sequelae included a wide range of behavioural abnormalities from hyperkinesis to Parkinsonism to personality changes and frank psychiatric illness. Not until the development of the electron microscope in the 1950s was the old debate on whether or not neurones represented a reticular mass of connective tissue or were separate entities finally settled with the clear delineation of the structure of neurones and the synaptic cleft. Shortly afterwards neurotransmitters—identified earlier in peripheral nerves—were detected within the central nervous system, and techniques for delineating various neurotransmitter pathways developed. In the past 20 years particularly, certain well-defined neurotransmitter systems—for example, the monoamine and peptide pathways and their role in moderation and alteration of behaviour—have become more clearly defined and understood. The group of illnesses often referred to as functional disorders—that is, those not clearly associated with structural disease and usually presenting as alterations of behaviour—seems to be related to alteration of activity in such pathways. Treatments such as psychotropic drugs emphasise the role of neurochemical mechanisms in the control and moderation of behaviour.

If the term functional is to have any useful meaning in the neurosciences, we must once again emphasise the physiological use of the term and abandon its psychological interpretations. Functional disorders are those which arise out of disturbed functioning of the nervous system. The goal is to find out which parts are affected most and how they become disordered. In this sense "functional" has heuristic value and ceases to be a meaningless term for undiagnosable symptomatology or a polite eponym for psychiatric disorder. It would thus have practical value and not be an expression of some metaphysical state that apparently stands in antithesis to so-called organic disease and has caused such confusion in the clinical neurosciences.

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Acute biochemical responses to moderate beer drinking

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Abstract

The consequences of drinking six pints of beer (3·3 l) over three hours were investigated in six healthy men. The expected rise in plasma osmolality, fall in plasma vasopressin concentration, and increase in free water clearance occurred; these variables had returned to normal by nine hours. There was a small but significant fall in plasma concentrations of urea and creatinine accompanied by a rise in plasma potassium concentration. Serum activities of alkaline phosphatase, gamma-glutamyl transferase, creatinine kinase, and lactate dehydrogenase did not change, and there was no alcohol-induced hypoglycaemia. All subjects had a slight hangover, but none was fluid depleted.

It is concluded that, apart from inducing changes in water balance, alcohol in this form causes remarkably little metabolic disturbance.

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Introduction

Long-term effects of excess alcohol ingestion are well known, but acute metabolic effects are less certain. Early work using alcoholic spirits defined the diuretic effect of alcohol[1] and implicated an inhibitory effect on secretion of vasopressin, which was subsequently confirmed by direct measurement.[2] In the early 1970s hyponatraemia was described in beer drinkers,[3 4] but whether this was related to an acute dilutional effect,[5] or to chronic sodium depletion was uncertain.[4 6] Beer drinking is such a common social pastime that we investigated its acute effects on sodium and water metabolism and other biochemical variables.

Subjects and methods

We studied six healthy men (mean age 25 years, range 21-32) of normal body weight (mean body mass index 22·4, range 20·9-24·8) who regularly drank moderate amounts of beer (six to 10 pints a week). The study had the approval of the local ethical committee. The investigation was carried out between 1800 and 0800 the next day, indwelling intravenous cannulae having been inserted beforehand. The subjects were not allowed to drink beer or spirits or smoke for 18 hours before the study, and during the study they did not drink tea or coffee or smoke. Blood samples (20 ml) were taken hourly from 1800 to 2400 and then at two-hourly intervals until 0800. Urine was voided at the same times; its volume was noted and an aliquot kept. Before blood sampling the subjects remained seated for 10 minutes. Blood pressure was also measured at these times. The following blood variables were measured: plasma urea, creatinine, electrolyte, arginine vasopressin, and glucose and serum ethanol concentrations; osmolality; and activities of alkaline phosphatase, γ-glutamyl transferase, creatine kinase, and lactate dehydrogenase. Urine was analysed for sodium and potassium and osmolality. Plasma arginine vasopressin

was measured by a sensitive radioimmunoassay[7]; other substances were measured by standard laboratory techniques.

The subjects were given a standard hospital meal (about 3·4 MJ (800 cals)) at 1830 and supper (about 1·3 MJ (300 cals)) at 2330. Beer (McEwan's Export; Scottish and Newcastle Breweries Ltd) was drunk between 2000 and 2300 at a rate of 550 ml (one pint) per 30 minutes (total 3·3 l (six pints) in three hours). A drink of about 250 ml of water or milk was allowed with supper. During the three hours' drinking subjects watched television, read, or played computer games. They went to bed at about 0030 and slept until 0800.

