# Mental Health Problems in Children with Prader-Willi Syndrome

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## Abstract

**Background:** Prader-Willi Syndrome (PWS) is a genetically determined neurodevelopmental disorder, which occurs in approximately one in 22000 births. **Aims:** This study aimed to investigate psychiatric characteristics of children diagnosed with PWS compared with an age-, gender- and IQ-matched control group. The parents of children with PWS were assessed for psychological distress in comparison to the parents of the control group. Methodological limitations identified in previous studies were addressed in the present study. **Methods:** Psychiatric problems were evaluated in a sample of children with genetically confirmed PWS and an age- and IQ-matched control group using the Child Behaviour Checklist 6-18. Parental psychological distress for both groups was evaluated with the Brief Symptom Inventory. **Results:** Children with PWS had more severe somatic, social, and thought problems, and were more withdrawn-depressed in comparison to controls. Borderline difficulties were detected for the affective, somatic, and attention deficit-hyperactivity CBCL DSM-orientated subscales in the PWS group. Parents of PWS children, in comparison to controls, had more somatization, phobic anxiety, obsessive-compulsive, and anxiety problems. **Conclusions:** PWS represents a complex psychological disorder with multiple areas of disturbances.

*Key words:* Prader-Willi Syndrome, comorbidity, depression, anxiety disorders, Attention Deficit/Hyperactivity Disorder

## Résumé

**Contexte:** Le syndrome Prader-Willi (SPW) et un trouble neurodéveloppemental génétique qui touche environ un enfant sur 22 000. **Objectif:** Étudier les caractéristiques psychiatriques d'enfants ayant reçu un diagnostic de SPW en les comparant à un groupe témoin d'enfants appariés pour l'âge, le et le QI. La détresse psychologique des parents dont les enfants souffraient du SPW a été comparée à celle des parents des enfants du groupe témoin. L'étude a tenu compte des limites méthodologiques constatées dans les études précédentes. **Méthodologie:** Les problèmes psychiatriques des enfants des deux groupes ont été analysés au moyen de la *Liste de contrôle du comportement de l'enfant âgé de 6 à 18 ans.* La détresse psychologique des parents des deux groupes a été évaluée au moyen de l'*Inventaire des symptômes—version courte.* Résultats: Les enfants qui souffrent du SPW ont de plus grandes difficultés au niveau somatique, social et conceptuel, et sont plus repliés sur eux-mêmes ou déprimés que les enfants du groupe témoin. Les sous-échelles État affectif, Somatisation et *Déficit d'attention avec hyperactivité* basées sur le DSM ont fait apparaître des difficultés à la limite de la pathologie. Les parents des enfants atteints du SPW avaient plus de symptômes somatiques, d'anxiété phobique, de symptômes obsessionnels-compulsifs et de problèmes anxieux que ceux du groupe témoin. **Conclusion:** Le SPW est un trouble psychologique complexe qui entraîne des perturbations à divers niveaux.

*Mots clés:* syndrome Prader-Willi, comorbidité, dépression, troubles anxieux, déficit d'attention avec hyperactivité

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# Introduction

Prader-Willi Syndrome (PWS) is a genetically determined neurodevelopmental disorder, which occurs in approximately one in 22000 births (Whittington et al., 2001). The critical region has been identified as 15q11-q13, with the majority of PWS cases (approximately 70%) resulting from a micro-deletion in the chromosome of paternal origin. One quarter of cases are due to maternal uniparental disomy (mUPD), in which two copies of the maternal chromosome are present, and a few cases (<5%) are caused by unbalanced translocations or imprinting centre defect (Bittel & Butler, 2005). Mild to moderate learning disability is usual, with an average IQ of about 70 (Whittington et al., 2001).

