

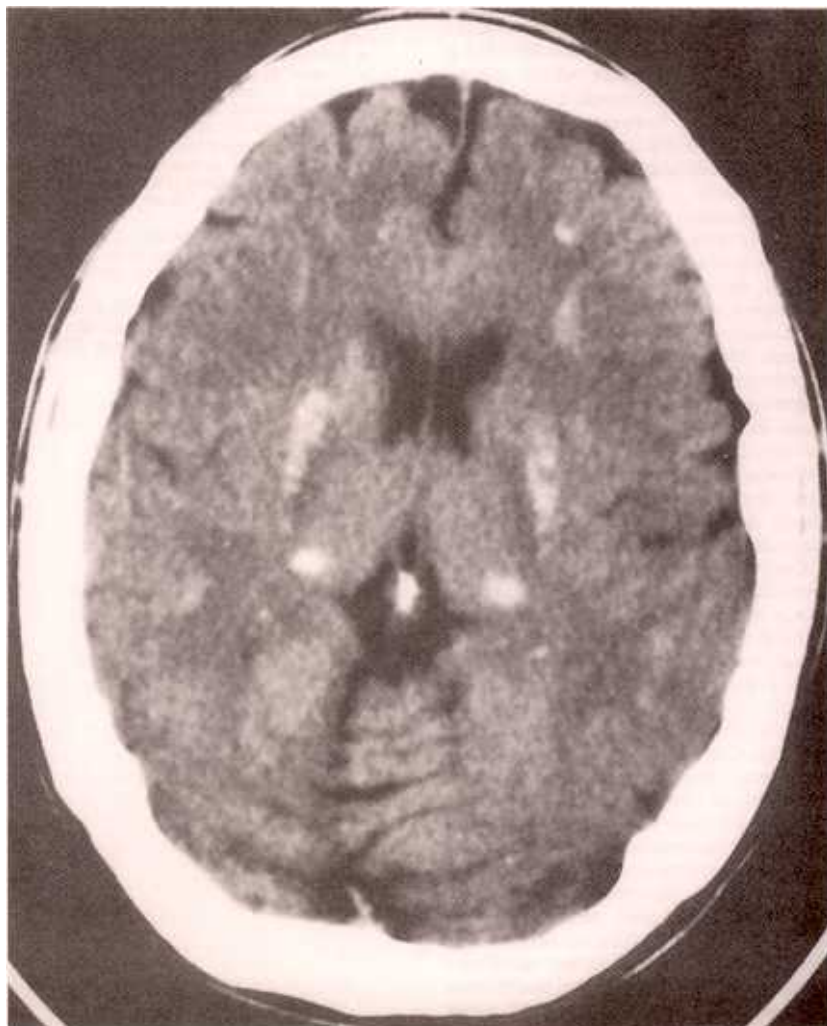
Fahr's disease¹—whether idiopathic or associated with hypoparathyroidism—previously been associated with this handicap. We present the case of a 24 year old man with Asperger's syndrome, primary hypoparathyroidism, and multifocal brain calcifications.

According to medical history, the patient's mother had received weekly injections of Depoprovera during pregnancy. A single child born after a normal term delivery, he underwent surgery for an inguinal hernia at 3 weeks. Developmental milestones were only moderately delayed. At 9 months, he rolled instead of crawling. He walked at 15 months, spoke at 2 years with poor articulation, and still speaks in short, unelaborated sentences. His social and language development lagged in grade school and he occasionally got into fights. In late adolescence, antisocial behaviour took the form of shoplifting and repeated long distance calls to pornographic hot lines. As an adult, his social adaptation remains poor: he currently lives with his mother and works irregularly as a dishwasher in a restaurant. He is indifferent, isolated, and resists novelty. He enjoys repetitive and solitary activities such as slot machine games and playing the piano.

