

## Detecting Psychiatric Profile in Genetic Syndromes: A Comparison of Down Syndrome and Williams Syndrome

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### Abstract

The occurrence and co-occurrence of psychiatric disorders have been more frequently reported in people with Intellectual Disability (ID) than in the general population. The present study was aimed at verifying whether the psychiatric profile of individuals with ID is just a consequence of ID or derives from a specific genotype. The psychiatric profile of 112 individuals with Down syndrome (DS) and 85 with Williams syndrome (WS) was examined. The interactions between psychiatric symptom clusters and the effect of age were also investigated.

Participants with WS had higher rates of psychiatric disorders, and, specifically, of Anxiety disorders and Psychosis than DS. However, the psychiatric profile changed by age, since Anxiety disorder was higher in individuals with WS compared to DS in young age, while Psychosis in old age. A relation between the occurrence of disorders, as Anxiety disorder and Mood Disorder, was found only in participants with WS. Moreover, distinct Anxiety and Behavior Disorder subtypes emerged between groups.

Results indicate that the genetic etiology of ID differently affects the psychiatric characteristics of the groups and suggest the importance of a targeted psychiatric care for individuals with WS and DS.

**Keywords:** Psychopathology; Intellectual disability; Comorbidity; Down and Williams syndromes

### Introduction

Psychiatric disorders in early childhood and delinquency in adolescence have been associated with low IQ [1,2] and more frequently reported in people with Intellectual Disability (ID) than in the general population [3-9]. However this greater vulnerability in people with ID has received little attention in research and it is still to clarify whether the psychiatric phenotype varies despite a common diagnosis of ID [10-12]. Examining psychopathology in individuals with known genetic diagnosis may clarify this heterogeneity, leading to an increase understanding of gene-behavior pathways. Thus, for example, the comparison of individuals with Down syndrome (DS) and Williams syndrome (WS) offers the opportunity to verify if the psychiatric features are just the effect of ID or a consequence of the genotype.

The rate of psychiatric disorders in these populations ranges from 30% to 50% [8]. Previous studies conducted in these two genetic syndromes independently documented variable percentage of psychiatric disorders, anxiety and behavior problems [1,9,13-20].

Individuals with WS usually display high sociability, excessive empathy (which may be inappropriate), anxiety, preoccupations and fears, impulsivity, inattention, sadness and depression, generalized anxiety disorder, phobias, and hyperactivity disorder - ADHD - [9,20,21]. Individuals with DS suffer from externalizing disorders and social problems as well as anxiety and obsessive-compulsive disorder, but rarely display depression [22-26]. Remarkable differences in patients' characteristic (age, IQ, social and cultural background) as well in measures adopted prevent comparisons of the results derived from different studies on the psychiatric phenotype of individuals with WS and with DS. Only one study has directly contrasted the psychiatric profile of children with DS and WS, documenting greater attentional deficits in children with WS than with DS, and greater attentional problems in both groups than in controls [27]. However, the study

focusing only on selected aspects of the psychopathological profile (i.e., ADHD) and used only teacher reports to collect the symptoms, without a direct psychiatric examination of the patients.

Even if much more frequent than in typically developing populations, also the co-occurrence of psychiatric disorders is an overlooked issue in people with ID [28]. The interaction between symptom clusters particularly affects adaptive functioning and it results in greater impairments and limitations in daily living [29]. To our knowledge only one study investigated the co-occurrence of different forms of psychopathology in persons with ID with unknown etiology, documenting a positive relation between mood, mania, and anxiety [8].

The present study was aimed at better understanding gene-behavior relations, verifying whether the psychiatric profile of individuals with known genetic syndromes is independent from genetic etiology. At this aim, individuals with WS and DS matched for chronological and mental age were compared on the prevalence of psychiatric disorders. The interactions between psychiatric symptom clusters and differences on the psychiatric profile based on ages were also investigated: two subgroups were distinguished by age (children/adolescents and adults) and the presence of psychiatric comorbidity was compared. The two

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contrasting hypothesis were considered: if psychiatric profile was independent from genetic etiology, participants with DS and WS will present comparable psychiatric comorbidity as an effect of the ID; on the contrary, if individuals with DS and WS will show distinct prevalence and distribution of psychiatric comorbidity, the specific contribution of the genotype will be supported.

