British Journal of Nutrition (1995), **74**, 115–123

Influences of dietary and intraduodenal lipid on alertness, mood, and sustained concentration

BY ANITA S. WELLS AND NICHOLAS W. READ

Centre for Human Nutrition, University of Sheffield, Northern General Hospital, Herries Road, Sheffield S7 5AU

AND ANGUS CRAIG

MRC/ESRC Social and Applied Psychology Unit, University of Sheffield, Mushroom Lane, Sheffield S10 2TN

(*Received 25 May 1994 – Revised 27 October 1994 – Accepted 7 December 1994*)

The effects of intraduodenal and dietary lipid on alertness, mood and performance in a task requiring sustained attention were investigated in two studies. The first experiment compared the effect of duodenal infusion of either 100 g/l Intralipid (8·36 kJ/min) or isotonic saline (9 g NaCl/l) in paired studies carried out on two non-consecutive days on five male volunteers. Two consecutive 3 h infusions, one of lipid, the other saline, were given blind on each day using a crossover design. Analysis of variance indicated that lipid significantly reduced alertness ($P < 0·05$) and affected the speed and accuracy of performance in a sustained attention task ($P < 0·05$). A second experiment compared the effects on eight male volunteers of two isoenergetic lunches of similar appearance, taste and protein content but differing fat and carbohydrate (CHO) contents (fat energy:CHO, 64:18 *v.* 7:76). Alertness was lower ($P < 0·05$) and responses to stimuli in a sustained attention task were slower after the high-fat meal than after the low-fat meal ($P < 0·05$). In conclusion, infusion of lipid into the small intestine, and the substitution of fat for carbohydrate while keeping energy and protein constant in a lunch, both cause an enhanced postprandial decline in alertness and concentration. This may be related to the presence of lipid in the small intestine.

Lipid: Postprandial alertness

Feeling drowsy after eating a large meal is a common experience. Psychological studies have demonstrated that human volunteers feel more lethargic, dreamy, feeble, clumsy, bored and mentally slow after lunch than they do before it, and this is associated with corresponding declines in performance particularly in tasks requiring sustained attention (Spring *et al.* 1982/3; Smith & Miles, 1986; Smith, 1988). Many different factors may be responsible for this post-lunch dip in alertness; the most important include circadian rhythm, boredom, sleep deprivation and meal composition. It has been suggested that carbohydrate-rich, low-protein meals may induce sleepiness by increasing plasma concentrations of tryptophan relative to other large neural amino acids, and thus increasing serotonin neurotransmission. However, there is little support for this occurring in humans (Ashley *et al.* 1982). Other studies, however, have shown that intraduodenal infusions of lipid make rats and cats sleepy (Fara *et al.* 1969; Murray *et al.* 1993). The aim of the present study was to investigate the influence of intestinal lipid on mood, alertness and sustained concentration in healthy human volunteers. Two experimental designs were used. In the first we investigated the effect of intraduodenal lipid infusions, and in the second we investigated the effect of substitution of carbohydrate with fat (while keeping protein and total energy constant) in a lunch-time meal.

https://doi.org/10.1079/BJN19950111 Published online by Cambridge University Press

METHODS

Subjects

Sixteen healthy male volunteer subjects (20–26 years, body mass index 20–25) were recruited from a cohort of present or past university students. The study was approved by the ethical committee of the Sheffield Health Authority (Northern General Hospital).

The effect of intraduodenal lipid infusions

Paired studies were conducted on eight volunteers and were separated by at least 4 d. Before each study an enteral feeding tube (Corsafe Inc., IL 60090, USA) was inserted via the nose into the duodenum with the aid of a guide wire. The position of the side opening infusion port at 0·85 m from the external nares was confirmed by measuring the potential difference between the end of this cannula, perfused with saline (9 g NaCl/l) (flowing saline electrode) and a subcutaneous cannula, filled with saline and inserted under the skin of the forearm (Read, 1980).

