The British Journal of Developmental Disabilities
Vol. 49, Part 2, JULY 2003, No. 97, pp. 111-116

A CASE REPORT OF THE MANAGEMENT OF BEHAVIOUR PROBLEMS IN IDENTICAL TWINS WITH RUBENSTEIN TAYBI SYNDROME

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Introduction

Rubenstein Taybi Syndrome (RTS) is a rare genetic condition, prevalence of which in the general population is estimated to range from 1/100,000 to 125,000 (Petrij *et al.,* 2001). The majority of reported cases are sporadic. Many of the patients with RTS are known to have the chromosome area 16p 13.3 affected. A micro deletion of chromosome at this site has been demonstrated in about 10 to 15% of the population (Petrij *et al.,* 2001 and Wallerstein *et al.,* 1997). Point mutation in the CREB binding protein (CBP) gene is reported as well. The CREB binding protein (CBP) gene which has also been mapped to chromosomal area 16p 13.3 has received much attention (Petrij *et al.,* 1995 and 2001) since the gene product is required for normal functioning of cells. Animal models and biochemical evidence point to the loss of one functional copy of CBP gene (haplodeficiency) during foetal development. However combined molecular and genetic investigations would reveal an abnormality only in 15 to 20% of the cases (Petrij *et al.,* 2001). The aetiology of this syndrome is considered to be heterogeneous and therefore the diagnosis is very much a clinical one. The syndrome affects both sexes.

Rubenstein and Taybi originally described this syndrome in 1963 (Rubenstein and Taybi). Physical features associated with the syndrome include hands and feet abnormalities such as broad thumbs and halluces, and characteristic facial dysmorphism such as microcephaly, prominent forehead, broad nasal bridge and beak like nose. This syndrome also is associated with delayed psychological and physical development (Stevens *et al.,* 1990). The general description of affected individuals is as loving and friendly although there are reports of maladaptive

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behaviour (Gorlin *et al.,* 2001). The behaviours reported include self-stimulatory behaviour such as rocking, hand flapping and spinning.

There are very limited published data on the psychiatric management of people with Rubenstein Taybi syndrome. The prevalence of psychiatric problems varies from one tenth to two third of the cases (Hellings *et al.,* 2002; Levitas and Reid, 1998). The main difficulty in estimating the prevalence is the lack of adequate sample size in most of the studies. There is a report of an adult female with severe learning disability and autism with symptoms of severe over-activity, mood lability, and aggressive outburtsts in a cyclical pattern, suggestive of mood disorder (Hellings *et al.,* 2002). This showed good response to treatment with sodium valporate, a mood stabiliser. The authors postulated from their experience that there may be a link between GABA or other neuro transmitter abnormalities and the chromosomal abnormalities noted in Rubenstein Taybi syndrome. Another study evaluated 13 people with Rubenstein Taybi syndrome, found a high prevalence of mood disorders and obsessive-compulsive disorders in this population (Levitas and Reid, 1998). There was also a high prevalence of neuroleptic induced movement disorders.

However, there are no published data on the use of any atypical antipsychotic drugs in people with Rubenstein Taybi syndrome. Atypical antipsychotic medications are increasingly used in the treatment of behaviour problems in people with learning disability. Risperidone in particular has been noted to be effective in people with learning disability and behaviour problems disorder (Sabaratnam, 1995; Purdon *et al.,* 1994). Risperidone has also been noted to be useful in the management of children with autism and behavioural problems (McCracken *et al.,* 2002). The present report is of identical twins with long standing behavioural problems requiring psychiatric intervention. The use of risperidone in one twin showed good clinical response and reduction in the intensity of behaviour in the other twin as well.

Rubenstein Taybi syndrome has been reported in identical twins before (Baraitser and Preece, 1983 and Robinson and Preece, 1993). These studies highlight the remarkable likeness of the twins in the physical phenotype. The present report highlights the difference in the behavioural phenotypes of the twins while resembling each other physically.

