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The relationship between compulsive behaviour and academic achievement across the three genetic subtypes of Prader–Willi syndrome

J. Zarcone¹, D. Napolitano¹, C. Peterson¹, J. Breidbord¹, S. Ferraioli¹, M. Caruso-Anderson², L. Holsen³, M. G. Butler⁴, T. Thompson⁵

¹Strong Center for Developmental Disabilities, University of Rochester Medical Center, Rochester, NY, USA

²The Kennedy Krieger Institute, Johns Hopkins University School of Medicine, Baltimore, MD, USA

³Waisman Center, University of Wisconsin-Madison, Madison, WI, USA

⁴Children's Mercy Hospitals and Clinics, University of Missouri-Kansas City, Kansas City, MO, USA

⁵University of Minnesota, Minneapolis, MN, USA

Abstract

Background—Prader–Willi syndrome (PWS) is a genetic syndrome associated with several physical, cognitive and behavioural characteristics. For many individuals with this syndrome, compulsive behaviour is often noted in both food and non-food situations. The focus of this paper is on the non-food-related compulsions in individuals with PWS and comparing differences across the three genetic subtypes of the syndrome.

Methods—Compulsive behaviours in 73 people with PWS were assessed using the Yale-Brown Obsessive Compulsive Scale and the Compulsive Behavior Checklist. Compulsive behaviour and its relation to IQ and academic achievement also were evaluated. Phenotypic differences were characterized for the three most common genetic subtypes of the disorder: 16 individual with the long type I(TI)15q deletion, 26 individuals with the short type II (TII) 15q deletion and 31 individuals with maternal disomy 15.

Results—There appeared to be important differences between the two deletion subtypes. Specifically, individuals with the TI deletion had more compulsions regarding personal cleanliness (i.e. excessive bathing/grooming), and their compulsions were more difficult to interrupt and interfered with social activities more than the other subtypes. Individuals with the TII deletion were more likely to have compulsions related to specific academic areas (i.e. rereading, erasing answers and counting objects or numbers).

Conclusions—These findings may help clinicians and researchers identify possible intervention strategies and supports based on the behavioural phenotype associated with genetic subtype in individuals with PWS.

Keywords

academic achievement; compulsion; obsessive-compulsive disorder; Prader–Willi syndrome

Introduction

Prader–Willi syndrome (PWS) is a complex genetic disorder that occurs in approximately one in 20000 live births (Whittington *et al.* 2001) and is associated with distinct cognitive and behavioural characteristics. PWS is caused by a chromosomal abnormality involving the typical paternal deletion of the proximal long arm of chromosome 15 (15q11–q13) in approximately 70% of individuals, maternal disomy of chromosome 15 in approximately 25% of individuals, and an imprinting-centre defect in the 15q11–q13 region for the remaining individuals (Butler & Thompson 2000; Bittel & Butler 2005). The PWS critical region on chromosome 15 contains three breakpoints (BPs) that are implicated in the distinct typical deletion patterns. The longer Type I (TI) deletion spans BP₁ and BP₃ (see Fig. 1) while the shorter Type II (TII) deletion involves only BP₂ and BP₃ (Butler *et al.* 2004). As a result, people with the TI deletion have approximately 500 kb less genetic material than people with the TII deletion, which may result in more significant clinical problems.

In addition to food preoccupations, individuals with PWS experience other compulsive behaviours unrelated to food that cannot be attributed to the presence of intellectual disabilities (IDs) (Feurer *et al.* 1998; Clarke *et al.* 2002). Dykens *et al.* (1996) demonstrated that these symptoms were similar to those of typically developing individuals with obsessive compulsive disorder (OCD) and included hoarding, ordering/arranging, concerns with symmetry and exactness, rewriting, and needs to tell, know, or ask. Others have demonstrated that individuals with PWS have levels of repetitive and ritualistic behaviour similar to those of children with autism (Descheemaeker *et al.* 2006; Greaves *et al.* 2006).

