

**Characterising anxiety in Williams Syndrome (WS): Identifying the frequency, type, causes and potential interventions**

**SUMMARY PROTOCOL**

**Brief Summary of the Study**

This study will explore and describe the profile of anxiety in WS using informant reports, self-reports, genetic data, implicit experimental measures and a measure of physiological arousal. It will also address individual and environmental variables which may act as risk factors or correlates of anxiety. The study is comprised of three stages; a parent/caregiver telephone interview, a parent/caregiver online questionnaire and direct assessments with the individual with WS and their caregiver. Comparison groups will also be included in the study where time and resources permit. These groups will receive the same standard and quality of research as the WS group. The timespan for this study is three years.

This study will be conducted in collaboration with colleagues at the University of New South Wales and Macquarie University in Australia and data will be shared to increase the applicability of results.

**Background and Rationale**

The prevalence of mental health problems within the intellectual disability (ID) population is estimated to be around 40-50% (Emerson et al., 2003). Despite these high rates, there is limited research focused on the presentation of these problems as well as little attention placed on the importance of developing treatment and management strategies (Hagopian & Jennett, 2008).

This research aims to investigate the profile of anxiety in the WS population, which is present at a remarkably high rate. Whilst anxiety can be an adaptive and natural response to threat, persistently high levels can cause severe disruptions to daily life functioning and may reduce an individual’s quality of life (Arnold et al., 2003). In these instances, the anxiety experienced is excessive, uncontrollable and is frequently associated with symptoms such as restlessness, fatigue, sleep problems and irritability (American Psychological Association, 2013). As reported rates for anxiety disorders in WS are approximately around 40-70% (Dodd & Porter, 2011; Green et al., 2003; Kennedy et al., 2006; Leyfer et al., 2012; Woodruff-Borden et al., 2010), this is an important issue to address.

Specific Phobias and Generalised Anxiety Disorder are amongst the top diagnoses of anxiety disorders in WS whilst rates of Social Anxiety Disorder are significantly lower than rates found in the general population and in other genetic syndromes (Cherniske et al., 2004; Crawford et al., 2014; Pegararo et al., 2013). The specificity in the forms of anxiety that are commonly presented suggests there may be a predisposition for certain anxiety disorders, linked to the WS phenotype. Even so, as there is individual variation in the presence and severity of anxiety, there may be environmental or individual variables which act to influence its development and maintenance (Kirk et al., 2003; Ng et al., 2014). Examining a range of variables which may be associated with anxiety will provide further understanding of the anxiety profile in WS and may highlight potential risk/protective factors.

Adults have been significantly underrepresented in the existing literature; therefore this research project primarily aims to focus on defining anxiety in adults (aged 18+). However, since it has already been established that anxiety is a predominant issue for children with WS, it will be interesting to examine whether there are changes in the forms, severity and presentation of anxiety during the progression from childhood to adulthood. This will also aid understanding regarding the development of anxiety in adults. For this reason, this research will also include individuals aged 12-17 years.

This study will investigate the frequency, severity and nature of anxiety in adolescents and adults with Williams Syndrome. It will identify how anxiety presents and the relationships between anxiety and environmental/individual variables. The research will also assess people’s readiness for Cognitive-Behavioural Therapy (CBT), a treatment used successfully for those with anxiety problems in the general population (Cartwright-Hatton et al., 2004). Understanding whether individuals with WS may benefit from CBT-type interventions will be a preliminary step towards future intervention research and incorporating effective reduction and prevention methods into clinical practice.

**Principal Research Questions**

1. What is the phenomenology of anxiety in individuals with Williams Syndrome?
2. How does anxiety develop across the lifespan? (looking at early trajectories and the changes from adolescence to adulthood)
3. Are there environmental or individual variables which may be risk factors or correlates of anxiety?
4. Is Cognitive Behavioural Therapy (CBT) a potential treatment option that could be trialled for individuals with WS? Do individuals have the skills indicating readiness for this type of intervention?
5. Is anxiety and its associated variables different between WS and other genetic syndromes/intellectually disabled comparison groups?

