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The Impact of Pediatric Basal Ganglia Stroke on Mental Health in Children: Report of 2 Cases

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Abstract

Background: The impact of basal ganglia stroke on mental health is better described in adults than in children. We report 2 children with significant mental health issues after basal ganglia stroke. **Case Reports:** Patient 1, an 8-year-old boy, had mild anxiety before his left basal ganglia stroke. Post-stroke, he developed severe anxiety, obsessions, depression, and attention deficit hyperactivity disorder, in addition to a right hemiplegia and some mild chorea. He gradually improved over 3 years with psychiatric care and medication but continued to have residual symptoms. Patient 2, a 10-year-old boy, had no history of mental health issues before his right basal ganglia stroke. Post-stroke, he developed significant anxiety and mild depression, along with a left hemiplegia. He improved over 9 months and returned to his mental health baseline. **Conclusions:** Mental health issues after basal ganglia stroke in children can be significant, and recovery can take months to years.

Keywords

basal ganglia, mental health, pediatric stroke, children, anxiety, depression

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Introduction

Basal ganglia stroke can affect mental health. This has been most studied in adults. Many adult stroke patients suffer from generalized anxiety, major depressive disorder, phobias, and/or obsessive-compulsive disorder following a stroke in which the basal ganglia was involved.[1-9] However, there are few studies describing mood disorders after pediatric basal ganglia stroke, and little data on how mental health issues in children after stroke affect the whole family, or how long recovery takes. This report presents 2 children with mental health issues after basal ganglia stroke and reviews the literature on the effects of basal ganglia stroke on mental health in adults and children. Possible mechanisms leading to mental health issues after basal ganglia stroke are described.

Case Reports

Case 1

An 8-year-old boy was referred to our hospital for subacute stroke. Three days prior, he fell and hit the right side of his head on a coffee table. He seemed fine immediately after, but the following 2 days, he had right facial weakness, difficulty concentrating, and was doing and saying things that did not make sense. His mother brought him to the pediatrician, who ordered magnetic resonance imaging (MRI) which revealed new large infarction of the left caudate and putamen. He was started on aspirin 81 mg daily and admitted to our hospital. On exam, he had significant executive function and concentration errors, while constructions were intact. He had some choreiform movements on the right with mild hyperreflexia distally in the right leg and positive right Babinski. Computed tomography angiogram was negative for dissection; repeat MRI

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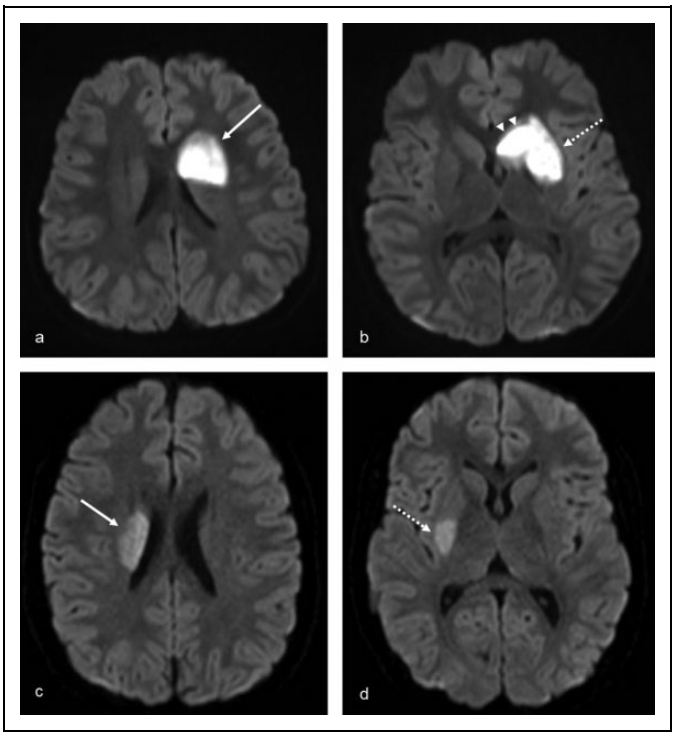

Figure 1. Legend MRI of Cases I and II. Figure 1a and 1b. are axial diffusion weighted images (DWI) at the level of the caudate body and the thalamus in patient 1 showing bright diffusion signal (diffusion restriction; corresponding dark signal on ADC map not shown) centered in the left anterior caudate body (solid arrow), head of the left caudate nucleus (arrowheads) and anterior aspect of the left putamen (dashed arrow). Adjacent portions of the anterior limb of the internal capsule, the globus pallidus and external capsule are also involved. Figure 1c. and 1d are axial diffusion weighted images (DWI) at the level of the caudate body and the thalamus in patient 2 showing bright diffusion signal (diffusion restriction; corresponding dark signal on ADC map not shown) centered in the right posterior caudate body (solid arrow) and posterior aspect of the putamen (dashed arrow).