Further analysis of the genetic subtypes of PWS indicates that individuals with the deletion subtype have more compulsive and self-injurious behaviour as compared with individuals with the maternal disomy who generally demonstrate higher Verbal IQ and academic performance scores (Roof *et al.* 2000). Individuals with maternal disomy may also be at increased risk for symptoms of autism (Milner *et al.* 2005; Veltman *et al.* 2005), psychiatric disorders (Boer *et al.* 2002; Vogels *et al.* 2004) and more symptom-related distress from obsessions and compulsions (Dykens *et al.* 1999).

Because of recent advances in genetic subtyping, there is evidence of additional differences between the two typical deletion subtypes of PWS. For example, Butler *et al.* (2004) demonstrated that individuals with the TI deletion were more likely to lack control over their compulsive behaviour and that their compulsions significantly interfere with social activities. In addition, they showed that individuals with the TI deletion had lower adaptive behaviour and IQ scores than those with the TII deletion. Milner *et al.* (2005) also identified possible

differences in Verbal IQ scores with individuals with the TII deletion having significantly higher scores than individuals with the TI deletion.

Interestingly, these authors did not find any significant differences in severity scores of compulsive behaviour on a modified version of the Yale-Brown Obsessive Compulsive Scale (YBOCS; Goodman *et al.* 1989a). Although these studies are preliminary, we are beginning to better characterize distinct behavioural phenotypes associated with each of the deletion subtypes and compare differences and similarities with individuals with maternal disomy.

The focus of the current study was to identify and describe differences in degree of compulsivity using the YBOCS Compulsions Checklist and the Compulsive Behavior Checklist (CBC; Gedye 1992) across the three genetic subtypes of persons with PWS (TI deletion, TII deletion and maternal disomy). Although the Compulsions Checklist of the YBOCS has not been validated with individuals with IDs, it is the primary instrument used to describe the topography and severity of compulsive behaviour in people the general population and has been used extensively with individuals with PWS (Stein *et al.* 1994; Dykens *et al.* 1999; Butler *et al.* 2004; Holsen & Thompson 2004; Milner *et al.* 2005). The CBC also has been used with individuals with IDs and has been well studied with individuals with PWS (Feurer *et al.* 1998; Dimitropoulos *et al.* 2001, 2006). Scores on these measures were also correlated with measures of intelligence and academic functioning to determine if there was a relationship between the type and severity of compulsions and academic skills.

Method

Participants

Participants in this study were volunteers recruited locally and nationally through the PWS Association (USA) website and annual conference for a large, 2-day investigation of compulsivity and abnormal food motivation in PWS. Seventy-three individuals with PWS (20 males and 45 females) participated, 16 with the TI deletion, 26 with the TII deletion and 31 with maternal disomy. Forty-five individuals were evaluated from 1995 to 1999 at the John F. Kennedy Center at Vanderbilt University, 23 individuals were evaluated from 2000 to 2004 at the University of Kansas Medical Center and five were evaluated in 2005 at the Department of Pediatrics at the University of Rochester Medical Center. Broad inclusion criteria for individuals with PWS were based on age (between 10 and 40 years), availability to travel and participate in a 2-day evaluation and documentation of genotype (i.e. deletion or maternal disomy) confirmed by diagnostic genetic testing. The demographic characteristics of each study group are described in Table 1. All individuals gave assent and carers signed informed consent approved by institutional review boards.

Genetic classification

High-resolution chromosome analysis, fluorescence *in situ* hybridization and DNA microsatellite analysis were used to confirm the deletion or maternal disomy genetic subtype status (Muralidhar & Butler 1998; Butler *et al.* 2002). Microsatellite markers proximal to *D15S541/S1035* and between *D15S541/S1035* and *D15S543* were used to identify TI and

TII deletions. These DNA markers are located between the two chromosome 15 proximal BPs (BP₁ and BP₂). The presence of a distal BP, between *D15S56* and *D15S165*, on 15q11–q13, was confirmed in all deletion participants by molecular genetic testing. Classification of TI and TII deletions was based on microsatellite analysis of parental DNA isolated from peripheral blood (see Fig. 1). Confirmation of classifications was achieved through quantitative polymerase chain reaction (PCR) using established protocols (Ungaro *et al.* 2001; Butler *et al.* 2002, 2004). TI deletion classification was made based on the absence of the paternal *D15S541/S1035* markers and classification of a TII deletion was based on the presence of the *D15S541/S1035* markers.