For each variable at each time of measurement the results for the six subjects were used to obtain 95% confidence limits for the mean response in the standard manner using Student's *t* distribution. To test for changes in the mean response with respect to time the first three observations made on each patient before beer drinking had started were used as a baseline and values obtained during and after drinking compared with the baseline mean. Standard *t* tests were then used to test the hypothesis that the population mean score was zero. Because measurements made at different times on the same subject are not necessarily independent, confidence limits for mean responses at different times do not in general give a reliable indication of the significance or otherwise of changes in the average response. Therefore a conservative test was made of the global hypothesis[8] of no change in mean response at any time after the baseline measurements were obtained. Separate tests of significance were then carried out for each of the eight post-baseline times if the global test showed significant differences.

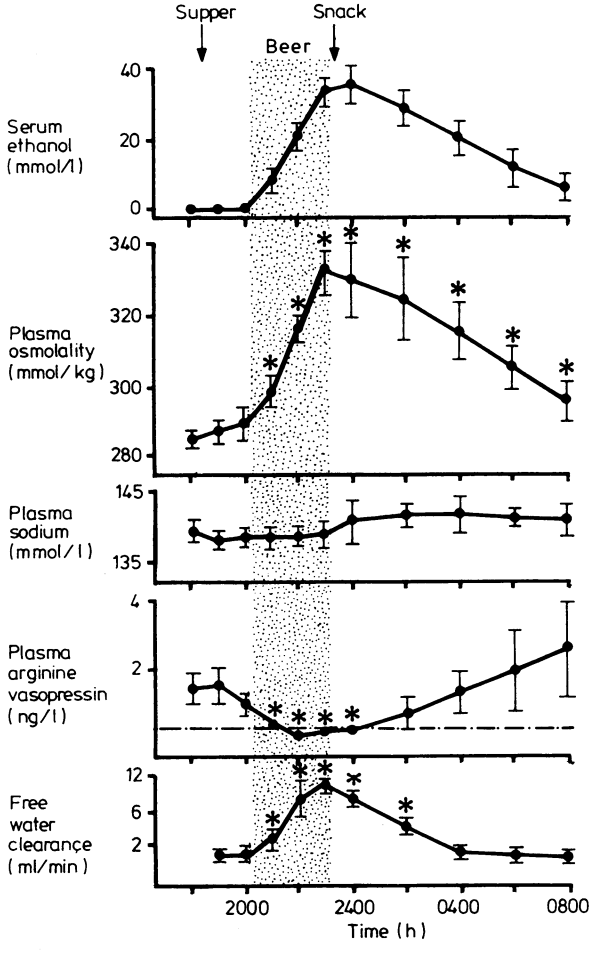

FIG 1—Effect of drinking six pints of beer over three hours on serum ethanol concentration; plasma osmolality and sodium and vasopressin concentrations; and free water clearance (values are means±95% confidence limits (n=6)). Dotted horizontal line indicates limit of detection.

Global test showed significance for plasma osmolality, vasopressin concentration, and free water clearance: *p<0·05.

Conversion: SI to traditional units—Ethanol: 1 mmol/l≈4·6 mg/100 ml. Osmolality: 1 mmol/kg≈1 mosmol/kg. Sodium: 1 mmol/l=1 mEq/l.

Results

Water and electrolyte balance (fig 1)—Serum ethanol concentration rose promptly when the subjects started to drink the beer; this rise was accompanied by a large increase in plasma osmolality. Plasma arginine vasopressin concentration was suppressed and free water clearance rose concurrently. Plasma sodium concentration did not change. Table I shows changes that occurred in plasma electrolyte concentrations. There were slight but significant decreases in plasma urea and creatinine concentrations, which both fell from mid-evening normal values. Plasma potassium concentration had risen slightly by 0600. All these changes were within the normal reference range. Figure 2 shows changes in urine volume, osmolality, and excretion of sodium and potassium. Minimum urine osmolality (94 mmol(mosmol)/

