

# Neurodevelopmental Influences in Psychosis: A Case of Left Cerebral Hemiatrophy and Schizoaffective Disorder

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## ÖZET:

Psikozda nörogelişimsel etkiler: bir olgu nedeniyle sol serebral hemiatrofi ve şizoaffektif bozukluk

Serebral hemiatrofi (veya Dyke-Davidoff-Masson Sendromu) serebral hemiatrofi ya da hipoplaziye eşlik eden aynı taraflı kalvarial değişiklikler ile karakterize nörogelişimsel bir bozukluktur. Bu durum klinik olarak kontralateral motor disfonksiyon, fasial asimetri, epilepsi ve entellektüel bozukluklar ile kendini gösterir. Psikiyatrik belirtiler daha seyrek olarak görülmekte olup hastalığın nöropsikiyatrik yönü henüz iyi tanımlanmamıştır. Bu yazıda, sol serebral hemiatrofi ve şizoaffektif bozukluğun beraber görüldüğü 26 yaşında bir kadın hasta sunulacak ve bu nadir birliktelik beyin lateralizasyonu ile ilişkili nöral gelişim bozukluğu, plastisite, şizofreni ve şizoaffektif bozuklukta sol hemisfer disfonksiyonu ile ilgili kanıtlar bağlamında tartışılacaktır.

**Anahtar sözcükler:** şizofreni ve psikotik özellikli bozukluklar, serebral hemiatrofi, Dyke-Davidoff-Masson Sendromu

**Klinik Psikofarmakoloji Bulteni 2013;23(4):368-72**

## ABSTRACT:

Neurodevelopmental influences in psychosis: a case of left cerebral hemiatrophy and schizoaffective disorder

Cerebral hemiatrophy (or Dyke-Davidoff-Masson Syndrome) is a neurodevelopmental disorder characterized by atrophy or hypoplasia of one cerebral hemisphere accompanied by ipsilateral calvarial changes. Clinically, the condition presents with contralateral motor dysfunction, facial asymmetry, epilepsy and intellectual impairment. Psychiatric manifestations are uncommon and the neuropsychiatric aspect of the disease is not well described. Here, we report a 26-year-old female who presented with left cerebral hemiatrophy and schizoaffective disorder. We discuss the relevance of left-sided neurodevelopmental cerebral atrophy in the context of disrupted neural development of brain lateralization, plasticity, and evidence regarding left hemisphere dysfunction in schizophrenia and schizoaffective disorder.

**Keywords:** schizophrenia and disorders with psychotic features, cerebral hemiatrophy, Dyke-Davidoff-Masson Syndrome

**Bulletin of Clinical Psychopharmacology 2013;23(4):368-72**

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Date of submission: January 21, 2013

Date of acceptance: March 13, 2013

## Declaration of interest:

A.D.T., A.D.Y., T.G.C.: The authors reported no conflict of interest related to this article.

## INTRODUCTION

Cerebral hemiatrophy (or Dyke-Davidoff-Masson syndrome [DDMS]) is a radiologically defined characteristic childhood syndrome, which consists of unilateral hemispheric atrophy accompanied by ipsilateral calvarial thickening and overgrowth of sinuses (1). This rare syndrome includes two forms comprising: [1] the congenital form, which may result from congenital malformations, infections or vascular etiology and [2] the acquired form related to perinatal birth

trauma, hypoxia and intracranial hemorrhage, or postnatal prolonged febrile convulsions, trauma, vascular insult or intracranial infections (2). The clinical symptomatology usually starts in early childhood and mainly includes contralateral motor impairment, facial asymmetry, epilepsy and intellectual dysfunction (3). Psychiatric manifestations are uncommon and have rarely been reported (4,5,6).

In this article, we aim to expand the neurobehavioral aspects of this rare syndrome with an unusual case, that presented with major

