duction including perseveration and echolalia; stereotyped body movements including flapping, clapping, and rocking; and persistent preoccupation with parts of objects reflecting a restricted range of interests. His Autism Behavior Checklist total score was 126 with the following subscale profile results: sensory 15, relating 33, body and object use 31, language 25, social and self-help 22. Speech and language testing indicated an age equivalency of 2.8 to 3.0 years old with severe delays of receptive and expressive language as well as speech articulation. MRI brain scan was unremarkable. Chromosomal analysis had confirmed a deletion at the Xp21 region. His family pedigree noted several female congenital adrenal hypoplasia carriers including his mother as well as male infants who had died from congenital adrenal hypoplasia with no family history of autism, nor other developmental, neurologic, or psychiatric conditions. The patient had been prenatally diagnosed with congenital adrenal hypoplasia and survived with in utero replacement therapy initiated at 40 weeks gestation with 100 mg of dehydroepiandrosterone sulfate infused into the amniotic space. Subsequent assessments revealed normalizing maternal estriol excretion. After birth at 43.5 weeks gestation, mineralocorticoid replacement therapy was administered during infancy. Later evaluations revealed steroid deficiencies as well as chronic failure to thrive. Progressive motor, language, and socialization delays followed as described.

Comment

Despite receiving replacement treatment, it is conceivable that congenital adrenal hypoplasia-related neurophysiologic abnormalities may have already been staged. Adrenal hormone imbalances have been linked to disturbances of development, language, memory, and mood.[1] Congenital adrenal hypoplasia can impact the function of the mineralocorticoid and glucocorticoid receptor systems for cortisol binding in the limbic system. The mineralocorticoid receptors, located in the lateral septum and hippocampus, affect tonic influences on brain function.[2] They demonstrate a 10-fold higher binding affinity for cortisol over glucocorticoid receptors.[1] Glucocorticoid receptors are more widely distributed in the lateral septum, central amygdala, locus coeruleus, and dentate nucleus having involvement with feedback action on stress-activated brain mechanisms.[2] Other studies demonstrated the selective loss of hippocampal granule cells after adrenalectomy suggesting adrenal hormones are a requirement for limbic structural integrity.[3] Adrenal deficiency causes hippocampal serotonin receptor density to selectively increase along with development of subsensitivity at presynaptic receptors.[4] Such impacts on serotonin receptors are particularly significant as alterations of serotonergic neurotransmission have been implicated in both autistic disorder and mental retardation.[5]

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Tyrosine Supplements for ADHD Symptoms With Comorbid Phenylketonuria

To the Editor: Phenylketonuria is the most common genetic disorder of amino acid metabolism with an incidence of 1 per 15,000 births. It is caused by a mutation in the gene coding for phenylalanine hydroxylase resulting in an inability to metabolize phenylalanine to tyrosine—a precursor of dopamine and norepinephrine.

Treatment for phenylketonuria involves restricting protein intake. If a low protein diet is commenced at birth and maintained throughout development, many patients achieve normal cognitive functioning. Failure to maintain the diet, however, leads to elevated serum phenylalanine with subsequent cognitive decline and potential mental retardation.[1]

As individuals with phenylketonuria are unable to metabolize phenylalanine to tyrosine, and tyrosine is an essential precursor to dopamine, some authors have suggested that tyrosine-enriched foods be included as part of the diet for patients with phenylketonuria. Several studies have investigated the use of tyrosine supplements to reverse the cognitive effects associated with hyperphenylalaninemia,

but the results have been mixed.[2] To our knowledge, however, no studies have investigated the use of tyrosine supplements for psychiatric conditions comorbid with phenylketonuria. We present the case of a young boy with phenylketonuria and comorbid attention-deficit/hyperactivity disorder (ADHD) who was treated with tyrosine supplementation.

Given that tyrosine is an essential precursor to dopamine, we hypothesized that the patient's ADHD symptoms may have been exacerbated by hypotyrosinemia. By supplementing his diet with tyrosine, we were able to achieve a reduction in his ADHD symptoms, and we suspect that the mechanism of action was an augmentation of dopaminergic activity.

Case Report

AA, a 4-year-old boy with phenylketonuria, was started at birth on a protein-restricted diet and was followed in a metabolic disease clinic. He was developing normally until age 3, when his parents noted behavioral problems characterized by impulsivity and poor frustration tolerance. At age 4, he was enrolled in an early intervention program and received psychosocial treatments to address worsening symptoms of inattention, hyperactivity, and aggression. After 4 months of treatment, AA showed little improvement. He underwent a comprehensive psychiatric evaluation, and a diagnosis of ADHD, Combined Type, was made. AA was started on a tyrosine supplement at a dose of 100 mg/kg/day. The treatment was well tolerated and after 4 weeks of treatment, he showed a dramatic improvement in his ADHD symptoms.

Standardized ratings are shown in Table 1.

