

Regional Cerebral Blood Flow in a Case of Bromide Psychosis

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Summary. A case of bromide psychosis is described. A course of repeated measurements of the *regional cerebral blood flow (rCBF)* was followed, using the ^{133}Xe inhalation method. At the first examination, when the serum bromide level was 45 mmol/l, the cerebral blood flow was reduced to about one-third of the normal. The regional flow pattern was also abnormal with low flows in frontal and parieto-occipital regions. Hemodialysis was performed with an overall improvement of the condition and a successive normalization of rCBF. The pronounced decrease of the cerebral blood flow, together with the positive effects of hemodialysis, seems to indicate that bromide psychosis is of a toxic origin and not an abstinence phenomenon.

Key words: Bromide psychosis – Regional Cerebral Blood Flow – ^{133}Xe inhalation method – Flow reduction.

Zusammenfassung. Bei einem Falle von Brom-Psychose wurde die regionale Hirndurchblutung (rCBF) mit der Xenon-Inhalationsmethode fortlaufend gemessen. Bei der ersten Untersuchung mit einem Bromspiegel von 45 mmol/l war die Hirndurchblutung auf $\frac{1}{3}$ des Normalen vermindert. Das regionale Blutflußmuster war abnorm mit erniedrigten Werten in den frontalen und parieto-occipitalen Hirnregionen. Nach Hämodialyse entstand eine allgemeine Besserung und eine zunehmende Normalisierung der Hirndurchblutungswerte. Die starke Hirndurchblutungsminde rung und die positive Wirkung der Hämodialyse weisen darauf hin, daß die Brom-Psychose toxischer Genese und kein Entziehungssymptom ist.

Schlüsselwörter: Brompsychose – Regionale Hirndurchblutung – ^{133}Xe Xenon-Inhalationsmethode – Durchblutungsminde rung.

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Introduction

Chronic bromide intoxication is characterized by the slow elimination of bromide (half-life 11.4 days; Poser et al., 1974) and by the high frequency of bromide psychosis, especially delirium (Levin, 1948). Early investigators described the delirium as a direct toxic reaction to bromide (Levin, 1948; Isbell and White, 1953) while in later studies the bromide delirium has been regarded more as a withdrawal syndrome. Carney (1971) reported on five cases, three of which started after a few days of abstinence. Further, Poser et al. (1974) doubted the value of treatment with hemodialysis because of the accelerated withdrawal.

In the present case of bromide psychosis the course of withdrawal was followed by repeated measurements of the regional cerebral blood flow (rCBF). A marked decrease of rCBF will be demonstrated as well as changes of the regional blood flow patterns. The effect of hemodialysis will also be discussed.

Methods

The regional cerebral blood flow (rCBF) was measured by the ^{133}Xe inhalation technique (Mallet and Veall, 1965) as modified by Obrist et al. (1975) and by Risberg et al. (1975). The patient inhaled ^{133}Xe mixed with air (3 mCi/l) for 1 min by means of a face mask and a rebreathing system. The 1 min inhalation period was followed by a 10 min period during which the patient was breathing normal air. The gamma radiation was recorded by 18 lead-shielded scintillation detectors ($\frac{3}{4}'' \times \frac{3}{4}''$ NaI(Tl) crystals; Meditronic, Denmark) placed in parallel at right angles to the left lateral surface of the patient's head. The detectors had lead collimators with a length of 20 mm and an ID of 22.5 mm. The radiation from a continuous sample of the expired air was recorded by a separate detector for determination of the end-tidal concentrations of ^{133}Xe (the 'air curve') used to correct the 'head curves' for recirculation of the tracer. The pulses from the 19 detectors were integrated in binary registers (Meditronic, Denmark) for 5 s for the head curves and for 0.625 s for the air curve. The counts were punched on paper tape (Facit, Sweden) for off-line computer analysis. The results presented here are based on the initial slope index (ISI), a cerebral blood flow parameter which is preferable due to its high reliability even in cases with very low cerebral flow rates, like the present one (Risberg et al., 1975). The arterial pCO_2 was estimated from recordings of end-tidal CO_2 concentrations (Beckman, LB 2-analyzer). Measurements were performed on the first, second, fifth, and fourteenth day after admission.

