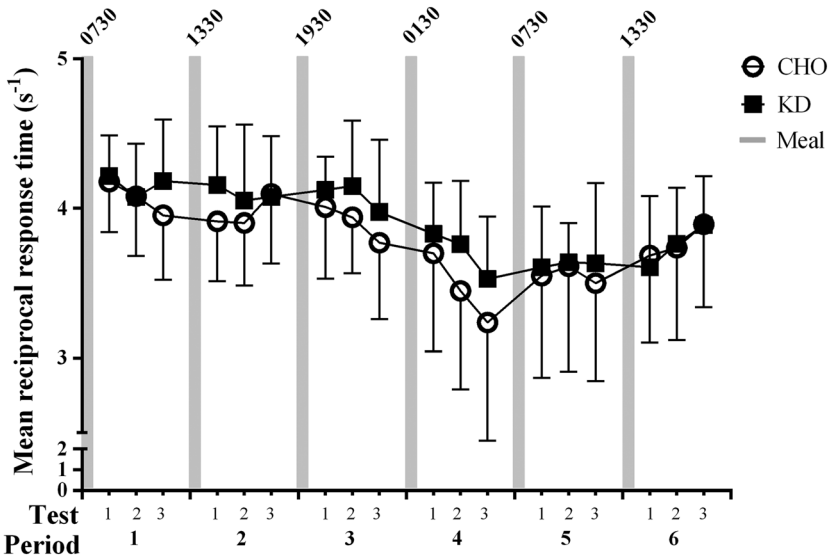

FIGURE 2 Mean reciprocal response time (responses s^{-1}) during 36 hours of extended wakefulness for the carbohydrate and ketogenic diet interventions. Values are presented as mean ± standard deviation.

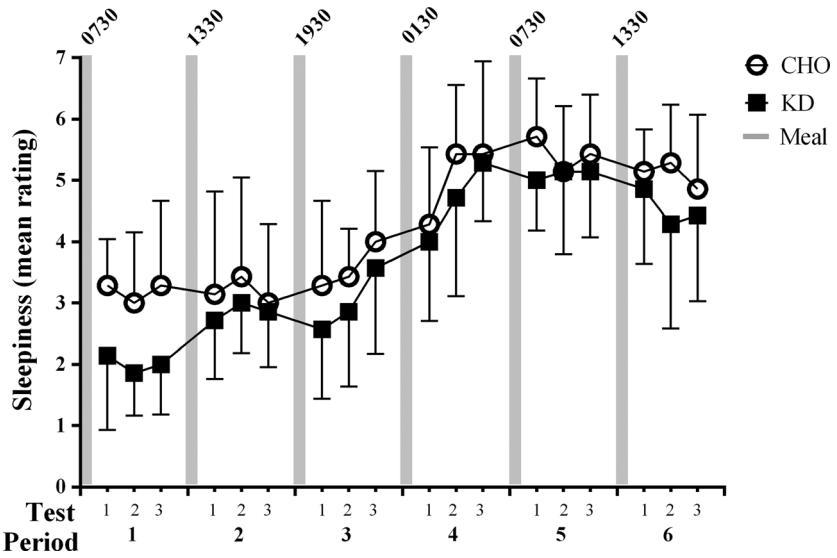

FIGURE 3 Subjective sleepiness during 36 hours of extended wakefulness for the carbohydrate and ketogenic diet interventions. Values are presented as mean ± standard deviation.

concentrations were higher in the KD compared with the CHO-based diet in week 1 (0.47 ± 0.33 mM vs 0.09 ± 0.07 mM) and 2 (1.07 ± 0.77 mM vs 0.08 ± 0.06 mM) (both $p < 0.001$), and higher in week 2 compared with week 1 on the KD ($p = 0.001$). Days to reach a D-βHB concentration of ≥0.4 mM for participants in the KD was 3.9 ± 1.1. The mean sleep duration for the 7 days prior to the extended wakefulness period did not differ between the KD (6.9 ± 0.9 h·day^{-1}) and CHO-based diet (6.7 ± 1.1 h·day^{-1}) ($p = 0.20$). On the night preceding the extended wakefulness period, participants slept for 6.8 ± 1.0 h (range, 5.2–8.2 h) on the KD and 6.5 ± 0.9 h (range, 4.8–7.1 h) on the CHO-based diet ($p = 0.63$).

For the extended wakefulness, summary tables of interactions and main effects can be found in Supporting Information, Tables S4–S16; only diet effects are reported here. Blood D-βHB was higher on the KD compared with the CHO-based diet (all $p < 0.001$). Psychomotor vigilance task performance was enhanced on the KD compared with CHO-based diet for the number of lapses, mean RRT (Figure 2), fastest 10% RT, and slowest 10% RT (all $p < 0.05$). For the ANAM tests, performance was enhanced on the KD compared with CHO-based diet for RMCPT RT and the number of correct responses per minute (both $p < 0.01$); however, there was no effect of diet for the 2-choice reaction time test RT ($p = 0.089$) and correct responses per minute ($p = 0.101$). Lower subjective sleepiness (Figure 3), higher vigour (Figure 4), and lower fatigue were also observed in the KD compared with the CHO-based diet (all $p \leq 0.001$).