## Materials and Method

### Participants

One hundred and twelve children, adolescents and adults with DS (mean age = 18.7, range=6-46; mean IQ = 49.0, SD=15.3; M/F=61/51) were selected for the study and were compared with eighty-five children, adolescents and adults with WS (mean age 18.0, range=6-39; mean IQ 51.2, SD=12.8; M/F = 43/42), comparable for sex distribution ( $\chi^2$  (1) =0.29; P=0.59), age (t=0.52; P=0.60) and IQ (t=1; P=0.32).

Participants were recruited at the Bambino Gesù Children's Hospital in Rome, at the Eugenio Medea Institute in Bosisio Parini (Lecco), at the Clinic of Physical Medicine and Rehabilitation in Marzana (Verona), and with the help of the Williams Syndrome Italian Association, Williams Syndrome Family Association (Marche Italian Region) and the Down Syndrome Family Association (Nardò, Lecce).

The individuals with WS exhibited a diagnosis established by FISH analysis and those with DS a diagnosis of free trisomy 21 determined by karyotyping. Exclusion criteria were the presence of neurosensory deficits, such as hypoacusia or serious visual impairment, the presence of epilepsy and the use of psychiatric medication both during the evaluation time and the clinical history.

### Every participant lived with their own families

Individuals with WS and DS were also split into two subgroups based on their chronological age (lower or equal/higher than 18 years) to verify potentially age effect on the psychiatric occurrence (see Table 1 for numerosity, sex, age and IQ). Observations were carried out after informed consent had been obtained from participants and their families. For evaluation purposes, participants were individually examined on two separate occasions over a period of about a week.

To overcome the limitation of some previous studies on ID, deriving psychiatric diagnosis only from questionnaires, the diagnosis was made by the psychiatric examination of an expert clinician interviewing patients and patients' caregivers [1,9,19,20,30]. The choice to interview patients with ID was based on studies indicating that adults with ID are reliable reporters of their psychological and emotional states [9,31].

### Instruments

The examination of the general intelligence was obtained by the Leiter International Performance Scale-Revised [32]. Short IQ measure was considered. For the adults whose ages extended beyond the norm

Group No.	Sex Male/Female	Age M (Range)	IQ M (SD)
Young WS 44	23/21	11.6 (6-17.1)	54.2 (14.6)
Young DS 69	32/37	11.7 (6-17.1)	52.4 (16.7)
	$\chi^2=0.37$ ; p=0.54	p=0.99	p=0.51
Old WS 41	20/21	24.9 (18-39)	47.6 (9.1)
Old DS 43	29/14	29.9 (18-46)	40.5 (5.7)
	$\chi^2=3.01$ ; p=0.08	p<0.001	p=0.35

WS, Williams's Syndrome; DS, Down Syndrome; Young, Children and Adolescents; Old, Adults

**Table 1:** Demographic data of the participants.

of the scale, IQ score was obtained by dividing mental age (derived from the scale) by chronological age and multiplying by 100.

The semi-structured psychiatric Diagnostic Interview Kiddie-Sads - Present and Lifetime Version (K-SADS-PL) - was addressed to the caregivers as well as to the patients in order to support the clinical diagnosis more effectively [33]. The K-SADS-PL is designed to assess psychopathology according to the DSM-IV criteria, namely includes specific questions relating to symptoms required to meet those criteria [34]. The primary diagnoses assessed with the K-SADS-PL include: Major Depression, Dysthymia, Mania, Hypomania, Cyclothymia, Bipolar Disorders, Schizoaffective Disorders, Schizophrenia, Schizophreniform Disorder, Brief Reactive Psychosis, Panic Disorder, Agoraphobia, Separation Anxiety Disorder, Avoidant Disorder of Childhood and Adolescence, Simple Phobia, Social Phobia, Overanxious Disorder, Generalized Anxiety, Obsessive Compulsive Disorder, ADHD, Conduct Disorder, Oppositional Defiant Disorder, Alcohol Abuse, Substance Abuse, Post-Traumatic Stress Disorder. Other disorders addressed by K-SADS-PL, such as Eating Disorders, Tic Disorders and Adjustment Disorders, were not considered in our research. We excluded participants with diagnosis of pervasive developmental disorder since the prevalence of this disorder, well documented in people with ID (e.g., in WS), may hide other psychiatric disorders [35].