Fahr's disease and Asperger's syndrome in a patient with primary hypoparathyroidism

Abnormal calcium phosphate metabolism has not previously been associated with Asperger's syndrome, a form of pervasive developmental disorder. Nor have symmetric calcifications of the basal ganglia, dentate nuclei and cortex, or

Neurological examination showed bilateral hyperreflexia, mild imprecision of fine finger movements, dysgraphaesthesia on sensory testing, and a manneristic gripping handshake. There were no extrapyramidal



Brain CT, axial section: dense calcific deposits in the basal ganglia, thalamus, and orbitofrontal cortex consistent with Fahr's disease.

symptoms. His IQ score was in the low range (WAIS-C=85 at the age of 13; Barbeau-Pinard=82 at the age of 17). He also presented an impairment on the Tower of London test, which measures executive function, and in a task assessing the understanding of other people's intentions. These two findings are reliably present in pervasive developmental disorders, in this IQ range. In addition, his performance on the Tower of Toronto test disclosed impaired performance in procedural learning. Psychiatric assessment showed scores above the cut off for autism according to the autism diagnostic interview (ADI),² a standardised interview that requires specific training and those administering it to have a 0.90 reliability with other researchers. The subject was positive for the diagnosis of autism, being above cut off values in the three relevant areas of communication, social interactions, restricted interests, and repetitive behaviours. Nevertheless, he did not present delay in language acquisition or morphological atypicalities in language development, which corresponds to DSM-IV criteria for Asperger's syndrome.

Brain CT showed dense calcium deposits in the basal ganglia, thalamus, cerebellar dentate nucleus, and orbitofrontal cortex, consistent with Fahr's disease (figure). SPECT showed increased activity in basal ganglia relative to the cerebral cortex. A fine banded karyotype was normal. Serum calcium was 1.55 mM/l (normal 2.15–2.55 mM/l), phosphate 1.69 mM/l (normal 0.70–1.5 mM/l). Ionised calcium was 0.80 mM/l at pH 7.4 (normal 1.19–1.34 mM/l); urinary calcium was 0.8 mM (normal 2.5–6.3 mM). Serum parathyroid hormone was below 0.6 (normal 1.0–6.55 µM/l), and a nuclear scan of the parathyroid glands showed an absence of activity. With a combination of vitamin D3-calcium supplementation and cognitive-behavioural therapy, serum calcium, and phosphate concentrations normalised and his behaviour improved marginally.

Asperger's syndrome is a subtype of pervasive developmental disorder of unknown aetiology. Evidence for involvement of specific brain regions in pervasive developmental disorder are scarce and inconclusive.³ Although the temporo-occipital region is the most often involved in pervasive developmental disorders^{4,5} abnormal functioning of the frontal lobes is also suspected from replicated findings of executive function deficits and from occasional findings of frontal hypometabolism or abnormal macroscopic brain morphology.³ Abnormal cell counts and morphology in the cerebellar hemispheres have also been reported, but the relation of these findings to autism is controversial.³

Fahr's disease consists of symmetric calcifications, located mainly in the basal forebrain and cerebellum, which are of various aetiologies. Cognitive and behavioural abnormalities may be present when calcifications occur early in development. A fortuitous association between pervasive developmental disorder and hypercalcaemia, given the paucity of published cases, is plausible in the presented patient. Nevertheless, our case suggests that abnormal phospho-calcium metabolism could produce an autistic syndrome when brain calcifications cause specific neuropsychological deficits, due to their localisation. For example, errors of social judgement may be related to calcifications of the orbitofrontal cortex, whereas dysfunction of frontal-basal ganglia circuits may contrib-

ute to repetitive and ritualistic activities. Additionally, developmental lesions of the basal ganglia and cerebellum may contribute to the abnormalities of sensory attention, procedural learning, and motor intention in this patient.

The finding that the clinical picture of autism can be found in a wide range of medical conditions giving rise to organic brain dysfunction is not new, but the relation between these conditions and autism are often considered meaningless.³ By contrast, this case, similarly to some others^{1,5} suggests that dysfunction in key brain circuits may result in behavioural and cognitive abnormalities currently indistinguishable from idiopathic pervasive developmental disorder. This case also suggests that careful biological assessment of this group of patients may disclose focal brain lesions associated with identifiable cognitive deficits. Could these clinical coincidences be instructive for a neurodevelopmental model of autism?

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