The original phenotypic characteristics described by Prader, Labhart and Willi consisted of obesity, short stature, mental retardation, and small hands and feet (Prader, Labhart & Willi, 1956). The physical phenotype now also includes a narrow bitemporal diameter, almond-shaped palpebral fissures, and a downturned mouth with thin upper lip, hypopigmentation, strabismus, scoliosis and hypogonadism (Bittel & Butler, 2005). Behavioral problems are also frequent and usually emerge around four years of age, and the characteristic profile is that of obsession with food, temper tantrums, aggression, stubbornness, skin-picking, and controlling and manipulative behavior (Dykens, Leckman, & Cassidy, 1996; Clarke et al., 2002). Compulsions are similar to the benign and transient rituals observed in normative child development (Feurer et al., 1998; Dykens, 2004). Skin picking has an early onset and shows stability over the time, and prevalence rates range from 65% to 95% (Feurer et al., 1998; Dykens, 2004). Variations in phenotype have been noted in relation to the underlying genetic anomaly: paternal deletions are associated with more severe maladaptive behaviours than mUPD mutations, even when IQ is taken into account (Dykens, Cassidy, & King, 1999). Patients with mUPD have also been shown to be less likely to display skin-picking and high pain-tolerance (Cassidy et al., 1997).

Anecdotally, children with PWS also exhibit other psychological difficulties outside of the described behavioural phenotype. In the past, several studies investigated a broader psychopathological phenotype for PWS. Previous studies did not, however, investigate comorbidity as a primary question, and consequently the potential for sources of artefact, previously described in the literature (Caron & Rutter, 1991; Wittchen, 1996) in detection of co-morbidity, may not have been considered. Some of the previous studies were purely descriptive in nature, with little or no use of standardized methods for assessing psychiatric problems, or using methods not standardized for subjects with learning difficulties. Other studies employed very small clinical samples (or just case series reports). An absence of control group or the use of control group not matched for age or level of disability is also a common weakness in PWS research (Table 1).

Investigation into parental psychopathology in PWS research in rare. Szatmari et al. investigated parental psychopathology and familial comorbidity in ASD parents, and in this case a PWS sample was used as a control group; other psychological difficulties in PWS parents were not addressed (Szatmari et al., 2008). Thus, there is a relative dearth of literature specifically focused on the mental health of parents with children with PWS.

# Aims

Based on the existent literature, we hypothesised that children with PWS would have a greater degree of psychopathology compared with an age and IQ matched control group. We further hypothesised that parents of children with PWS would have a greater degree of psychological distress compared with children of an age and IQ matched control group. We were interested in exploring the type of psychopathology present in both groups. The present study attempted to address some of the identified methodological limitations in previous investigations.

# Methods

## Subjects

Children with PWS (57) and their parents participating in the First National Irish PWS study were invited to participate. Children only with confirmed PWS based on FISH (fluorescence in situ hybridization) karyotyping were included. Parents were asked to fill in a demographic questionnaire, The Child Behaviour Checklist 6-18, Brief Symptom Inventory. IQ was assessed using Leiter International Performance Scale-Revised. The age, gender and IQ matched control group was collected through Special Schools. Exclusion criteria for this group included children or adolescents with a known clinical diagnosis of PWS, autistic spectrum disorder or any other confirmed genetic syndrome.

## Assessment Instruments

The Child Behaviour Checklist 6-18 (CBCL/6-18) has 118 items which are grouped into Internalising, Externalising and Total scales. The CBCL/6-18 also provides six DSM orientated scales. The CBCL/6-18 has been shown to have good satisfactory reliability and validity in general, clinical, and intellectual disability populations (Borthwick-Duffy, Lane, & Widaman, 1997; Achenbach & Rescoria, 2001; Dekker, Koot, van der Ende, & Verhulst, 2002; Koskentausta, Iivanainen, & Almqvist, 2004; de Ruiter, Dekker, Verhulst, & Koot, 2007). Parents reported their own psychological distress using the Brief Symptom Inventory (BSI). The BSI consists of 53 items covering nine symptom dimensions: Somatization, Obsession-Compulsion, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic anxiety, Paranoid ideation and Psychoticism; and three global indices of distress: Global Severity Index (GSI), Positive