Measures

Throughout the 2-day session, both participants and carers completed the following measures.

Parent/Carer measures—Given impaired cognitive capacity in some individuals with PWS, the following behavioural scales were administered to the parents or carers of all participants.

1. The YBOCS is a standardized clinical measure of obsessive and compulsive behaviour in typically developing individuals. Two sub-scales are derived from the questionnaire: a Compulsions Checklist and an Obsessions Checklist. Each checklist contains a list of possible symptoms and the severity and prevalence of each behaviour over the past week is noted. Following this symptom section on each checklist, there are six questions on the frequency and severity of these behaviours or thoughts regarding control over, distress experienced by, and resistance to the behaviours/thoughts. For this study, we only examined the scores on the Compulsions Checklist which included nine subcategories of behaviour on which to rate participants: washing/cleaning, checking, repeating, counting, ordering/arranging, hoarding/saving, excessive magical games or superstitious behaviours, rituals involving other persons and 10 miscellaneous compulsions (e.g. need to tell, ask, confess; ritualized eating behaviours; need to touch, tap, rub). In addition, we evaluated the total number of compulsions endorsed out of a possible 35 items.

High levels of reliability (inter-rater agreement ranging from 0.95 to 0.98) for this scale have been established for OCD populations (Goodman *et al.* 1989b). In addition, high convergent validity (strong correlation between YBOCS scores and scores on other OCD measures) and discriminant validity (low correlation between YBOCS and depression and anxiety measures) have been reported for people with OCD (Woody *et al.* 1994).

2. The CBC is an assessment of compulsive behaviour written specifically for people with IDs (Gedye 1992). It includes 25 items covering five categories of behaviours (ordering, completeness/incompleteness, cleaning/tidiness, checking/touching and deviant grooming); additional items on the degree to which the compulsions interfered with regular activities and response to being interrupted when engaging in a compulsion were also scored. Although not standardized, the CBC is a reliable measure for obtaining information on the compulsive

behaviours of people with developmental disabilities (Bodfish *et al.* 1995) and also has been used reliably with people who have PWS (Feurer *et al.* 1998).

Participant measures

3. The Woodcock-Johnson Psychoeducational Battery was used to determine academic achievement. The Woodcock-Johnson Battery provides a normed set of tests for measuring general intellectual ability, specific cognitive abilities, scholastic aptitude, oral language and academic achievement. Participants at Vanderbilt University were tested with the revised version (Woodcock & Johnson 1989) and all subsequent participants were tested using the Woodcock-Johnson III (Woodcock *et al.* 2001). Given the significant differences between the two versions of the scale, only the math, reading, calculation, applied problems and letter-word identification subtests were used for this study.
4. IQ was assessed through standardized age-appropriate tests using either the Wechsler Adult Intelligence Scale-Revised (Wechsler 1981) or the Wechsler Intelligence Scale for Children-III (Wechsler 1991).
5. Other variables: in addition to age and gender, information was collected on any current psychotropic medications including selective serotonin reuptake inhibitors (SSRIs), which are often prescribed to reduce symptoms associated with anxiety and compulsivity in individuals with PWS (Stein *et al.* 1994). The number of individuals receiving SSRI treatment within each genetic subtype group is indicated in Table 1.

Procedures

The behavioural questionnaires were completed by the primary carer of the person with PWS and were based on the informant's assessment of the individual's degree of compulsivity. Trained research staff conducted the academic and IQ testing with each PWS participant. Data were analysed using SPSS (2005) 14.0 for Windows. Individual items on both scales relating to specific compulsive behaviours were analysed by genetic subtype.