**Stage 1: Semi-structured Interviews**

***Aims***: To obtain information regarding the process and experiences of anxiety in individuals with WS, using parent/caregiver interviews. This will indicate which measures and constructs may be important to address in Stage 2 of the study and will aid the development of a tailored and specific anxiety triggers questionnaire and a mood diary app.

***Research Questions***: How does anxiety present in individuals with WS? What are the antecedents and consequences?

*Participants*: Parents/carers of individuals with WS. Participants will have varying levels of ability.

*Sample size*: 10-15. Proposed number of adults with WS (aged 18+): 7-10. Proposed number of children with WS (aged 12-17): 3-5

*Recruitment*: Williams Syndrome Foundation (WSF)

*Data collection*: via telephone interviews, consent process online via software limesurvey

*Time required per participant*: 30 minutes to one hour

*Assessments*: Questions regarding developmental history, antecedents, behavioural markers, cognitions, management strategies and the impact of anxiety. Questions are asked in an open format to allow parents/carers to freely express issues that are of real concern to them.

**Stage 2: Survey Study**

Although the prevalence of anxiety is high, the severity varies between individuals and not all people with WS will present with anxiety. This suggests there may be interacting variables which strengthen or attenuate the anxiety experienced, or increase/decrease the risk of developing the disorder. For instance, individuals with WS tend to have many health problems and frequently require medical attention (Pober & Morris, 2007). Increased health complications may be associated with the increased rates of specific phobias reported in WS relating to hospitals, injury, doctors and injections (Green et al., 2012; Leyfer et al., 2006; Stinton et al., 2010; Woodruff-Borden et al., 2010). Moreover, whilst there is indication that quality of life and hypersensitivity to sound may be correlated with anxiety ([Arnold et al., 2003](#_ENREF_1); Blomberg et al., 2006), these are also factors which have received little attention in WS anxiety research.

***Aims:*** To obtain information regarding quality of life, sensory processing, self-help skills, general health and data regarding emotions, mood and behaviour.

***Research Questions:*** Are there any individual or environmental variables which may be associated with the risk/development of anxiety. Do any of the measures correlate with anxiety? Do these variables differ in other genetic syndromes/intellectually disabled comparison groups?

*Participants*: Parents/carers of individuals with WS. Parents/carers of individuals in comparison groups. We will aim to include two comparison groups (we will be sensitive to ensure chosen comparison groups are not currently being over researched). Participants will have varying levels of ability.

*Sample Size:* 200-300. Proposed number of adults with WS (aged 18+): 50-100. Proposed number of children with WS (aged 12-17): 50. Proposed number of adults per comparison group (aged 18+): 50-100. Proposed number of children per comparison group (aged 12-17): 50

*Recruitment*: WSF database, the Cerebra Centre for Neurodevelopmental Disorders (CCND) database, syndrome support groups and conferences/forums.

*Data collection*: online

*Time required per participant*: 30-45 minutes

*Assessments*:

**Measures (See Appendix A for further details):**

* Background Information Questionnaire
* Health Questionnaire: looks at current health symptoms and long term health problems
* Developmental Behaviour Checklist: assesses presence of emotional and behavioural disorders
* Anxiety, Depression and Mood Scale: measures psychiatric symptoms
* Anxiety Triggers Measure (to be developed specifically): will identify common triggers/antecedents of anxiety
* Waisman Activities of Daily Living Scale: measures level of independence in daily activities and self-help skills
* WHOQOL-BREF & Disabilities Module: assesses quality of life
* Sensory Experiences Questionnaire: identifies sensory processing patterns in the context of daily life/activities

**Stage 3: Direct Assessments**

***Aims***: To obtain genetic information through the collection of saliva samples for confirmation of syndrome diagnosis and to look at whether the size of the deletion present in an individual may be associated with their behavioural profile and the severity of anxiety. To carry out detailed clinical interviews and assessments to look at the types and impact of anxiety disorders and the presence of comorbid disorders. To measure cognitive abilities, communication skills and adaptive behaviours and how they are associated with anxiety. To use a variety of different assessment methods to identify which are the most appropriate and reliable for individuals with WS. To assess an individual’s readiness for intervention.