Personal and Developmental History

Twins were delivered at 37 weeks by emergency caesarian section due to breech presentation. No particular problems were noted at birth or immediately afterwards. A diagnosis of Rubenstein Taybi syndrome was made based on the physical features. Rubenstein who originally described this syndrome assessed the twins and confirmed that they have most of the features of the Rubenstein Taybi syndrome. Genetic analyses carried out more than 10 years ago did not reveal any specific abnormalities on chromosome 16. The twins have the physical features as described in TABLE I.

Both showed significant delay in the developmental milestones. They were poor feeders, had limited speech \and were much smaller for age (growth retardation). An assessment using the Vineland scale of adaptive functions (Sparrow *et al.,* 1984) revealed them to be functioning at the level of moderate

learning disability. There were no significant differences between the twins in adaptive functions. Both have epilepsy. While twin A has generalised tonic clonic seizures, twin B has mixed seizure types with generalised tonic clonic, atonic and absence seizures.

As children they are described as pleasant in manners. Twin A is described as obsessive (obsessed with jigsaw puzzles) and would get upset if his routine was interrupted. Twin B did not have this problem. However, parents do not report any significant behavioural problems requiring input from professionals. The twins lived with their parents and had their education at home with support from educational services, social service

TABLE I
The twins' physical features

	Twin A	Twin B
Height	147 cms	145 cms
Head circumference	52 cms	55 cms
Eyes		
Hypertelorism	Present	Present
Slant of Palperbral fissures	Present	Present
Cataract	Absent	Absent
Strabismus	Present	Present
Long eye lashes	Present	Present
Nose		
Long curved nose	Present	Present
Hypoplastic alae	Present	Present
Mouth		
High arched palate	Present	Present
Skeletal		
Narrow shoulders	Present	Present
Pectus excavatum	Present	Present
Rib defects	Present	Present
Scoliosis	Present	Present
Hands and feet		
Broad thumbs	Present	Present
Broad terminal phalanges	Present	Presen
Other features		
Excess body hair	Present	Present
Medical Conditions		
Epilepsy	Present	Present
Respiratory problems		
(Recurrent Bronchiecstasis)	Present	Absent
Duodenal ulcer	Absent	Present

respite and a voluntary organisation until they were 19 years old.

They were then admitted to a specialist centre for epilepsy for assessment for long-term residential care. The behavioural problems were first noted during their stay in that centre.

Twin A has now autistic features such as strict adherence to routine and obsessions with jigsaw puzzles. However, he enjoys company and generally reciprocates well to others. An assessment using the Childhood Autism Rating Scale (Schopler *et al.,* 1998) revealed that he does not have autism. He is described as hyperactive as well. Apart from the hyperactivity, he does not have any features of ADHA (Attention Deficit Hyperactivity Disorder). It was noticed that he had more severe behaviour problems, such as setting off fire alarms, playing with fire extinguishers, tearing up clothes, smashing other patients' glasses and spitting. Twin B had comparatively less severe problems, and limited to a short period of self-biting and being agitated. He eventually settled down well. Both were eventually moved to the current residential home where they have been staying now for nearly 18 months.

During this period the residential home staff has noticed increasing intensity of behaviour problems requiring input from the psychiatry of the learning disability service based at Leicester Frith Hospital, Leicester. Twin A continued to have the problems described above with increased intensity. The main behavioural problems were setting off fire alarms, grabbing belongings of other residents and smashing those, ripping clothes, and throwing food. Staff at the residential home described twin A's behaviour as deliberate to draw attention from staff and other residents. He was having 4-6 such behavioural incidents daily requiring staff intervention. The behaviour problems displayed by twin B in the residential home included escorting vulnerable residents out of the home, pulling down curtains and generally being mischievous. Twin A was described as having more severe problems in terms of both number of incidents and severity.

