Brief Report

Behavioural change in Prader–Willi syndrome during COVID-19 pandemic

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Abstract

Background Prader–Willi syndrome (PWS) is a rare genetic disorder that in many cases is associated with mental health disorders, in addition to characteristic symptoms such as hyperphagia. The current Sars-CoV-2 coronavirus pandemic has led to massive restrictions in health care and social life worldwide. People with PWS represent a particularly vulnerable population group to these restrictions, with unknown impact on their mental health.

Methods We conducted an online questionnaire to assess the impact of the restrictions associated with the COVID-19 pandemic on the mental health of people with PWS.

Results One hundred and eight caregivers completed the survey about individuals with PWS. Individuals with PWS > 6 years (n = 89) were included for evaluation with regard to psychopathological change. Respondents frequently reported an increase in psychopathological symptoms associated with PWS during the lockdown, with 51.7% reporting increased temper outbursts, 43.8% showing signs of sadness, 38.2% being anxious, 55.0% more irritable, and 39.3% showing more food seeking behaviour. Adjusted for the type of accommodation food seeking behaviour and irritability is increased to a significantly lesser extent in people with PWS accommodated in specialised care facilities compared with those living in their family home. No significant difference could be found between the sexes.

Conclusion The COVID-19 pandemic has had a significant effect on the mental health of individuals with PWS, evidenced by an increase in behaviours associated with PWS, including temper outbursts, food-seeking, and irritability, which again underlines their need for specialised care. Individuals living with their families were particularly vulnerable, indicating that they and their families are in special need of support.

Keywords COVID-19, intellectual disability, mental health, Prader–Willi syndrome

Introduction

Since December 2019, the novel coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been spreading pandemically across the globe. The resulting disease is known as COVID-19 and is characterised by a variety of symptoms, most of which include fever, cough and shortness of breath, but more specific symptoms such as loss of taste have also been described. The course of the disease...
appears to be variable with mild flu-like symptoms, sometimes unnoticed infections up to a severe course with fatal consequences (Esakandari et al. 2020). As part of German government’s measures to contain the Sars-CoV-2 pandemic, the operation of healthcare facilities was reduced to a minimum. Childcare facilities such as daycare centres and schools were closed, and far-reaching restrictions of social contacts were implemented with restrictions on visits to hospitals, nursing homes and institutions for people with disabilities.

Prader–Willi syndrome (PWS) is a rare genetically determined neurodevelopmental disorder with an estimated birth incidence between 1:10 000 and 1:30 000 births (Vogels et al. 2004; Lionti et al. 2015; Bar et al. 2017). PWS is caused by a lack of paternally expressed genes on chromosome 15q11.2-13, which can occur via three mechanisms. In most cases (70%), PWS is caused by a deletion of the 15q11-13 region on the paternal chromosome 15. In about 25% of cases, it is caused by a uniparental disomy, and in the remaining 5% of cases, deficits in the imprinting centre lead to PWS (Angulo et al. 2015). Infants with PWS typically present with muscle hypotonia, a failure to thrive and feeding difficulties, followed by the later development of severe hyperphagia with excessive eating leading to morbid obesity if food intake is not controlled. Individuals with PWS are in need of intensive monitoring, especially with regard to food intake. A low-calorie diet and regular physical activity are recommended. In nearly all cases, a mild to moderate intellectual disability and an overall developmental delay in language and motor skills are present. Dysregulated body temperature, high pain tolerance and sleep disturbances are also typical symptoms of PWS, most of which can be attributed to hypothalamic dysfunction (Muscoliuri et al. 2019).