***Research Questions*:** Is the size of the genetic microdeletion present in WS associated with the behavioural features/severity of anxiety expressed? Are cognitive abilities/communication skills/adaptive behaviours associated with anxiety? Do self-reports of anxiety match with informant reports? What is the association between physiological measures and informant/self-reports of anxiety? Are there any commonly reported comorbid disorders? Do individuals have the skills indicating a readiness for CBT interventions?

*Participants*: Parents/carers of individuals with WS and the individual

*Sample Size*: 50-60. Proposed number of adults with WS (aged 18+): 40. Proposed number of children with WS (aged 12-17): 20

*Recruitment*: WSF, conferences and forums and the CCND database

*Data collection*: via video, diaries, telephone and face-to-face assessments

*Time required per participant*: 4 hours (breaks included)

*Assessments*:

**Measures prior to the assessment day (See Appendix B):**

* Vineland Adaptive Behavior - assessment of adaptive behaviour (approx. 1 hour interview over the telephone with parents/carers)
* KSADS Psychiatric Interview – approx. 1 hour interview with parents over the telephone

**Assessment day:**

Assessments will be carried out in the participant’s home or at the University of Birmingham. This will take a maximum of four hours (breaks included). Once a date has been decided, informant measures that can be completed in advance will be sent via post to parents/carers and may also be carried out using telephone calls.

Saliva sample kits (Oragene- DNA OG-575) will be provided to the participants on the assessment day and instructions will be provided and also explained verbally by the researcher. This kit is ideal for participants who are unable to spit. These samples may be collected with the researcher present or at a later date depending on which parents/carers/participants feel most comfortable with. Latex gloves will be provided to increase sanitation. Full consent will be obtained prior to collection. These samples will then be delivered by researchers to a licensed human tissue biorepository, the Human Biomaterials Resource Centre (HBRC) at the University of Birmingham. These samples will be analysed by Mr Andy Beggs (Clinical Scientist) and Dr Jo Stockton at the Institute of Cancer Studies. Samples will then be stored appropriately as per standard procedures at the HBRC.

**Post Assessment Day**

* Mood diary app - for parents/carers to fill out for 28 days about their child/person they care for
* Video diary - we will ask individuals with WS to film a daily five minute video answering questions about their emotions for 28 days

**Measures (See Appendix B):**

* Wechsler Abbreviated Scale of Intelligence - assessment of intellectual functioning in adults and children (for individuals with a mental age of 6-90).
* One Word Receptive & Expressive Picture Vocabulary Test - measures understanding of the meanings of words and ability to name objects, actions or concepts.
* Glasgow Anxiety Scale - measures state anxiety
* Spence Children’s Anxiety Scale - evaluates symptoms of anxiety disorders
* Kiddie-Schedule of Affective Disorders – semi-structured interview to identify presence of psychiatric disorders
* Experimental Task
* Physiological measurement: to measure skin responses and heart rate during the experimental task
* Readiness for Cognitive Behavioural Therapy - assesses participant’s cognitive capacity and ability to benefit from CBT methods
* The Behavior Rating Inventory of Executive Function Adult Version – measures executive functioning and self-regulation in everyday life.
* Loneliness and Social Satisfaction Questionnaire – measures social competence

**PLEASE NOTE:**

* Wording of questions and statements will be modified where necessary to ensure the participant fully understands what is being asked
* We may not use all of the assessments listed above in the studies. We will decide which assessments are the most suitable and relevant for the participants and will keep time burden in mind when making this decision
* Feedback will be provided back to participants at every stage of the study (except regarding genetic information and this will be made clear during the consent process)

**Collection of saliva samples and access to medical records:**

Participants will be asked whether they consent to giving a saliva sample for the research project. They will be made aware that they will not receive feedback on any of these results. The reason for this is because we do not have the resources or training to provide such sensitive feedback. In line with practices by several large UK research studies, including the NIHR BioResource for Rare Disease and the Deciphering Developmental Disorders (DDD) study, incidental findings unrelated to the syndrome diagnosis will not be disclosed.