(Figure 1) with MR angiography (MRA) and MR venography (MRV) demonstrated restricted diffusion within the left caudate, anterior lentiform nucleus, anterior limb of the internal capsule, and deep white matter of the frontal lobe consistent with acute infarct, but no evidence of dissection or venous thrombosis. His past medical history was remarkable only for mild anxiety and an itchy rash 1 month earlier that did not look like varicella. His family history was remakable for a pulmonary embolism in his mother following cardiac ablation for Wolff-Parkinson-White and a maternal grandfather with multiple strokes starting at age 56; there was no known family history of mental health issues. Echocardiogram and electrocardiogram were unremarkable. His prothrombotic workup was remarkable only for mild anemia with mean cell volume of 78 fL and hemoglobin of 11.8 GM/dL; heterozygosity for the PAI 14G gene variant, and homozygosity for the MTHFR 1298C gene variant, with normal homocysteine. His alertness and concentration improved during his 3-day hospitalization, and he was discharged home on aspirin, iron, and folate with outpatient rehabilitation.

However, after discharge home, his family noted severe anxiety, depression, impulsivity, aggression, hyperactivity, trouble with concentration, mouthing objects, restlessness, and no remorse for his actions. He was fighting, biting, kicking, punching, and spitting at family members. He lost interest in toys and only wanted to watch television. He was unable to return to school and was started on homebound instruction. He was started on cyproheptadine for decreased appetite, guanfacine for poor attention, and as-needed hydroxyzine for anxiety by his pediatrician. He returned to the hospital a month and a half post discharge with chest pain, but was discharged the next day when no cardiac pathology was found. At his follow up stroke clinic exam 2 months post discharge, he was uncooperative, and his insight and judgment appeared poor. He was referred urgently to psychiatry clinic, where he was diagnosed with a personality change due to cerebrovascular accident and combined type attention-deficit/hyperactivity disorder, specifically disinhibited and aggressive features. The mother quit her job to stay home and care for him.

Over the next year, multiple medications were tried and discontinued by the pediatrician and psychiatry clinic. Cyproheptadine was stopped because it did not help. The initial guanfacine did not help. Amphetamine sulfate caused headaches. He became suicidal on atomoxetine. His aggression worsened on extended-release guanfacine. Atomoxetine was retried at a lower dose, but he became aggressive on that, and security was called to psychiatry clinic. Risperidone helped behavior, particularly rage outbursts, but caused weight gain and was sedating, so the dose was readjusted multiple times. Low dose methylphenidate was added approximately 16 months post discharge, and that helped impulsivity and inattention. In addition to medication, he received individual counseling and family counseling. The family was noticing definite improvements by 1 ½ years post discharge; then, he developed worsening anxiety and depression and an eye-blinking tic. Counseling, which had been stopped when he improved, was restarted. He was switched from short-acting to extended-release methylphenidate. Clonidine was added to help the tic and anxiety. He was weaned off risperidone, then it was restarted, and fluoxetine was added when he became anxious in school. At his last follow up, 3 years post stroke, he was doing well on aspirin, clonidine, dexmethylphenidate, and fluoxetine and was feeling back to his old self. However, he still got anxious in large crowds, and his family reported he acted like a younger child in the mornings until he got his morning medications.

The behavior symptoms had a significant impact on the child's family due to the disruption of the behavioral symptoms. His motor symptoms had resolved much faster than the psychiatric symptoms and were barely noticeable after a few months. The mother finally returned to work 3 ½ years after his stroke.

Case II

A 10-year-old boy presented to his local hospital with left-sided numbness, along with weakness of the left side of his face and left arm and leg. There was history of head trauma; about

2 months prior, he had hit his head on the bathroom sink, but did not lose consciousness. MRI demonstrated acute infarction in the right basal ganglia involving the caudate and lentiform nucleus and extending to the corona radiata, and MRA was normal. He had a left hemiparesis with distal flaccidity in the left upper and lower extremities, but some preserved shoulder abduction and hip flexion. His past medical history was unremarkable. His family history was negative for early stroke and clotting disorders, but positive for anxiety and depression in several family members. Transthoracic echo with bubble study, prothrombotic workup, and infectious workup were all unremarkable. He was treated with aspirin 162 mg daily and heparin, which was transitioned to enoxaparin for about 2 weeks. He was referred to our hospital for rehabilitation 3 weeks post stroke. Both psychiatry and neuropsychology were consulted during rehabilitation, but no major problems with depression or anxiety were noted, though he did have some mood swings. He made significant motor improvements in the early weeks post stroke. He was discharged on aspirin. He was referred to outpatient counseling.

