perfused hollow fibre. Neurosci. Lett., *29:* 111 (1982).
21. Requests for reprints should be addressed to: Dr. H. Lagercrantz, Nobel Institute for Neurophysiology, Karolinska Institutet, Box 60400, S-104 01 Stockholm, Sweden.
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Letter to the Editor

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We would like to comment on the interesting observation by P. Landrieu and coworkers (Pediatr. Res., *16:* 977, 1982). Contrary to the statement of the authors, "it seems unlikely that sodium valproate (SV) played an important role," we suggest that SV could have been of major importance in the development of acute hepatic failure for the following reasons. Liver function tests were stated to be normal before the start of SV. Three days after the start of SV blood ammonia and serum GPT rose and PTT decreased. It must be noted that SV was given in an unusually high dosage of 100 mg/(kg·d) [normal dosage, 10–20 mg/(kg· d)]. The changes in urinary amino acids between d 2 (start of SV) and d 3 cannot be explained by the OTC deficiency but are typical for SV therapy [increase of alanine and glycine, decrease of glutamic acid, glutamine and tyrosine (4, 5)]. Furthermore, there was an important decrease of orotic acid which can be explained by the inhibitory effect of SV on the first step of the urea cycle (2). By giving SV in high doses a second block was introduced into the urea cycle besides the existing OTC deficiency. The observed accumulation of fat droplets in the cytoplasm could be ascribed to SV which is known to cause steatosis (3) and to decrease serum levels of carnitine, necessary for the oxidation of fatty acids (1, 6). Recently, a boy with OTC deficiency died at the age of 13 mo after the introduction of SV [33 mg/(kg·day)] for febrile convulsions (8).

We agree with the authors that the changes in peroxisomes are unlikely to be specifically related to the OTC deficiency. The possibility that SV or SV in association with OTC deficiency caused the peroxisomal changes rather than the OTC deficiency itself cannot be excluded as SV is a short chain fatty acid and fatty acids are known to induce peroxisomal changes (7). It would be of interest to know whether the recovery of this patient occurred during SV therapy or after SV had been stopped or diminished.

REFERENCES AND NOTES

1. Böhles, H., Richter, K., Wagner-Thiessen, E., and Schäfer, H.: Decreased serum carnitine in valproate induced Reye syndrome. Eur. J. Pediatr., *139:* 185 (1982).
2. Coude, F. X., Rabier, D., Cathelineau, L., Grimber, G., Parvy, P., and Kamoun, P. P.: Letter to the editor: a mechanism for valproate-induced hyperammonemia. Pediatr. Res., *15:* 974 (1981).
3. Gerber, N., Dickinson, R. G., Harland, R. C., Lynn, R. K., Houghton, D., Antonias, J. I., and Schimschock, J. C. Reye-like syndrome associated with valproic acid therapy. J. Pediatr., *95:* 142 (1979).
4. Jaeken, J., Corbeel, L., Casaer, P., Carchon, H., Eggermont, E., and Eeckels, R., Dipropylacetate (valproate) and glycine metabolism Lancet, *2:* 617 (1977).
5. Kamoun, P., and Parvy, P.: Effet du n-dipropyl acétate sur l'elimination urinaire des acides aminés. Helv. Paediatr. Acta, *33:* 379 (1978).
6. Ohtani, Y., Endo, F., and Matsuda, I.: Carnitine deficiency and hyperammonemia associated with valproic acid therapy. J. Pediatr., *101:* 782 (1982).
7. Tolbert, N. E.: Metabolic pathways in peroxisomes and glyoxysomes. Ann. Rev. Biochem. *50:* 133 (1981).
8. Tripp, J. H., Hargreaves, T., Anthony, P. P., Searle, J. F., Miller, P., Leonard, J. V., Patrick, A. D., Oberholzer, V. G.: Sodium valproate and ornithine carbamyl transferase deficiency. Lancet, *1:* 1165 (1981).