If participants choose to not consent to this, we will ask participants whether they consent for the research team to contact their doctor/relevant professional to obtain a copy of medical records confirming a participant’s diagnosis. Participant’s do not have to consent to this either however if they do, we will provide them with a letter which needs to be signed and then sent to the professional/clinician. This letter will request for the medical records to be sent to the CCND.

**Off-site Research Activity Policy:**

This study will be conducted in line with the CCND’s off-site research activity policy.

**Timeline**

* March 2015-Oct 2015: Recruitment and completion of interviews (Stage 1), start data analysis
* Oct 2015 – Jan 2015: Complete data analysis, Create anxiety triggers questionnaire and pilot. Set up limesurvey with online screen measures, begin recruitment for Stage 2.
* Jan 2015 – March 2016: On-going recruitment and data collection for online screening measures, dissemination of data from Stage 1, Start preparing stage 3
* March – May 2016: Data analysis for stage 2. Contact parents who expressed an interest in taking part in the clinical assessments and agreed to future contact from the Cerebra Centre. Send recruitment flyers to the WSF to advertise to members.
* March - June 2016: On-going recruitment and collection of data for Stage 3, dissemination of data from Stage 2
* July 2016 – December 2016: Begin recruiting from the comparison groups (if resources are available), continue with recruitment and collection of data from Williams Syndrome group.
* January 2017 – April 2017: finish data collection and start analysis
* April 2017 – September 2017: Further data analysis, dissemination of data (Stage 3), final report preparation.

**Appendix A**

**Background Information Questionnaire (Moss et al., 2009)**

This asks about an individual’s mobility (ability to walk), verbal ability, date of birth, gender, vision, hearing and diagnostic status. There are some further questions which are directed towards the parent/carer, asking about factors such as education, marital status and income levels.

**Health Questionnaire (Burbridge et al., 2007)**

This assesses the presence and severity of 15 health problems and is answered by parents/carers. Informants will be required to rate the presence and severity (0 = never occurred to 3 = severe problem) of problems occurring ever in the person’s life and over the last month. The total numbers of health problems during the person’s life and the previous month will also be calculated. Inter-rater reliability was collected on a sample of 24 individuals. Mean item level reliability Kappa co-efficient for health problems ever occurring was 0.72. Mean item level reliability for the occurrence of health problems over the last month was 0.76.

**Developmental Behaviour Checklist - Child and Adult Versions (Einfeld & Tonge, 1995)**

This questionnaire measures emotional and behavioural disorders in children and adults with intellectual disabilities from the past six months. Behaviour is scored on a 0, 1, 2 scale whereby 0 = ‘not true as far as you know’, 1 = ‘somewhat or sometimes true’ and 2 = ‘very true or often true’. The DBC-P has been reported to have good test-retest reliability with a coefficient of 0.83 and good inter-rater reliability (Einfeld & Tonge, 1995). This version will be used alongside the DBC-A which is a modified version for adults aged over the age of 18 and contains 107 items. The DBC-A has shown high internal consistency (α=.95) and high test-retest reliability at two weeks for both paid carers and family carers at 0.75 and 0.85 respectively (Mohr, Tonge & Einfeld, 2005).