At neurology clinic follow up 2 months post stroke, he was making some slow improvement and was in physical therapy. He had some persistent left sided weakness and a hemiplegic gait, was struggling with post-stroke fatigue, headaches, concentration, anxiety, and mood changes, describing feeling "down" for a while. He had not started counseling yet. He became visibly distraught and anxious when blood work was mentioned. He was put on a vitamin D supplement for a slightly low vitamin D level.

At the next stroke clinic follow up, 5 months post stroke, his fatigue had improved slightly, and his left motor strength had improved significantly, with minimal residual weakness. He continued to have mood issues. He admitted to feeling depressed and anxious. He had an episode of whole body shaking, thought to be due to a panic attack at the thought of more blood work at an upcoming visit to neurology. His trouble with concentration and coordination had improved, but he had continued to have issues with feeling depressed and anxious. He was put on an increased dose of melatonin to help him sleep and was encouraged to see a counselor.

At stroke follow up 9 months post stroke, his depression had resolved, and he had only mild residual anxiety. His fatigue had improved, and he had stayed in physical therapy. He still had mild weakness on his left side, but his neurologic examination was unremarkable otherwise. He remained on the aspirin, and his melatonin was decreased from 3 mg to 2 mg.

His family had struggled with the notable change in behavior post stroke, which was not immediately evident after discharge from rehabilitation. They had described him as a "happy go lucky kid" prior to his stroke. They were encouraged by the gradual improvement in mood without additional therapy or medication.

Discussion

Many adult patients suffer from major depressive disorder, along with several other mood disorders, post-stroke.[1] Damage to the basal ganglia in particular has been associated with many mood disorders. Murakami et al.[4] found that out of 149 adult stroke patients, 83 patients (55.7%) had affective and/or apathetic post-stroke depression (PSD) that was related to lesions involving the basal ganglia, brain stem, and frontal cortex. More recent work has reported an association between basal ganglia infarctions and the development of obsessive-compulsive disorder (OCD).[7-9] Akaho et al.[9] conducted a literature review which demonstrated that out of 21 cases of OCD following stroke, the most frequent site of lesion was the basal ganglia, with 12 cases.

Literature describing the impact of basal ganglia stroke on pediatric mental health is far smaller; a PUBMED search identified 4 studies (Table 1). In a study of 44 children with stroke involving the basal ganglia ($n = 32$) or thalamus ($n = 12$), Westmacott et al.[10] found that diagnoses of attention deficit hyperactivity disorder (ADHD) and anxiety disorder were more prevalent after basal ganglia stroke. Similarly, Max et al.[11] determined that ADHD or traits of the disorder were more prevalent among children with putamen lesions (6 out of 7 children) than among those without (2 out of 6 children). Kwak and Jankovic[12] described 2 children who exhibited ADHD and OCD after suffering from stroke involving the basal ganglia. Ledochowski et al.[13] studied 75 children with stroke involving the basal ganglia and/or thalamus and reported that a higher degree of anxiety and depression was present in those with post-stroke dystonia versus those with no dystonia. Both of our patients struggled with anxiety, depression, and attention after basal ganglia stroke, which is consistent with these previously described cases of children with basal ganglia stroke. Neither had post-stroke dystonia, though the first patient did have mild chorea.

Animal models and functional imaging have helped clarify the motor functions of the basal ganglia, but the neurobiological mechanisms leading to mood disorders after basal ganglia stroke are less clear. The basal ganglia are a group of subcortical nuclei that are strongly interconnected with several brain areas, including, but not limited to, the cerebral cortex and the thalamus.[10,14] Parallel frontal to subcortical neuronal circuits that connect specific regions of the frontal cortex to the striatum, globus pallidus and the thalamus are implicated in neuropsychiatric disorders.[15] Although the main anatomical structures that are involved are similar, the anatomical positions of the circuits are segregated in the caudate, putamen, and other deep gray structures.[15] Therefore, injury to different regions may be associated with potentially differential impact on motor function, mood and behavior.[16] Specifically, decreased volume in the caudate nucleus has been associated with depression,[17] and caudate nucleus stroke has been implicated in transient psychosis.[18] Basal ganglia involvement in neuronal pathways connected with the prefrontal cortex may contribute to the pathogenesis of several disorders affecting mood regulation, such as depression, anxiety, OCD, and attention.[10,13,14] Murakami et al.[4] proposed that post-stroke apathetic depression might be associated with the intracranial dopamine pathway since it includes projections to

Table 1. Previously Reported Cases of Mental Health Issues After Basal Ganglia Stroke in Children.