Results

YBOCS

Overall, there was no significant difference across the three genetic subtypes in the mean number of items endorsed on the Compulsions Checklist, although there was a greater degree of variability for the maternal disomy group (TI deletion mean = 7.9 ± 4.1 , TII deletion mean = 6.5 ± 4.2 , maternal disomy mean = 8.0 ± 9.6). For each item on the Compulsions Checklist, a chi-square was constructed for YBOCS severity ratings (no problem, mild problem, moderate problem and severe problem) by genetic subtypes (TI deletion, TII deletion and maternal disomy). Results of the chi-square analysis indicated that there was a significant difference in the degree of excessive bathing/grooming ($P=0.02$) for individuals with the TI deletion (see top panel of Fig. 2). In addition, individuals with the TII deletion had more severe repeating compulsions regarding excessively counting numbers and objects ($P=0.04$) and rereading and erasing ($P=0.06$) (see middle and bottom panel of

Fig. 2). There was no significant difference across the three groups regarding the global severity of compulsive behaviour.

CBC

A chi-square was also constructed for severity ratings on the CBC and genetic subtypes. There were several subtype differences on the extent to which the compulsion interfered with daily living. First, compulsions were more likely to significantly interfere with social activities for individuals with the TI deletion ($P=0.002$) and take more than an hour of the day, although only at a marginally significant level ($P=0.08$) (see top and bottom panels of Fig. 3). In addition, for individuals with the TI deletion, interrupting compulsions was more likely to make them upset ($P=0.02$) (see top panel of Fig. 4). Second, individuals with maternal disomy were more likely to halt momentarily, but then resume the compulsive activity when interrupted ($P=0.025$) (see bottom panel of Fig. 4). There were no significant differences between the number of compulsions endorsed and the number of categories represented across the three subtypes.

Woodcock-Johnson

T-tests were conducted to determine areas of significance. Persons with the TI deletion were shown to have significantly lower overall scores than persons with the TII deletion or maternal disomy. Additionally, persons with the TII deletion had significantly higher scores ($P=0.019$) on the calculation sub-scale than either TI deletion or maternal disomy groups. See Table 2 for mean scores on the Woodcock-Johnson for each group.

IQ

Consistent with previous studies, there was not a significant difference in Full-Scale IQ score for the three groups, although persons with the maternal disomy had significantly higher Verbal IQ scores than those of the two deletion subtypes ($P=0.008$). See Table 3 for mean IQ scores for each group.

Use of SSRIs

We conducted a chi-square analysis to determine whether there were any differences in the number of individuals in each group using SSRIs. Results indicated that there was no significant difference in SSRI use across subtypes.

Discussion

These data provide further evidence of distinct behavioural profiles or phenotypes across the genetic subtypes of PWS. Consistent with prior studies (Butler *et al.* 2004), individuals with the TI deletion exhibited more compulsive behaviours than either TII deletion or maternal disomy groups. These compulsions are similar to those commonly experienced by typically developing individuals with OCD (e.g. arranging objects, excessive cleaning or grooming). Interestingly, individuals with the TII deletion demonstrated compulsions related to academic factors (i.e. counting, rereading, erasing). Although these three groups of participants did not differ significantly according to Full-Scale IQ, there were differences in Verbal IQ and performance on the Woodcock-Johnson Psychoeducational Battery subtests.

Specifically, individuals with the TI deletion did not perform as well on the Woodcock-Johnson across all subtests as did participants with the TII deletion or maternal disomy.

Although this study is limited because of the number of statistical comparisons and the small sample of individuals with the TI deletion, it expands the growing body of evidence that distinct behavioural phenotypes characterize individuals within the deletion subtypes and demonstrate additional differences as compared with individuals with the maternal disomy. This information may be useful when planning behavioural and medical interventions. For example, an understanding that persons with a TI deletion may experience more difficulties around grooming tasks might indicate a need for increased support during those activities. Additionally, given the greater severity of their compulsions, the difficulty they have when compulsions are interrupted, and the greater amount of time spent engaging in compulsions, persons with a TI deletion may be more likely candidates for medications shown to decrease compulsive behaviours. Other therapeutic interventions such as cognitive-behaviour therapy may also be appropriate for this group. Finally, because of significant differences in the compulsions displayed by persons with a TII deletion specific to academic tasks, greater support in school may be necessary in order to increase their academic success. This information may provide caregivers with the documentation necessary to obtain such support.