## Table 1. Psychiatric Problems in PWS: Literature Review

| Authors | Sample size; instruments employed | Main findings | Limitations |
|---|---|---|---|
| (Whitman & Accardo, 1987) | 35 adolescents with PWS; Survey Diagnostic Instrument (SDI) which screens for the DSM-III criterion-based diagnostic categories of neurosis, and hyperactivity | The following diagnostic pattern was reported: neurosis, dysphoric, (1 probable); neurosis, compulsive, 3 (6 probable); neurosis, anxious, 4 (and 10 probable); somatization, 0; conduct disorder, violent 0; conduct disorder, antisocial, 0; hyperactivity, 1 (and 1 probable) | DSM-III criterion-based diagnostic categories were employed, SDI has no single standardized quantitative scoring system, no control group |
| (Curfs, Verhulst, & Fryns, 1991) | 27 individuals with PWS, CBCL | 87% had Total problem scores in the clinical range. No significant difference was found in the proportion of PWS patients scored in the clinical range on the Internalizing over the Externalizing syndrome | Small clinical sample, control group was not match for IQ |
| (Dykens, Hodapp, Walsh, & Nash, 1992) | 23 adults and adolescents with PWS, CBCL, Vineland Adaptive Behavior Scale | Externalising behaviours were significantly higher than internalising across all age groups and adolescent group had the highest externalising domain score | Small clinical sample recruited from a private service, no control group |
| (Dykens & Cassidy, 1995) | 25 children and 61 adults with PWS; The Reiss Scales for Children's Dual Diagnosis and The Reiss Screen for Maladaptive Behavior scales | 56% of children were distracted and irritable, 52 had communication problems; 56 adults/adolescents were socially inadequate, 74% impulsive | Sample recruited from one PWS Association meeting, no control group |
| (Dykens & Kasari, 1997) | 43 children with PWS, CBCL | 72% obtained clinically elevated Total Scale score in contrast to 23% and 39% of the Down Syndrome and mentally retarded samples. PWS scored significantly higher on externalizing behaviour problems than the Down Syndrome sample | Parents were notified of the study through syndrome-specific parent organizations, groups were not matched on weight, and IQ |
| (Beardsmore, Dorman, Cooper, & Webb, 1998) | 25 adults with PWS; Psychiatric Present State-Learning Disabilities, Adaptive Behaviour Scales | The PWS group was found to have higher rates of affective disorders (17.4%), in which psychotic symptoms were common, but similar rates of schizophrenia/delusional disorders (4.3%) compared with the control group. None was found to have generalized anxiety or phobic disorders | Small sample, control group not matched for age, IQ |
| (Clarke, 1998) | 95 adults with PWS; Psychopathology Assessment Schedule for Adults with Developmental Disability (PAS-ADD) checklist | 6.3% had a possible psychotic disorder in the month before the assessment was made | Some reported psychotic symptoms may not be truly indicative of psychotic disorder as a checklist and not a diagnostic tool was employed |
| (Dykens et al., 1999) | 23 individuals with PWS due to paternal deletion and 23 age- and gender-matched subjects with maternal uniparental disomy: CBCL | "deletion" group had significantly higher Internalizing, Externalizing, and Total Child Behaviour Checklist mean raw scores, than did the uniparental disomy group | Small clinical sample, in some cases old IQ test results used |
| (State, Dykens, Rosner, Martin, & King, 1999) | 8 individuals with PWS, aged 4 to 20; Yale-Brown Obsessive Compulsive Scale | PWS subjects had greater numbers of obsessive compulsive symptoms resulting in significant impairment | Very small clinical sample recruited from a tertiary centre |
| (Akefeldt & Gillberg, 1999) | 44 individuals with PWS, age 0.8 to 36.3; Modified Greenswag Interview of parents with SSBP-PQ, Rutter parent questionnaire and ASSQ. Older Subjects completed the Birleson Depression Inventory and Eating Attitudes Test | Individuals with PWS had more behavior problems than those in the comparison group. Younger PWS cases had fewer behavior problems than older PWS cases. One woman with PWS developed psychotic symptoms, including agitation, abnormal beliefs and violent aggression problems | A large proportion of the parents in the non-PWS group also had ID, possibly influencing reporting of behaviours |

