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The effect of *bis*-(2,2,2-trifluoroethyl)ether on brain electrolytes and water distribution in the rat

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IN OUR studies with the anesthetic, trifluoroethyl vinyl ether, we observed that a closely related fluorinated ether $CF_2{\cdot}CH_2{-}O{-}CH_2{\cdot}CF_3$, *bis*-(2,2,2-trifluorethyl)ether (BTE) evoked marked convulsive seizures upon inhalation in laboratory animals.[1] This observation prompted us to use the agent as a substitute for electroshock in the treatment of mentally depressed patients.[2] In studies of the mechanism of action of BTE, Ling *et al.*[3] showed that the convulsive seizure in rats was accompanied by a mobilization of brain acetylcholine from its storage sites. Woodbury[4] observed that intracellular brain sodium was increased by electroshock in rats.

These studies describe the effect of BTE-evoked convulsive seizures on the brain electrolytes Na^+ and K^+, and water distribution.

The BTE used in these studies was Indoklon®, used in human convulsive therapy. Male albino rats (150 to 200 g) were convulsed with BTE (0·5 ml in a 3·4-liter chamber). During the convulsion each rat was decapitated, and the brain *in toto* was removed. Adequate blood samples were collected for serum electrolyte determinations. The brains were dried to constant weight (Yannet and Darrow[5]) and the content of brain water was determined. Each whole brain was homogenized in deionized-distilled water, deproteinized with 10% trichloroacetic acid, and diluted with deionized-distilled water. After centrifugation, supernatant samples of the brain preparation were taken and analysed for brain sodium and potassium by means of the Baird-Atomic model KY-1 flame photometer with lithium as the internal standard. Standard curves were constructed with each series of determinations.

The results of these studies, in Table 1, show a significant decrease in brain potassium with a concomitantly significant increase in serum potassium during BTE-induced convulsions. There is also a significant elevation in brain sodium during the convulsion. No significant change was noted with serum sodium or brain-water content.

TABLE 1. THE EFFECT OF BTE SEIZURES ON BRAIN Na^+, K^+, AND WATER

Fraction	Mean value
Control (10 rats)	
Serum Na^+	151·7 ± 4·34 mEq/L
Serum K^+	6·8 ± 0·44 mEq/L
Brain Na^+	244·5 ± 17·84 μEq/g dry wt
Brain K^+	427·0 ± 24·30 μEq/g dry wt
Brain H_2O A	3·5 ± 0·03 (g/g dry wt) —or—
Brain H_2O B	77·8 ± 0·16% (g H_2O/total brain dry wt)
BTE (14 rats)	
Serum Na^+	153·7 ± 4·92 mEq/L
Serum K^+	8·1 ± 0·16 mEq/L *
Brain Na^+	389·3 ± 41·11 μEq/g dry wt*
Brain K^+	206·8 ± 18·36 μEq/g dry wt*
Brain H_2O A	3·5 ± 0·04 g/g dry wt —or—
Brain H_2O B	77·9 ± 0·22% (g H_2O/total brain dry wt)

* Significant: based on *t* test for paired means with the differences from control being at least at the 1% level of probability.

Henry,[6] Welt *et al.*,[7] and Colfer and Essex[8] demonstrtaed that convulsions induced electrically or by pentylenetetrazole are accompanied by a decrease in brain potassium with an increase in serum potassium. There is lack of agreement among these workers concerning the changes in sodium and water fractions of brain and blood during convulsive activity. More recently, Cummins and McIlwain[9] observed an efflux of potassium from slices of cerebral cortex of guinea pig after electrical stimulation. Our studies with BTE conform with the findings of Woodbury,[4] who used electroshock, indicating an increase in brain Na^+ evoked by the convulsive seizure.

In summary, *bis*-(2,2,2-trifluoroethyl)ether elicits marked convulsive seizures in rats upon inhalation of low concentrations of its vapors. These studies show that the seizure is accompanied by a decrease in brain potassium and a concomitant increase in serum potassium. There is also a significant elevation in brain sodium. No significant changes were observed in serum sodium or brain-water content.

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