STUDY PROTOCOL

Official title: Early treatment for children with mental health problems and genetic abnormalities through a parenting intervention (The GAP): A pragmatic randomized controlled trial

NCT Number: NCT ID not yet assigned

Document date: October 13th, 2023

TITLE
Early Treatment for children with Mental health Problems and Genetic Abnormalities through a Parenting intervention (The GAP): a pragmatic randomized controlled trial

Keywords: intervention; parenting; randomized controlled trial; pragmatic; genetic syndromes; mental health, development.

ABSTRACT
Children with genetic abnormalities are at increased risk for a wide range of mental health problems, and parental distress is more significant within these families. These genetic and family factors can negatively impact children and parents' mental health. Early parenting interventions, such as the Incredible Years Autism Spectrum and Language Delays (IY-ASLD®), have demonstrated the potential to improve children emotional, behavioral and social communication symptoms, as well as parental distress. However, the efficacy of such interventions has yet to be determined for children with genetic abnormalities. This group of infants has complex phenotypic presentations, but they have not been studied through careful developmental lens, and major gaps in knowledge exist on effective treatment options. Clinicians face a lack of guidance regarding which evidence-based interventions could improve their developmental pathways, particularly when patients have impairing language or social communication symptoms but do not meet criteria for a full-blown diagnosis of an Autism Spectrum Disorder (ASD). This study aims to fill this gap, providing preliminary evidence on the efficacy of the IY-ASLD® intervention for children with genetic abnormalities who present impairing developmental difficulties but do not meet criteria for ASD. We designed a multicenter pragmatic randomized controlled trial with a treatment as usual (TAU) condition. Approximately 68 children aged 3–7 years will be recruited. The IY-ASLD® intervention will be delivered online, as these families tend to be scattered over the territory and the feasibility and acceptability of this format has already been piloted within the Spanish Mental Health System. The results of this study could shed light on early treatment options for this often overlooked group of infants. This could represent an effective treatment for a key developmental period, sharpening the trajectories for such vulnerable children.

BACKGROUND

Early intervention for neurodevelopmental problems in children with genetic syndromes

Children with genetic abnormalities commonly present developmental problems and mental health comorbidities. The manifestation of these difficulties can often be identified in the early stages of childhood, such as the development of social communication, emotion regulation and behavioral problems. The persistence of these difficulties has implications for children's trajectory, including the emergence of social dysfunction, comorbid mental disorders, and future maladaptation. Early intervention is crucial to improve these outcomes in children with neurodevelopmental problems. Thus, early troubling signs, such as communication difficulties, should be targeted and treated with no need to wait for a full-blown diagnosis. This dimensional approach allows treatment to reach young children with a wide range of neurodevelopmental difficulties, not only being limited to particular diagnostic categories.
Young children with genetic abnormalities have complex clinical presentations defined by particular behavioral phenotypes (i.e. a characteristic pattern of motor, cognitive, linguistic, and social abnormalities), which are not included within the Diagnostic and Statistical Manual classification (DSM) but commonly overlap with recognized diagnosis such as ASD, ADHD or Anxiety Disorders. Despite the high prevalence of ASD in children with genetic syndromes (13% in Prader Willi, 12% in Williams and 11% in 22q11.2 deletion) (Morel 2018, Veltman et al 2005; Richards et al 2015), a growing body of evidence suggests that these individuals might have an atypical profile of ASD phenomenology, distinct from idiopathic ASD (Richards et al 2015). More than 21 genetic syndromes have been described to present autistic like behaviours, such as social deficits and repetitive behaviors, which might not meet full criteria for an ASD diagnosis (Moss and Howlin 2009). For instance, difficulties in the social domain and expressive language delays may represent key characteristics of the 22q11.2 deletion Syndrome (Lavoy 2016); Prader Willi Syndrome do not present specific impairments in face processing, social cognition, or communication but could show solitary behavior, social withdrawal, poor peer relations, and pronounced repetitive and compulsive behaviors (Dykens 2011, Veltman 2005); Sotos Syndrome often presents difficulty with peer group relationships, lack of awareness of social cues and speech delays (Lane 2016); and many others syndromes as Crit-du-chat, 1p36 deletion, 15q11q13 duplication, 16p11 deletion, 1q21 duplication, Smith–Magenis, Kleefstra, and Williams present language delays, difficulties in the social domain and restricted or repetitive patterns of behavior, but do not meet full criteria for an ASD diagnosis (Lu Y 2020, Bernier 2016, Smith ACM, 2001, Ciacio 2018, Feinstein 2007).
Unfortunately, these patients are less likely to access interventions targeting their impairing symptoms, as there is a lack of evidence regarding effective treatment options, and only the most severe cases with salient symptoms in all domains are referred to ASD care-pathways.