Because our analysis only addressed the differences in compulsive behaviour across the three subtypes, we did not evaluate how they differ from individuals with IDs, OCD, autism, or typically developing individuals. Thus, our findings were somewhat different from other studies indicating that individuals with PWS engage in a high degree of hoarding, checking, or other repetitive behaviours (Dykens *et al.* 1996; Clarke *et al.* 2002). The next step may be evaluating the relationship between PWS and other endophenotypes such as autism (Dykens *et al.* 2004). In our study, mean scores for the maternal disomy group indicated that they are more likely to return to their compulsions when interrupted which is similar to the repetitive behaviour associated with autism. Additional research may lead to a possible common genetic or neurodevelopmental origin linking the two disorders.

Future studies could also target how the compulsions exhibited by individuals with PWS compare with the compulsions demonstrated by individuals with OCD. Recent research has indicated that OCD symptoms cluster into four factors: factor I (aggressive, sexual, religious and somatic obsessions, and checking compulsions), factor II (obsessions of symmetry and repeating, counting and ordering/arranging compulsions), factor III (contamination obsessions, and cleaning/washing compulsions) and factor IV (hoarding obsessions and compulsions) (Leckman *et al.* 2001; Nestadt *et al.* 2003). Delineation of OCD phenotypes according to these factors may indicate that individuals with the TI deletion fit within the OCD factor III phenotype and individuals with the TII deletion fit within the OCD factor II phenotype. Further delineation of the OCD subtypes may indicate differences with comorbid diagnoses across the OCD phenotypes (Hasler *et al.* 2005) and between children/adolescents and adults with OCD (Delorme *et al.* 2006). Extending these findings to determine whether individuals with PWS also show differences in comorbid diagnoses and across age groups with regard to severity of compulsive behaviour would indicate that at least a portion of their compulsivity parallels individuals with OCD.

Because food compulsions are typically associated with PWS, further research needs to be conducted on the differences in the severity and types of food-related compulsions across the three genetic subtypes of PWS. Unfortunately, most behavioural questionnaires focusing on compulsive behaviour do not specifically measure food-related compulsions. This may indicate the need to develop additional questionnaires that are directly relevant to individuals with PWS so that we may begin to validate them (e.g. Clarke *et al.* 2002; Russell & Oliver 2003).

Further analysis of the genes that play a critical role in the phenotypic characteristics of the three genetic subtypes may also provide us with further evidence of possible gene-brain-behaviour relationships. For example, four genes (*NIPA1*, *NIPA2*, *CYFIP1* and *GCP3*) have been identified in the chromosomal region between BP₁ and BP₂ in the critical region of chromosome 15 and their expression may distinguish further the phenotypes associated with the TI and TII deletion subtypes (Bittel *et al.* 2006). These genes may be implicated in relation to differences in compulsive behaviour and academic skills in PWS individuals with TI versus TII deletions (Butler *et al.* 2005). Research is underway to further examine gene expression using quantitative RT-PCR to assess their contribution to behavioural and cognitive differences found between PWS individuals with the TI or TII deletion.