Author	Year	No. of Patients	Gender	Age at Stroke	Lesion Laterality	Seizure History	Mood Disorders
Max et al.[11,a]	2002	Putamen: 6/7					
		Patient 1	M	5 years	R	Yes	ADHD/ADHD traits
		Patient 2	F	4 years	R	No	ADHD/ADHD traits
		Patient 3	M	Unclear [b]	R	No	ADHD/ADHD traits
		Patient 4	F	Prenatal	L	Yes	ADHD/ADHD traits
		Patient 5	F	Prenatal	L	No	ADHD/ADHD traits
		Patient 6	M	8 years	R	No	ADHD/ADHD traits
Kwak & Jancovic[12]	2002	2	M	8 years	R	No	ADHD OCD
Westmacott et al.[10,c]	2018	16	Unclear	Unclear	Unclear	Unclear	[d] ADHD: 7 Depression: 6 Anxiety: 5
Ledochowski et al.[13,e]	2020	Unclear	Unclear	Unclear	Unclear	Unclear	[d] *Dystonia*: Depression Mild-Moderate = 8 Severe = 6 Anxiety Mild-Moderate = 7 Severe = 7 *No dystonia*: Depression Mild-Moderate = 7 Anxiety Mild-Moderate = 10 Severe = 2

Abbreviations: M, male; F, female; m, months; R, right; L, left.

[a] This study looked for the presence of ADHD/traits, no other mood disorders. Only 1 out of the 7 patients with putamen lesions did not exhibit ADHD/traits.

[b] Age was listed as 3:05, but it is unclear if it means at 3 minutes or hours of life.

[c] 32 patients who had childhood basal ganglia stroke were studied, and 16 were diagnosed with mood disorders. The genders, ages, lesion laterality, and seizure history were unspecified for those 16. Of the 32, M = 21 and F = 11; the age range was between 5 months and 13 years; R = 15, L = 13, bilateral = 3; and 1 patient had a seizure disorder.

[d] Some patients may have had multiple diagnoses of mood disorders, but the overlap was unspecified.

[e] 75 children were studied (dystonia n = 24, no dystonia n = 51). 21 showed concerns for depression, and 26 for anxiety. They were considered individually, and the overlap was unspecified, so it is unclear how many patients out of the 75 showed concern for at least 1. The genders, ages, lesion laterality, and seizure history were also unspecified for those patients. Of the 24 with dystonia, M = 10, F = 14; the mean age was 3.13 years; R = 13, L = 11; and 2 had seizure disorders. Of the 51 with no dystonia, M = 39, F = 12; the mean age was 3.72 years; R = 20, L = 31; and 7 had seizure disorders.

the bilateral striatum. The cortico-striatal-thalamic-cortical circuit is heavily involved in the development of Tourette syndrome, and it has been reported that dysfunction in this pathway is linked to OCD.[12] Popa et al.[7] also observed that abnormal hyperactivity within the mesio-prefrontal-cingulo-striatal circuit was linked to OCD. Additionally, dysfunction of the prefrontal cortical-striatal-pallidal pathways is thought to be involved with ADHD.[11] Further research is needed to clarify specific mechanisms within this complex system that contribute to mood disorders after basal ganglia stroke. It is not clear which mechanisms caused our first patient to have a far more severe mental health course than the second, though we speculate that stroke size and pre-existing anxiety may have both played a role.

Mental health issues can be significant after pediatric basal ganglia stroke, as our patients demonstrate. These issues can be exacerbated by the presence of barriers to psychiatric care. While both of our patients received psychiatric care, many patients are not so fortunate. In the United States, approximately only one third (36.2%) of adolescents with mental health disorders accessed mental health services.[19] Through an intensive literature review regarding the barriers to psychiatric care as perceived by parents, Reardon et al.[20] found those barriers to center around issues with the mental health system, stigma associated with mental health services and treatment, understanding the mental health problem and possible solutions, and familial circumstances. Many states, including Indiana, have suboptimal access to mental health care for adults and children.[21] Mental Health America released its 2020 rankings of how the states performed in mental health care in several categories, and Indiana was among the lowest-ranked states in almost every single one—it was ranked 33rd in prevalence of mental illness, 19th in prevalence and care for youth, 26th in access to care, and was ranked 33rd overall.[21]

This study has limitations. This is a small series, with only 2 cases described, limiting the ability to draw generalizable conclusions. In the second case, it is possible that the anxiety was related to post-traumatic stress after his hospitalization, rather than the stroke itself; post-traumatic stress after hospitalization in children has been well-described.[22-24] To fully understand the complete relationship between the basal ganglia and mood disorders in children, how these mood disorders impact the family, and the time to recovery, larger studies are necessary.

Anxiety, depression, and difficulty with attention can follow pediatric basal ganglia stroke.[10-13] We describe 2 children with basal ganglia strokes who had all of these issues; both families were impacted by these issues, and the first child took several years to have significant recovery, while the second recovered over months. Further research is still needed to clarify the neurobiological mechanisms leading to mood disorders after basal ganglia stroke in both children and adults.

Declaration of Conflicting Interests

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