Parenting group interventions (the Incredible Years Autism Spectrum and Language Delays program: IY-ASLD®)

Parent-mediated group interventions can have a large and sustained effect on children outcomes at a relatively low cost (Sanders 1993). With this aim, evidence-based early parenting interventions have increasingly been developed for children with neurodevelopmental problems (Webster-Stratton 2018). However, these interventions are insufficiently available within our Public Mental Health System, and they have not been studied in children with neurodevelopmental problems related to genetic syndromes.

Group interventions show promise as a valuable resource to help parents cope with children's behavioral, social, and emotional difficulties. This therapeutic approach has demonstrated effectiveness improving dysfunctional parenting styles, reducing children's behavioral problems and increasing parents' ability to facilitate their children's communication skills and vocabulary (Whittingham 2009). Group interventions also provide social support for parents. This is especially important for parents of children with genetic syndromes, who present high stress levels as well as a lack of structured guidance on effective ways to promote their children's development and mental health.

The Incredible Years® parenting programs are a set of interventions recommended by the NICE guidelines, primarily focused on strengthening the parent-child interaction and improving parenting skills in order to prevent or reduce children's behavioral problems (Jamila Reid 2001). The effectiveness of the Incredible Years program has been widely demonstrated in multiple randomized controlled trials, showing an improvement in parental stress levels, depression, and parental coping, as well as in children's behavior difficulties (Hutchings 2007, Webster-Stratton 2001). A range of developmentally appropriate interventions for different age groups is offered. The IY-ASLD® program has been specifically developed to target the needs and concerns of parents of young children in the autistic spectrum or with language delays. The program encourages positive parent-child relationships to promote children's emotion regulation, social competence, language skills, pre-academic coaching, and peer relationships. The intervention teaches parents how to play in a child-directed way but with a specific focus on encouraging children's communication and social engagement. It also focuses on how to use positive discipline to set limits and handle misbehavior. A pragmatic randomized controlled trial has supported the feasibility and acceptance of delivering this intervention for children with ASD in the UK National Health Service (Williams 2020). However, it has yet to be implemented for children with genetic syndromes and neurodevelopmental problems.

The IY-ASLD® intervention has recently been piloted within the Spanish Mental Health system (Valencia 2021). Due to the COVID-19 pandemic, the program was piloted in an online format, including all the elements of the face-to-face intervention with families and therapist connected online. Preliminary results showed that parental compliance and satisfaction with the intervention was very high (Villalta in press), and several advantages of the online format were highlighted (such as better family logistics and improved access to therapy). In view of these results, and taking into account that families of infants with genetic abnormalities are scattered all over the territory, we aim to examine the feasibility and initial effectiveness of delivering the IY-ASLD® intervention in an online format in spite of the pandemic context. It is also of note that support groups are an important resource for many families living with children with rare diseases, and it has been described that meeting via teleconference is a facilitating factor.

