

Psychotic Behaviour and Folic Acid Medication Preliminary Report on Two Cases

Jerome LeJeune¹

The general hypothesis of a disturbance of monocarbon metabolism in mental retardation has been previously discussed¹ and experimentally confirmed in fragile X syndrome², and in trisomy 21^{3,4}.

Systemic examination of cases referred for psychosis or autism has shown a normal chromosomal constitution in the majority of patients. Two cases have been followed during a trial of folic acid medication.

Case 1 — 26633

K.L., an eumorphic girl 6 years and 7 months old, was referred with mental retardation (IQ = 0.33) and psychotic behaviour. She did not speak, and at monthly intervals became excited with severe temper tantrums. Chromosomal examination was normal (no fragile site detected), but an excess of various chromosomal breaks were noted. At the time of the examination K.L. was going through a very "difficult" period. Another test at 7 years in a "good" period did not reveal any breaks. A third examination at 7 years 2 months again showed some breaks; K.L. was again at the beginning of a "difficult" period. At 7 years 8 months K.L. received 15 mg of folic acid per day for a body weight of 21 kg.

After a week her behaviour was quieter and aggressive behaviour was diminished "80%" according to her mother. Educators (totally ignoring the medication) noted a remarkable improvement in behaviour.

After a year of continuous medication at 0.70 mg/k/d, behaviour was stable except for a 15 day period during which the treatment was suspended. In a week, K.L. again became extremely "difficult" (aggressive, nervous, regressed). When treatment was resumed behaviour became normal again in a week.

1. Institut de Progenese (Centre Claude Bernard) 45 Rue des Saints-Peres 75270 Paris cedex 06. Work supported by grants from the Micahel Fund.

After nearly three years of continuous folic acid medication, the parents finally agreed to another suspension of medication. K.L. was now 10 years 11 months old. Four days after folic acid was withdrawn, K.L. became tense, aggressive against herself and her brothers, could not concentrate on ordinary tasks, and sleeping time was very much shortened.

All these symptoms forced the parents to resume folic acid medication after only 20 days (instead of the 3 months prescribed). The recovery, slower than previously, took three weeks, but this was possibly related to an intercurring mumps infection.

After three months of folic acid medication (0.80 mg/k/d), K.L. had fully recovered her normal behaviour.

The two episodes of worsening during the withdrawal of medication has totally convinced the parents (and partially the observer) that another trial is not appropriate.

It must be stressed that IQ has not changed significantly. Non-verbal tests gave the following mental ages: 2 years 9 months at 8 years 4 months of age; 3 years 2 months at 10 years 6 months of age. Only behaviour seems to have been modified.

Case 2 - 4.514

D.H., an eumorphic boy 3 years old, was referred for severe mental retardation with psychotic behaviour: when disturbed he hit his head on the wall, bit his fingers, and could not control his gaze. The diagnosis of autism had been previously made by competent psychiatrists. Hand movements were stereotyped, he nodded his head, frequently lifted his pants, and whirled around every few steps. No chromosomal anomaly was noted.

Folic acid medication was prescribed (5 mg per day for a body weight of 12 kg).

A progressive decrease in the stereotypic was noted by his parents, and after a year at 0.42 mg/k/d of folic acid the behaviour was

"normal". His mental age (Binet-Simon) was then 3 years 6 months for 4 years 5 months of chronological age, and D.H. began to go to a normal school.

Some difficulty in coordination of eye movements was noted, and the right iris was a little larger than the left one with horizontal strabismus.

At 7 years 1 month of age his mental age was 5 years 2 months, and at 8 years 2 months his mental age was 6 years 9 months. Hence his IQ (Binet-Simon) was 0.70 at 4 years 5 months (after one year of medication), and is now 0.83 at 8 years 2 months of age.

At 7 years 1 month of age it was decided to stop the treatment for 3 months, to resume it for three months, and to stop it again for another three months.

During *both* vitamin-free periods the *same* observations were made by the parents. During the first three weeks of withdrawal nothing was noted. Then all the stereotypies progressively reappeared: playing with his hands, nodding his head, compulsive lifting of pants, turning himself around every few steps when walking, and talking aloud to himself in a deep voice.

When the folic acid was resumed (0.20 mg/k/d) all the stereotypies persisted unchanged for three weeks and, then, disappeared progressively and completely.

These facts and this time schedule of three weeks latency was observed very clearly by the parents during the two trials. They were convinced that a third attempt to withdraw the folic acid was not appropriate, and the medication was continued at 0.30 mg/k/d.

These two observations seem worthy of consideration because some abnormal demands upon monocarbon metabolism are related to behavioural disturbances. This is particularly well-known in the Lesch Nyhan disease (loss of purines due to inefficiency of the salvage pathway of HGPRT)⁵, in the so-called "purine autism"⁶, with over-excretion of uric acid, or in the very rare adenylo succinase deficiency⁷, often related to clinical autism.

If the general hypothesis of monocarbon deficiency is taken into account, it seems logical

that some behaviour problems could be sensitive to folic acid medication, although many others could be totally unresponsive because the biochemical difficulty can be such that the uptake or the reduction of folic acid is not efficient. Even some cases of worsening by folic acid are theoretically expected, and one instance has been quoted in a case of 5-10 methylene tetrahydrofolate deficiency⁸.

This preliminary report must not be interpreted as a proposal that folic acid per se can be a treatment for behavioural difficulties in psychotic conditions. It is only intended to draw attention to a specific field of research.

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