During the morning (09.45 to 12.45 hours) and afternoon (12.45 to 15.45 hours) of each test day either 100 g/l Intralipid (Kabi Pharmacia Ltd, Milton Keynes, Bucks), or isotonic saline were perfused into the duodenum, at a rate of 2 ml/min in a crossover, balanced design (Fig. 1). This provided a total of 40 g lipid (1500 kJ, 360 kcal). The subjects were unaware of the nature of the infusion; four subjects had lipid infused on their first afternoon and second morning, and four subjects received lipid on their first morning and their second afternoon.

Measures of mood, alertness and sustained concentration (described below) were collected at hourly intervals throughout the day. These were followed after a 5 min rest by a clerical task, which lasted for the remainder of the hour. Every attempt was made to match the two study days for other variables as far as possible by familiarizing the subjects with the performance tasks before the study, asking them to go to bed and get up at the same times on the night before the study and fasting before arrival at the Centre for Human Nutrition. External factors such as noise, known to influence arousal, were controlled for by subjects being studied on their own in a quiet room.

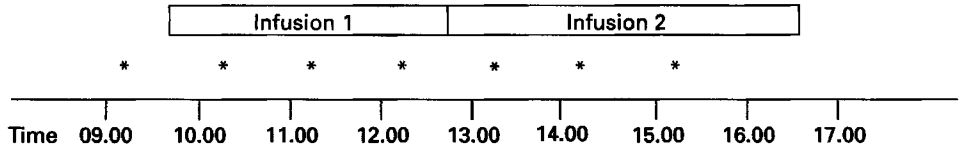
The effect of replacement of carbohydrate with fat

Paired studies were carried out in eight volunteers, and the 2 d were matched for non-nutrient variables as described above. Fasted subjects arrived at 08.30 hours and ate a breakfast consisting of cornflakes, semi-skimmed milk, orange juice, toast, butter, marmalade and decaffeinated tea or coffee (3225 kJ/760 kcal).

The experimental protocol (Fig. 2) was designed to represent a typical working day for an office-based clerical assistant. Between 09.00 and 17.00 hours measures of mood, alertness and sustained concentration were collected at hourly intervals and in the remaining time subjects performed a clerical analysis task. In order to control for other factors known to influence arousal, subjects worked alone in a quiet room. There was a 30 min lunch break at 12.45 hours, and 10 min breaks for decaffeinated coffee and tea at 10.45 and 16.45 hours in which they were permitted to talk to one other person.

The two test lunches were identical in protein and energy contents, but varied widely in fat and carbohydrate contents (Table 1). The high- and low-fat food components, beef and courgette lasagne and raspberry fromage frais, looked and tasted very similar. This manipulation was achieved in the lasagne by varying the proportions of meat, vegetables and cheese sauce, and by using a roux sauce containing whole milk, full-fat cheese, and single cream for the high-fat version, and using a cornflour sauce containing skimmed milk

https://doi.org/10.1079/BJN19950111 Published online by Cambridge University Press



Order of infusions	Day 1		Day 2	
	Infusion 1	Infusion 2	Infusion 1	Infusion 2
Group 1	Saline	Lipid	Lipid	Saline
Group 2	Lipid	Saline	Saline	Lipid

Fig. 1. Timetable for the intraduodenal infusion study. * Indicates the time at which rating scales were assessed and the sustained attention task was performed. For details of infusions and procedures, see pp. 116–118.

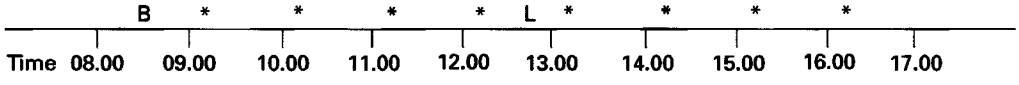


Fig. 2. Timetable for each test day during the meals study. B, breakfast; L, lunch. * Indicates the time at which rating scales were assessed and the sustained attention task was performed. For details of meals and procedures, see Table 1 and pp. 116–118.