Distinct behavioural traits are common, among them stubbornness, compulsions, temper outbursts and skin-picking (Whittington and Holland 2018). Repetitive questioning and difficulties in dealing with change are also characteristic and were described by caregivers as resulting in frequent misconduct (Feighan et al. 2020). Furthermore, individuals with PWS seem to have a higher susceptibility to psychiatric disorders, mainly obsessive compulsive behaviours, depression, autism spectrum disorders and psychosis (Soni et al. 2007; Soni et al. 2008). With regard to the most common behavioural disorders, individuals with PWS benefit from structured, recurring daily routines with increased support from family or other caregivers and certain medical treatment options may be beneficial (Dyken and Shah 2003; Deest et al. 2020).

Above all, a structured environment seems essential for the well-being of people with PWS. This stable environment is likely to be considerably disturbed by the effects of national responses to the COVID-19 pandemic. Recent studies showed a loss of educational or healthcare services and social-engagement opportunities in most families of people with intellectual or developmental disorders during the COVID-19 pandemic (Jeste et al. 2020; Neece et al. 2020).

In this study, we investigate the effect of the current COVID-19 pandemic and its associated restrictions on daily life on the mental health of people with PWS in Germany, using an online questionnaire.

Methods

Completion and demographics

A total of 141 informants participated in the survey, of which 108 gave complete responses. Only complete responses were statistically processed and included in our study. Of the caregivers completing the questionnaire, 85 were female (78.7%) and 23 male (21.3%) with an average age of 50.69 years (min. 24 years and max 79 years) The vast majority of respondents (n = 106, 98.1%) stated to be parents of individuals with PWS (Table 1).

As psychopathological changes may be difficult to observe in very young participants, we had to limit our analysis to a specific age group. Preliminary work on PWS has shown that psychopathological abnormalities become apparent already in infancy (Dimitropoulos et al. 2001). Therefore, we assume that these can be safely assessed from the age of 6 years or older. Hence, only children with PWS > 6 years (n = 89) were included for evaluation with regard to psychopathological change.

Of these 89 individuals 43 (48.3%) were female and 46 (51.7%) male. Age of people with PWS ranged from 6 to 56 years, with a mean age of 21.3 years. Body weight ranged from 16.0 to 130.0 kg with a mean of 65.1 kg.

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To evaluate the results in regard of the type of accommodation, we split up the people with PWS into two groups, namely, those living with their families and those living in specialist care facilities. As the youngest individual with PWS accommodated in a specialist care facility was 14 years old, we limited this analysis to participants being 14 years or older. Of those 53 people with PWS, 28 (52.8%) were living with their families without any professional support, 25 (47.2%) in specialist care facilities. There is an age difference of 10 years in terms of mean age between the two groups (20.8 years in those living with family to 30.8 years in those accommodated) (Table 1 for demographic characteristics).

**Table 1** Demographics of participants

| Demographics | Informants (n = 108) | PWS (>6-year included for evaluation) (n = 89) | PWS living in family (n = 28) | PWS accommodated (n = 25) |
|--------------|----------------------|---------------------------------|----------------------------|---------------------------------|
| Sex          | 23 male (21.3%)      | 46 male (51.7%)                | 14 male (50%)             | 14 male (56%)                   |
|              | 85 female (78.7%)    | 43 female (48.3%)              | 14 female (50%)           | 11 female (44%)                 |
| Age          | 24–79 years (mean 50.7 years) | 6–56 years (mean 21.3 years) | 14–39 years (mean 20.8 years) | 14–54 years (mean 30.8 years) |

PWS, Prader–Willi syndrome.

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**Ethical considerations**

This study was approved by the local Ethics Committee of Hannover Medical School and adhered to the Declaration of Helsinki. All informants in this study were informed and gave their written consent for participation in this study and publication of the results.

Data were obtained using a web-based questionnaire for self-completion. The questionnaire was not addressed to the people with PWS themselves, but to their caregivers. The online questionnaire was administered using the survey administration tool SoSci Survey (Leiner 2019) and made available to participants at www.soscisurvey.de. The link to the survey was sent to potential participants via the mailing list of the Prader–Willi Syndrome Association Germany e.V. Therefore, the survey was limited to participants from Germany.