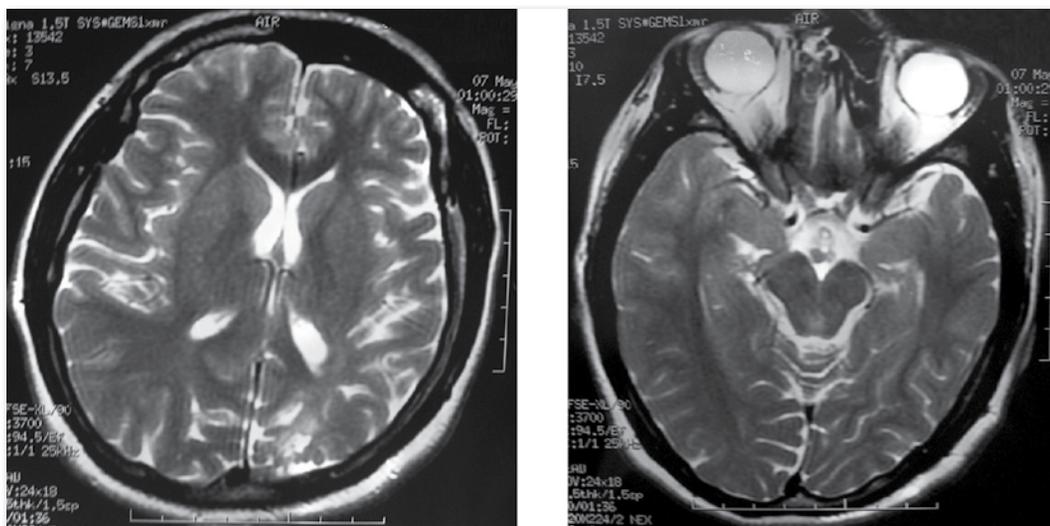
depression and psychosis in addition to the hallmark components of DDMS.

## CASE

E.S. was a 26-year-old female followed by our epilepsy outpatient clinic for her epileptic seizures. She was born on time with low-birth-weight; however, her mother reports no developmental delay in milestones until age 3, when she had meningitis. Following the infection, the family did not notice an apparent motor dysfunction but learning was reportedly slower. Her epilepsy started at age 5 and included complex partial seizures characterized by interrupted behavior, unresponsiveness and motionless staring at a fixed point; these seizures rarely evolved to secondarily generalized tonic-clonic seizures. At age 7, she started her education in the primary school and learning difficulties became clear. She was able to read and write but could not proceed further and dropped out after three years of education. She was living with her family and did not work outside the home. At age 19, she had her first severe major depression episode and was admitted to a psychiatry clinic following a suicidal attempt. At that time, her reference and persecutory delusions

became apparent; she also showed aggressive behavior, frequent excitation and violent outbursts. Until age 26, the patient was reported to have numerous depressive periods mostly characterized by depressed mood, anhedonia, decreased functionality in all activities, psychomotor agitation, remarkable changes in sleep and appetite and recurrent thoughts of suicide which led to several suicidal attempts. The psychotic symptoms persisted during the remission periods and primarily included delusions of reference (believing almost everybody was talking about her) and persecution (believing her relatives would kill or mutilate her). A diagnosis of schizoaffective disorder (depressive type) was made. Her family history was unremarkable for neurological or psychiatric disease.

On mental status examination, her cooperation was intermittent. Her affect was blunt or inappropriate while her mood was variable. General intellectual functioning revealed an IQ score of 64, which indicated a mild mental impairment. Her Beck Depression Inventory score excluded the presence of depression at the time of examination. Her neuropsychological examination showed impairments in simple and complex attention, planning, abstraction and judgment.



**Figure 1:** Cranial magnetic resonance imaging of the patient. (Left) This axial T2-weighted section shows left cerebral hemiatrophy along with prominent reduction in gray and white matter and noticeable atrophy in the left thalamus. The hyperpneumatization of the left frontal sinus is accompanied by widening of the diploe space and left calvarial hypertrophy. (Right) Atrophy in the left cerebral peduncle and enlargement of the left frontal sinus is notable in this axial T2-weighted section.

Language tests revealed moderate impairments in confrontation naming and decreased verbal fluency. Verbal memory was impaired indicating deficits both in encoding and retrieval stages. Her Mini-Mental Status Examination score was 24 out of 30. Neurological examination revealed mild right-sided hemiparesis and brisk deep tendon reflexes on the right with no clonus or extensor plantar response.

The EEG revealed mild amplitude depression over the left hemisphere and diffuse slow-wave activity in the range of 6-6.5 c/s on the left and 7-7.5 c/s on the right hemisphere. An MRI showed marked calvarial changes on the left side comprising enlarged diploic spaces and hyperpneumatization of paranasal sinuses. Her left cerebral hemisphere showed diffuse atrophy including the white matter, thalamus and brain stem accompanied by ischemic gliotic areas in the left frontal and parietooccipital regions (Figure 1). Taken together, the neuroimaging findings and clinical presentation confirmed the diagnosis of left-sided cerebral hemiatrophy (DDMS).