Accordingly with the K-SADS-PL, psychiatric disorders were then grouped into four clusters: Mood Disorder (Major Depression, Dysthymia, Mania, Hypomania, Cyclothymia, Bipolar Disorders); Psychosis (Schizoaffective Disorders, Schizophrenia, Schizophreniform Disorder, Brief Reactive Psychosis); Anxiety (Panic Disorder, Agoraphobia, Separation Anxiety Disorder, Avoidant Disorder of Childhood and Adolescence, Simple Phobia, Social Phobia, Overanxious Disorder, Generalized Anxiety Disorder, Obsessive Compulsive Disorder, Post-Traumatic Stress); Behavior Disorder (Oppositional Defiant Disorder, ADHD, Conduct Disorder, Alcohol Abuse, Substance Abuse).

### Statistics and significance level

One-way ANOVAs and t-tests have been applied on parametric measures (IQ and age), while Chi-square tests, Fisher Exact Test, Phi 4-point correlation test, Odds ratio index and Cochran Q test were performed on nonparametric data (gender and the prevalence of psychiatric disorders). Post-hoc analyses were conducted by means of Tukey HSD test and McNemar test. The Statistical Program for Windows, Version 8.1 (StatSoft, Inc., Tulsa, OK, USA) and the SPSS statistical software (SPSS version 21.0, for windows, SPSS Inc., Chicago, IL) were used. The level of significance was set at p=0.05.

### Results

A higher prevalence rate of psychiatric disorders was found in individuals with WS (47.1%) compared to individuals with DS (32.1%) ( $\chi^2$ (1) =4.54, P=0.03).

By considering the four psychiatric clusters (Table 2), a higher prevalence rate of Anxiety ( $\chi^2$ (1) 5.81 P=0.01) and Psychosis ( $\chi^2$ (1) =7.53, P after Yates' correction=0.006) was found in individuals with WS than in individuals with DS. However, groups did not differ in the prevalence rate of Mood Disorder and Behavior Disorder.

Although individuals with WS show higher rate of Anxiety than DS, the prevalence of Anxiety subtypes did not differ between groups ( $\chi^2$ (5) =3.8, P=0.58, P after Yates's correction 0.97). In WS, 16.5% of participants

	Psychopathology Prevalence Rate	Anxiety	Mood Disorder	Behavior Disorder	Psychosis
WS No. (%)	40 (47.1)	24 (28.2)	9 (10.6)	13 (15.3)	9 (10.6)
DS No. (%)	36 (32.1)	16 (14.3)	9 (8.0)	15 (13.4)	1 (0.9)
$\chi^2$	4.5*	5.8**	0.4	0.1	7.5**
Young WS No. (%)	22 (50.0)	14 (31.8)	3 (6.8)	9 (20.5)	2 (4.5)
Young DS No. (%)	21 (30.4)	9 (13.0)	3 (4.4)	13 (18.8)	-
$\chi^2$	4.4*	5.8*	0.1	0.1	1.1
Old WS No. (%)	18 (43.9)	10 (24.4)	6 (14.6)	4 (9.8)	7 (17.1)
Old DS No. (%)	15 (34.9)	7 (16.3)	6 (14.0)	2 (4.7)	1 (2.3)
$\chi^2$	0.72	0.67	0.01	0.23	3.72*

WS, Williams Syndrome; DS, Down Syndrome; Young, Children and Adolescents; Old, Adults; \* $P < 0.05$ ; \*\* $P \leq 0.01$

**Table 2:** Distribution of psychiatric disorders.

received a diagnosis of Simple Phobia, 11.8% of Generalized Anxiety Disorder, 4.7% of Obsessive Compulsive Disorder, 2.4% of Social Phobia, 1.2% of Separation Anxiety Disorder and 0% of Panic Disorder. In DS, 7.1% of participants received a diagnosis of Simple Phobia, 4.5% of Generalized Anxiety Disorder, 1.8% of Obsessive Compulsive Disorder, 1.8% of Separation Anxiety Disorder, 1.8% of Panic Disorder and .9% of Social Phobia. However, the distribution of Anxiety subtypes significantly differed within each group (respectively, WS:  $Q(5) = 28.16$ ;  $P < 0.0001$ ; DS:  $Q(5) = 11.52$ ;  $P = 0.04$ ). In particular, the McNemar test indicated that in WS the rate of Simple Phobia was higher than that of Separation Anxiety Disorder ( $P = 0.001$ ), Panic Disorder ( $P < 0.001$ ) and Social Phobia ( $P < 0.013$ ); the rate of Generalized Anxiety Disorder was higher than that of Social Phobia ( $P = 0.021$ ), Separation Anxiety Disorder ( $P = 0.004$ ) and Panic Disorder ( $P = 0.002$ ). In DS, only the rate of Simple Phobia was significantly higher than that of Social Phobia ( $P < 0.016$ ).