4 | DISCUSSION

We investigated the effect of a 2 week KD compared with a CHO-based diet on cognitive performance, mood, and subjective sleepiness during 36 h of extended wakefulness in male military personnel. Participants were compliant with all dietary and sleep requirements

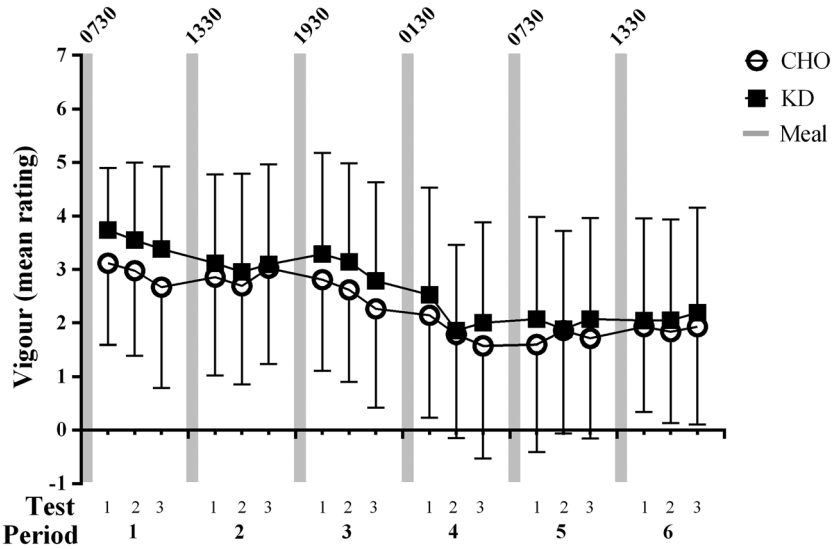

FIGURE 4 Vigour during 36 hours of extended wakefulness for the carbohydrate and ketogenic diet interventions. Values are presented as mean ± standard deviation.

during the dietary adaptation phase, as reported previously (Shaw et al., 2022). In support of our hypothesis, the KD attenuated SD-related impairments for all PVT and RMCPT variables, mood, and subjective sleepiness during the 36 h. This suggests that increases in the availability of KBs and underlying metabolic adaptations to a short-term KD may provide a metabolic benefit to the brain during SD.

In the present study, the interaction between increasing homeostatic sleep pressure and circadian processes elicited expected cognitive and mood impairments from which to assess possible effects of diet. Differences between dietary conditions were observed across the 36 h of extended wakefulness but appeared greatest in period 4 (0130–0630; that is, the circadian low). This was similar to a previous study comparing a 1 week, non-ketogenic (40% energy intake as CHO) high-fat diet with a high-CHO diet (65% energy intake from CHO) diet over 24 h of SD (Lowden et al., 2004), which found that irresistible sleepiness increased to a greater extent for the high-CHO diet during 1200–1600 and 2400–0400. Together, these observations suggest that the effects of a high fat, or KD, may be more beneficial during circadian lows.

We speculated that the metabolic effects of the KD would mitigate cognitive impairments that stemmed from reductions in brain glucose metabolism caused by SD. In the present study, adaptation to the KD lowered blood glucose concentration, which elicited hyperketonaemia via increased ketogenesis. Whilst we did not measure differences in brain metabolism, the 2-week adaptation period prior to extended wakefulness likely shifted substrate oxidation from glucose to KBs. For example, in a previous study, a 4-day KD increased plasma KBs concentrations (acetoacetate + D-βHB) to 4.8 mM, which increased the metabolism of cerebral KBs from ∼5% (on the CHO diet) to ∼33% (Courchesne-Loyer et al., 2017). Although blood KB concentrations were lower in our study (i.e., D-βHB <2 mM), which would theoretically reduce the oxidation of cerebral KBs (Courchesne-Loyer et al., 2017), the longer dietary adaptation period may have augmented the oxidation of KBs by increasing ketolytic enzyme activity (Mey et al., 2020) and possibly the transport of KBs.

In conclusion, the 2 week KD, compared with the CHO-based diet, demonstrated beneficial effects on cognitive performance, mood, and sleepiness during 36 h of extended wakefulness in male military personnel. Our study suggests that a KD may provide a cognitive benefit during periods of SD. Further research using study designs with more ecological validity and larger, more diverse sample populations to assess the effects on safety and performance as they relate to real-world military operations are required prior to their implementation in this community.