Table 1. *Nutrient composition of lunch-time meals (% energy)**

	High-fat, low-carbohydrate	Low-fat, high-carbohydrate
Fat	64·0	6·7
Carbohydrate	17·8	75·6
Protein	18·2	17·7

* Calculated using CompEat nutritional analysis programme (Lifeline Nutritional Services Ltd, London W2 3EN).

and low-fat cheddar cheese in the low-fat version. The high-fat raspberry fromage frais contained added vegetable oil, double cream and Canderel spoonful (NutraSweet, High Wycombe, Bucks), whereas the low-fat version contained cornflour and sugar. A glass of water was served with the high-fat meal, whereas with the low-fat meal, subjects were given a glass of Lucozade (Smith Kline Beecham, Brentford, Middx).

Four subjects ate the high-fat, low-carbohydrate lunch on their first test day and the low-fat, high-carbohydrate lunch on their second test day. The remaining subjects ate the two meals in the reverse order. The proportions were individually prepared to provide each subject with one third of his estimated daily energy requirement (Department of Health, 1991; 3675 (SD 310) kJ, 875 (SD 74) kcal).

Measures of mood and alertness

Rating scales. Each hour subjects rated their alertness, cheerfulness and calmness, three critical dimensions of mood and arousal (Thayer, 1989), on twenty-point bipolar visual analogue scales. In the infusion study subjects were also asked to report any sensations of

https://doi.org/10.1079/BJN19950111 Published online by Cambridge University Press

hunger, nausea, bloatedness, discomfort and stomach-ache on twenty-point monopolar visual analogue scales.

Sustained attention task. This high-paced task places heavy demands on the capacity to pay continuous attention and reliably indicates failures to maintain the speed and accuracy of performance for longer than a few minutes (Neuchterlein *et al.* 1983). It has proved sensitive to variations in arousal associated with time-on-task, time-of-day (Craig *et al.* 1987) and alcohol (Rohrbaugh *et al.* 1988). In the present version of this widely used task a sequence of single digits was displayed in the centre of a personal computer visual display unit. To make the task sufficiently demanding the appearance of the digits was degraded by reversing the polarity of a random 30% of the pixels that defined the digits and their background, thereby producing images that were fuzzy and grainy. Each digit was displayed for less than one second, and subjects were required to press the space-bar each time a zero appeared. The task lasted continuously for 10 min, during which a total of 600 randomly selected digits was presented, containing an average of 150 zeros. Data analysis of this task is confined to the final 9 min, the first minute providing an initial 'warm-up' period.

Data analysis

For the infusion study. As the design depicted in Fig. 1 shows, each subject was observed under each of the two infusions (lipid and saline) in the morning and also in the afternoon, data being collected after periods of 0·5, 1·5 and 2·5 h from the start of each infusion; one group began with saline on their first morning, the other with lipid. Accordingly, the data were analysed as a $2 \times 2 \times 3 \times 2$ (infusion × time of day × period × group) factorial design, with repeated measures on the first three factors. In addition, the baseline measures, taken at 09.15 hours before the infusions, were compared using a paired Student's t test.

The data from the final 9 min of the sustained attention task were further divided into three, 3 min blocks, in order to determine the duration for which attention could be sustained, and the data analysed as a $2 \times 2 \times 3 \times 3 \times 2$ (infusion × time of day × period × block × group) factorial design with repeated measures on the first four factors. Performance indicators included the number of correctly detected targets (hits), detection latencies, number of incorrect responses (false alarms) and indices of perceptual sensitivity and of response bias. Due to the skewed nature of the frequency distribution of the reaction times, a reciprocal transformation was performed before the variance analysis.

Post hoc comparisons between means were made using the paired two-tailed Student's t test, appropriately adjusted by the Fisher–Tukey method to reveal only 'honestly significant differences', recommended when more than two means are available for comparison.

For the meals study. The data were analysed in a similar way to that described for the infusion data, except that pre-lunch scores were included as covariates. The between-subjects grouping variable was again the order in which subjects received the meals, and the dependent variables were the responses collected at 13.15, 14.15, 15.15 and 16.15 hours. Within-subject factors were 'food' (low- or high-fat lunch), 'time of day' (13.15, 14.15, 15.15 or 16.15 hours), and, for the sustained attention task, the 3 min blocks of trials.