Responses submitted between 3 August 2020 and 25 August 2020 were included in the evaluation.

**Questionnaire**

In addition to collecting sociodemographic data (age, sex, body mass index and type of accommodation) and data on affectedness by COVID-19 (positive test results, restrictions in care and daytime activity), the caregivers were asked to report observed psychopathological changes in the individuals with PWS under their care during the Sars-CoV-2 pandemic. The respondents were asked to indicate the changes on a five-level Likert scale (Likert 1932). They rated statements such as ‘The PWS person showed temper outbursts’ from ‘Strong increase’ to ‘Strong decrease’. PWS-typical psychopathological abnormalities such as irritability, social behaviour, eating behaviour, sleep disturbance, affect, compulsive behaviour and cognitive functioning were assessed (items of the questionnaire can be found in Data S1).

**Analysis**

Statistical analysis was conducted in R (R Core Team 2019) and Statistical Package for Social Sciences (SPSS, IBM).

A χ² test of independence was performed to examine differences in psychopathological alteration with respect to sex and type of accommodation. Significance level was set at 5%. Differences of >10% between groups were categorised as considerable. ‘Strong increase’ and ‘increase’ on the Likert scale were cumulatively combined as an overall increase.
‘Strong decrease’ and ‘decrease’ were cumulatively combined as overall decrease. Free-choice-answers were categorised depending on their content and then counted. A logistic regression analysis was performed to ascertain the effect of age and type of accommodation on psychopathological changes.

Results

Implications of COVID-19 in Prader–Willi syndrome

Of the 108 individuals, 23 (21.3%) were tested for the Sars-CoV-2 corona virus, resulting in positive tests for Sars-CoV-2 in three cases (2.8%). In addition, seven (6.5%) positive tests in the immediate vicinity were reported. Family, partner, roommates and caregivers were specified as immediate vicinity in the corresponding question. The proximity to these other people is considered as potential exposure to Sars-CoV-2.

Restrictions in the provision of care (Yes 67.3%, n = 72) and employment/daytime activity (including childcare, school and work) (Yes 82.4%, n = 89) in the context of the COVID-19 pandemic were reported frequently. Asked to explain this in more detail in free text, most interviewees report that therapy measures (e.g. physiotherapy or occupational therapy; n = 14), sports activities (n = 9), leisure activities, such as excursions (n = 12) and doctor’s appointments (n = 9), had been cancelled.

The majority of respondents stated that they have sufficient resources (e.g. masks, disinfectants) to implement protective measures (Strongly agree 43.9%, n = 47, Agree 15.9%, n = 17) and that the individuals with PWS were able to implement the governmental measures (Strongly agree 44.4%, n = 48, Agree 33.3%, n = 36).

Behavioural alterations in people with Prader–Willi syndrome

Because we assume that psychopathological changes in PWS already become apparent in childhood, the age group > 6 years was considered for the evaluation of psychopathological changes in the context of the Sars-CoV-2 pandemic.

Overall, the respondents frequently described an increase in psychopathological symptoms in people with PWS > 6 years. Specifically, 51.7% of those surveyed reported an increase in temper outbursts (decrease 4.5% and no change 43.8%), 46.1% an increase in conflicts with other people (decrease 5.6% and no change 48.3%), and about 55.0% an increase in irritability (decrease 1.1% and no change 43.8%).

Of those PWS individuals, 43.8% showed a reported increase in depressed mood (decrease 0.0% and no change 56.2%). In 38.2% of cases, the informants reported an increase in anxiety (decrease 0.0% and no change 66.3%), with 33.7% of those surveyed reporting increased social withdrawal (decrease 0.0% and no change 66.3%).

Increased daytime sleepiness (increase 40.4%; decrease 1.1%; no change: 58.4%) and an increased desire to eat were described (increase 39.3%, decrease 0.0% and no change 60.7%).