After trying several drug combinations, the seizures were well-controlled with an antiepileptic therapy comprising carbamazepine 1000 mg/day and leviratracetam 500 mg/day. Of note, the psychotic symptoms were unrelated to seizure control and were present regardless of response to antiepileptic therapy ruling out forced normalization. Her final psychiatric treatment included biperidene 4 mg/day, haloperidol 20 mg/day and thioridazine 25 mg/day and the family reported that she still showed frequent excitation and violent outbursts.

## DISCUSSION

Intellectual dysfunctioning and the extent of cognitive impairment in DDMS shows differences depending on the affected hemisphere (1,3,7,8). In right hemiatrophy, spatial processing and orientation discrimination were reported to be consistently impaired while attention, executive functions and verbal memory domains showed variable deficits (7). When the left hemisphere was

affected, repetitive speech patterns, lack of spontaneity or jargon were clinically observed (3); language representation was mostly found to be reorganized to the right cerebral hemisphere and the cognitive outcome was poor with variable impairments on measures of verbal and visual memory (8). While our patient had no apparent language difficulties during the clinical interview, the neuropsychological assessment revealed a clear language dysfunction and a marked impairment in verbal memory; attention and executive functions also showed severe impairments. Further, our patient was left-handed indicating right hemisphere dominance despite a negative familial sinistrality, conceivably due to early extensive damage or delayed development of the left hemisphere (9). Atypical patterns of cerebral dominance and disorders of cerebral lateralization have been reported to occur in schizophrenia and schizoaffective disorder (10,11). Our findings appear to be in agreement with the abnormal language processes and mixed or ambiguous handedness that has been associated with schizophrenic psychopathology.

While psychiatric manifestations of cerebral hemiatrophy have rarely been reported, the presented psychiatric symptomatology meets the DSM-IV criteria for schizoaffective disorder. Currently, there are only three reports, that describe the manifestation of psychotic symptoms during late adolescence and adulthood concomitant with DDMS (4-6). Two of these patients had a diagnosis of schizophrenia and neuroimaging revealed central and periventricular atrophy in both cases indicating a possible hypoxic/ischemic etiology (5,6). The third case was reported to have a schizoaffective disorder with psychosis triggered during a major depressive episode; loss of white matter was detected along with gliosis in the frontal, temporal, and posterior areas (4). In the same vein, the neuroimaging in this case showed ischemic gliotic areas in the left frontal and parietooccipital regions accompanied by loss of white matter. Importantly, in all three cases, as well as in our case, the hemiatrophy occurred in the left hemisphere. There is a

considerable amount of evidence indicating left hemisphere dysfunction in schizophrenia and schizoaffective disorder (12-15). A recent meta-analysis suggested a morphological lateralization of the schizophrenic brain impairments to the left hemisphere and superior temporal structures (16). Connectivity studies have indicated marked abnormalities in the left frontotemporal white matter in schizophrenia and schizoaffective disorder (17-20). It is quite intriguing that abnormalities in the normal neural development of the left hemisphere might also present with the psychotic symptoms of schizophrenia. Future prospective evidence from neurodevelopmental studies implementing functional neuroimaging and connectivity measures may add to the suggested specificity of the pathological brain processes in schizophrenia and schizoaffective disorder.

Overall, this rare case of DDMS manifesting with concurrent schizoaffective disorder expands the available sparse evidence concerning the neuropsychiatric aspect of cerebral hemiatrophy and adds to the evidence that this condition may present with psychotic abnormalities particularly when left hemiatrophy is present. As a disorder of neural development confined to a unilateral cerebral hemisphere, DDMS is especially interesting in the context of lateralization of brain functions associated with neuropsychiatric disorders and neurodevelopmental models of schizophrenia and schizoaffective disorder (21,22). The influence of abnormalities in neural connectivity, changes in plasticity following early hemispheric damage and functional reorganisation of neural networks contributing to the pathogenesis of psychotic disorders remain to be elucidated.