RESULTS

Lipid infusion experiments

The data from three subjects were disregarded due to a lack of positive confirmation of the position of the infusion point. However, this did not appreciably change the pattern of the results. There were no significant differences ($P > 0{\cdot}05$) in the baseline scores between the two study days.

https://doi.org/10.1079/BJN19950111 Published online by Cambridge University Press

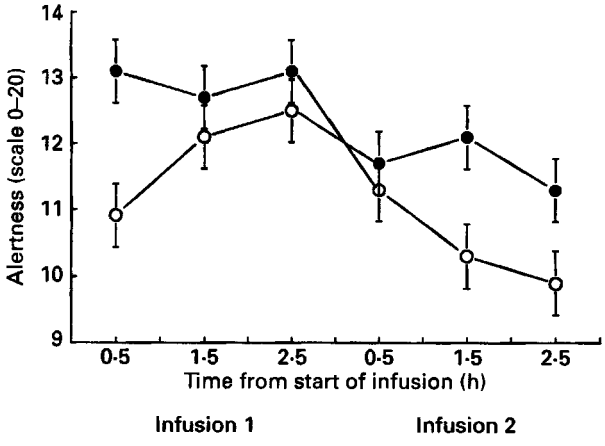


Fig. 3. Alertness ratings measured during 3 h intraduodenal infusions of (○) lipid and (●) saline in human volunteers. Values are means for five subjects, with their standard errors indicated by vertical bars. For details of infusions and procedures, see pp. 116–119.

Subjective ratings of alertness and mood. Subjects felt significantly less alert during lipid infusions than during saline infusions, irrespective of the time of day or order of infusion (F 8·92; df 1,9; $P = 0·048$), (Fig. 3). Independently, the time of day also affected alertness and cheerfulness, with subjects feeling less alert and less cheerful during the afternoons than during the mornings (alertness: F 7·71; df 1,9; $P = 0·012$; cheerfulness: F 7·22; df 1,9; $P < 0·025$). Subjects also tended to feel less cheerful and less calm when lipid rather than saline was infused although these effects just failed to achieve statistical significance ($P = 0·054$). Analysis of the interaction between infusate, time of day and period revealed significant effects of lipid on calmness and cheerfulness occurring immediately after commencement of the infusion in the morning and somewhat later in the afternoon.

Gastrointestinal sensations. There were no significant differences in ratings of nausea or overall discomfort between the two infusions or between different times of day. However, feelings of bloatedness were significantly enhanced by lipid irrespective of the time of day (F 16·09; df 2,6; $P = 0·028$), and there were significant interactions between infusate, time of day, and period (F 5·75; df 2,6; $P = 0·040$) for ratings of hunger, and between infusate and period for the presence of stomach-ache (F 6·93; df 2,6; $P = 0·028$). During lipid infusions subjects felt less hungry in the early part of the morning and reported more stomach-ache during the first periods of both morning and afternoon.

Sustained attention task. The effects of infusate on the speed and accuracy of performance were similar. In each case there was significant evidence of an interaction with time-on-task ($P = 0·031$; F 6·52; df 2,6, and $P = 0·023$; F 42·13; df 2,2). Subjects receiving lipid were unable to maintain efficient attention for more than 3 min; whereas those receiving saline only exhibited a decrement in the final block of trials (Fig. 4). These effects were particularly noticeable in the morning, when overall accuracy was poorer. Apart from these interactions, the tendency for lipid to result in less efficient levels of attention failed to reach significance. However, subjects' inclination to report the occurrence of a zero, as indexed by response bias (the number of responses made divided by the number of zeros presented), did alter according to the infusion. Subjects were less inclined to report a zero with lipid than with saline in the first and second periods of the morning and the second and third periods of the afternoon (F 6·14; df 2,6; $P = 0·035$).

https://doi.org/10.1079/BJN19950111 Published online by Cambridge University Press