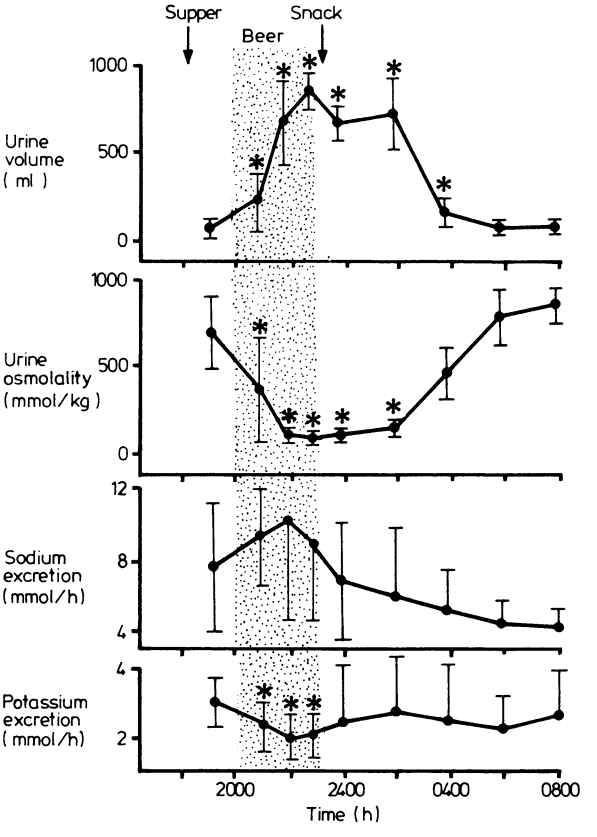

FIG 2—Changes in urine volume and osmolality and sodium and potassium excretion in response to drinking six pints of beer in three hours (values are means±95% confidence limits (n=6)).

Global test showed significance for urine volume and osmolality and for potassium excretion: *p<0·05.

Conversion: SI to traditional units—Osmolality: 1 mmol/kg=1 mosmol/kg. Sodium and potassium excretion: 1 mmol/h=1 mEq/h.

TABLE I—*Mean plasma concentrations of sodium, potassium, urea, and creatinine with beer drinking (±95% confidence limits)*

Time	Sodium (mmol/l)	Potassium (mmol/l)	Urea (mmol/l)	Creatinine (μmol/l)
Mean basal value	138·6±1·0	3·8±0·1	5·6±0·8	91±7
2100†	138·4±1·9	3·7±0·2	5·3±1·1*	86±5*
2200†	138·8±1·0	3·8±0·1	5·0±0·8**	84±6*
2300†	138·8±2·2	3·9±0·1	4·6±0·8**	82±6
2400	140·8±3·1	3·7±0·2	4·4±0·8***	84±6*
0200	141·8±2·3	3·8±0·2	4·2±0·7***	84±6
0400	142·0±2·7	4·0±0·2	4·3±0·7***	80±8***
0600	141·5±1·6	3·9±0·1*	4·1±1·3***	81±5**
0800	141·3±2·1	4·1±0·1**	4·4±0·9***	79±5***
Global test p value	0·136	0·032	0·002	0·016

Difference from basal value: *p<0·05, **p<0·01, ***p<0·001.
†Period during which beer was drunk.
Conversion: SI to traditional units—Sodium, potassium: 1 mmol/l=1 mEq/l. Urea: 1 mmol/l≈6 mg/100 ml. Creatinine: 1 μmol/l≈11·3 μg/100 ml.

kg) occurred at the end of the beer-drinking session. There was no change in sodium excretion. Calculations showed a mean (±SD) urine output of 3·588 ± 0·507 l in the 14-hour period.

Serum enzyme activities did not change significantly at any stage during the study (table II).

Plasma glucose concentrations showed the expected trend in response to carbohydrate intake, with no late hypoglycaemia (table III).

Blood pressure (both systolic and diastolic) did not change significantly, remaining normal at all times.