Psychiatric assessment did not reveal any evidence of a mood disorder or psychotic symptoms. The epilespy was well controlled with sodium valporate (800mg) in twin A and Carbamazepine (400mg) in twin B. Both twins have not had any seizures in the last five years. The staff had support from the behavioural intervention team in managing the behaviour problems but the success was limited. As twin A was clearly more unmanageable in the home setting, risperidone at a dose of 0.5mg twice daily was prescribed for him. Twin B did not have any specific treatment. Twin A showed a significant reduction in the number of behavioural incidences from the second week after being given risperidone, and at the time of the next psychiatric review (at three months), the occurrence of behavioural incidences had become once in a week or less. Residential staff reported also an overall improvement in his functioning; he was calmer, less agitated and more communicative. There was no evidence of any extra pyramidal side effects from risperidone. Although twin B's behaviours became more intense and frequent for a short while following twin A's treatment, there was a subsequent improvement with interventions from the behavioural intervention team.

Discussion

The psychological aspect of the Rubenstein Taybi syndrome is not clearly

described in the literature. Although people with this condition are generally described as pleasant and well mannered, there may be a substantial proportion who have psychological problems. The current report shows that at least in a few the behaviour problems can be long lasting and severe requiring psychiatric input.

There is evidence from the literature that people with Rubenstein Taybi syndrome who have behaviour problems which have cyclical course respond well to mood stabilisers such as sodium valporate. Twin A described in this report was already on sodium valporate for the treatment of epilepsy. While the epilepsy was well controlled, sodium valporate was not effective in the management of the behaviour problems. The behaviour problems reported here did not have a cyclical nature or any other evidence of a mood disorder. It is possible that people with Rubenstein Taybi syndrome have behaviour problems of a varying nature, intensity and course requiring different types of interventions.

The use of risperidone has been found to be useful for people with learning disability and behaviour problems. This is the first report of the use of risperidone in a person with Rubenstin Taybi syndrome. The use of risperidone was associated with significant improvement in the behaviour without any side effects. High prevalence of neuroleptic induced movement disorders is noted in the literature as one of the difficulties in the psychiatric management of people with Rubenstein Taybi syndrome (Levitas and Reid, 1998). Risperidone was used at a lower dose than for the treatment of schizophrenia. This particular use of risperidone has been noted to be effective for the management of behaviour problems in people with learning disability (Sabaratnam, 1995). The use of psychotropic medications in people with particular genetic syndromes such as Rubenstein Taybi syndrome needs to be explored further.

The interesting aspects of this case report are the possible links between the problems of the twins. Twin A is clearly described as the more disturbed person requiring staff attention and support. However, a careful evaluation revealed that twin B follows twin A closely and at times shows appreciation by laughing and nodding. Twin B can at times also encourage twin A to behave in a disturbed manner. Treatment with risperidone has reduced behavioural problems in twin A. There was a transient increase in intensity of behaviour problems in twin B following this reduction of problems. However, residential staff managed these problems with support from the behavioural intervention team. While behavioural intervention strategies, like limit settings and positive reinforcement tried earler, were not successful, the use of risperidone in twin A was followed by a good effect of these interventions in twin B. This reveals that the problems of the twins were interlinked and difficult to address in isolation.

Summary

Rubenstein Taybi syndrome is a rare genetic syndrome. Although the actual prevalence of psychiatric problems seems to vary widely between studies (10-76%), a significant proportion of people with this syndrome experience psychiatric and behavioural problems during the life span. However, there is very little information on the use of psychotropic medications for these people. The available evidence suggests that there is a high risk

of neuroleptic induced movement disorder in this population. This is a case report of identical twins with a Rubenstein Taybi syndrome. One of the twins was treated with a low dose of risperidone, an atypical antipsychotic drug, which produced a significant improvement without any side effects. This report highlights the need for further studies on the use of psychotropic medications in people with such genetic syndromes.

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