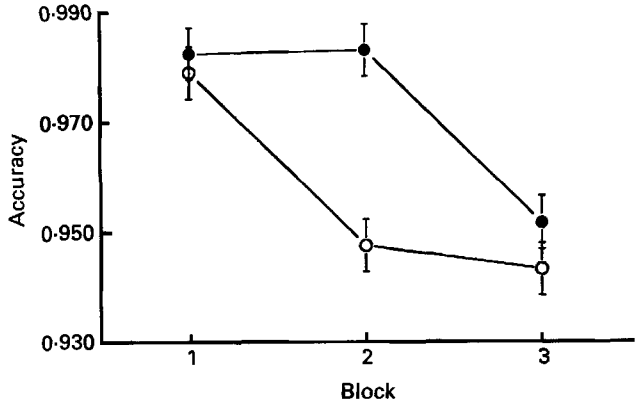


Fig. 4. Mean accuracy of responses in sustained attention tasks (performed in three 3 min blocks) carried out during intraduodenal infusions of (○) lipid and (●) saline. Values are means for five subjects, with their standard errors indicated by vertical bars. For details of infusions and procedures, see pp. 116–119.

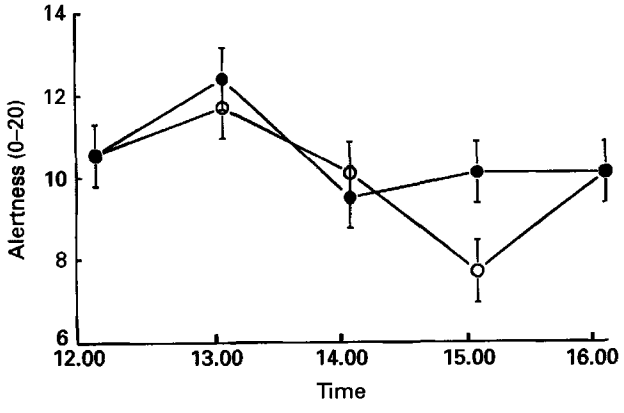


Fig. 5. Alertness ratings in healthy male volunteers given isoenergetic lunches at 12.30 hours. (○), High-fat, low-carbohydrate lunch; (●), low-fat, high-carbohydrate lunch. Values are means for eight subjects with their standard errors indicated by vertical bars. For details of lunches and procedures, see Table 1 and pp. 116–119.

Results from the meal study

Subjective rating of alertness and mood. There were significant changes in alertness after both types of lunch ($P < 0{\cdot}0001$). Scores increased initially but then declined below the pre-lunch scores. By 2·5 h after lunch the postprandial decline in alertness was significantly greater after the high-fat, low-CHO lunch than after the low-fat, high-CHO lunch (t 3·07; df 7, $P = 0{\cdot}018$) (Fig. 5).

Subjects also tended to be less cheerful after the high-fat meal, although the effect just failed to achieve statistical significance ($0{\cdot}05 < P < 0{\cdot}10$). Scores for calmness did not vary significantly with the meal.

Sustained attention task. Both the accuracy and speed of responses in this task were affected by the type of lunch eaten. The speed of correct responses was slower after the high-fat lunch than after the low-fat lunch (F 10·38; df 1,5; $P < 0{\cdot}023$), the mean correct response time in the four tests after the high-fat meal was 684 ms compared with 679 ms after the low-fat meal (SE comparison 1·4). There was also a significant interaction between time on task and lunch ingested. Following the low-fat, high-CHO meal there was a linear

https://doi.org/10.1079/BJN19950111 Published online by Cambridge University Press

decline in accuracy across the three blocks, whereas after the high-fat, low-CHO meal, accuracy waned between the first and second blocks but thereafter remained constant (F 13·21; df 2,3; $P = 0·033$).

DISCUSSION

The results from the infusion study indicate that subjects felt significantly less alert during intraduodenal lipid infusions than during saline infusions. These results occurred in addition to the usual afternoon dip in arousal and were endorsed by a significant reduction in performance in the middle of the sustained attention task, indicating an impairment of the ability to sustain attention.

Despite the relatively small number of participants in this study, statistically significant differences were observed, and examination of the analyses and the power of the tests revealed that the only marginal effects that may have reached significance with a larger study of practicable size were differences in feelings of calmness and cheerfulness during lipid and saline infusions.

