

# Concordant response to pharmacotherapy in monozygotic twins with schizoaffective disorder

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**Abstract.** – **BACKGROUND:** Schizoaffective disorder (SAD) represents one of the most confusing and controversial concepts in psychiatry. Prevalence is less than 1%, but despite that it has a major influence on an individual and community. There is an increased risk for schizophrenia and mood disorders in first degree relatives with SAD, according to DSM IV. This paper describes the concordant clinical response of a pair of monozygotic twins with SAD when treated with risperidon and valproic acid. We found that their clinical symptoms were very similar and both brothers expressed hypomanic and depressive episode prior to full onset of SAD-psychotic symptoms with correlations of elevated mood, and first psychiatric hospitalization at the age of 19 (patient A) and 18 (patient B). Their response to the combined treatment with risperidon and valproic acid has been also similar both in intensity and in the pattern of symptoms that have improved.

*Key Words:*

Schizoaffective disorder, Monozygotic twins, Valproic acid.

## Introduction

Schizoaffective disorder (SAD) represents one of the most confusing and controversial concepts in psychiatric nosology<sup>1</sup>. It was invoked in 1933 to describe “acute schizoaffective psychosis” in patient presented with conterminous severe affective and psychotic symptoms<sup>2</sup>.

To date the debate continues as to whether schizoaffective disorder is a form of schizophrenia, a form of affective disorder, a completely separate condition or the mid-point of a continuum between schizophrenia and bipolar disorder<sup>2</sup>.

Despite its low prevalence, the disorder has a significant impact on an individual and community, and increased research is needed to better understand the disorder and inform treatment.

The SAD has a low temporal stability, when patients were followed two years after the first hospitalization for a SAD, the diagnoses were stable in only 36% of cases<sup>1</sup>. Schizoaffective disorder bipo-

lar type may be more common in young adults, whereas schizoaffective disorder- depressive type may be more often in older patients. Compared with schizophrenia, SAD probably occurs more often in woman. Substantial occupation and social dysfunction is also common<sup>3</sup>.

According to DSM IV there is substantial evidence that there is an increased risk for schizophrenia and mood disorders in first degree relatives of individuals with SAD. In family studies, relatives of probands with SAD have elevated risks of SCH (schizophrenia), SAD and bipolar depression<sup>4</sup>. Gershon’s family study reports lifetime prevalence of major affective disorder (including SAD) as 37% in relatives of probands with SAD<sup>5</sup>.

Patients suffering from schizoaffective disorder seem to receive complex pharmacological treatment regimes including antipsychotic drugs, mood stabilizers and antidepressants<sup>6</sup>.

One of the mood stabilizers that has been frequently used in the treatment of SAD is Valproic acid. The most common adverse effects are gastrointestinal disturbances (dyspepsia, nausea, anorexia, particularly at the start of therapy), weight gain, CNS effects (tremor, drowsiness, ataxia) and transient hair loss<sup>7</sup>.

Here, we present a case of a pair of male monozygotic twins suffering from schizoaffective disorder with early onset of disorder and the same adverse effect of hair loss to the therapy with valproic acid.

## Case Report

Twins A and B are 20 years old monozygotic twins, diagnosed as suffering from schizoaffective disorder according to the ICD-10 (International Statistical Classification of Diseases and Related Health Problems – 10<sup>th</sup> Revision). They were spontaneously delivered in gestational age of 30 weeks, they spent two weeks incubated, further there were no specific developmental problems, their walking and language began within the period of normal range. Both twins shared close relationship since child-

hood, they enrolled to the same highschool, went to the same class, with the proviso that twin A was being dominant of the two. Concerning family history, no individuals had any psychiatric problem among second-degree relatives of the twins except for their mother's sister, who suffered from depression.

Patient A was first seen at the age of 15, in first grade of high school, when symptoms of elevated mood were observed - he was logorrhoeic, very active in class at school, always raising his hand, he started multiple activities at the same time not finishing them. He had a feeling he was omnipotent or „almighty“. This episode of slightly elevated mood (hypomanic episode) was managed in outpatient terms, including only advisory conversation, no medications were included. In the same year he had a depressive episode which passed without the supervision of psychiatrist. His first hospital treatment was at the age of 19 when his psychiatric status indicated psychotic symptoms- paranoid delusions, ideas of reference, he felt that his life was threatened. At that time his mood was elevated, he slept very poorly, lost about 11 kg in body weight. There wasn't evidence from the history, physical examination or laboratory tests indicating that the symptoms are the consequence of specific general medical condition. Psychological testing showed significant disbalance between patients verbal abilities, which were highly above the average, contrary to his manipulative abilities which were under the average - this result could be elucidated by current illness. Projective testing material was extremely creative and rich in associations, spoke in favor of rapid flow of thoughts, with correlates of hypomanic mood, tension and increased vulnerability. Also discrete indicators of morbidly bizarre elaboration with schizophrenic quality could be observed. Results of CT scan of endocranium and EEG results were in the range of normal. Indicators of thyroid function were also correct. He was initially treated with a combination of risperidon (3 mg/day), valproic acid and benzodiazepines. After two months of treatment his psychotic symptoms reduced, his mood was euthymic, also his social functioning was satisfying. However, after a two months of treating with 1500 mg/day with valproic acid, he showed scalp hair loss which led first to reduction of the dose (1000 mg/day) and finally to the discontinuation of the drug, and this mood stabilizer was replaced with lamotrigin (200 mg/day). Three months after hospital treatment he had exacerbation in the form of paranoid ideas and symptoms of depersonalisation combined with depressive mood. This episode was successfully treated in outpatient terms

by increasement of risperidon doses to 4 mg/day.