**Anxiety, Depression and Mood Scale (Esbensen et al., 2003)**

This informant report questionnaire will be used to assess anxiety, depression and mood. The 28 item questionnaire, scored on a four-point rating scale, contains five subscales labelled manic/hyperactive behaviour, depressed mood, social avoidance, general anxiety and compulsive behaviour. The questionnaire has shown to have good test-retest reliability (r = .81). Internal consistency for the subscales has coefficients ranging from .75 to .83, with a mean of .80 (Esbensen et al., 2003).

**Anxiety Triggers Measure (to be developed)**

This measure will be developed using the information gathered during Stage 1 with parents/carers. This will allow us to further identify whether there is a syndrome specific appearance of anxiety in WS or whether these issues are individually variable. The measure will take approximately 5-10 minutes to complete, will be piloted and will use an appropriate coding scheme.

**Waisman Activities of Daily Living Scale (Maenner et al., 2013)**

This 17-item parent/carer questionnaire assesses the level of independence an individual has for performing daily living activities. Items are rated on a three-point scale: 2 = ‘Independent or does on own’, 1 = ‘does with help’ and 0 = ‘does not do at all’. The W-ADL has high reported internal consistencies within these samples (Cronbach’s Alphas ranging from 0.88-0.94).

**WHOQOL-BREF & Disabilities Module (Power & Green, 2010)**

This assesses quality of life in adults with physical or intellectual disabilities. The proxy informant measure consists of 39 items, which relate to the past two weeks, and are rated on a five-point scale, ‘not at all’, ‘a little’, ‘moderately’, ‘mostly’ and ‘totally’. Caregivers are asked to bear in mind what is important to the person they are answering for and what makes them happy/sad. Internal consistency was found to be acceptable (Cronbach’s Alpha: 0.60 – 0.79) and high for the additional WHOQOL-DIS module in an intellectually disabled group (Cronbach’s Alpha: 0.8).

**Sensory Experiences Questionnaire (Baranek, David, Poe, Stone & Watson, 2006)**

This is a brief caregiver questionnaire used to assess how well young children with autism and developmental delays process sensory information in daily tasks. The items reflect five sensory domains: Gustatory-Olfactory, Tactile, Auditory, Visual and Vestibular-Proprioceptive. Caregivers are asked to report the frequency of sensory behaviours on a five-point scale; ‘almost never’ to ‘almost always’. The SEQ has excellent internal consistency, Cronbach’s Alpha, 0.8 and test-retest reliability, ICC=.92 (Little et al., 2011).

**Appendix B**

**Mood diary**

Parents/carers will be asked to assess their child's mood over 28 days at home. This will be available to download as a free app and will include a series of multiple choice and short answer questions. Individuals who do not own a smart device for the app will be provided with the appropriate equipment from the CCND for the duration of the study. This assessment aims to document the frequency and severity of anxiety in individuals with WS and to report the potential triggers of negative moods and elevated anxiety. This should take no longer than 5 minutes each day in order to minimise disturbance to the participant’s daily routine. Data inputted on this app will be stored securely and the information will only be made accessible to the individuals themselves and relevant researchers at the CCND. We will aim to produce an informational video in order to explain how to use the app and how to record the video diaries.

If we are unable to develop an app, we will use paper versions of the diaries or will provide the diaries through a secure online system. This would only be accessible by parents/carers and by researchers working on the project and data will be collected and stored in accordance with the Data Protection Act.

**Video diary**

We will ask individuals with WS to complete a daily 5 minute video diary (during the same period as the app). We will provide a camera for the duration of the study and will request that parents/carers assist individuals with reminders and with setting up the recordings each day. We will provide information to parents expressing the importance of giving their child/person they care for privacy during the recordings. We will also provide instructions for parents/carers on how to set up the camera and record the videos and a set of questions for the individuals to answer each day. Recordings will be stored securely on an SD card and will be date and time stamped. Using video cameras to record individuals with intellectual disabilities has been used in previous research and we will follow a similar method and protocol to Jahoda et al. (2010). The video diary will be used by the individual with WS to record their own thoughts and feelings about each day. Questions will focus on both positive and negative emotions.