Although groups did not differ in the Behavior Disorder rate, results revealed a difference between individuals with DS and WS in the prevalence rate of Behavior Disorder subtypes as ADHD and Oppositional Defiant Disorder ( $\chi^2(1) = 20.1$ ,  $P < 0.0001$ ,  $P$  after Yates's correction 0.0001). Indeed, the rate of participants with WS diagnosed with ADHD (15.3%) was higher than DS (1.8%) (Fisher Exact test  $P = 0.001$ ) and the rate of participants with DS diagnosed with Oppositional Defiant Disorder (10.7%) was higher (Fisher Exact test  $P = 0.001$ ) than WS (0%).

It was not analyzed Psychosis and Mood Disorders subtypes since only Schizophrenia and Major Depression subtypes were documented in both syndromic groups.

Concerning the comorbidity or two or more psychiatric disorders, groups did not differ in the prevalence rate of psychiatric comorbidities ( $\chi^2(1) = 0.5$ ,  $P = 0.3$ ,  $P$  after Yates's correction = 0.45). Specifically, 31.8% of individuals with WS showed one psychiatric disorder and 15.3% showed two or more psychiatric disorders; similarly, 25% of individuals with DS showed one psychiatric disorder and 7.1% showed two or more psychiatric disorders. However, to detect possible correlations between the co-occurrence of two or more psychiatric disorders, a Phi 4-point correlation test was conducted between the disorders clusters. In the group with WS, the occurrence of an Anxiety disorder positively correlated with the occurrence of a Mood Disorder (Phi 4-point correlation = 0.21;  $P = 0.049$ ) with a moderate to high probability of the co-presence of the two disorders (Odds ratio = 5.48;  $Z = 2.3$ ;  $P = 0.02$ ). No significant correlation was found in the group with DS.

The distribution of psychiatric disorders was also analyzed considering possible age effects. At this aim, participants with WS

and DS were split in two subgroups (lower or equal/higher than 18 years): children and adolescents (or young subgroup) and adults (or old subgroup). When the WS and DS age subgroups were directly compared (Table 2), results revealed a significantly higher prevalence rate of psychopathology in the young participants with WS compared to participants with DS ( $P = 0.04$ ). Specifically, Anxiety Disorder ( $\chi^2(1) = 0.24$ ;  $P = 0.02$ ) was found higher in the young subgroup with WS than in the young subgroup with DS. Conversely, no difference in the general prevalence of psychiatric disorders emerged comparing the two subgroups of adults ( $\chi^2(1) = 0.24$ ;  $P = 0.39$ ), but the prevalence of Psychosis was higher in participants with WS than in participants with DS ( $P$  after Yates' correction = 0.05).

## Discussion

Results of the present study documented different prevalence and distribution of psychiatric disorders in two genetic syndromes associated with ID. Our results extend the 'syndrome-specific' view to the psychopathology, suggesting development may be asynchronous among different etiological groups with ID because of different characteristics of their brain development. In the last twenty years a mass of findings supports the existence of specific cognitive profile in genetic syndromes as a consequence of neurobiological factors caused by the genetic abnormalities and expressed in abnormal brain maturation [36-45]. Similar to cognitive findings, our results indicate that psychiatric comorbidity is related to the specific genetic alteration pertaining to the syndrome and not to ID per se.

Our results found higher rate of psychiatric disorders in participants with WS than in participants with DS. This high prevalence (more than 47%) in people with WS is particularly impressive, especially if we consider data on the general population that is around 8.2% [46]. Our results are consistent with those found by Dodd and Porter, reporting a prevalence of around 58% of psychiatric disorder in individuals with WS [47]. However, Stinton and colleagues found that only 29% of 92 adults with WS had a diagnosable or currently diagnosed psychiatric disorder [21]. It is possible that this difference of results is due to the exclusion of some disorders in the study by Stinton and colleagues [9]. Specifically, the authors adopted the Psychiatric Assessment Schedule for Adults with Developmental Disabilities, a semi-structured interview for psychiatric assessment based on ICD-10 that does not consider ADHD, Dystimia, Manic Depression, Obsessive Compulsive Disorder, Post Traumatic Stress Disorder, Separation Anxiety, and Sexual Impulse Disorder [48].