The serum bromide level was determined with the technique described by Wuth (1927).

Case Report

The patient was a 58-year-old woman, a former chemical engineer, now a high school teacher of science. She had always been in excellent physical health. She regarded herself as a good-tempered woman with few nervous symptoms and had previously never visited a psychiatrist. She had used bromide (mainly NaBr) on and off during the last 30 years, sometimes in excess, but had never developed psychotic symptoms. She was also a heavy drinker but had no indications of physical dependence on alcohol.

She became progressively more tired during February 1976 and was confused during short periods at the end of the month. During this period there was no positive indication of excessive drinking of alcohol or use of drugs other than bromide. The condition deteriorated continuously and she was admitted to hospital on the 10th of March. On admission she was profoundly disorientated with visual and auditory hallucinations. Paranoid symptoms were also prominent.

She was atactic and bedridden. Blood pressure 120/80 mm Hg. Heart rate 80 b.p.m. Electrocardiogram normal. Hemoglobin 155 g/l. Serum sodium 141 mmol/l. Serum potassium 4.7 mmol/l. Serum calcium 2.65 mmol/l. Serum creatinine $48\mu\text{mol/l}$.

The day after admission the serum bromide level was 45 mmol/l (360 mg/100 ml). Therefore hemodialysis was initiated. On the second day after admission the serum bromide level was 20 mmol/l (160 mg/100 ml) and the hemodialysis was interrupted. Now the patient was much less atactic and the psychotic symptoms had diminished slightly. The delirium ceased on the fourth day after admission. A psychometric investigation on the 11th day revealed no obvious signs of mental impairment. The patient left the ward 3 weeks later in excellent condition.

Results

The average initial slope index (ISI) values (corrected for apCO_2) for the hemisphere are shown in Figure 1. It is seen that on the first day the cerebral blood flow was reduced to about one-third of the normal (Normal ISI: 50 ± 7 ; Wilson et al., 1977). The patient was much less drowsy after the hemodialysis and the cerebral blood flow on the second day was also considerably increased but still subnormal. The measurement on the fifth day, when the delirium had ceased, showed a further increase and after 14 days the flow results were normal. The estimated apCO_2 values at the times of the four measurements were: 40, 42, 43, and 34 mm Hg respectively, and the BP: 120/80, 135/110, 155/105, and 130/80 mm Hg respectively. Correction of the flow values to a standard apCO_2 of 40 mm Hg was performed with a correction factor of 4% per mm Hg (Olesen et al., 1971). The regional flow variations in the first three measurements are shown in Figure 2. The flow distribution on the first day showed the lowest values in frontal and occipitoparietal regions. This pattern is never seen in normal subjects and has some resemblance to what has been found in presenile dementia (Gustafson and Risberg, 1974). The distribution on the second day was more close to the normal but lacked the typical 'hyperfrontal' normal pattern (Wilkinson et al., 1969; Sveinsdottir et al., 1971), which, however, was seen in the measurements on the fifth and fourteenth days.

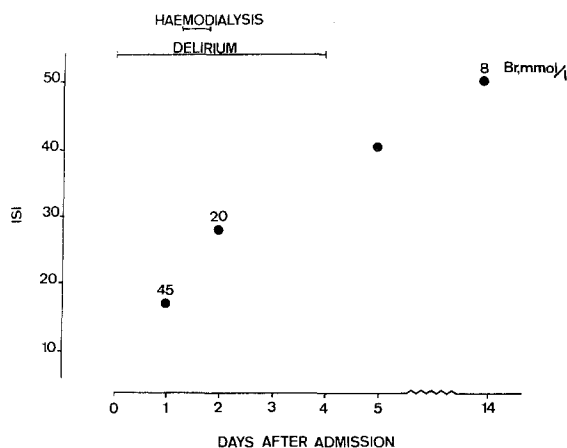


Fig. 1. Mean hemispheric values of the initial slope index (ISI), corrected for apCO_2 , are marked with filled dots. A normalization of the cerebral blood flow after a pronounced reduction at admission is seen