We will provide verbal instructions/questions which can be played by the participant during the recordings and this will be available via a function on the parent app. We will also provide instructions/questions on a symbol information sheet.

These are some examples of the types of questions we may ask:

1. What made you feel happy today?
2. Did anything make you feel sad today?
3. Did anything make you feel scared today?
4. What was the best thing that you did today?

**Vineland Adaptive Behaviour Scale (Sparrow, Cicchetti & Balla, 2005)**

Parent/carer interview measure that assesses adaptive behaviour in four key domains: daily living, communication, socialisation and motor skills. It is used for typically developing children (aged from birth to 18) and is also widely used for children and adults with intellectual disabilities. Response options are scored on a 0, 1, 2 and DK scale whereby 2 = ‘Usually’, 1 = ‘Sometimes/Partially, 0 = Never and DK = ‘Don’t Know’. Internal consistency for the total score was high when tested in children and adolescents with intellectual disabilities (Cronbach’s Alpha = .99) and the VABS is highly correlated with the Social Functioning Scale for the Mentally Retarded (r=.93) (de Bildt et al., 2005).

**Wechsler Abbreviated Scale of Intelligence** **(WASI; Weschler, 1999):**

Psychometric assessment designed to assess intellectual functioning in adults and children (ages 6-90). It is comprised of two verbal IQ tests (Vocabulary and Similarities) and two performance IQ tests (Block design and Matrix Reasoning). Administration of the WASI takes approximately 30 minutes. Internal consistency for the entire scale has been shown to be high (.961) (Axelrod, 2002).

**One Word Receptive & Expressive Picture Vocabulary Test** **(Brownell, 2012):**

These tests take 20 minutes each to administer and are norm referenced verbal intelligence assessments which measure an individual’s understanding of the meanings of words and their ability to name objects, actions or concepts. Internal consistency for the EOWPVT-4 is high, ranging from 0.93-0.97 and test-retest reliability is 0.97 for standard scores. Similarly, internal consistency for the ROWPVT-4 ranges between 0.94-0.98 for various age groups and test-retest reliability is 0.91 for standard scores.

**Glasgow Anxiety Scale (GAS-ID; Mindham & Espie, 2003):**

This 27 item self-report measure is designed to assess state anxiety in those with intellectual disabilities on a 3 point scale of ‘never’, ‘sometimes’ or ‘always’. An anchor event (one week prior to testing) is established and questions are asked in relation to how the participant has been feeling since the event. A cut-off score of 13 has been established as an indicator of an anxiety diagnosis. The questionnaire has high internal consistency (Cronbach's Alpha: 0.96) and test-retest reliability at one-month (0.93). There is also an informant report version which will also be used in the study.

**Spence Children’s Anxiety Scale** **(Spence, 1978):**

This is a 44-item child self-report measure designed to evaluate symptoms relating to separation anxiety, social phobia, obsessive-compulsive disorder, panic agoraphobia, generalized anxiety and fears of physical injury. It has a 4-point rating scale ranging from ‘never’ to ‘always’. Internal consistency for the full scale was high (Cronbach's Alpha = 0.92). Test-retest reliability after 6 months was acceptable for the total score (0.60). The scale was also found to have good convergent, divergent and construct validity. There is also an informant report version which will also be used in the study.

**Kiddie-Schedule of Affective Disorders** **(K-SADS; Endicott & Spitzer, 1978):**

This is a semi-structured interview based on the DSM-IV. It consists of an unstructured introductory interview (10-15 mins), a screening assessment (82 items) and then five diagnostic supplements (affective disorders, psychotic disorders, anxiety disorders, behavioural disorders, substance abuse and other disorders). The majority of items are scored using a 0-3 point rating scale, 0 = ‘no information is available’, 1 = ‘symptom not present’, 2 = ‘subthreshold levels of symptomatology’, 3 = ‘threshold criteria’. The K-SADS-PL has strong psychometric properties and test-retest reliability is high (Kaufman et al., 1997). This interview has also been successfully used in a previous study with individuals with Williams Syndrome (Dodd & Porter, 2009).