AIMS AND HYPOTHESIS

The main aim of the present study is to examine the feasibility and initial effectiveness of the IY-ASLD® intervention for parents of children with developmental difficulties of a genetic basis. We specifically aim to describe the compliance and satisfaction of these parents with the program, from a quantitative and qualitative perspective, and provide initial evidence on its effectiveness in terms of improving parental distress, parenting skills, as well as overall mental health difficulties in their children.

In order to achieve these goals, we designed a controlled randomized pragmatic trial where families will be randomly allocated to the intervention group (receiving the IY-ASLD® intervention online) or to the treatment as usual condition (TAU). We recruited children from the three pediatric hospitals that have a specialized unit in genetic diseases and in child mental health.

The research hypotheses are as follows:

I. Parents' compliance with the program is acceptable (attending at least 15 of the 22 online sessions and a minimum of 50% of parents finishing the intervention).
II. Parents report acceptable levels of satisfaction with the program.
III. Parents who received the intervention present reduced levels of parental stress when compared to the control group.
IV. Parents who received the intervention show reduced levels of depressive symptoms and expressed

emotions when compared to the control group.

V. Parents who received the intervention present an increase in their positive parenting skills when compared to the control group.

VI. Parents who received the intervention report a decrease in the levels of children's externalizing and internalizing symptoms when compared to the control group.

METHODOLOGY

The GAP project will be implemented in three Pediatric Hospitals (Hospital Sant Joan de Déu in Barcelona, Hospital Vall d'Hebron in Barcelona, Hospital Parc Taulí in Sabadell). Participating families will be recruited from specialist paediatric genetic units within each hospital, and will be randomly allocated to the TAU condition or to the intervention group. Clinical psychologists and child psychiatrists working in specialised mental health services for neurodevelopmental disorders within the hospitals will deliver the intervention. Before the intervention takes place, between 4 and 8 focus groups will be carried out with a subsample of families to explore their needs, challenges, preferences and expectations. After the intervention, interviews will be conducted with parents of the intervention group and with clinicians who delivered the intervention.

A mixed-methods approach will be used, considering the benefits of combining quantitative and qualitative methods in health psychology clinical trials (Bishop 2015).

Sample size:

For the sample size calculation, we used the outcome parental stress, measured through the questionnaire Parental Stress Index Short Form (PSI-SF). This is a 36-item scale, with a range of 180 points. There is data showing that a decrease of 16.5 points in the total scale stress score can be seen after attending an IY program. Given that this study will be conducted with parents of children presenting neurodevelopmental difficulties, we anticipated that the decrease in the PSI-SF score would be lower. We estimated the necessary sample size considering a power of 80%, $\alpha = 0.05$, a difference between pre- and post-test of 10 points, and a standard deviation of 20, using a paired-samples t test. We estimated 34 participants needed per arm of the study. Thus, we aim to recruit approximately participants. The drop-out rate has not been included when calculating the sample size, considering that a sample of 68 participants is similar than previous studies and in line with recommendations by the National Institute of Health Research.

For the focus groups that will be conducted before the intervention, each group will have between 4 and 6 participants (mothers or fathers), considering the recommendations provided by Tausch & Menold (2016). Taking into account potential drop-outs, 6 parents will be contacted per focus group.
For the post-intervention individual interviews with parents, parents will be selected from the 4 intervention groups conducted in the 3 sites: a minimum of 2 parents per group will be interviewed, therefore at least 8 interviews will be conducted. Parents who dropped out of the study will also be invited to participate to explore their experiences. Data saturation will be used to determine the final sample size.
For the post-intervention individual interviews with clinicians, all clinicians that delivered the intervention will be interviewed after the intervention phase.