TABLE II—*Mean serum enzyme activities with beer drinking (± 95% confidence limits)*

Time	Alkaline phosphatase (U/l)	γ-Glutamyl transferase (U/l)	Creatine kinase* (U/l)	Lactate dehydrogenase (U/l)
Mean basal value	48 ± 10	9 ± 3	77 ± 38	130 ± 28
2100†	49 ± 11	9 ± 4	73 ± 35	125 ± 12
2200†	49 ± 13	9 ± 4	76 ± 36	133 ± 28
2300†	45 ± 10	9 ± 4	76 ± 36	128 ± 24
2400	48 ± 12	9 ± 3	75 ± 38	128 ± 26
0200	46 ± 12	9 ± 3	74 ± 35	129 ± 18
0400	45 ± 11	9 ± 3	68 ± 30	125 ± 19
0600	44 ± 10	9 ± 3	62 ± 27	120 ± 25
0800	43 ± 10	8 ± 3	61 ± 27	126 ± 27
Global test p value	0·120	1·000	0·096	1·000

*Values for creatine kinase are rather high because in one subject they were all slightly above the upper limit of the reference range. Subsequent measurements on this subject were normal, and he did not have heart or muscle disease.
†Period during which beer was drunk.

TABLE III—*Mean plasma glucose concentrations with beer drinking (± 95% confidence limits)*

Carbohydrate intake	Time	Plasma glucose (mmol/l)
	1800	5·2 ± 0·4
Supper at 1830 (80 g)		
	1900	8·0 ± 0·9
	2000	6·8 ± 1·2
Beer drinking from 2000 to 2300 (120 g in three hours)	2100	7·8 ± 1·9*
	2200	6·6 ± 1·4
	2300	6·8 ± 0·9
Snack at 2330 (30 g)		
	2400	6·1 ± 1·1
	0200	5·4 ± 0·4
	0400	5·2 ± 0·6
	0600	5·2 ± 0·5
	0800	5·1 ± 0·4

*One subject with a plasma glucose concentration of 11·3 mmol/l (204 mg/100 ml) at 2100 subsequently yielded a normal result to a glucose tolerance test.
Conversion: SI to traditional units—Plasma glucose: 1 mmol/l ≈ 18 mg/100 ml.

Discussion

Drinking large volumes of beer is a common pastime, and in this study we tried to mimic a typical night's drinking and to document biochemical abnormalities that must occur in thousands of people each night. Beer is a hyperosmolar fluid (due to alcohol) with a low sodium content (the beer that we used, McEwan's Export, contained 4·3% ethanol by volume, had an osmolality of 612 mmol/kg, and contained 2 mmol(mEq)sodium/l and 7·6 mmol(mEq)potassium/l. While our subjects were drinking the beer their serum ethanol concentration rose quickly to peak at a mean of 35 mmol/l (161 mg/100 ml) at 2400. This was reflected in appreciable plasma hyperosmolality (mean peak value 332 mmol/kg). Calculated osmolalities were similar, suggesting that the addition of alcohol was the sole cause of the raised measured osmolality.[9] Plasma arginine vasopressin concentration was promptly suppressed by the raised ethanol concentrations, though it later began to rise at a time when serum ethanol concentrations were still high. Free water clearance rose and fell in relation to the changing arginine vasopressin concentrations. The later increase in arginine vasopressin concentration despite high ethanol concentrations suggests that other factors were stimulating the posterior pituitary or that the effect of ethanol on inhibiting secretion of arginine vasopressin is only temporary. Possible non-osmotic factors include hypotension, hypovolaemia, and vomiting, but none of these was apparent in our subjects.

An increase in extracellular osmolality is usually a potent stimulus to secretion of arginine vasopressin.[6] During beer drinking hyperosmolality is associated with suppression of antidiuretic hormone and diuresis. Ethanol, however, is freely distributed across cell membranes, and the hyperosmolality will be equal inside and outside cells. Thus there will not be any "shrinkage" stimulus to osmoreceptor cells and water will not move from inside to outside cells to cause hyponatraemia. Beer drinking, however, may induce lowered plasma sodium concentrations if sufficient volume is drunk quickly enough[5] by a direct dilution effect due to rapid addition of water to the body. This did not occur with the rate of ingestion of beer in our study. The previously described "beer drinker's hyponatraemia"[3,4] is a more complex condition; in those studies the patients generally took large amounts of beer for long periods, ate little, and sometimes had liver damage. The cause of the hyponatraemia in these patients was probably multifactorial, and many may have been chronically salt depleted.[4] Chronic alcohol ingestion may also lead to hyponatraemia associated with concentrated urine,[3,10] possibly due to persistent secretion of antidiuretic hormone.[11]

Our urine results (fig 2) showed the expected increase in urine flow and maximal urine dilution with return to normal of both variables after 0400. The mild natriuresis reported by other workers and believed to be due to suppression of secretion of aldosterone[12] was not documented in this study.