**NB.** The K-SADS-PL is based on the DSM-IV and we are currently unaware of an updated version for the DSM-5. Whilst the psychometric properties of the current version are strong, we will use a newer version if one is released, as this will be a better option for our participants. We anticipate that the language, format and length of a new version will be similar to the existing version. Alternatively, we may develop a modified version of the K-SADS-PL, in order to bring it up to date with the DSM new criteria.

**Experimental Tasks:**

* **Task 1 – Interpretation Bias Task (developed by Researchers at the University of Reading):** This e-prime task has been newly developed at the University of Reading and has been developed for use in typically developing children aged 4+. It follows the same principles of existing measures in the field but has been adapted to be appropriate for those with a younger developmental age. The computer based space-themed task assesses interpretation bias using high and low pitched tones. These are listened to through headphones at a standardised volume. The tones are presented for a period of 250ms and are based on five different musical instruments (e.g. the guitar and piano). Learning and practice trials are utilised to teach participants the associations with high tones for ‘happy aliens’ and low tones for ‘angry aliens’. Pictures of happy and angry aliens are included to facilitate learning. Practice trials continue until participants achieve a 60% accurate response rate. Each experimental trial is preceded by a learning block to account for memory recall bias. The four experimental trials involve the presentation of 7 or 8 tones (5 ambiguous and 2/3 high/low tones). Participants are required to indicate whether the tone is from a happy or angry alien (even when the tone is ambiguous). Reaction times are recorded. It is hypothesised that those participants with high anxiety will interpret more of the ambiguous tones as ‘angry’ compared with participants who are less anxious. This task will take approximately 20 minutes to complete. Task validity and the collection and analysis of normative data is currently in progress.
* **Task 2 – Intolerance of Uncertainty HiLo Card Game (developed by Researchers at the University of Reading):** The first part of the task checks labelling of emotional faces and takes 2/3 minutes to complete. Participants are asked to state whether pictures of faces are happy, sad, angry or neutral (or a neutral object). The e-prime computerised card game includes seven cards with circles of different sizes. Participants are presented a fixation dot in the centre of the screen, followed by one of the seven cards and a mystery card. Participants are asked to decide whether the mystery card will be bigger or smaller than the presented card, and indicate their answer using two keys on a keyboard. There is a practice round and then 3 experimental rounds for uncertainty (26 trials each) followed by 3 experimental rounds for uncertainty + threat (26 trials each). The uncertainty and threat condition involves the presentation of an angry face on the screen each time the mystery card is shown to be a bigger circle. These angry faces may produce mild anxiety. Reaction times are recorded. After completing the 3 rounds for condition, subjective anxiety is measured by asking the participant how certain and how anxious they felt answering questions about each card. This will be rated on a scale of 1-10 (1=very anxious/very uncertain to 10=not anxious at all/very certain. Task validity and the collection and analysis of normative data is currently in progress.

**Physiological measurement:**

We will record electrodermal activity (skin responses) and pulse rate to measure the individual’s level of arousal whilst they are completing the experimental task using the BioNomadix Wireless Pulse and EDA device from Biopac systems. This equipment is non-invasive and simply requires two electrodes to be stuck to two of the participants fingers on one hand (can also be connected to another body part if this is not suitable, e.g. foot). These electrodes will be connected by two wires to a transmitter watch that the participant will also be required to wear on their wrist/foot. The watch wirelessly connects to the recording system and transmits the information from the electrodes to a laptop computer. This measures skin conductance and is painless, quick to set up and a simple yet robust method of measuring arousal. The measurement of electrodermal activity and pulse rate has been used in a variety of studies in the intellectually disabled population to measure autonomic arousal (Doherty-Sneddon et al., 2009; Lane, Reynolds, & Dumenci, 2012; Skwerer et al., 2008; Vos et al., 2012); we will follow similar guidelines and protocols to these studies.