With regard to obsessive-compulsive behaviour, an increase was described in 33.0% (decrease 0.0% and no change 67.0%), with respect to skin picking about 50.6% describing an increase (decrease 0.0% and no change 49.4%).

When asked about psychotic experiences (increase 26.4%, decrease 0.0% and no change 73.6%) and in particular suicidal thoughts (increase 5.6%, decrease 1.1% and no change 93.3%), the majority of respondents did not report any change in those with PWS.

In 85.4% of cases, the person with PWS was reported to be concerned about the current pandemic situation and its consequences, and in 58.0% to be concerned about their own health (Fig. 1)

Adjusted for type of accommodation, the data show a considerably higher percentage increase in anxiety among those accommodated in a specialist care facility (increase specialist care facility 56.0% and family 42.9%). In contrast, those living in specialist accommodation were reported as showing a considerably lower percentage increase in temper outbursts (increase specialist care facility 36.0% and family 57.1%), conflicts with other people (increase specialist care facility 40.0 and family 60.7%), concentration problems (increase specialist care facility 28.0% and family 39.3%), sleep problems (increase specialist care facility 12.5% and family 35.7%), compulsive behaviour (increase specialist care facility 24.0% and family 42.9%) and skin-picking (increase specialist care facility 32.0% and family 57.1%) compared with those living with their families. However, a significant difference

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between the types of accommodation could only found in the $\chi^2$ test for irritability (increase specialist care facility 32.0% and family 78.6%; $X^2(1, N = 53) = 11.662, P < 0.001$) and food seeking behaviour (increase specialist care facility 24.0% and family 57.1%; $X^2(1, N = 53) = 5.975, P = 0.016$) with a significant lower increase in those in the specialist accommodation. A logistic regression was performed to ascertain the effects of age and type of accommodation on the likelihood of psychopathological changes. Of the predictors, only type of accommodation but not age was significant for

**FIGURE 1.** Alteration in the psychopathology of 89 PWS individuals (age > 6 years) under the COVID-19 pandemic.

**FIGURE 2.** Comparison of the psychopathological changes under COVID-19 between the accommodation types. We compared those living with their families ($n = 28$) versus those living in specialist care facilities ($n = 25$). As the youngest person living in a specialist care facility, only individuals with an age of 14 or older have been included.

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irritability ($B = -1.392$, SE = 0.704, Wald = 3.911, df = 1, $P = 0.048$, odds ratio = 0.249, lower confidence interval = 0.063, upper confidence interval = 0.988). For the remaining items, no significance could be found (results of logistic regression analysis are shown in Data S2).

The percentage increases in daytime sleepiness, sadness, psychosis and suicidality were only slightly different between the groups (<10%) (Fig. 2).

Adjusted for sex, no significant differences between female and male could be found (data not shown).

Discussion

In this study, we evaluated the effect of the current COVID-19 pandemic on the mental health of people with PWS.

Previous studies on the impact of quarantine measures on mental health showed predominantly negative effects, such as confusion, anger and post-traumatic stress symptoms, in the general population (Cava et al. 2005; Wu et al. 2009; Sprang and Silman 2013). Particular stressors include fear of infection, frustration and boredom as well as insufficient information and care (Bai et al. 2004; DiGiovanni et al. 2004; Reynolds et al. 2008). Our results show that a vast majority of the caregivers reported people with PWS to be concerned about the pandemic and about half of them to be concerned about their own health.

People with PWS have certain behavioural traits such as stubbornness, temper tantrums, compulsions and skin-picking. They have difficulties in dealing with change and stress, and anxiety is common among them (Whittington and Holland 2018). The caregivers in our study frequently reported worsening of those symptoms during the lockdown with a marked increase in temper outbursts, sadness and anxiousness as well as an increase in irritability and compulsions.