*continued*

## Table 1. Psychiatric Problems in PWS: Literature Review (continued)

| Authors | Sample size; instruments employed | Main findings | Limitations |
|---|---|---|---|
| (Einfeld, Smith, Durvasula, Florio, & Tonge, 1999) | 46 individuals with PWS; Developmental Behaviour Checklist (DBC) | 63% had mood swings without a reason, 43% were anxious | 30% of the controls were in the mild learning disability range and ascertainment of this group may well be biased towards those with greater behaviour disturbance |
| (Boer et al., 2002) | 25 individuals with PWS; clinical assessment | 28% had severe affective disorder with psychotic features, with a mean age of onset of 26 | No standardised assessment, small clinical, sample no control group |
| (Verhoeven, Tuinier, & Curfs, 2003) | 23 adults with PWS referred for neuropsychiatric assessment; diagnosed according to ICD-10 | 18 diagnosed as cycloid psychosis, 5 with bipolar affective disorder | Subjects selected from those referred for specialist assessment, no standard instrument used in diagnosis, no comparison between ratters |
| (Vogels, Matthijs, Legius, Devriendt, & Fryns, 2003) | 59 adults with the PWS; clinical assessment | 15.7% had experienced a psychotic episode with an age of onset varying from 13 to 19 yrs | No standardised instruments, no control group |
| (Steinhausen, Eiholzer, Hauffa, & Malin, 2004) | 58 individuals with PWS, aged 3 to 29; DBC | Behavioural disturbances and psychiatric symptoms increase with increasing age (apart from food-related behaviours) | Subjects recruited from tertiary care centre/parental support groups, lack of formal IQ and genetic information in a sizeable proportion of the sample |
| (Wigren & Hansen, 2005) | 58 children with PWS; Childhood Routines Inventory and Conner's Parent Rating Scale | One-fourth showed clinical indices of ADHD, 3.4% - of anxiety | Cross-sectional data were collected using postal questionnaires and parents were informants; instruments not validated for ID population |
| (Kim, Yoo, Cho, Hong, & Kim, 2005) | 14 individuals with Prader-Willi syndrome, CBCL | 71.4% had social problems, 35% had attention problems | Small clinical sample, PWS diagnosis was made based on clinical assessment |
| (Descheemaeker, Govers, Vermeulen, & Fryns, 2006) | 59 adults with PWS, Pervasive Developmental Disorder Mentally Retardation Scale | 19% met the full diagnostic DSM-III-R criteria for PDD | Findings rely on informant-ratings of a screening questionnaire |
| (Hiraiwa, Maegaki, Okaa, & Ohnoa, 2007) | 165 individuals with PWS in Japan assessed by postal questionnaire to parents | Young adults with PWS had significantly more behavioural and psychiatric symptoms than those with non-PWS ID with psychotic symptoms in up to 27.6% over the previous five years | Questionnaire was not a standardised, validated instrument, no evidence of explanation to parents of terms such as 'hallucination', 'delusion' etc. Parents asked to comment on the prior five years, recall bias likely |
| (Soni et al., 2007) | 46 individuals with PWS, Psychiatric Assessment Schedule for Adults with Developmental Disability, Operational Criteria Checklist for psychotic and Affective illness | In deletion group (N=24): 41.7% Non-psychotic depressive illness, 37.5% Depressive psychosis, 20.8% Psychotic illness, in mUPD (n=22) 4.5% Non-psychotic depressive illness, 27.3% Depressive psychosis, 50% bipolar affective disorder, 18.2% psychotic illness | Initial screening was performed with invalidated screening questionnaire |
| (Reddy & Pfeiffer, 2007) | 73 children and adolescents with PWS; Devereux Scales of Mental Disorders | The PWS sample exhibited significantly more attention and acting out and anxiety problems than their peers with mental retardation-only | Sample was drawn from residential treatment facilities, only one standardized assessment procedure was employed to measure emotional and behavioural problems |