Eligibility criteria:

The following are the inclusion criteria:

1. Children aged 3.0 – 7.11 years at recruitment
2. Children with a diagnosis or in diagnostic process for high suspicion of a genetic abnormality
3. For children up to 5.11 years with withdrawn (defined as CBCL/1.5-5 scores above the borderline clinical range, T-score> 65) AND/OR pervasive developmental problems (defined as CBCL/1.5-5 scores above the borderline clinical range, T-score> 65) AND/OR socialization difficulties (defined as Vineland-III scores below 1SD in the socialization subdomains).
4. For children over 6 years with social problems (defined as CBCL/6-18 scores above the borderline clinical range, T-score> 65) AND/OR thought problems (defined as CBCL/6-18 scores above the borderline clinical range, T-score> 65) AND/OR socialization difficulties (defined as Vineland-III scores below 1SD in the socialization subdomains).
5. Parents/caregivers showing good understanding of the Spanish or Catalan language
6. Parents/caregivers consenting to take part in the study and signing the informed consent

The following are the exclusion criteria:

1. Children diagnosed with an Autism Spectrum Disorder
2. Children scoring above diagnostic cut-off for Autism or Autism Spectrum Disorder in the ADOS-2.
3. Attending another structured parenting program
4. Children in the care of their local authority

Recruitment:

Parents will be recruited from the three specialist units in paediatric genetic abnormalities within the three Hospitals. A leaflet with the inclusion and exclusion criteria will be handed out to clinicians working in the services. Clinicians will discuss the study with eligible families and will ask the families permission to be contacted by the study researchers. If they agree to be contacted about the project, a research assistant will call the family to discuss the study further. If the family is interested in participating in the study the researcher will set up an appointment to evaluate all the inclusion criteria (including the Autism Diagnostic Observation Schedule-ADOS-). During this visit, researchers will make sure that participants receive all the necessary information and have the opportunity to ask any questions. If participants meet the inclusion criteria, parents will be asked to sign the informed consent and to complete the pre-intervention assessment. Any children excluded from the study due to scoring above diagnostic cut-off for ASD (ADOS) will be referred to specialised assessment within the mental health public system. Participants will be able to discontinue the treatment sessions or drop out from the control group at any point at their request. The participation in the study will not affect their usual treatment.

Randomization:
Randomization will take place once all the participating families have completed baseline measures. They will be randomly allocated to the intervention group or to the TAU condition. An independent researcher will carry out the randomization process, and researchers who are responsible for patient recruitment or intervention delivery will not be involved. Due to the pragmatic and clinically focused nature of the study, further blinding procedures will not be possible.

Intervention:
The IY-ASLD® program is a 14-session group-based intervention for parents of children presenting neurodevelopmental difficulties. During the COVID-19 pandemic, the Incredible Years developers adapted the intervention to be performed online (22 sessions approximately). Each online group will include approximately 6-10 participants. The intervention includes video modelling and emphasizes the importance of practice-based learning through role-playing. Weekly home tasks will be assigned to parents, and families will be phoned each week to encourage home-based practice. Fidelity to the treatment manual will be ensured in different ways. Group interventions will be conducted by experienced psychiatrists and clinical psychologists, officially trained in the IY-ASLD® model and its online adaptation by an accredited trainer. Group leaders will complete weekly fidelity checklists and will be supervised by certified supervisors throughout the intervention. The TAU condition involves outpatient appointments with neuropediatricians to monitor children's developmental level and drug prescription when needed. All infants are also treated in Early Years Centers based in the community, where they receive individual unstructured interventions to foster children's development. Families allocated to the intervention group will also receive TAU.

Measures:
Baseline and sample descriptors:
Sociodemographic and child clinical variables will be collected from clinical notes and parent reports. Socioeconomic status will be determined using Hollingdale's Index of Social Position.