Early longitudinal studies on the effects of COVID-19 on mental health in the general population show divergent findings between increasing mental health problems and no detectable effects (O’Connor et al. 2020; Wang et al. 2020a). In this respect, we consider the effects we observed to be substantial.

However, COVID-19 pandemic led to an increase in PWS-characteristic behaviours like compulsions and temper outbursts. Other characteristics of PWS, like seeking for food and skin-picking also deteriorated during this time period.

Interestingly, the increase in irritability and food-seeking behaviour was significantly lower among those accommodated in specialist care facilities. Likewise in general (with the exception of anxiety), the increase in various psychopathological traits was shown to be considerably lower among those living in specialist accommodation. Our data may suggest that PWS living at home with their families are more vulnerable to the effects of the Sars-Cov-2 pandemic than those living in specialist facilities. The structured environment in these facilities may have helped people with PWS better overcome the effects of the pandemic. Families providing care to their child with PWS may benefit from additional professional support during such difficult times. It must be taken into account that the difference of the mean age between the groups could have influenced the difference in psychopathology. However, we performed a logistic regression analysis that did not show a significant effect of age on psychopathological changes. Furthermore, we did not assess data like level of intellectual disability or psychiatric comorbidities. These factors could also contribute to the differences between those two groups in our study.

The trade-off between restrictive measures, with their impact on mental health, and the potential risk of viral infection remains difficult. As the respondents particularly reported limited therapy and daytime activity in times of restricted face-to-face contact, the use of telemedicine or remote education could be promising options, although availability and feasibility remain challenging (Duis et al. 2019; Jeste et al. 2020).

On a positive note, an overwhelming majority of respondents reported that the PWS individuals could implement the measures recommended by the state, such as wearing mouth and nose protection or following social distancing rules. We interpret this as a positive detail to report, after a previous study showed that adherence to general hygiene measures is associated with less depression and lower stress levels (Wang et al. 2020b).

There are certain limitations to this study. Our approach aimed at reaching as large a cohort as possible in a short period of time. The use of an online
questionnaire appeared to be the most appropriate means of achieving this, but it also required reducing the demands on the respondents to the essentials. Individual psychopathologies were assessed by informants using only a five-level Likert scales rather that by using established psychometric test procedures for the detection of depression, anxiety or obsessive–compulsive disorders that would have enabled a more differentiated evaluation. Of course, retrospective surveys also tend to suffer from recall bias. It should also be considered that parents, whose children live in specialist facilities, probably not have daily contact, so their assessment of psychopathology may be less accurate. This assumption could also contribute to the differences in psychopathology between the types of accommodation. Our study, as the first of its kind, should be seen as pilot study in this respect. Subsequent studies could try to replicate our results using standardised psychometric testing. The problem however is in the detection of change over time in the absence of baseline data.

The procedure was also influenced by the situation of the COVID-19 pandemic itself. Face-to-face contact with individuals with PWS and their caregivers, which would have enabled a more differentiated and objective assessment using psychometric test procedures, could not be carried out under the government measures and also appeared irresponsible from an ethical point of view. Further limitations are that the study population is restricted to Germany and that the cohort size of 89 is small. However, PWS is a rare genetic syndrome a study population of 89 is comparable with those published in previous studies.

In summary, we can show that the COVID-19 pandemic has had a major effect on the mental health of individuals with PWS. An increase in psychological stress was reported by informants in people with PWS during the pandemic, whereby the challenging behaviours characteristically associated with PWS increased, which again underlines their need for specialist support.

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**Conflict of interest**

All authors declare that they do not have a conflict of interest.

**Ethical considerations**

This study was approved by the local Ethics Committee of Hannover Medical School and adhered to the Declaration of Helsinki. All participants in this study were informed and gave their written consent for participation in this study and publication of the results.

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**Data Availability Statement**

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Supporting Information

Additional Supporting Information may be found online in the supporting information tab for this article.

Data S1. Questionnaire

Data S2. Results of logistic regression analysis