*continued*

| Table 1. Psychiatric Problems in PWS: Literature Review (continued) | | | |
|---|---|---|---|
| Authors | Sample size; instruments employed | Main findings | Limitations |
| (Zarcone, Peterson, Breidbord, Ferraioli, & Caruso-Anderson, 2007) | 73 individuals with PWS were assessed using the Yale-Brown Obsessive Compulsive Scale and the Compulsive Behavior Checklist | Individuals with the TI deletion had more compulsions regarding personal cleanliness and their compulsions, Individuals with the T II deletion were more likely to have compulsions related to specific academic areas | Although this study is limited because of the number of statistical comparisons and the small sample of individuals with the TI deletion (n=14) |
| (Dykens & Roof, 2008) | 88 individuals with PWS aged 5 to 51; CBCL | No compelling behavioral differences across PWS paternal deletion subtypes were found | Cross sectional nature, CBCL was used to assess mental health problems in adults |
| (Soni et al., 2008) | 46 individuals with genetically confirmed PWS; PAS-ADD, Family History and Life Events Questionnaires | The profile of psychiatric illness resembled an atypical affective disorder with or without psychotic symptoms | No control group |
| (Sinnema et al., 2011) | 98 adults with PWS; Developmental Behavior Checklist for Adults (DBC-A) | DBC-A total scores were higher in the consecutive age groups, with the most behavioral problems in the oldest age groups. Persons with mUPD had higher total scores on the DBC-A than persons with a deletion | No IQ measure, the study population is characterized by a predominance of older persons with PWS as the sample was "borrowed" from the study "Ageing in PWS" |

Symptom Distress Index (PDI), and Positive Symptom Total Index (PSI) (Derogatis, 1993). The presence of T-scores greater than 63 on two or more BSI subscales indicates possible psychopathology. A GSI T-score of 63 or greater also indicates possible psychopathology (Derogatis, 1993).

*Ethics*

The Irish Health Service Executive's Ethics Committee approved this study. Parents of the children had all signed informed consent forms prior to participation.

### Statistical Analysis

Descriptive statistics were used to characterize the children's and parents' demographic variables, and to evaluate the results of the BSI and the CBCL/6-18. Correlation analyses using Pearson's Correlation co-efficient were used to compare the results of CBCL/6-18 and BSI to determine the extent to which parents' distress was associated with the identification of externalizing and internalizing problems in PWS children. Analyses were performed with SPSS version 18.0.2.

## Results

### Psychopathology in Children with PWS

Both groups (PWS and controls) were comprised of 24 children. In both groups there were 11 (45%) girls and 13 (55%) boys. Mean age for PWS boys was nine years (SD=3.1 years) and for PWS girls 11.03 years (SD=3.4). In the control group mean age for boys was 12 years (SD=2.67 years) and for girls 12 years (SD=2.67 years).

The two groups did not differ significantly with regards to mean age, mean IQ scores, gender. Parents of PWS children were significantly older in comparison to control's parents (Table 2).

The total T mean score on the CBCL/6-18 was elevated within the clinical range in PWS and elevated within the borderline range for the control group. No significant differences were found between the two groups for externalizing behaviour problems. The score for internalizing problems score higher in the PWS than controls (T mean score (62.02 (SD=10.17) vs. 58.13 (SD=7.53) p<. 05) (Table 3)).

The CBCL/6-18 syndromes profile T-scores were elevated within the clinical range for the PWS group for the majority of syndromes. In the PWS group the thought problems item received the highest score (mean T=67.71 SD=9.71) and reached clinically significant range along with the: Withdrawn-depressed (mean T=67.71 SD=8.01); Somatic complaints (mean T=63.50 SD=8.41); Social problems (mean T=64.71 SD=8.95); and, Attention problems (mean T=65.92 SD=9.82) items. In the control group clinically significant ranges were reached in rule-breaking behaviour (mean T=63.21 SD=7.2) and attention problems, with attention problems receiving the highest score (mean T=64.83 SD=8.93). Borderline clinical ranges were reached on the aggressive problems item in the control group (mean T= 61.79 SD=7.84). In the PWS group the rest of the problems (which did not reached clinical range) were within borderline range (Table 3).