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References

- Bittel DC & Butler MG (2005) Prader–Willi syndrome: clinical genetics, cytogenetics, and molecular biology. *Expert Reviews in Molecular Medicine* 7, 1–20.
- Bittel DC, Kibiryeva N & Butler MG (2006) Expression of 4 genes between chromosome 15 breakpoints 1 and 2 and behavioral outcomes in Prader–Willi Syndrome. *Pediatrics* 118, e1276–83. [PubMed: 16982806]
- Bodfish JW, Crawford TW, Powell SB, Parker DE, Golden RN & Lewis MH (1995) Compulsions in adults with mental retardation: prevalence, phenomenology, and comorbidity with stereotypy and self-injury. *American Journal on Mental Retardation* 100, 183–92. [PubMed: 8527113]
- Boer H, Holland A, Whittington J, Butler J, Webb T & Clarke D (2002) Psychotic illness in people with Prader–Willi syndrome due to chromosome 15 maternal uniparental disomy. *Lancet* 359, 135–6. [PubMed: 11809260]
- Butler MG & Thompson T (2000) Prader–Willi syndrome: clinical and genetic findings. *Endocrinologist* 10, 3S–16S. [PubMed: 27570435]
- Butler MG, Bittel DC & Talebizadeh Z (2002) Prader–Willi syndrome and a deletion/duplication within the 15q11–q13 region. *Journal of Medical Genetics* 107, 69–70.
- Butler MG, Bittel DC, Kibiryeva B, Talebizadeh Z & Thompson T (2004) Behavioral differences among subjects with Prader–Willi syndrome and TI or Type II deletions and maternal disomy. *Pediatrics* 113, 565–74. [PubMed: 14993551]
- Butler MG, Kibiryeva N & Bittel DC (2005) Correlation of phenotype and expression of four genes between breakpoints BP1 and BP2 in Prader–Willi syndrome 55th Annual American Society of Human Genetics Meeting, 10 27, Salt Lake City, Utah.

- Clarke DJ, Boer H, Whittington J, Holland A, Butler J & Webb T (2002) Prader–Willi syndrome, compulsive and ritualistic behaviours: the first population-based survey. *British Journal of Psychiatry* 180, 358–62. [PubMed: 11925360]
- Delorme R, Bille A, Betancur C, Mathieu F, Chabane N, Mouren-Simeoni MC & Leboyer M (2006) Exploratory analysis of obsessive compulsive symptom dimensions in children and adolescents: a prospective follow-up study. *BioMed Central Psychiatry* 6, 1. [PubMed: 16396684]
- Descheemaeker MJ, Govers V, Vermeulen P & Fryns JP (2006) Pervasive developmental disorders in Prader–Willi syndrome: the Leuven experience in 59 subjects and controls. *American Journal of Medical Genetics* 140, 136–42.
- Dimitropoulos A, Feurer ID, Butler MG & Thompson T (2001) Emergence of compulsive behavior and tantrums in children with Prader–Willi syndrome. *American Journal on Mental Retardation* 106, 39–51. [PubMed: 11246711]
- Dimitropoulos A, Blackford J, Walden T & Thompson T (2006) Compulsive behavior in Prader–Willi syndrome: examining severity in early childhood. *Research in Developmental Disabilities* 27, 190–202. [PubMed: 15950435]
- Dykens EM, Leckman JF & Cassidy SB (1996) Obsessions and compulsions in Prader–Willi syndrome. *Journal of Child Psychology and Psychiatry* 37, 995–1002. [PubMed: 9119946]
- Dykens EM, Cassidy SB & King BH (1999) Maladaptive behavior differences in Prader–Willi syndrome due to paternal deletion versus maternal uniparental disomy. *American Journal on Mental Retardation* 104, 67–77. [PubMed: 9972835]
- Dykens EM, Sutcliffe JS & Levitt P (2004) Autism and 15q11–q13 disorders: behavioral, genetic, and pathophysiological issues. *Mental Retardation and Developmental Disabilities Research Review* 10, 284–91.
- Feurer ID, Dimitropoulos A, Stone WL, Roof E, Butler MG & Thompson T (1998) The latent variable structure of the Compulsive Behavior Checklist in people with Prader–Willi syndrome. *Journal of Intellectual Disability Research* 42, 472–80. [PubMed: 10030443]
- Gedye A (1992) Recognizing obsessive-compulsive disorder in clients with developmental disabilities. *Habilitative Mental Healthcare Newsletter* 11, 73–7.
- Goodman WK, Price LH, Rasmussen SA, Mazure C, Fleischmann RL, Hill CL, Heninger GR & Charney DS (1989a) The Yale-Brown Obsessive Compulsive Scale: I. Development, use, and reliability. *Archives of General Psychiatry* 46, 1006–11. [PubMed: 2684084]
- Goodman WK, Price LH, Rasmussen SA, Mazure C, Delgado P, Heninger GR & Charney DS (1989b) The Yale-Brown Obsessive Compulsive Scale: II. Validity. *Archives of General Psychiatry* 46, 1012–16. [PubMed: 2510699]
- Greaves N, Prince E, Evans DW & Charman T (2006) Repetitive and ritualistic behaviour in children with Prader–Willi syndrome and children with autism. *Journal of Intellectual Disability Research* 50, 92–100. [PubMed: 16403198]
- Hasler G, LaSalle-Ricci VH, Ronquillo JG, Crawley SA, Cochran LW, Kazuba D, Greenberg BD & Murphy DL (2005) Obsessive-compulsive disorder symptom dimensions show specific relationships to psychiatric comorbidity. *Psychiatry Research* 135, 121–32. [PubMed: 15893825]
- Holsen L & Thompson T (2004) Compulsive behavior and eye blink in Prader–Willi syndrome: neurochemical implications. *American Journal on Mental Retardation* 109, 197–207. [PubMed: 15072522]
- Leckman JF, Zhang H, Alsobrook JP & Pauls DL (2001) Symptom dimensions in obsessive-compulsive disorder: toward quantitative phenotypes. *American Journal of Medical Genetics* 105, 28–30. [PubMed: 11424988]
- Milner KM, Craig EE, Thompson RJ, Veltman MWM, Thomas NS, Roberts S, Bellamy M, Currant SR, Sporikou CM & Bolton PF (2005) Prader–Willi syndrome: intellectual abilities and behavioural features by genetic subtype. *Journal of Child Psychology and Psychiatry* 46, 1089–96. [PubMed: 16178933]
- Muralidhar B & Butler MG (1998) Methylation PCR analysis of Prader–Willi syndrome, Angelman syndrome, and control subjects. *American Journal of Medical Genetics* 80, 263–5. [PubMed: 9843050]