The following questionnaires will be administered:

- Social Communication Questionnaire (SCQ): it is a 40-item parent report measure, yes/no format, based on the Autism Diagnostic Interview-Revised (ADI-R). The Lifetime version of this questionnaire will be administered before the intervention to describe children's social communication difficulties. It is a robust tool that has shown good validity, and it has been widely adopted by both the research and clinical community.
- Child Behavior Checklist (CBCL 1.5-5): this is a parent-reported 99-item inventory that addresses specific externalizing and internalizing behaviors. The sum of scores forms a total problem score, and it also includes scores for pervasive developmental problems and withdrawn subdomains. It will be collected before and after the intervention. It has shown good internal consistency, also in children with neurodevelopmental problems.
- Child Behavior Checklist (CBCL/6-18): it is a 113-item parent-response instrument that provides information about behavioral and emotional problems in children aged 6-18 years. It will be administered before the intervention to obtain information on social problems score and withdrawn-depressed score. It has shown good internal consistency.
- Vineland Adaptive Behavior Scale-III (VABS-III, parent/caregiver report form): it assesses adaptive functioning in different areas: communication (receptive, expressive, written), socialization (interpersonal/play and leisure time/coping), daily living skills (personal, domestic, community), and motor skills (fine and gross). It also generates a final adaptive composite score. This instrument will be used before the intervention to collect the level of functioning in different developmental areas. It has been considered a very efficient tool to measure the adaptive behavior profile of preschool children with developmental problems and shown excellent test-retest reliability.
- Developmental Profile-3 (DP-3): this is a 180-item parental questionnaire assessing developmental delays in different domains: motor, adaptative, socio-emotional, cognitive, and communication. It also computes an overall general development score. It will be used before the intervention to collect the child developmental level. It has shown good internal consistency.

- Autism Diagnostic Observation Schedule (ADOS-2): it is a semi-structured assessment of social interaction, communication and play exposing the child to situations that elicit spontaneous behaviors in standardized contexts. The Toddler Module will be used for children between 24 and 30 months, and Modules 1 to 3 will be selected in accordance to the children's language level. An experienced psychologist research assistant, trained to ADOS research standards, will conduct the assessment. To receive an autism or autism spectrum diagnosis by the ADOS-2 algorithm an individual`s score must exceed a total cut-off score.

Outcomes:
Feasibility outcomes (primary outcomes):
- Parents' engagement with the program and participant retention: parents' attendance at the sessions will be monitored throughout the intervention, expecting they will attend at least 15/22 sessions with a minimum of 50% of parents finishing the program.
- Compliance and satisfaction throughout the study: the questionnaire Autism Program Parent Weekly Evaluation is part of the IY-ASLD® program materials and will be administered after each session to collect information regarding compliance and satisfaction throughout the study.
- Parents' acceptability and satisfaction with the program: this outcome will be evaluated quantitatively and qualitatively. From a quantitative perspective, parents' overall acceptability and satisfaction with the program will be assessed with the Autism Program Parent Final Satisfaction Questionnaire (included within the IY-ASLD® program). Data will be collected after the last session. From a qualitative perspective, individual interviews will be conducted after the last session of the intervention to explore parents' acceptability, satisfaction and overall experience with the intervention.

Effectiveness outcomes (secondary outcomes):
- Parental stress will be measured with the Parent Stress Inventory-Short Form (PSI-SF). This is a 36-item questionnaire that specifically focuses on assessing parental stress associated with the care of their offspring. It has three domains: parental distress, parent-child dysfunctional interaction, and difficult child, which combine to form a total stress scale. This tool will be administered before and after the intervention. It has shown good internal consistency.
- Parents' depressive symptoms will be measured using the Beck Depression Inventory (BDI). The BDI is a 21-item screening tool assessing the severity of depressive symptoms. It is a standardized and validated questionnaire, often used in mood disorder assessments. It will be collected before and after the intervention. It has good reliability.
- Parenting skills will be assessed with the Alabama Parenting Questionnaire-Preschool revision (APQ-Pr). The APQ-Pr is a 32-item parent-reported questionnaire measuring parenting practices that are consistently associated with disruptive child behaviors. This version has 3 dimensions: positive parenting, inconsistent parenting, and punitive parenting. It will be collected before and after the intervention. This measure has shown good internal consistency and validity.
- Parental-expressed emotions will be evaluated with the Autism-Specific Five Minute Speech Sample (ASFMFSS). This is a narrative 5-min interview used to measure parental-expressed emotions for children with ASD and related disorders. Parents are asked to speak about their child and the parent-child relationship —"I'd like you to speak for 5 minutes, telling me what kind of person (child name) is and how the two of you have got along together over the past 6 months." Speech samples are audiotaped, transcribed, and coded following four global categories: (a) initial statement, (b) warmth, (c) relationship, (d) emotional over-involvement, (e) critical comments, and (f) positive comments. Expressed emotions will be measured before and after the intervention. Benson et al. [49] assessed 30 randomly selected speech samples by three different raters. Inter-rater reliability and code-recode reliability on two separate occasions, for all six AS-FMSS components and for total EE score, were both in the good to excellent range.
- Semi-structured individual interviews will be conducted after the last session of the intervention to qualitatively explore: (1) parents' perceived changes in their parenting skills and distress, and (2) clinicians' experiences with the intervention delivered.

