Prader–Willi syndrome (PWS) is a rare genetic disorder, with a UK population prevalence of ~1 in 25 000.1 PWS is caused by a lack of a paternal contribution to the critical chromosome region at 15q11-13, because of deletion on the paternally inherited chromosome (del PWS, 70%) or maternal uniparental disomy (mUPD PWS, 25%). Imprinted genes are monoallelically expressed in a parent-of-origin dependent manner. PWS is associated with a distinct physical phenotype including short stature, small hands and feet, hypogonadism and a characteristic facial appearance; and a behavioural phenotype characterised by increased appetite, mood swings, stubbornness, temper tantrums, aggression and repetitive speech.2 PWS is also associated with high rates of psychopathology, including affective psychosis such as major depressive disorder (MDD).5 Pathophysiological mechanisms of psychosis in those with mUPD PWS have been proposed, with higher rates of serotonin dysregulation.6,7 Serotonin is a neurotransmitter, involved in mood regulation, appetite, sleep and thermoregulation, and is involved in the development of affective disorders such as major depressive disorder.8 Serotonin is synthesised from the amino acid tryptophan, which is transported into the brain by the serotonin transporter (5-HTT) and acts with 5-HTTs to regulate mood.9,10

The serotonergic system is a prime candidate for explaining the high rates of affective disorders, and particularly affective psychosis in mUPD PWS. It is well established that serotonin plays a crucial role in brain development and emotional regulation and has been implicated in the development of affective disorders such as major depressive disorder (MDD).5 Through examining the role of imprinted genes in brain serotonin neurochemistry it may be possible to shed light on the neurobiological basis of higher rates of affective psychosis in those with mUPD PWS. Previous research has shown greater serotonergic turnover, including increased monoamine-oxidase activity in platelets and increased 5-hydroxyindoleacetic acid (breakdown product of serotonin) in the cerebrospinal fluid of patients with PWS.6,7 The aim of this study was to explore if serotonergic activity in platelets and increased 5-hydroxyindoleacetic acid (breakdown product of serotonin) in the cerebrospinal fluid of patients with PWS.6,7 The aim of this study was to explore if serotonergic activity in platelets and increased 5-hydroxyindoleacetic acid (breakdown product of serotonin) in the cerebrospinal fluid of patients with PWS.6,7 The aim of this study was to explore if serotonergic activity in platelets and increased 5-hydroxyindoleacetic acid (breakdown product of serotonin) in the cerebrospinal fluid of patients with PWS.6,7 The aim of this study was to explore if serotonergic activity in platelets and increased 5-hydroxyindoleacetic acid (breakdown product of serotonin) in 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Method

This was a UK-wide, cross-sectional study, comparing 5-HTT availability in eight adults with mUPD PWS and ten with del PWS, approved by the West of Scotland Research Ethics Committee and the Administration of Radioactive Substances Advisory Committee.

Results

We scanned eight participants with mUPD PWS and ten participants with del PWS. The SPECT scan from one of the participants with del PWS did not pass quality control and was discarded. Demographic and clinical details are shown in Table 1. The mUPD group had higher GDS-LD scores (non-significant) and had more past episodes of psychosis (non-significant) compared with the del group. On the general linear model, PWS variant was a significant predictor of 5HT BPND (F(1,12) = 3.59; P < 0.014). The mUPD group had significantly lower 5HT BPND compared with the del group (mean difference = 0.09; t = −2.85, P = 0.014, 95% CI 1.12–3.59) (see supplementary Fig. 1, available at https://doi.org/10.1192/bjp.2017.7).

Discussion

This is the first study to explore brain-stem 5-HTT availability in PWS.11 Our findings reveal an association between PWS genotype and brain-stem 5-HTT availability. The mUPD group had lower...
with the mUPD group of patients, and the potential reasons why drugs such as selective serotonin reuptake inhibitors are effective in treating this cohort of patients.

**Table 1** Demographic and clinical variables in the two patient groups with Prader–Willi syndrome (PWS)

<table>
<thead>
<tr>
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<th>mUPD group</th>
<th>Deletion group</th>
<th>( \chi^2 )</th>
<th>( t )</th>
<th>( P ) (two tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years: mean (s.d.)</td>
<td>31.25 (9.09)</td>
<td>29.78 (7.13)</td>
<td>0.37</td>
<td>0.72</td>
<td></td>
</tr>
<tr>
<td>Gender, female: ( n ) (%)</td>
<td>6 (75)</td>
<td>6 (66.7)</td>
<td>0.14</td>
<td>0.71</td>
<td></td>
</tr>
<tr>
<td>GDS-LD score, mean (s.d.)</td>
<td>6.75 (5.11)</td>
<td>4.55 (2.65)</td>
<td>1.09</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>Past History of psychosis, ( n ) (%)</td>
<td>5 (62.5)</td>
<td>3 (33.3)</td>
<td>1.45</td>
<td>0.23</td>
<td></td>
</tr>
<tr>
<td>mUPD, maternal uniparental disomy PWS, GDS-LD, Glasgow Depression Scale for people with Learning Disability.</td>
<td></td>
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Supplementary material

Supplementary material is available online at https://doi.org/10.1192/bjp.2017.7

References