The comparison of the PWS group and control group along CBCL/6-18 syndromes profiles indicated that children with

**Table 2. Demographic characteristics of PWS and control samples**

|  | PWS group (N=24) Mean (SD) | Control group (N=24) Mean (SD) | Test | P |
|---|---|---|---|---|
| Age, years | 9.92 (3.6) | 11.75 (3) | t | >.05 |
| Gender, male:female | 13:11 | 13:11 | t |  |
| IQ | 64.03 (3.1) | 65.85 (2.9) |  | >.05 |
| Parents' age, years | 45.5 (6.2) | 51.0 (9) | t | <.05 |

**Table 3. CBCL syndrome profiles in PWS and control groups**

| CBCL/6-18 syndromes profile | PWS group Mean T score | PWS group SD | Control group Mean T score | Control group SD |
|---|---|---|---|---|
| Anxious/depressed | 62.79 | 8.01 | 59.54 | 5.59 |
| Withdrawn/depressed | 64.04 | 9.11 | 55.46* | 6.48 |
| Somatic complaints | 63.50 | 8.41 | 56.13* | 6.31 |
| Social problems | 64.71 | 8.95 | 58.79* | 9.41 |
| Thought problems | 67.71 | 9.71 | 58.04* | 7.17 |
| Attention problems | 65.92 | 9.82 | 64.83 | 8.93 |
| Rule breaking behaviour | 62.88 | 7.2 | 63.21 | 7.4 |
| Aggressive behaviour | 62.75 | 11.48 | 61.79 | 7.84 |
| Internalizing Problems | 62.02 | 10.17 | 58.13* | 7.53 |
| Externalizing problems | 62.25 | 9.66 | 62.46 | 7.66 |
| Total | 64.00 | 10.10 | 62.29 | 5.71 |

*P < 0.05

PWS had more severe somatic problems (mean T 63.50 SD=8.41 vs. 56.13 SD=6.31, p<.05), social problems (mean T 64.71 SD=8.95 vs. 58.79 SD=9.41, p<.05), thought problems (mean T 67.71 SD=9.71 vs. 58.04 SD=7.17, p<.05) and were more withdrawn/depressed (mean T 64.04 SD=9.11 vs. 55.46 SD=6.48, p<.05).

Several behaviours/CBCL items are commonly observed as part of the PWS phenotype (e.g. 'picks nose skin or other parts of the body', 'under active', 'secretive', 'keeps things to self", 'withdrawn', overeats', 'hoards', 'bites fingernails', 'acts too young for his/her age'). These items were analysed separately across the groups (Table 4).

Clinically significant difficulties were not reached for any of CBCL DSM-orientated subscales in either of the groups. Borderline difficulties were detected for the affective, somatic, and attention deficit-hyperactivity CBCL DSM-orientated subscales in the PWS group, with PWS children having significantly more somatic (mean T 63.05 SD=8.33 vs. 52.00 SD=6.48, P<.05) and affective (mean T 66.22 SD=8.51, vs. 60.08 SD=6.829 P<.05) problems than controls (Table 5).

### Parental Psychopathology
The analysis of BSI scales revealed that parents of PWS children in comparison to controls had more somatization, phobic anxiety, obsessive compulsion, and anxiety

**Table 4. Individual CBCL domains in PWS and controls**

| Domain | PWS group % (N) | Control group % (N) |
|---|---|---|
| Underactive | 83 (20) | 45 (11) |
| Secretive, keeps things to self | 79(19) | 33.3 (8) |
| Withdrawn | 75 (18) | 33.3 (8) |
| Picks nose skin or other parts of the body | 96 (23) | 8.3 (2) |
| Overeats | 96 (23) | 33.3( 8) |
| Hoards | 66.6 (16) | 45.8 (11) |
| Bites fingernails | 58 (14) | 50 (12) |
| Acts too young for his/ her age | 66.6 (16) | 62.5 (15) |

problems (Table 6). Neither group, however, reached clinically significant levels on the GSI scale.

Correlation analyses were used to determine the extent to which parents' distress was associated with the identification of externalising and internalising problems in children with PDW. Table 7 indicates that scores on the BSI indices significantly correlated with scores on the CBCL/6-18 (Table 7).