Data collection:
Quantitative data collection:
Data will be collected at baseline (before performing randomization) and after finishing the IY-ASLD® intervention. Parents consenting to participate will be offered a hospital appointment before the intervention with a research assistant to evaluate inclusion criteria (parental questionnaires and ADOS). If they meet inclusion criteria they will then be contacted on the phone to complete the baseline assessment (including self-report measures, children outcome measures, and a voice recording for the ASFMSS tool). If both parents participate in the study, they will fill out the children's outcome measures together (by consensus) and the parental outcome measures individually.

Qualitative data collection:
Qualitative data will be collected at baseline (focus groups) and after finishing the IY-ASLD® intervention (interviews). Parents included in the study will be contacted on the phone to be invited to participate in an online focus group. We will aim for a representative sample in terms of children's diagnosis, age, gender

and cognitive status (according to DP-3 cognitive subscale score). If a parent declines to participate in a focus group, another parent will be contacted until 6 individuals per focus group are recruited. The focus groups will be delivered online and will be conducted by a psychologist trained in qualitative methods, external to the clinical team, and they will be audio-recorded and transcribed verbatim.
The same psychologist will conduct the individual interviews to parents and clinicians, which will have an online format and will be audio-recorded and transcribed verbatim.

SCIENTIFIC AND SOCIAL INTEREST

Genetic and early environmental factors are crucial for children's development and future mental health. Genetic load can be difficult to modify, but environmental factors affecting critical developmental periods can shape phenotypic expression. Being exposed to responsive, sensitive and encouraging relationships with core adult figures allows young children to develop communication, social and emotional regulation skills. Such abilities are more difficult to acquire for children with developmental genetic syndromes, and their parents face the challenge to provide an enhanced environment despite presenting higher stress levels. Most children with developmental genetic syndromes in the Spanish system attend child development centers for individual therapy, but parents do not usually receive structured evidence-based interventions to enhance children's development and mental health symptoms from an early stage. Indeed, the evidence to treat these children is very limited, and there is no guidance on parent-mediated interventions for this particularly vulnerable group of patients.
The GAP project has great scientific interest, as it will provide unprecedented data on a novel evidence-based treatment option for children that develop mental health difficulties of a genetic basis. The study participants are a very unique and hard-to-ascertain sample, as neurodevelopmental genetic syndromes are very rare, and its associated mental health difficulties have particular clinical presentations. This study will generate novel scientific data on both, the phenotype description of early mental health problems of infants with genetic syndromes, as well as on treatment options for such difficulties. Thus, The GAP study will provide new scientific data while setting up initial guidelines to implement standards of mental health treatment in the public mental health system.
This scientific gap is also worrying from a societal point of view. Families whose infants are diagnosed with a genetic abnormality face high stress levels related to parenting children with behavior, communication and social difficulties, and in relation to how the diagnosis will affect their children's mental health. In this regards, parents tend to look for peer-to-peer support in family associations. The GAP project will bring families with similar problems closer, creating opportunities for peer-to-peer support while providing rigorous and specialized treatment options to improve parent and children mental health.
Finally, The GAP study represents a scientific and clinical challenge as it involves the collaboration between the three hospitals with specialized mental health and genetic diseases units within our public health system. The collaborative approach of the current project is set not only for recruitment purposes, but also for implementation of joint treatment strategies, as patients will be allocated to one of the online intervention groups according to their clinical profile, and not according to the recruitment site. The design of this project goes beyond health institutions catchment areas, brings together centers for child development and children mental health, and integrates physical and mental health with the ultimate aim of providing the best possible assistance to this often overlooked group of infants.