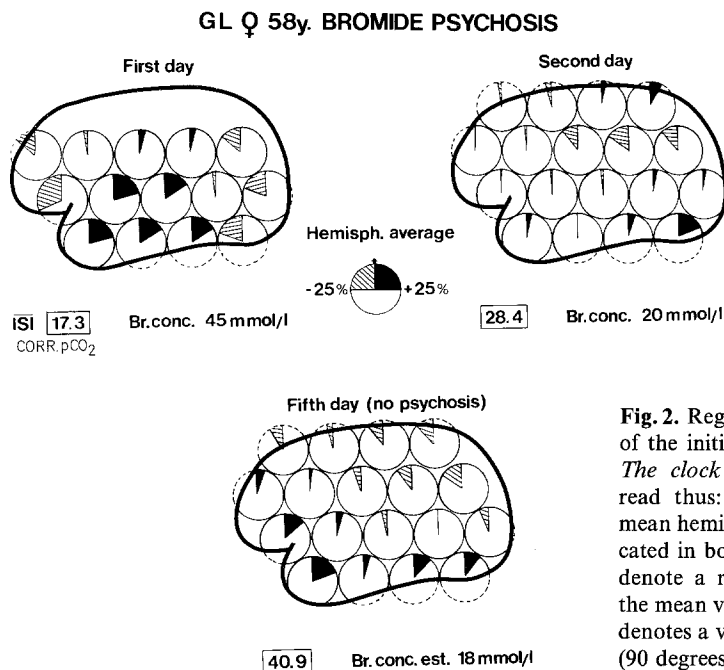


Fig. 2. Regional flow variations of the initial slope index (ISI). The clock symbols should be read thus: 12 o'clock denotes mean hemispheric value as indicated in boxes. Black markings denote a regional value *above* the mean value and striped field denotes a value *below* the mean (90 degrees = 25 per cent)

Discussion

The present findings during a bromide delirium differ from findings with similar measurement techniques in alcoholics with delirium tremens. Compared to predeliric values the cerebral blood flow was reported to be unchanged during delirium tremens (Marx et al., 1975). Also, the regional pattern found during the first study has not been found in an ongoing study of alcohol withdrawal (Berglund and Risberg, 1977). Therefore it seems plausible to assume that different mechanisms are active in alcohol delirium and bromide delirium, the bromide being characterized by a more marked decrease of cerebral blood flow and most likely also of oxygen metabolism.

Previous EEG studies have given results which support the present finding of a decrease of the rCBF. Greenblatt et al. (1945) reported high voltage activity as slow as 2 Hz in some of the confused patients with high blood bromide levels, even if an activity in the 5 to 8 Hz range was most frequent. Harenko and Humar (1967) reported a case with a serum bromide level of 260 mg/100 ml and with delta waves as slow as 1 Hz, and Meyer (1974) reported diffuse slow waves in high serum bromide levels.

Hemodialysis drastically reduces the half-life of bromide in blood plasma from 11 days to a few hours. Thus the withdrawal is strongly accelerated. The condition of the patient was markedly improved after hemodialysis. Thus our observations support the hypothesis that bromide delirium is released by a direct effect of bromide and not by bromide abstinence.

A clear understanding of the etiology of the bromide psychosis is important for proper therapy. According to the present results the treatment ought to be active until the delirium ceases. Hemodialysis is one possibility but this is unnecessary in most cases according to Wieth and Funder (1963). They recommended treatment by forced halogen excretion. With this method bromide will have a half-life of 16 h and the serum bromide concentration can almost always be brought under toxic level in less than 24 h.