Moreover, looking at the four psychiatric clusters (see Table 2), it was found a higher rate of Anxiety disorder and Psychosis in individuals with WS compared to individuals with DS.

The higher rate of Anxiety disorder showed by participants with WS



(28.2%) is consistent with previous reports in people with WS [48,49]. Conversely, a study adopting the Anxiety Disorders Interview Schedule for DSM-IV Parent Interview Schedule (ADIS-IV) documented an even higher rate (53.8%) in 119 participants with WS aged 4-16 years [17,50]. A possible reason for the discrepancies between our results and those of the previous study is that the parent version of the ADIS-IV overestimates prevalence of some disorders, as the Anxiety disorder [17,51]. Nevertheless, in all cases the high prevalence of Anxiety in WS is the most consistent result in this population with ID, which is at almost twice the rate of the other psychopathological disorders.

Even if the present study confirmed previous data of a relatively high prevalence of Anxiety disorder also in individuals with DS (more than 14%), results from the direct comparison between participants with DS and participants with WS support evidence indicating how Anxiety disorder is less common in DS than in other populations with ID [52-54].

Moreover, differences between the groups also emerged for the distribution of the Anxiety disorder subtypes. In the group with WS, the Anxiety disorder profile was characterized by the highest prevalence of Simple Phobia and Generalized Anxiety disorder, while in the group with DS Anxiety disorders subtypes were equally distributed, with the exception of Simple Phobia rate, more prevalent than Social Phobia. An accumulating literature consistently indicates that psychopathology pertaining to anxiety and abnormal fear is among the most common diagnosis within the population with WS, and that the symptoms also appear relatively stable across the development [1,17,19,49,55-57]. For example, in a large-scale study, Leyfer et al. [56] examined the prevalence of Anxiety disorder in a group of 132 children with WS by administering the Anxiety Disorder Interview Schedule (ADIS-IV) to their caregivers. Compared to children with ID, those with WS were more likely to meet criteria for Specific Phobia, General Anxiety disorder, and Separation Anxiety, with over 60% of the participants likely to have at least one type of Anxiety disorder. In another study, Cherniske et al. [58] reported that over 60% of the 20 adults with WS exhibited moderate to severe Anxiety and Simple Phobias. However, few studies have investigated the distribution of specific Anxiety disorders in individuals with DS. Some works suggested that children with DS show less Social Phobia and Separation Anxiety disorder than typically developing children, and others reported higher levels of distress and greater latency when approached with novel stimuli [59-61]. The present study confirmed previous results showing a higher level of Simple Phobia than other subtypes of Anxiety disorders in participants with DS.

As for the Anxiety disorders, a higher rate of Psychosis was found in individuals with WS compared to DS. Literature pointed out that Psychosis comorbidity is rarely considered in WS [62]. However, our results pointed out that the presence of Psychosis should be established in individuals with WS and that targeted treatment should be considered. Conversely, in DS the presence of Psychosis is very rare, as documented by our data and by previous studies on the topic [13-16]. It has been suggested that the effect of unknown resilience factors associated with DS may protect against the development of Psychosis [63].

A relevant number of participants with WS also showed Behavioral problems, which have been exclusively related to ADHD (15.3%). An opposite profile emerged in the group with DS, mainly characterized by Oppositional Defiant disorder (10.7%). Our results are consistent with previous studies examining separately the two groups and confirm that individuals with WS may be at risk for developing ADHD while individuals with DS may be at risk for developing Oppositional Defiant

disorder and Conduct disorder [9,47,64-66].

The co-occurrence of Anxiety disorder with other disorders also differed between our groups with ID. A positive correlation between the occurrence of Anxiety disorder and Mood Disorder was found in individuals with WS, suggesting the presence of an internalizing pattern of comorbidity. However, no significant relations between disorders were found in individuals with DS. At our knowledge, only a study in literature evaluated the co-occurrence of psychiatric disorders in DS documenting a negative relation between Anxiety disorder and Behavioral problems, as if Anxiety inhibited disruptive behaviors [61]. Nevertheless, our results are not directly comparable to those of Evans et al. [61] since they focused only on impulsivity and hyperactivity behaviors by adopting self-report instruments.