REFERENCES

Ae, L. A. O., Mchugh, L., Jo, A. E., Ae, S., & Reed, P. (2007). Parenting Stress Reduces the Effectiveness of Early Teaching Interventions for Autistic Spectrum Disorders. http://doi.org/10.1007/s10803-007-0497-7

Bernier, R., Steinman, K. J., Reilly, B., Wallace, A. S., Sherr, E. H., Pojman, N., … Wenegrat, J. (2016). Clinical phenotype of the recurrent 1q21.1 copy-number variant. *Genetics in Medicine*, *18*(4), 341–349. http://doi.org/10.1038/gim.2015.78

Bishop, F. (2015). Using mixed methods research designs in health psychology: an illustrative discussion from a pragmatist perspective. *British Journal of Health Psychology, 20*(1), 5-20. https://doi.org/10.1111/bjhp.12122

Ciaccio, C., Scuvera, G., Tucci, A., Gentilin, B., Baccarin, M., Marchisio, P., … Milani, D. (2019). New Insights into Kleefstra Syndrome: Report of Two Novel Cases with Previously Unreported Features and Literature Review. *Cytogenetic and Genome Research*, *156*(3), 127–133. http://doi.org/10.1159/000494532

Dababnah, S. (2014). Pilot trial of the Incredible Years for parents of preschool children with autism spectrum disorder.

Dababnah, Sarah, & Parish, S. L. (2016). Feasibility of an empirically based program for parents of preschoolers with autism spectrum disorder. *Autism : The International Journal of Research and Practice*, *20*(1), 85–95. http://doi.org/10.1177/1362361314568900

Dykens, E. M., Lee, E., & Roof, E. (2011). Prader-Willi syndrome and autism spectrum disorders: An evolving story. *Journal of Neurodevelopmental Disorders*, *3*(3), 225–237. http://doi.org/10.1007/s11689-011-

