Nx produced the clinical effects observed in our patient (Cuello 1983).

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References

Bluym I, Munitz H, Shalev A, Roberts E (1984): Naloxone may be beneficial in the treatment of tardive dyskinesia. *Clin Neuropharmacol* 7:265–267.

Brambilla F, Facchinetti F, Petraglia F, et al (1984): Secretion patterns of endogenous opioids in chronic schizophrenia. *Am J Psychiatry* 141:1183–1189.

Cuello AC (1983): Central distribution of opioid peptides. *Br Med Bull* 39:11–16.

Gillman MA, Sandyk R (1984): Evidence for underactivity of the opioid system in neuroleptic-induced akathisia. *Psychiatry Res* 13:187.

Hornykiewicz O (1982): Brain catecholamines in schizophrenia: A good case for noradrenaline. *Nature* 299:484–486.

Sandyk R, Gillman MA (1984): Noradrenaline and tardive dyskinesia. *Br J Psychiatry* 145:217.

Lithium and RBC Water Permeability

To the Editor:

The concentration of choline in the red blood cell (RBC) increases in lithium-treated patients at the same time that the choline carrier system appears to be inhibited (see Domino et al. 1981). Water permeates the RBC membrane primarily via hydrophilic protein channels, which also provide an important route for the passive flux of monovalent cations (Vieira et al. 1970). Hence, alterations in intracellular steady-state levels of choline may correlate with changes in the hydrophilic protein channels, therefore affecting water permeability. Our experiment measured RBC water permeability in lithium-treated patients and normal volunteers.

The mean lifetime of a water molecule in an average RBC (τ) was determined using a modification of the ^{1}H-NMR method of Conlon and Outhred (1972). Adding Mn^{2+} to whole blood diluted 1:4 with 0.9% NaCl shortens the plasma spin–spin relaxation time. This allows the water external to the RBC to be "pulsed-away" using a Standard Carr-Purcell-Meiboom-Gil (CPMG) pulse sequence on a JEOL-FX90Q NMR spectrometer. The CPMG conditions were an 18.5-μsec pulse to induce a 90° spin flip, a 39.0-μsec pulse for a 180° spin flip, and an interpulse interval of 30 msec. The second half of the spin echo was Fourier transformed after an 8-Hz exponential apodization. The internal water peak linewidth ($\nu_{1/2}$) is related to τ by $\tau = \pi/\nu_{1/2}$.

Titrating blood samples with Mn^{2+} from 2.5 to 30 mM showed that the internal peak width depended linearly on Mn^{2+} concentration. Each blood sample was titrated with Mn^{2+} and the titration curve extrapolated to zero to determine $\tau_{1/2}$ without Mn^{2+}.

This method was applied to blood from eight lithium carbonate-treated patients and four normal volunteers. The lithium-treated patients had a mean water lifetime of 8.4 ± 1.2 msec, whereas the normal volunteers had a mean water lifetime of 8.1 ± 0.6 msec. The treated versus normal groups did not differ significantly by Student's *t*-test. The two groups compare to the mean water lifetime of approximately 8 msec reported by Solomon (Vieira et al. 1970).

No differences in water permeability were observed between lithium-treated patients and normal volunteers, suggesting that the choline accumulation is not due to modification of the membrane protein channels responsible for passive efflux of water. Lithium, in fact, may alter

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the properties of a specific RBC membrane choline carrier or may affect endogenous choline metabolism.

This present investigation may be limited by the small sample size of the two groups studied, making the results vulnerable to type II statistical error. It would also be interesting to compare the same patients before and during lithium treatment.

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References

Conlon T, Outhred R (1972): Water diffusion permeability of erythrocytes using an NMR technique. *Biochim Biophys Acta* 288:354–361.

Domino EF, Mathews B, Tait SK, Demetriou SK, Fucek F (1981): Red blood cell/plasma choline ratio—a possible biological marker of lithium therapy—clinical correlations and limitations. In Pepeu G, Ladinsky H (eds), *Advances in Behavioral Biology 25: Cholinergic Mechanisms*. New York: Plenum Press, pp 891–900.

Vieira FL, Shaaf RI, Solomon AK (1970): The state of water in human and dog red cell membranes. *J Gen Physiol* 55:451–465.