**Readiness for Cognitive Behavioural Therapy (Dagnan & Chadwick, 1997):**

This 15 minute assessment has been used previously with individuals with intellectual disability to assess participant’s cognitive capacity and ability to benefit from CBT methods.

This assessment first involves testing an individual’s ability to recognise five facial expressions from makaton symbols (Walker, 1985). These emotions are: happy, sad, frightened, anxious and angry. The ability to link activating events to emotions is measured by giving individuals six scenarios and a corresponding emotion. For example: ‘you want to go on a special trip but there is only one place and your friend is chosen to go instead and you feel sad’. Individuals will then be asked ‘What would you be thinking or saying to yourself?’ If an individual can get all scenarios correct then it is judged that they will be able to benefit from CBT interventions. This assessment should not be seen as concerned with excluding people from cognitive therapy. Instead it assesses the abilities that a person has in order to identify the best form of intervention that will be most advantageous to an individual and allows researchers/clinicians to made suitable decisions about the necessary adaptations to be made to therapy.

**The Behavior Rating Inventory of Executive Function Adult** **Version** (**BRIEF-A; Roth, Isquith & Giola, 2005):**

The BRIEF-A is an informant measure of executive functioning and self-regulation for adults 18-90 years. It is comprised of 75 items which correspond to the clinical scales: inhibit, self-monitor, plan/organise, shift, initiate, task monitor, emotional control, working memory and organisation of materials.

**Loneliness and Social Dissatisfaction Questionnaire (LSSQ; Asher, Hymel & Renshaw, 1984):**

This self-report questionnaire has 24 items and measures social adequacy and feelings of loneliness. Eight of the items are filler items which focus on hobbies and preferred activities in order to encourage participants to be more open and relaxed when giving their attitudes on various topics. Each item is scored on a five-point scale of how true the statements are to a person, ‘always true’, ‘true most of the time’, ‘true sometimes’, ‘hardly ever true’ and ‘not true at all’. Higher scores indicate more loneliness and social dissatisfaction. The questionnaire has been found to have high internal consistency in a sample of children with learning disabilities (Cronbach’s alpha = .92) (Al-Yagon, 2007).

***Repetitive Behaviour Questionnaire***(RBQ; Moss & Oliver, 2008)

The RBQ is an informant questionnaire for use with children and adults with a range of intellectual abilities. It is suitable for use with verbal and non-verbal individuals. The RBQ consists of 19 items that comprise five subscales: stereotyped behaviour, compulsive behaviour, insistence on sameness, restricted preferences and repetitive speech. Informants rate the frequency of behaviour over the preceding month on a five-point Likert-type scale ranging from ‘never’ to ‘more than once a day’. Internal consistency was good at the full-scale level (Cronbach’s Alpha = .80). Test-retest reliability ranged from .61 to .93, and concurrent validity and content validity between the RBQ and the repetitive behaviour subscale of the Autism Screening Questionnaire was good (.6, *p*<.001) (Moss, Oliver, Arron, Burbidge, Berg, 2009).

***Intolerance of Uncertainty Scale*** (Rodgers et al., 2012)

This parent 12-item scale measures an important construct that appears to be related to anxiety. Parents are asked to indicate the extent to which a list of statements is like their child, on a scale from 1 (not at all like them) to 5 (entirely like them). Scores across the 12 items are summed to yield a total score; higher scores reflect greater levels of intolerance of uncertainty. The parent version of the Intolerance of Uncertainty scale has been found to have excellent internal consistency in both parents of children with autism (α = 0.90) and parents of typical children (α = 0.90; Boulter et al. [2014](http://link.springer.com/article/10.1007/s10803-016-2721-9/fulltext.html#CR5)).

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