Comment

Attention-deficit/hyperactivity disorder is a heterogeneous condition characterized by inattention, hyperactivity, and impulsivity. Although its precise pathophysiology is unknown, neuropsychological studies have found deficits in executive functions, including inhibitory control and set shifting.[3] Moreover, consistent with longstanding data that psychostimulants reduce the symptoms of ADHD, functional imaging studies have implicated abnormalities in the dopaminergic pathways of the anterior attentional system.[4]

Our findings suggest that our patient's symptoms of ADHD may have been exacerbated by a deficiency in tyrosine and suggest a potential approach for treating patients with comorbid phenylketonuria and ADHD. Moreover, our findings suggest that inquiring into dietary habits may be important when evaluating children with ADHD.

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TABLE 1. Neuropsychological Assessment of ADHD Symptoms

	Pre-treatment		Post-treatment		Change	
CRS-R*	Parent t-score	Teacher t-score	Parent t-score	Teacher t-score	Parent t-score	Teacher t-score
Oppositional	86	75	65	60	**−21**	**−15**
Hyperactivity	79	69	67	52	**−12**	**−17**
Cognitive problem/inattentive	54	88	51	67	**−3**	**−21**
ADHD Index	75	73	59	54	**−16**	**−19**
CBCL**	Parent t-score	Teacher t-score	Parent t-score	Teacher t-score	Parent t-score	Teacher t-score
Externalizing	83	74	60	56	**−23**	**−18**
NEPSY***	Scaled Score		Scaled Score			
Statue	8		10		+2	
Visual Attention	8		11		**+3**	

*The Parent and Teacher versions of the CRS-R (Conners' Rating Scales-Revised) are standardized instruments that use observer ratings to assess symptoms of ADHD. T-scores > 70 are in the clinical range (borderline range is 60-69).

**The CBCL (Child Behavior Checklist) is a reliable and valid parent-report measure for assessing problem behavior and adaptive functioning in children and adolescents. T-scores > 70 are in the clinical range (borderline range is 65-69).

***The NEPSY is a standardized neuropsychological assessment for preschool and school-aged children. The statue and visual attention subtests assess impulsivity and attention, respectively. Subtest results are reported as scaled scores (mean=10, 1 SD=1.5).

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Musical Hallucination in a Patient After Cochlear Implantation

To the Editor: Musical hallucinations are still poorly understood clinical phenomena. There is an association between acquired deafness and musical hallucination, but no case report could be found with musical hallucination after a cochlear implantation.

Case Report

A 66-year-old woman was referred to the psychiatric service because of musical hallucinations after a cochlea implantation. The patient experienced no hallucinations before the implantation. In 2002, the patient had a sudden onset of acute deafness due to a defect of the middle right ear. In January 2003, after an additional deafness in her left ear, she had a cochlea implantation. In 2005 the patient admitted hearing music. In the beginning, the music was soft and did not interfere with her daily life. Later on, the loudness of the music increased. Finally, she heard a rhythmic humming, sometimes so loud that she could not hold a conversation with her husband. There was no mental illness known and no previous psychiatric admission or family history of psychiatric illness. The symptoms were still present when the cochlea implantation was inactive. A CT scan revealed generalized cortical atrophy but without any pathological significance. The EEG indicated muscular artifacts in the frontal lobe but otherwise presented as a normal alpha EEG without seizer potential. The patient scored an 8 on the Beck Depression Inventory (0-9 indicates that a person is not depressed). A treatment with risperidone up to 2 mg/day or olanzapine up to 10 mg did not have an effect on her symptoms. There are some case reports in the literature that suggest that mood stabilizers have an effect on musical hallucinations. But due to the medical history (cardiac arrhythmia and hepatitis C) this was not considered for possible treatment. Therefore mirtazapine was started up to 30 mg and the patient showed slight improvement. The musical hallucinations were still persistent but not as disturbing.

Discussion

Musical hallucinations have been related to female sex; social isolation;[1] age; hearing impairments;[2] brain diseases (particularly epileptic foci, tumor, or stroke) affecting the nondominate hemisphere;[3] temporal lobe lesions;[4,5] and mental disorders including depression,[2,5] schizophrenia,[6] and obsessive-compulsive disorder.[7] Klostermann et al.[8] reviewed 32 cases in the literature, but treatment with antipsychotic medication or anticonvulsants remained unsatisfying in all cases. In single case reports neuroleptic, antidepressive, and in particular anticonvulsive drugs were successful, but no general recommendations for treatment could be made. Keshavan et al.[9] suggested that musical hallucinations derive from memory tracts, which they refer to as a concept of "parasitic memory." Musical hallucinations are a possible result of sensory deprivation, similar to the effects of sensory deprivation in Charles Bonnet syndrome or patients with phantom limbs. Griffiths et al.[10] revealed the similarity of activation produced by musical hallucination. However it is still unknown why these memory traces are released, apparently spontaneously, in the absence of specific brain stimulation. New to this case are musical hallucinations after a cochlea implantation. Therefore, is sensory deprivation the most likely explanation?

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