**Table 5. CBCL DSM orientated scales**

| DSM orientated scales | PWS | | Control group | |
|---|---|---|---|---|
| | Mean T score | SD | Mean T score | SD |
| Affective problems | 66.22 | 8.516 | 60.08* | 6.829 |
| Anxiety problems | 60.37 | 6.334 | 60.88 | 8.027 |
| Somatic problems | 63.05 | 8.334 | 52.00* | 6.487 |
| Attention deficit/hyperactivity problems | 63.53 | 7.259 | 63.13 | 8.582 |
| Oppositional defiant problems | 61.58 | 5.846 | 58.58 | 7.625 |
| Conduct problems | 62.50 | 7.372 | 63.17 | 6.829 |
| *P < 0.05 | | | | |

**Table 6. BSI Symptom dimension in PWS and control group parents**

| | PWS group | | Control group | |
|---|---|---|---|---|
| | Mean T score | SD | Mean T score | SD |
| Somatization | 60.15 | 5.66 | 55.81* | 6.54 |
| Depression | 57.00 | 6.89 | 57.32 | 5.43 |
| Phobic Anxiety | 63.02 | 4.67 | 55.21* | 5.33 |
| Obsessive-Compulsive | 68.96 | 5.66 | 59.96* | 6.02 |
| Anxiety | 64.08 | 3.55. | 54.15* | 5.03 |
| Interpersonal Sensitivity | 65.13 | 7.64 | 58.67 | 6.43 |
| Paranoid Ideation | 57.94 | 6.54 | 58.44 | 6.23 |
| Hostility | 59.56 | 6.32 | 58.08 | 4.65 |
| Psychoticism | 54.88 | 6.43 | 58.2 | 3.56 |
| GSI | 62.29 | 5.34 | 58.38 | 5.65 |
| *P < 0.05 | | | | |

**Table 7. Correlations between BSI scores and CBCL/6-18**

| | CBCL | |
|---|---|---|
| | Internalising | Externalizing |
| BSI GSI Pearson Correlation Sig. (2-tailed) | .623* | .702* |
| BSI PDI Pearson Correlation Sig. (2-tailed) | .429* | .412* |
| BSI PSI Pearson Correlation Sig. (2-tailed) | .611* | .509* |
| *Correlation is significant at the P < .01 level (two-tailed) | | |

## Discussion

The present study investigated psychiatric problems in children diagnosed with PWS, their parents' psychological problems, and compared them with an age-, gender- and IQ-matched control group and their parents. The main findings from this study can be summarized as follows. The Internalizing problems score was higher in children with PWS than controls. On CBCL/6-18 syndromes profiles the PWS group showed significantly more somatic, social, thought problems and were more withdrawn-depressed and

then control group. Borderline difficulties were reached on the affective, somatic and attention deficit/hyperactivity CBCL DSM orientated subscales in the PWS group, with PWS children having significantly more somatic and affective problems than controls. Parents of PWS children in comparison to controls had more somatization, phobic anxiety, obsessive compulsion, and anxiety problems.

While the internalizing problems score was higher in children with PWS than controls, the internalising problems score was smaller in the PWS subjects compared with externalising problems; this is in keeping with several previous studies (Dykens et al., 1992; Dykens & Kasari, 1997). One older study however, found no significant difference in the proportion of PWS patients scored in the clinical range on the Internalizing over the Externalizing syndrome (Curfs et al., 1991).

It has been well documented that children with learning difficulties show a greater risk for psychopathology compared to typically developing children and several studies have shown that, within a given mild intellectual disability population, between 24% and 54% of subjects present serious emotional, social and behavioural problems (Dekker et al., 2002; Capozzi et al., 2008). In our study, children and adolescents with PWS exhibited more comorbid psychological

problems than their peers matched for age, IQ, and gender. Indeed, our findings illustrate that children with PWS exhibit psychological difficulties that extend beyond the historical perception that the syndrome is marked only by maladaptive behaviours, obsessive-compulsive traits, and skin picking.

Our study has found that PWS subjects displayed very high levels of thought problems on CBCL/6-18. It has to been explained that CBCL "thought problems" domain includes items such as "seeing things", "hearing voices", "strange ideas". Several previous reports and studies have suggested an association between PWS and psychotic episodes and few studies reported that psychotic symptoms were present in almost a half of the sample (see Table 1). However in the present study (and in other studies which employed CBCL/6-18), high levels of "thought problems" on CBCL/6-18 reflect not only a potential link between psychotic problems and PWS, but also a very clear link between skin picking and PWS because the "thought problems" item also includes a question about skin picking (Table 3).