The small but significant changes that occurred in plasma potassium, urea, and creatinine concentrations (table I) are interesting but difficult to explain. We did not measure urinary urea or creatinine concentrations, but the diuresis may have induced increased clearance of these substances with an accompanying slight reduction in their plasma concentrations. The increase in plasma potassium concentration may have been due to the potassium content of the beer, though it occurred rather late. Some or all of these changes might possibly represent normal daily variations, though this is not supported by previous diurnal studies of these biochemical variables,[13-15] though the conditions were not comparable. Ideally, our subjects should be restudied in control conditions drinking, firstly, nothing and, secondly, similar volumes of water. Our volunteers, however, were not prepared to perform these experiments again.

Long-term high alcohol intake may produce increased serum γ-glutamyl transferase activity.[16] Such increases are the result of enzyme induction, and previous studies have found only small (about 10%) increases after one[17] or three[18] evenings of moderate alcohol intake. Our findings confirm that in the short term such drinking does not alter serum activity of γ-glutamyl transferase in the healthy. The fasting state is believed to lower alkaline phosphatase activity,[19] but our study failed to confirm this.

Hypoglycaemia may occur after alcohol ingestion, especially when both alcohol and carbohydrate are taken together,[20] which is basically what happens when beer is drunk. A study from South Africa,[21] however, failed to show hypoglycaemia after ingestion of two litres of beer. Interestingly, when the same subjects drank gin and tonics of equivalent alcohol content significantly lower blood glucose concentrations were recorded. Our results (with over three litres of beer drunk) also showed no suggestion of hypoglycaemia in any subject.

At the end of the study (the "morning after") all our subjects had something of a hangover, with headache, nausea, dry mouth, and malaise. They were not, however, in obvious fluid imbalance (mean output 3·588 l, mean input 3·630 l). Even allowing for insensitive losses during the 14-hour period, they cannot have been more than 200-300 ml in deficit. They also had normal blood glucose concentrations, no evidence of electrolyte imbalance or liver dysfunction, and fairly low serum ethanol concentrations. Whether impurities in the beer or other factors are responsible for the hangover remains undetermined.

We conclude that drinking six pints of beer has no serious acute biochemical consequences in healthy young men.

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The gap in your knowledge: gender on wheels

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Abstract

Among a group of young car drivers the size of the gap perceived as necessary to allow them to drive their cars through was related to their degree of measured fatness. This relationship extended to measured height and shoulder breadth in women and self-perception of shoulder breadth in men. No relationship could be found with the premenstrual phase in women. These findings may have important social implications!

Introduction

Some claim that man's hypochondriasis, obsessionality, potency, and gender are nowhere more apparent than when extended to his car—his vision of it and his vision of the outside world when he is in it. Some of us, it seems, also considerably distort our vision of ourselves, at least in our reports to others in terms of our body shape.[1] Several years ago AHC suggested to his female research colleagues and assistants that there might be a relation between such known gross distortions by many women of their perception of their shape and their obvious inability to drive their cars through perfectly reasonably sized gaps in the traffic confronting them. His colleagues' fierce resistance to this proposal confirmed him in his belief. At the time it was considered that only pubertal and adolescent women experienced such shape and other body experience misconceptions, but now we know that so too do men.[2] No longer would the men have to act as controls: the way was clear for a dispassionate study of both sexes!

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Hypothesis

There will be a direct relation between the perceived size of the gap through which a car driver in his or her driving position will report being prepared to drive the car and his reported estimate of his own body width. Such relationships will not extend to people's reported estimates of the size of an inanimate object.

Method

The sample consisted of 25 male and 19 female car-owners aged 18-31, who were asked to estimate the width of various parts of their body, plus a neutral object, in terms of the horizontal separation between moveable lights, as described elsewhere.[1] They were also asked to estimate the width of their car along a chalk line on the laboratory floor.

To measure the perception of the size of gap through which subjects were prepared to drive their car, portable barriers made to resemble width markers in roads were constructed and set up in a car park. The subjects drove into the car park and were asked to stop their car on a white T painted a standard distance from the width barriers.

They were instructed: "The size of the gap in front of you will be altered a number of times. On each occasion please assess whether you can drive your car through the gap. If you can, indicate how much room there is to spare. If you cannot, indicate how much too small the gap is. At any point you may be asked to act on your decision." The