Patient B, the twin brother, was first hospitalized at the age of 18, one year earlier than patient A. His psychiatric status also indicated psychotic symptoms with elevated mood. On admission to hospital he was nearly agitated, logorrhoeic, with lots of paranoid delusions, ideas of reference religious in character. Noticable was echolalia, verbigerations and manerism - crossing himself all the time, thouching his hands and shaking them. Auditory halucinations were also present, speaking to himself, being apsent from time to time. Heteroanamnesic data from mother points out that the adolescent had his first mood swing episode during previous summer when he was 17. At that time he had a manic episode followed by a depressive episode in autumn, similar to his twin brother. While in hospital he was also initially treated with the combination of risperidon (4 mg/day), valproic acid (2000 mg/day) and benzodiazepins. Psychological testing took place at the near end of the hospital treatment, so he was in good remission but personality profile showed correlations of emotional immaturity, hypersensitivity and perfectionism. Results of CT scan of endocranium and EEG results were in the range of normal. Laboratory analysis were also correct. The answer to the medications was similar as his brother-psychotic simptoms faded out, mood was stabilized. Due to hair loss valproic acid had to be replaced with lamotrigin. After this, one more hospitalization took place a year after, when auditory hallucinations dominated his complaints with cenestopathic ideas. Therapy was improved with haloperidol (1 mg/day).

At present time both brothers are in satisfactory remission which now lasts for two years, patient A is enrolled to the Faculty of Economics and is achieving good results and patient B is enrolled to the Faculty of Physical Education.

## Discussion

Systematic psychiatric research using twins has been going on since 1928, shifting from population to molecular genetic strategies<sup>8,9</sup>. The classical twin method - comparing similarity of a trait in identical, or monozygotic twins to that in fraternal, or dizygotic twins - has had a significant impact on our current understanding of etiologic factors in psychiatric diseases<sup>10</sup>. Heritability of SAD is still controversial. Cardno et al<sup>11</sup> analyzed 224 proband-wise-ascertained twin pairs from the Maudsley Twin Psychosis Series. Heritability estimates for schizophrenia, schizoaffective disorder and mania

were between 82% and 85%. Although incomplete, the data support SAD as a genetic intermediary between bipolar disorder and schizophrenia. According to results from a recent large-scale study, the relative risk of SAD was 2.76 if a first-degree relative had a history of mental illness compared with control subjects with no such family history. More precisely, the relative risk of SAD was 3.23, 2.57, or 1.92 if the first degree relative had bipolar disorder, schizophrenia, or SAD, respectively<sup>12</sup>. However, only one study investigated concordance rate within monozygotic twin pairs with schizoaffective syndrome and found that it is 39.1%<sup>13</sup>.

This paper describes the concordant clinical response of a pair of monozygotic twins with SAD when treated with risperidon and valproic acid. We found that their clinical symptoms were very similar and both brothers expressed hipomanic and depressive episode prior to full onset of SAD – psychotic symptoms with correlations of elevated mood, and first psychiatric hospitalization at the age of 19 (patient A) and 18 (patient B). Their response to the combined treatment with risperidon and valproic acid has been also similar both in intensity and in the pattern of symptoms that have improved. Side effects of hair loss to the therapy with valproic acid have been observed in both patients.

Up to 28% of patients who take valproate suffer temporary alopecia<sup>14,15</sup>. In most cases, hair loss is associated with long-term valproate pharmacotherapy and this was not a case in our twin brothers. Hair loss appears to be dose-related<sup>15</sup> and may be more common in women than in men. Usually patients will report gradual but steady hair loss, commonly beginning 2 to 6 months after initiating treatment<sup>16</sup>. Our patients reported hair loss 2 months after initiating treatment and it was very frustrating event for them since they were adolescents. Complete hair loss is rare and new hair growth typically begins approximately 2 to 3 months after alopecia onset<sup>16</sup>. The mechanism by which valproic acid induces effects on hair remains to be elucidated<sup>17</sup>. Nevertheless, both twins responded very well to the replacement of valproic acid with lamotrigin.

### Conclusions

To our knowledge, this is the first report describing monozygotic twins with SAD and similar illness characteristics who showed a similar response to risperidon and valproic acid treatment. Our finding supports the view that genetic factors may be important in predicting response to psychopharmacotherapy.

### Conflict of Interest

The Authors declare that there are no conflicts of interest.

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