## References:

- Jacoby CG, Go RT, Hahn FJ. Computed tomography in cerebral hemiatrophy. *AJR Am J Roentgenol* 1977;129(1):5-9.
- Zilkha A. CT of cerebral hemiatrophy. *Am J Neuroradiol* 1980;135(2):259-62.
- Parker CE, Haris N, Mavalwala J. Dyke-Davidoff-Masson syndrome: five case studies and deductions from dermatoglyphics. *Clin Pediatr* 1972;11(5):288-92.
- Amann B, García de la Iglesia C, McKenna P, Pomarol-Clotet E, Sanchez-Guerra M, Orth M. Treatment-refractory schizoaffective disorder in a patient with dyke-davidoff-masson syndrome. *CNS Spectr* 2009;14(1):36-39.
- Honer WG, Kopala LC, Locke JJ, Lapointe JS. Left cerebral hemiatrophy and schizophrenia-like psychosis in an adolescent. *Schizophr Res* 1996;20(1-2):231-34.
- Puri BK, Hall AD, Lewis SW. Cerebral hemiatrophy and schizophrenia. *Br J Psychiatry* 1994;165(3):403-05.
- Demirtas-Tatlidede A, Yalcin AD, Uysal E, Forta H. Right cerebral hemiatrophy: neurocognitive and electroclinical features. *Epilepsy Behav* 2010;17(4):536-40.
- Mirsattari SM, Wilde NJ, Pigott SE. Long-term cognitive outcome of hemiconvulsion-hemiplegia-epilepsy syndrome affecting the left cerebral hemisphere. *Epilepsy Behav* 2008;13(4):678-80.
- Geschwind N, Galaburda AM. Cerebral lateralization: Biological mechanisms, associations and pathology. *Arch Neurol* 1985;42(5,6,7):428-59,521-52,634-54.
- Crow TJ. Schizophrenia as failure of hemispheric dominance for language. *Trends Neurosci* 1997;20(8):339-43.
- Reite M, Teale P, Rojas DC, Sheeder J, Arciniegas D. Schizoaffective disorder: evidence for reversed cerebral asymmetry. *Biol Psychiatry* 1999;46(1):133-36.
- Gur RE. Left hemisphere dysfunction and left hemisphere overactivation in schizophrenia. *J Abnorm Psychol* 1978;87(2):226-38.
- Hugdahl K, Løberg EM, Nygård M. Left temporal lobe structural and functional abnormality underlying auditory hallucinations in schizophrenia. *Front Neurosci* 2009;3(1):34-45.
- Kwon JS, McCarley RW, Hirayasu Y, Anderson JE, Fischer IA, Kikinis R, et al. Left planum temporale volume reduction in schizophrenia. *Arch Gen Psychiatry* 1999;56(2):142-48.
- Li X, Branch CA, Ardekani BA, Bertisch H, Hicks C, DeLisi LE. fMRI study of language activation in schizophrenia, schizoaffective disorder and in individuals genetically at high risk. *Schizophr Res* 2007;96(1-3):14-24.
- Vita A, De Peri L, Deste G, Sacchetti E. Progressive loss of cortical gray matter in schizophrenia: a meta-analysis and meta-regression of longitudinal MRI studies. *Transl Psychiatry* 2012;2:e190.
- Antonius D, Prudent V, Rehani Y, D'Angelo D, Ardekani BA, Malaspina D, et al. White matter integrity and lack of insight in schizophrenia and schizoaffective disorder. *Schizophr Res* 2011;128(1-3):76-82.

18. Hao Y, Yan Q, Liu H, Xu L, Xue Z, Song X, et al. Schizophrenia patients and their healthy siblings share disruption of white matter integrity in the left prefrontal cortex and the hippocampus but not the anterior cingulate cortex. *Schizophr Res* 2009;114(1-3):128-35.
19. Konrad A, Winterer G. Disturbed structural connectivity in schizophrenia primary factor in pathology or epiphenomenon? *Schizophr Bull* 2008;34(1):72-92.
20. Szeszko PR, Ardekani BA, Ashtari M, Kumra S, Robinson DG, Sevy S, et al. White matter abnormalities in first-episode schizophrenia or schizoaffective disorder: a diffusion tensor imaging study. *Am J Psychiatry* 2005;162(3):602-05.
21. Palomo T, Kostrzewa RM, Archer T, Beninger RJ. Neurodevelopmental liabilities in schizophrenia and affective disorders. *Neurotox Res* 2002;4(5-6):397-408.
22. Gursu Hariri A, Uzuner Ozer G, Ceylan ME, Ceylan N, Yazan B, Onal AO. Schizophrenia: neurodevelopmental hypothesis. *Klinik Psikofarmakoloji Bülteni-Bulletin of Clinical Psychopharmacology* 1999;9(2):99-103. (Turkish)