References

- Berglund, M., Risberg, J.: Variations in the regional cerebral blood flow during the withdrawal period in alcoholics. A study with the ^{133}Xe inhalation method. (in preparation, 1977)
- Carney, M. W. P.: Five cases of bromism. *Lancet* **1971** *II*, 523—524
- Greenblatt, M., Levin, S., Schegloff, B.: Electroencephalographic findings in cases of bromide intoxication. *Arch. Neurol. Psychiat. (Chic.)* **53**, 431—436 (1945)
- Harenko, A., Humar, E.: EEG changes in chronic Bromisolvalum poisoning. *Ann. Med. Int. Fenn.* **56**, 79—85 (1967)
- Isbell, H., White, W. M.: Clinical characteristics of addiction. *Amer. J. Med.* **14**, 558—565 (1953)
- Levin, M.: Bromide psychoses: Four varieties. *Am. J. Psychiat.* **104**, 798—800 (1948)
- Mallet, B. L., Veall, N.: Investigation of cerebral blood flow in hypertension, using radioactive Xenon inhalation and extracranial recording. *Lancet* **1963** *I*, 1081
- Marx, P., Neundörfer, B., Potz, G., Hoyer, S.: Cerebral blood flow and amino-acid metabolism in chronic alcoholism. In: *Blood flow and Metabolism in the Brain*. (Ed. Harper et al.) Edinburgh: Churchill Livingstone 1975
- Meyer, G.: Klinische Untersuchungen bei chronischen Bromintoxikationen. *Schweiz. Arch. Neurol.* **114**, 169—194 (1974)
- Obrist, W. D., Thompson, H. K., Wang, H. S., Wilkinson, W. E.: Regional blood flow estimated by ^{133}Xe inhalation. *Stroke* **6**, 245—256 (1975)
- Olesen, J., Paulson, O. B., Lassen, N. A.: Regional cerebral blood flow in man determined by the initial slope of the clearance of intraarterially injected ^{133}Xe . *Stroke* **2**, 519—540 (1971)
- Poser, W., Poser, S., Echterkamp, M.: Mißbrauch bromhaltiger Schlaf- und Beruhigungsmittel. Ein aktuelles Suchtproblem. *Dtsch. med. Wschr.* **99**, 2489—2497 (1974)
- Risberg, J., Ali, Z., Wilson, E. M., Wills, E. L., Halsey, J. H.: Regional cerebral blood flow by ^{133}Xe inhalation. Preliminary evaluation of an initial slope index in patients with unstable flow compartments. *Stroke* **6**, 142—148 (1975)
- Sveinsdottir, E., Torlöf, P., Risberg, J., Ingvar, D. H., Lassen, N. A.: Calculation of regional cerebral blood flow (rCBF): Initial-slope-index compared to height-over-area values. In: *Brain and blood flow, proceedings of the 4th international symposium on the regulation of cerebral blood flow*. (Ed. Ross Russel). London: Pitman 1971
- Wieth, J. O., Funder, J.: Treatment of bromide poisoning. Comparison of forced halogen turnover and haemodialysis. *Lancet* **1963** *II*, 327—329
- Wilkinson, I. M. S., Bull, J. W. D., Boulay, du G. H., Marshall, J., Ross Russel, R. W., Symon, L.: Regional blood flow in the normal cerebral hemisphere. *J. Neurol. Neurosurg. Psychiat.* **32**, 367—378 (1969)
- Wilson, E. M., Wills, E. L., Risberg, J., Halsey, J. H., Gerard, J. D., May, C. P.: Measurement of regional cerebral blood flow by the ^{133}Xe inhalation method with an on-line computer. *Computers in Biol. and Med.* (in press, 1977)
- Wuth, O.: Rational Bromide Treatment. *J.A.M.A.* **88**, 2013—2017 (1927)