AUTHOR CONTRIBUTIONS

The study was designed by David M Shaw and Margo van den Berg; data were collected by Lydia Rose Henderson and David M Shaw; actigraphy was scored by Margo van den Berg; data were analysed and interpreted by Lydia Rose Henderson, David M Shaw, and Margo van den Berg; initial manuscript preparation was by Lydia Rose Henderson; the final manuscript was co-written and approved by Lydia Rose Henderson, David M Shaw, and Margo van den Berg.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

Caldwell, J. A., Caldwell, J. L., Thompson, L. A., & Lieberman, H. R. (2019). Fatigue and its management in the workplace. *Neuroscience and Biobehavioral Reviews*, *96*, 272–289. https://doi.org/10.1016/j.neubiorev.2018.10.024

Courchesne-Loyer, A., Croteau, E., Castellano, C. A., St-Pierre, V., Hennebelle, M., & Cunnane, S. C. (2017). Inverse relationship between brain glucose and ketone metabolism in adults during short-term moderate dietary ketosis: A dual tracer quantitative positron emission tomography study. *Journal of Cerebral Blood Flow and Metabolism*, *37*(7), 2485–2493. https://doi.org/10.1177/0271678X16669366

Dinges, D. F., & Powell, J. W. (1985). Microcomputer analyses of performance on a portable, simple visual RT task during sustained operations. *Behavior Research Methods, Instruments, & Computers*, *17*(6), 652–655. https://doi.org/10.3758/BF03200977

Hoddes, E., Zarcone, V., Smythe, H., Phillips, R., & Dement, W. C. (1973). Quantification of sleepiness: A new approach. *Psychophysiology*, *10*(4), 431–436.

Iacovides, S., Goble, D., Paterson, B., & Meiring, R. M. (2019). Three consecutive weeks of nutritional ketosis has no effect on cognitive function, sleep, and mood compared with a high-carbohydrate, low-fat diet in healthy individuals: A randomized, crossover, controlled trial. *American Journal of Clinical Nutrition*, *110*(2), 349–357. https://doi.org/10.1093/ajcn/nqz073

Johnson, D. R., Vincent, A. S., Johnson, A. E., Gilliland, K., & Schlegel, R. E. (2008). Reliability and construct validity of the automated neuropsychological assessment metrics (ANAM) mood scale. *Archives of Clinical Neuropsychology*, *23*(1), 73–85. https://doi.org/10.1016/j.acn.2007.10.001

Lowden, A., Holmbäck, U., Åkerstedt, T., Forslund, J., Lennernäs, M., & Forslund, A. (2004). Performance and sleepiness during a 24 h wake in constant conditions are affected by diet. *Biological Psychology*, *65*(3), 251–263. https://doi.org/10.1016/S0301-0511(03)00114-5

Mergenthaler, P., Lindauer, U., Dienel, G. A., & Meisel, A. (2013). Sugar for the brain: The role of glucose in physiological and pathological brain function. *Trends in Neurosciences*, *36*(10), 587–597. https://doi.org/10.1016/j.tins.2013.07.001

Mey, J. T., Erickson, M. L., Axelrod, C. L., King, W. T., Flask, C. A., McCullough, A. J., & Kirwan, J. P. (2020). β-Hydroxybutyrate is reduced in humans with obesity-related NAFLD and displays a dose-dependent effect on skeletal muscle mitochondrial respiration in vitro. *American Journal of Physiology - Endocrinology and Metabolism*, *319*(1), E184–E195. https://doi.org/10.1152/ajpendo.00058.2020

R Core Team. (2013). *R: A language and environment for statistical computing*.

Reeves, D. L., Winter, K. P., Bleiberg, J., & Kane, R. L. (2007). ANAM® genogram: Historical perspectives, description, and current endeavors. *Archives of Clinical Neuropsychology*, *22*(SUPPL. 1), 15–37. https://doi.org/10.1016/j.acn.2006.10.013

Shaw, D. M., Henderson, L., & van den Berg, M. (2022). Cognitive, sleep, and autonomic responses to induction of a ketogenic diet in military personnel: A pilot study. *Aerospace Medicine and Human Performance*, *93*(6), 507–516. https://doi.org/10.3357/AMHP.6015.2022

Shaw, D. M., Merien, F., Braakhuis, A., Maunder, E. D., & Dulson, D. K. (2019). Effect of a ketogenic diet on submaximal exercise capacity and efficiency in runners. *Medicine and Science in Sports and Exercise*, *51*(10), 2135–2146. https://doi.org/10.1249/MSS.0000000000002008

Thomas, M., Sing, H., Belenky, G., Holcomb, H., Mayberg, H., Dannals, R., Wagner, H., Thorne, D., Popp, K., Rowland, L., Welsh, A., Balwinski, S., & Redmond, D. (2000). Neural basis of alertness and cognitive performance impairments during sleepiness. I. Effects of 24 h of sleep deprivation on waking human regional brain activity. *Journal of Sleep Research*, *9*(3), 335–352. https://doi.org/10.1016/S1472-9288(03)00020-7

Wu, J. C., Gillin, J. C., Buchsbaum, M. S., Hershey, T., Hazlett, E., Sicotte, N., & Bunney, W. E. (1991). The effect of sleep deprivation on cerebral glucose metabolic rate in normal humans assessed with positron emission tomography. *Sleep*, *14*(2), 155–162. https://doi.org/10.1093/sleep/14.2.155

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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