- Nestadt G, Addington A, Samuels J, Liang KY, Bienvenu OJ, Riddle M, Grados M, Hoehn-Saric R & Cullen B (2003) The identification of OCD-related subgroups based on comorbidity. *Biological Psychiatry* 53, 914–20. [PubMed: 12742679]
- Roof E, Stone W, MacLean W, Feurer ID, Thompson T & Butler MG (2000) Intellectual characteristics of Prader–Willi syndrome: comparison of genetic subtypes. *Journal of Intellectual Disability Research* 44, 25–30. [PubMed: 10711647]
- Russell H & Oliver C (2003) The assessment of food-related problems in individuals with Prader–Willi syndrome. *British Journal of Clinical Psychology* 42, 379–92. [PubMed: 14633414]
- Statistical Package for the Social Sciences (2005) SPSS for Windows, Release 14.0. (Computer Software). SPSS Inc., Chicago.
- Stein DJ, Keating J, Zar HJ & Hollander E (1994) A survey of the phenomenology and pharmacology of compulsive and impulsive-aggressive symptoms in Prader–Willi syndrome. *Journal of Neuropsychiatry* 6, 23–9.
- Ungaro P, Christian SL, Fantes JA, Mutirangura A, Black S, Reynolds J, Malcolm S, Dobyns WB & Ledbetter DH (2001) Molecular characterization of four cases of intrachromosomal triplication of chromosome 15q11–q14. *Journal of Medical Genetics* 38, 26–34. [PubMed: 11134237]
- Veltman MWM, Craig EE & Bolton PF (2005) Autism spectrum disorders in Prader–Willi and Angelman syndromes: a systematic review. *Psychiatric Genetics* 15, 243–54. [PubMed: 16314754]
- Vogels A, De Hert M, Descheemaeker MJ, Govers V, Devriendt K, Legius E, Prinzie P & Fryns JP (2004) Psychotic disorders in Prader–Willi syndrome. *American Journal of Medical Genetics* 127, 238–43.
- Wechsler D (1981) Wechsler Adult Intelligence Scale-Revised. The Psychological Corporation, San Antonio, TX.
- Wechsler D (1991) Wechsler Adult Intelligence Scale for Children, 3rd edn. The Psychological Corporation, San Antonio, TX.
- Whittington JE, Holland AJ, Webb T, Butler J, Clarke D & Boer H (2001) Population prevalence and estimated birth incidence and mortality rate for people with Prader–Willi syndrome in one UK health region. *Journal of Medical Genetics* 38, 792–8. [PubMed: 11732491]
- Woodcock R & Johnson M (1989) Woodcock-Johnson Tests of Achievement-Revised. DLM, Allen, TX.
- Woodcock RW, McGrew KS & Mather N (1994) Examiner's Manual. Woodcock-Johnson III Tests of Cognitive Ability. Riverside Publishing, Itasca, IL.
- Woody SR, Steketee G & Chamnless DL (1994) Reliability and validity of the Yale-Brown Obsessive Compulsive Scale. *Behaviour Research and Therapy* 33, 597–605.