In the present study we reported high scores on the CBCL Withdrawn-depressed item in children with PWS. Kim et al. reported much lower scores on the withdrawn-depressed item (mean T-score 52.21 SD=10.28 vs. mean T-score 64.04 SD=9.11), yet these authors acknowledged a possibility that their results might have been influenced by factors associated with sociocultural characteristics i.e. Korean parents being less sensitive to their children's emotional states, such as depression, and the greater weight they give to externalizing problems (Kim et al., 2005). Studies carried out in Western Europe and North America have produced similar rates of affective problems in children with PWS to this study (Boer et al., 2002).

In the past, very little attention was paid to ADHD-type difficulties in children with PWS. A prior study investigating ADHD in PWS, found that a quarter showed clinical indices of ADHD (Wigren & Hansen, 2005). In our study attention deficit-hyperactivity CBCL DSM orientated subscale has reached borderlines scores in 21% of the children with PWS. Previously it has been reported that autism spectrum disorders (ASD) could be linked with maternally-derived duplications or triplications of chromosome 15q11-13, and therefore might occur more frequently in people with PWS due to uniparental disomy (UPD), than in other forms of chromosomal abnormality involving this region (Veltman et al., 2004). Our study did not employ ASD diagnostic instruments yet children with PWS exhibited more severe social problems in comparison with controls.

Distress and psychiatric problems in parents of children with PWS have received surprisingly very little attention in previous research. Few previous studies have investigated stress levels and profiles in parents of children with PWS, and none looked at their psychiatric difficulties. Hodapp reported that parents of children with PWS showed higher

levels of parent and family problems, and comparable levels of pessimism to parents of children with mixed aetiologies of retardation (Hodapp, Dykens, & Masino, 1997). This study, however, did not have clear inclusion criteria, and the control sampled was "borrowed" from other studies. Wulffaert et al. reported that parenting stress was high for 26% of PWS cases when measured with the Nijmegen Parenting Stress Index-Short (Wulffaert, Scholte, & Van Berckelaer-Onnes, 2010).

To our knowledge our study is the first study to investgate psychological difficulties in parents of PWS children. The present study found that parents of PWS children in comparison to controls had more somatization, phobic anxiety, obsessive compulsion, and anxiety problems and that these correlate with measures of psychopathology in PWS children.

Our study has several limitations and strengths. Firstly, the PWS sample was not large. Based on an estimated incidence of one in 22000 live births (Whittington et al., 2001), our nationwide sample nonetheless constitutes about 14% of the total Irish PWS population. Our sample consisted of subjects aged from 6 to 18, and the representation would be even higher within this age range. Accurate epidemiological data regarding the Irish PWS population within the age range of 6-18 is unfortunately not available at present. Secondly, in our study only one standardized instrument was employed to measure emotional and behavioural problems in children with PWS. A third limitation is that we did not match across the two groups on the degree of obesity.

Despite the limitations described above, this was the first study in Ireland to investigate psychiatric and behavioural characteristics of children with PWS, and our study extends the findings of other studies regarding the presence of specific psychiatric difficulties, which requires psychiatric attention, and in some case psychiatric interventions. Moreover this was the first study, which specifically investigated psychological difficulties in parents of children with PWS and compared them with parents of children with learning disabilities.

## Conclusions and Future Directions:

1. PWS represents a complex psychological disorder with multiple areas of disturbances.

2. Children with PWS had more somatic, social and thought problems, and were more withdrawn-depressed and then were those in the control group.

3. Parents of PWS children in comparison to those of controls had more somatization, phobic anxiety, obsessive compulsion, and anxiety problems.

4. Parents' distress was associated with the severity of psychological problems in children with PWS.

5. Epidemiological samples are required to further explore psychiatric problems in chidren with PWS

and their parents, and future studies should employ a multimodal assessment approach, which includes multiple measures and multiple informants across settings.

## Acknowledgements / Conflicts of Interest

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