Enhanced ethanol consumption following portal-systemic shunting in rats

J.R. Martin, J. Bircher and H. Porchet

Institute for Behavioral Science, Swiss Federal Institute of Technology, Turnerstrasse 1, CH-8092 Zürich (Switzerland), and Department of Clinical Pharmacology, University of Bern, Murtenstrasse 35, CH-3010 Bern (Switzerland), 21 January 1982

Summary. Following surgical construction of a chronic end-to-side portacaval shunt, rats consumed more 6% ethanol than their controls in a schedule-induced polydipsia paradigm during the baseline condition and during intermittent food delivery. Blood ethanol was higher in rats with portacaval shunts than in controls following the final test session.

The rat with a portacaval shunt serves as an animal model for many of the biochemical effects of chronic liver disease with portal-systemic shunting of the circulation[1]. Surgical construction of a portacaval shunt in patients with severe liver cirrhosis is often followed by the development of hepatic encephalopathy with debilitating cognitive and neuromuscular disturbances[2]. Recently, attempts have been made to determine whether the rat with a portacaval shunt (PCS) also exhibits behavioral abnormalities[3,4]. The present experiment provides evidence that the rat with a portacaval shunt consumes more ethanol and exhibits a higher blood ethanol concentration than sham-operated controls in a schedule-induced polydipsia paradigm used to produce acutely a high level of ethanol intake.

Methods. 16 male Sprague-Dawley rats (Süddeutsche Versuchstierfarm, Tuttlingen, FRG) underwent behavioral testing beginning 3-4 months after the surgical construction of an end-to-side portacaval shunt (N = 8) or sham surgery (N = 8). These surgical procedures are described elsewhere[4]. Animal quarters were illuminated in a 12:12 h light-dark cycle and all behavioral testing was done during the light half of the cycle. Food and water were available ad libitum except during the fasting periods. Prior to the start of the present experiment, it was verified that, as in earlier research[3,4], the rats with portacaval shunts exhibit lower spontaneous activity than controls in maze tests of long duration and overconsume palatable solutions (e.g., 5% glucose) when compared with sham-operated rats. The subjects were initially habituated to a daily 8-h fast and to the test chamber prior to the start of the present experiment. On 11 consecutive days the 8-h fasted rats received a daily 1-h session in an operant chamber with a bottle containing 6% ethanol (w/w) attached. On day 1, a baseline test was done with 30 food pellets (each 45 mg) given together in the food receptacle at the start of the session. On the subsequent 10 days, 30 pellets were delivered intermittently on a FT-2 min schedule (i.e., 1 pellet delivered every 2 min) during the 1-h sessions. The procedure was then modified so that a 24-h fast preceded each 1-h test session, with 2-3 days between successive sessions. A baseline test was given following a 24-h fast and then 5 sessions with intermittent pellet delivery on a FT-2 min schedule. Other details concerning this schedule-induced polydipsia paradigm are provided elsewhere[5]. A blood sample was taken from the tail of each rat 30 min following the completion of the final test session and was analyzed for ethanol by the method of von Wartburg[6], adapted for small samples of blood. In a subsequent necropsy, the liver weight was measured for all subjects and the portacaval shunt in each experimental rat was anatomically verified.

Results and discussion. Under the baseline condition and during intermittent food delivery, fasted rats with portacaval shunts consumed significantly more ethanol (given as a 6% solution) than their sham-operated controls. The blood ethanol concentration of the rats with portacaval shunts was significantly higher than that of their controls following the final test session with food pellets presented intermittently. In the necropsy, the rats with portacaval shunts were anatomically verified to have open portacaval shunts and the wet liver weights of these experimental rats was found to be significantly lower than that of control rats. Ethanol consumption, blood ethanol level, and liver weight data are shown in the table. Despite a very drastic reduction of liver weight, after experimental portal-systemic shunting of the circulation, the fasted rats with portacaval shunts consumed significantly more ethanol than their controls in a schedule-induced polydipsia paradigm and, not surprisingly, had a significantly higher blood ethanol concentration than their controls at the conclusion of the final test session. Within this context, it is interesting to note that when cirrhotic patients with a history of alcoholism were subjected to a portal-systemic shunt they frequently returned to alcoholism[7]. Thus, the shunting of the portal circulation directly into the vena cava may, by an as yet unexplained mechanism, influence the tendency to consume ethanol in both rats and man.

Ethanol intake (calculated as g 100% ethanol) during baseline tests and tests with food intermittently delivered on a FT-2 min schedule, blood ethanol concentrations, and liver weights (mean ± SEM) of rats with portacaval shunts (PCS) and sham-operated rats (SHAM)

	Baseline[a] (trial 1)	FT-2 min[a] (trials 2-6)	FT-2 min[a] (trials 7-11)	Baseline[b] (trial 12)	FT-2 min[b] (trials 13-17)	Blood ethanol concentration (mg/dl)	Liver weight (g/100 g)
PCS	0.64 ± 0.11*	0.82 ± 0.12**	1.14 ± 0.13**	0.69 ± 0.09**	1.35 ± 0.08**	40.1 ± 8.1*	1.8 ± 0.1**
SHAM	0.24 ± 0.08	0.30 ± 0.11	0.29 ± 0.08	0.16 ± 0.06	0.83 ± 0.16	14.2 ± 6.8	3.5 ± 0.1

[a]Tested after 8-h fast; [b]tested after 24-h fast. *$p < 0.05$, **$p < 0.01$ for a comparison with the SHAM group using a 2-tailed Mann-Whitney U-test.

1 R. Herz, V. Sautter, F. Robert and J. Bircher, Eur. J. clin. Invest. *2*, 390 (1972).
2 R.H. Resnick, T.C. Chalmers, A.M. Ishihara, A.J. Garceau, A.D. Callow, E.M. Schimmel, E.T. O'Hara and the Boston Inter-Hospital Liver Group, Ann. intern. Med. *70*, 675 (1969).
3 J.R. Martin, K. Bättig and J. Bircher, Physiol. Behav. *25*, 713 (1980).
4 J.R. Martin, K. Bättig and J. Bircher, Behav. neural Biol. *32*, 54 (1981).
5 J.R. Martin and K. Bättig, Pharmac. Biochem. Behav. *14*, 857 (1981).
6 J.P. von Wartburg and M.M. Ris, Experientia *35*, 1682 (1979).
7 M.M. Howard, K.G. Swan, B.F. Rush, Jr, and C.M. Leevy, Gastroenterology *78*, 1308 (1980).