As the subjects were blind to the nature of the infusions and did not experience any of the sensory properties of lipid in their mouths or throats, there is no possibility that cognitive or gustatory factors influenced their feelings and performance. While the lipid and saline infusions were associated with different gastrointestinal sensations, there was no difference in overall discomfort, and although the feelings of bloatedness and stomach-ache may have caused distraction in the sustained attention task, these sensations would tend to cause an increase in alertness rather than a decline. Thus we can conclude that the decline in alertness was a response related either to the presence of lipid within the intestine or the post-absorptive effects of lipid on behaviour.

The results of the infusion experiments, however, do not specifically implicate lipid as the mediator of the behavioural changes. Such changes could occur with any source of energy and previous experiments have shown that CHO-rich meals are also associated with postprandial lassitude and inferior performance (Spring *et al.* 1982/83). The second study controlled for the effect of energy by substituting fat for carbohydrate in isoenergetic meals of similar appearance and taste and identical protein content. The results from the dietary study supported a more potent effect of fat on behaviour by showing that the high-fat, low-CHO meal caused a grater decline in alertness and an inferior performance on the sustained attention task than the low-fat, high-CHO meal. The possibility that the differences in alertness and performance between the two meals were related more to an alerting effect of carbohydrate rather than a somnogenic effect of fat is refuted by the results. They indicate that both meals tended to cause a reduction in alertness and performance, but this was greater and only achieved statistical significance with the high-fat, low-CHO meal. Moreover, previous cognitive performance studies have never shown an arousing effect of CHO (see Smith & Kendrick, 1992 for a review).

It is noted that although statistically significant, the changes in reaction time and accuracy during the sustained attention task were very small. Changes of this magnitude are not unusual, and attest to the sensitivity of such tasks. For example, Laming (1988) has drawn attention to significant differences in reaction time of less than 5 ms in studies investigating the effects of drugs and other stressors. While one may be sceptical about the practical significance of the obtained effect sizes, it would be incorrect to dismiss them as of no consequence, since there is no guarantee that effects in the laboratory and field will be the same order of magnitude, and the cumulative effects of small alterations of reaction time in a complex task may result in a much larger change. Moreover, the small drop in accuracy depicted in Fig. 4 actually corresponds to a two- to three-fold increase in error rate, which might prove critical in practice.

https://doi.org/10.1079/BJN19950111 Published online by Cambridge University Press

In the present study the maximum postprandial decline in alertness and performance occurred between 1·5 and 2·5 h after ingestion of the high-fat meal. Since the start of this investigation Lloyd *et al.* (1994) have similarly reported that subjects felt drowsier 2·5 h after ingestion of a high-fat meal than after ingestion of an isoenergetic low-fat meal. A lag of this order coincides with the time at which most fat would have emptied from the stomach. The average half time for gastric emptying of high-fat meals of similar energy density has been reported to be just over 2 h (Sepple & Read, 1990). In contrast, when lipid was infused directly into the duodenum the decline in alertness occurred within 30 min of starting the infusion, as can be seen in Fig. 3. These observations suggest that the changes in behaviour are directly related to the exposure of the small intestine to lipid.

The mechanisms implicated in postprandial somnolence are uncertain. The presence of lipid in the duodenum releases a variety of peptides, including cholecystokinin (CCK). Intravenous infusion of CCK has been shown to make male and female volunteers feel drowsy and cause a decline in performance in a task requiring sustained attention (Stacher *et al.* 1979). CCK, released by the presence of fat in the small intestine, probably acts on vagal afferent terminals to induce effects on mood and behaviour. Infusions of CCK have been shown to increase vagal afferent discharge in rats (Schwartz *et al.* 1993). Moreover, low-voltage stimulation of the intestinal mucosa induces sleepiness in cats and this effect is abolished by severing the vagus nerve. Postprandial sleepiness is associated with feelings of satiety and could be triggered by the same mechanisms. Recent studies have demonstrated that apoprotein A-IV secreted from the intestine after a fatty meal may act on receptors in the central nervous system to alter eating behaviour, but so far no change in sedation has been observed (Fujimoto *et al.* 1993).

In conclusion, infusion of lipid into the small intestine and the substitution of fat for CHO while keeping energy and protein constant in a lunch both cause an enhanced postprandial decline in alertness and concentration. This may be related to the presence of lipid in the small intestine.