Overall, our results documented, in a large group of individuals with ID, the presence of specific psychiatric profiles linked to specific genetic conditions.

Little attention has been directed toward targeted treatment of psychiatric disorders in populations with ID and genetic syndromes. Indeed, only few studies exist on psychopharmacological treatment of psychiatric disorders in population with ID and genetic syndromes. A study on Depression treatment in DS found an association between antidepressant use and delayed dementia onset and increased longevity [67]. A study on individuals with WS showed that the combination of SSRIs and low doses of low-potency antipsychotics seems to be the most suitable medication to treat Generalized Anxiety disorder [68]. In a study on response to methylphenidate treatment of individuals with WS and with ADHD, a decrease in the rate of Anxiety disorders and clinically significant improvement were reported [69]. However, the evidence base for specific psychopharmacologic treatment in populations with ID is limited and warrants future prospective controlled trials for a more targeting intervention.

Evidence for the psychological support in people with ID is even more limited. Much of the research on cognitive behavioral therapy in ID has come from forensic secure units and has shown it to be effective for conditions such as Depression, Anxiety, anger management and sex offending [70]. No syndrome-specific psychological treatment is still available and this is likely to be an important psychological intervention that needs further investigation.

While cognitive features in people with ID have been deeply examined, the behavioral and psychopathological characteristics have not been fully explored, despite being of primary importance to implement appropriate strategies for care and treatment. Several studies have investigated the correlation between genotype and cognitive phenotype and the role played by the specific genes involved in DS and WS. Yamamoto and colleagues have underlined the clinical importance of DSCR region, containing up to 25-50 genes, that plays a crucial role for cognitive abilities both in DS and in other developmental disorders. In transgenic mice with DS it has been demonstrated the weight of DYRK1A as candidate gene responsible for learning and memory [71-75]. Also studies in WS have underlined the importance of genotype-phenotype correlation. For instance, Fusco and colleagues suggested that larger deletions extending distally in individuals with WS give more severe developmental delay and ID [76]. Moreover, hemizygosity of LIMK1, CLIP 2, GTF2IRD1 and GTF2I is generally associated with a better cognitive profile in WS [77,78]. Nevertheless, little is still known about the genotype-phenotype correlation related to psychopathological symptoms in individuals with DS and WS. As pointed out, DYRK1A overexpression was found in mouse model of

DS [79]. Influencing synaptic excitation/inhibition balance, DYRK1A induced excessive synaptic inhibition in the transgenic mice with DS [80]. Speculatively, since increased synaptic excitability was documented in psychiatric disorders as schizophrenia, the synaptic inhibition found in mouse model of DS may represent a possible resilience factor against the development of Psychotic symptoms in DS [81]. As concerns WS, some authors suggested that the HTT gene is relevant for influencing the phenotypic spectrum of WS [82]. Considering the association of the HTT promoter polymorphism with Anxiety-related traits, it could be argued that the HTT gene is linked to the Anxiety symptoms found in WS [83]. However, in the present study the direct correlations between specific genes involved in the chromosomal abnormalities causing DS and WS and the presence of specific psychiatric disorders in the two groups it was not investigated. Studies that directly compare population with ID and different etiology and that look at the genotype-phenotype correlation of the psychopathological profile are then mandatory to clarify the overlooked issue of diagnosis and treatment of psychiatric disorders in ID.

In summary, present findings show differences in prevalence of psychiatric disorders between individuals with WS and individuals with DS and suggest the need for a targeted care of psychiatric disease in these populations. Moreover, the syndrome-specific intervention should be age-focused, given that the psychiatric profile changes by age according to the different etiology of ID. Indeed, individuals with WS showed on the whole higher rate of Anxiety disorders and Psychosis than individuals with DS but Anxiety disorder was more evident in young age and Psychosis in old age. These age-related changes should be taken into account by clinicians in the management of psychopathological disorders of individuals with ID of known etiology. Particularly, in populations with WS an early life program to screen Anxiety disorders should be targeted and in the follow-ups the examination of Psychosis symptoms should be provided. Healthcare professionals need to be familiar with this behavioral phenotype of different genetic syndromes with ID to tailor focused treatment and psychological support [84].

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