Figure 1.
Chromosome 15 ideogram indicating the Type I and Type II deletion areas. BP, breakpoint.

Figure 2.

Proportion of caregiver ratings (none, mild, moderate, or severe) by PWS subtype for three compulsions that were significantly different on the YBOCS (excessive bathing/grooming, counting and rereading/erasing). PWS, Prader-Willi syndrome; YBOCS, Yale-Brown Obsessive Compulsive Scale; TI, Type I; TII, Type II.

Figure 3.

Proportion of caregiver ratings (none, mild, moderate, or severe) by PWS subtype for two areas of interference were significantly different on the CBC (compulsion interferes with social activities and compulsions takes more than an hour a day). PWS, Prader-Willi syndrome; CBC, Compulsive Behavior Checklist; TI, Type I; TII, Type II.

Figure 4.

Proportion of caregiver ratings (never, rare, some, or often) by PWS sub-type for two areas of interference were significantly different on the CBC (becomes upset when compulsion interrupted and halts momentarily then resumes compulsive activity). PWS, Prader–Willi syndrome; CBC, Compulsive Behavior Checklist; TI, Type I; TII, Type II.

Table 1

Demographic characteristics for each PWS subgroup

	TI deletion	TII deletion	Maternal disomy
No.	16	26	31
Mean age $\pm$ SD (years)	25.68 $\pm$ 9.03	20.3 $\pm$ 8.4	23.3 $\pm$ 10.2
Gender			
Male	7	8	13
Female	9	18	18
SSRI treatment	3	6	11

PWS, Prader–Willi syndrome; TI, Type I; TII, Type II; SSRI, selective serotonin reuptake inhibitor.

Table 2

Woodcock-Johnson mean scores and standard deviations for the reading and mathematics cluster scores, calculation, letter-word identification and applied problems subtests across genetic subtypes

Genetic subtype	Cluster scores				
	Reading	Math	Calculation	Letter-word identification	Applied problems
TI deletion (<i>n</i> = 16)	44.8 ± 26.6	45.5 ± 21.5	48.6 ± 25.7	47.5 ± 26.2	50.4 ± 16.7
TII deletion (<i>n</i> = 24)	68.1 ± 18	65.8 ± 16.7	69.5 ± 18.4	71.7 ± 18.3	66.1 ± 13.3
Maternal disomy (<i>n</i> = 29)	68.3 ± 29.9	62.5 ± 23.5	57 ± 24.9	68.2 ± 28.4	65.4 ± 16.8

TI, Type I; TII, Type II.

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Table 3

Mean scores and standard deviations for Full-Scale IQ, Verbal IQ and Performance IQ across genetic subtypes TI, Type I; TII, Type II.

Genetic subtype	Full-Scale IQ	Verbal IQ	Performance IQ
TI deletion (<i>n</i> = 14)	62.1 ± 95.6	61.9 ± 8.6	66.1 ± 9.6
TII deletion (<i>n</i> = 27)	62.4 ± 9.8	64 ± 9.7	65.5 ± 9.3
Maternal disomy (<i>n</i> = 30)	65.2 ± 12.1	71.3 ± 11.9	63.1 ± 11.3