Primary disorders of neurotransmitter metabolism: experience of a tertiary center

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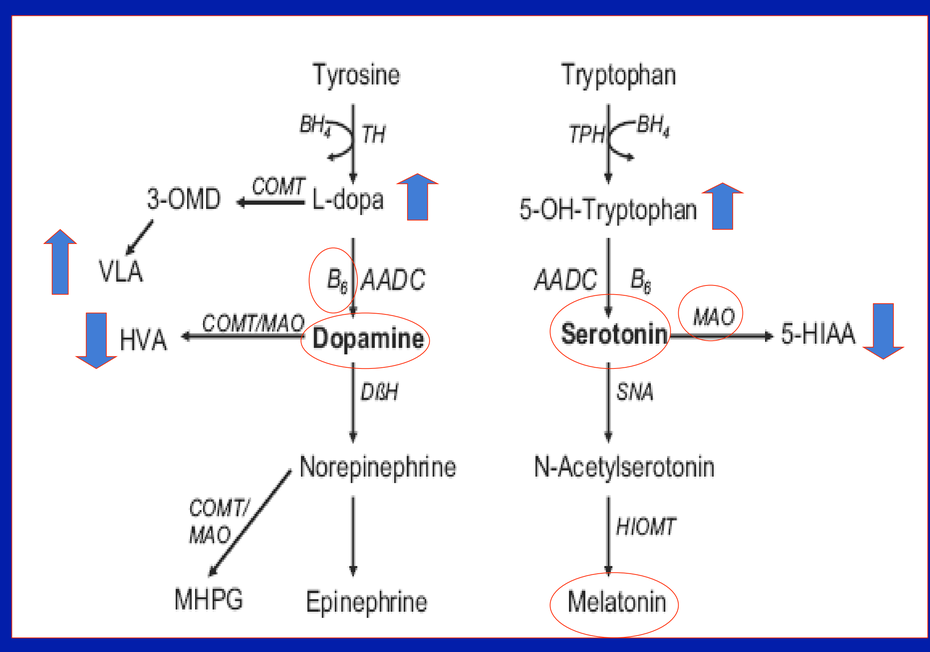
Background: Neurotransmitter diseases are a group of inherited disorders attributable to a disturbance of neurotransmitter metabolism. Biogenic amines are neurotransmitters with multiple roles including psychomotor function, hormone secretion, cardiovascular, respiratory and gastrointestinal control, sleep mechanisms, body temperature and pain. Given the multiple functions of monoamines, disorders of their metabolism comprise a wide spectrum of manifestations, with motor dysfunction being the most prominent clinical feature.

Methods: Case review of 12 patients from 4 families, with primary disorders of biogenic amine metabolism.

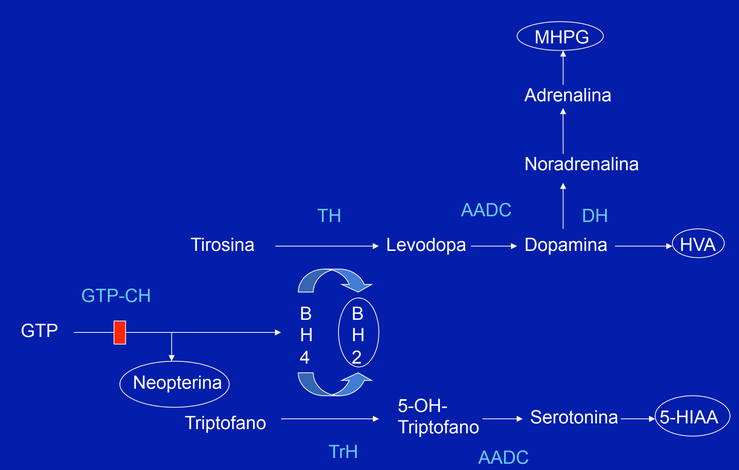
Pt	Onset Age/ Sex	Main clinical features	Neuro imaging	Treatment	Treatment Response	Evolution
1	2 m/M	Irritability, Oculogyric crisis, Truncal Hypotonia Limb Dystonia, Sleep and temperature regulation disturbance Feeding Difficulties Psichomotor Delay	Normal	Pyridoxine Bromocriptine Selegiline	Mild and transitory	Deceased
2	4 m/F	Irritability Truncal Hypotonia Limb Dystonia, Temperature regulation disturbance Feeding Difficulties Psichomotor Delay	Normal	Pyridoxine Bromocriptine Selegiline	Absent	Deceased
4	2m/F	Bilateral Ptosis Facial Hypomima Extreme Hypotonia, Psichomotor Delay	Not Performed	Pyridoxine Bromocriptine Selegiline	Absent	Tetraparesis. Hypotonia
3	2,5 m/ M	Bursts of irritability and involuntary movements. Oculogyric crisis, Limb Dystonia Bilateral Ptosis, Facial Hypomima Feeding Difficulties Psichomotor Delay	Normal	Pyridoxine Bromocriptine Selegiline	Absent	Tetraparesis Hypotonia Irritability

Table 1. Clinical and neuroradiological features of the patients with Aromatic Amino Acid Descarboxylase deficiency.



Pt	Onset Age/ Sex	Main clinical features	Treatment	Treatment response	Evolution
5	6a/F	Limb dystonia with diurnal flutuation	L-Dopa	Very good	Asymptomatic
6	3a /F	Toe walking that evolved to spastic paraparesis	L-Dopa	Gait improvement Involuntary movements	Gait disturbance Choreic Movements
7	…/M	Mild limb dystonia.	–	–	Mild motor disturbance
8	?/F	Bradikynesia, hypomimia, Limb Hypertonia with dystonia. Depression. Psichomotor Delay	L-Dopa	Motor improvement Psychosis with higher dosis	Parkinsonism Cognitive deficit
9	?/F	Dystonia Cognitive deficit	–	–	?
10	?/M	Cognitive deficit Psychosis	Neuroleptic agents	Moderate Improvement	?
11	?/F	Bradikynesia, hypomimia, dystonia. Psichomotor Delay	L-Dopa	Motor improvement	?
12	?/F	Bradikynesia. Psichomotor Delay	L-Dopa	Motor improvement	?

Table 2. Clinical and neuroradiological features of the patients with GTP cyclohydrolase deficiency.



Discussion

- Regarding AADC deficiency, symptoms began early in life and, as previously described, truncal hypotonia, hypokinesia, dystonia, oculogyric crisis and sleep/temperature regulation disturbance were present. The prognosis is most frequently severe and treatment response is variable and transitory, although a therapeutic trial is indicated.
- Regarding GTP-CH deficiency, the most frequent features were dystonia, rigidity and hypokinesia, with diurnal fluctuation. Hypereflexia has been described but the presence of other pyramidal signs, like in the case of pte 6, is not frequent. Cognitive deficit is atypical and the psychiatric symptoms described in the literature are mostly obsessive-compulsive and sleep disturbance. In one of the families in this series, depression and psychosis were the psychiatric symptoms.
- In accordance with published cases, after the index case diagnosis, other members of the family are diagnosed, exhibiting minimal signs and symptoms with latter onset age.

- These disorders should be considered in the differential diagnosis of paediatric neurodegenerative diseases, in order to allow an adequate therapeutic trial that can favor prognosis.