9092-5
Feinstein, C., & Singh, S. (2007). Social Phenotypes in Neurogenetic Syndromes. *Child and Adolescent Psychiatric Clinics of North America*, *16*(3), 631–647. http://doi.org/10.1016/j.chc.2007.03.006
Flint J, Yule W. 1994. Behavioural phenotypes. In: Rutter M, Taylor E, Hersov L, editors. Child and adolescent psychiatry, 3rd edition. Oxford, England: Blackwell Scientific. pp. 666–687
Furlong, M. & McGilloway, S. (2011). The *Incredible Years Parenting program* in Ireland: A qualitative analysis of the experience of disadvantaged parents. *Clinical Child Psychology and Psychiatry, 17*(4), 616-630. https://doi.org/10.1177/1359104511426406
Hutchings, J., Bywater, T., Daley, D., Gardner, F., Whitaker, C., & Jones, K. (2007). Parenting intervention in Sure Start services for children at risk of developing conduct disorder: pragmatic randomised controlled trial. http://doi.org/10.1136/bmj.39126.620799.55
Jamila Reid, M., Webster-Stratton, C., & Beauchaine, T. P. (2001). Parent training in head start: a comparison of program response among African American, Asian American, Caucasian, and Hispanic mothers. *Prevention Science : The Official Journal of the Society for Prevention Research*, *2*(4), 209–227. http://doi.org/10.1023/A:1013618309070
Landa, R. J. (2018). Efficacy of early interventions for infants and young children with, and at risk for, autism spectrum disorders. *International Review of Psychiatry (Abingdon, England)*, *30*(1), 25. http://doi.org/10.1080/09540261.2018.1432574
Lane, C., Milne, E., & Freeth, M. (2016). Cognition and Behaviour in Sotos Syndrome: A Systematic Review. http://doi.org/10.1371/journal.pone.0149189
Lavoy. (2016). Developmental Trajectories in 22q11.2 Deletion HHS Public Access. *Physiology & Behavior*, *176*(12), 139–148. http://doi.org/10.1002/ajmg.c.31435.Developmental
Lu, Y., Liang, Y., Ning, S., Deng, G., Xie, Y., Song, J., … Qin, Y. (2020). Rare partial trisomy and tetrasomy of 15q11-q13 associated with developmental delay and autism spectrum disorder. *Molecular Cytogenetics*, *13*(1). http://doi.org/10.1186/s13039-020-00489-z
Morel, A., Peyroux, E., Leleu, A., Favre, E., Franck, N., & Demily, C. (2018). Overview of social cognitive dysfunctions in rare developmental syndromes with psychiatric phenotype. *Frontiers in Pediatrics*, *6*. http://doi.org/10.3389/fped.2018.00102
Moss, J., & Howlin, P. (2009). Autism spectrum disorders in genetic syndromes: implications for diagnosis, intervention and understanding the wider autism spectrum disorder population. *Journal of Intellectual Disability Research*, *53*(10), 852–873. http://doi.org/10.1111/j.1365-2788.2009.01197.x
Richards, C., Jones, C., Groves, L., Moss, J., & Oliver, C. (2015). Prevalence of autism spectrum disorder phenomenology in genetic disorders: A systematic review and meta-analysis. *The Lancet Psychiatry*, *2*(10), 909–916. http://doi.org/10.1016/S2215-0366(15)00376-4
Sanders, M. R., & Dadds, M. R. (1993). *Behavioral family intervention.* (A. & Bacon., Ed.).
Tausch, A. P. & Menold, N. (2016). Methodological aspects of focus groups in health research: Results of qualitative interviews with focus group moderators. *Global Qualitative Nursing Research, 3*, 2333393616630466. https://doi.org/10.1177/2333393616630466
Valencia, F., Urbiola, E., Romero-González, M., Navas, I., Elías, M., Garriz, A., ... & Villalta, L. (2021). Protocol for a randomized pilot study (FIRST STEPS): implementation of the Incredible Years-ASLD® program in Spanish children with autism and preterm children with communication and/or socialization difficulties. *Trials*, *22*(1), 1-10.
Veltman, M. W. M., Craig, E. E., & Bolton, P. F. (2005). Autism spectrum disorders in Prader-Willi and Angelman syndromes: A systematic review. *Psychiatric Genetics*, *15*(4), 243–254. http://doi.org/10.1097/00041444-200512000-00006
Webster-Stratton, C. (2001). The incredible years: Parents, teachers, and children training series. *Residential Treatment for Children & Youth*, *18(3),* 31-45.
Webster-Stratton, Carolyn, Dababnah, S., Olson, E., Webster-Stratton, C., Dababnah, S., & Olson, E. (2018). Handbook of Parent-Implemented Interventions for Very Young Children with Autism. *Autism and Child Psychopathology Series*. http://doi.org/10.1007/978-3-319-90994-3_17
Whittingham, K., Sofronoff, K., Sheffield, J., & Sanders, M. R. (2009). Stepping Stones Triple P: an RCT of a parenting program with parents of a child diagnosed with an autism spectrum disorder. *Journal of Abnormal Child Psychology*, *37*(4), 469–480. http://doi.org/10.1007/S10802-008-9285-X
Williams, M. E., Hastings, R. P., & Hutchings, J. (2020). The incredible years autism spectrum and language delays parent program: A pragmatic, feasibility randomized controlled trial. *Autism Research*, *13*(6), 1011-1022.