REFERENCES

Ashley, D. V., Barclay, D. V., Chauffard, F. A., Monnoz, D. & Leathwood, P. D. (1982). Plasma amino acid responses in humans to evening meals of differing nutritional composition. *American Journal of Clinical Nutrition* **36**, 143–153.

Craig, A., Davies, D. R. & Matthews, G. (1987). Diurnal variation, task characteristics, and vigilance performance. *Human Factors* **29**, 675–684.

Department of Health (1991). *Dietary Reference Values for Food Energy and Nutrients for the United Kingdom. Report on Health and Social Subjects* no. 41. London: H.M.Stationery Office.

Fara, J. W., Rubinstein, E. H. & Sonnenschein, R. R. (1969). Visceral and behavioural responses to intraduodenal fat. *Science* **166**, 110–111.

Fujimoto, K., Fukagawa, K., Sakata, T. & Tso, P. (1993). Suppression of food intake by apolipoprotein A-IV is mediated through the central nervous system in rats. *Journal of Clinical Investigation* **91**, 1830–1833.

Laming, D. (1988). Some boundary conditions of choice reaction performance. In *Pharmacology and Reaction Time*, pp. 65–77 [I. Hindemarch, B. Aufdembrinke and H. Ott, editors]. New York: Wiley.

Lloyd, H. M., Green, M. W. & Rogers, P. J. (1994). Mood and cognitive performance effects of isocaloric lunches differing in fat and carbohydrate content. *Physiology and Behaviour* **56**, 51–57.

Murray, B. E., Clarke, K. A. & Rumsey, R. D. E. (1993). The effect in rats of intestinal intraluminal lipid on post prandial activity determined by Doppler shift radar. *Proceedings of the Nutrition Society* **52**, 359A.

Neuchterlein, K. H., Parasuraman, R. & Jiang, Q. (1983). Visual sustained attention: image degradation produces rapid sensitivity decrement over time. *Science* **220**, 327–328.

Read, N. W. (1980). Kinetic study of small intestinal transport in man determined by measurement of transmucosal potential difference. MD Thesis, University of Cambridge.

Rohrbaugh, J. W., Stapleton, J. M., Parasuraman, R., Frowein, H. W., Adinoff, B., Varner, J. L., Zubovic, E. A., Lane, E. A., Eckardt, M. J. & Linniila, M. (1988). Alcohol intoxication reduces visual sustained attention. *Psychopharmacology* **96**, 442–446.

Schwartz, G. J., McHugh, P. R. & Moran, T. H. (1993). Gastric loads and cholecystokinin synergistically stimulate rat gastric vagal afferents. *American Journal of Physiology* **265**, R872–R876.

Sepple, C. P. & Read, N. W. (1990). Effect of prefeeding lipid on food intake and satiety in man. *Gut* **31**, 158–161.

https://doi.org/10.1079/BJN19950111 Published online by Cambridge University Press

Smith, A. (1988). Effects of meals on memory and attention. In *Practical Aspects of Memory: Current Research and Issues. Volume 2: Clinical and Educational Implications*, pp. 447–482 [M. M. Gruneberg, P. E. Morrison and R. N. Sykes, editors]. Chichester: Wiley.

Smith, A. & Kendrick, A. M. (1992). Meals and performance. In *Handbook of Human Performance, vol. 2*, pp. 1–23 [D. M. Jones and A. P. Smith, editors]. London: Academic Press.

Smith, A. & Miles, C. (1986). Effects of lunch on selective and sustained attention. *Neuropsychobiology* **16**, 117–120.

Spring, B., Maller, O., Wurtman, J., Digman, L. & Cozolino, L. (1982/3). Effects of protein and carbohydrate meals on mood and performance; interactions with sex and age. *Journal of Psychiatric Research* **17**, 155–167.

Stacher, G., Bauer, H. & Steinringer, H. (1979). Cholecystokinin decreases appetite and activation evoked by stimuli arising from the preparation of a meal in man. *Physiology and Behaviour* **23**, 325–331.

Thayer, R. E. (1989). *The Biopsychology of Mood and Arousal*. Oxford: University Press.

Printed in Great Britain

https://doi.org/10.1079/BJN19950111 Published online by Cambridge University Press