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Behavioural Neurology

Increased persuadability and credulity in people with corpus callosum dysgenesis

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ABSTRACT

Corpus callosum dysgenesis is one of the most common congenital neurological malformations. Despite being a clear and identifiable structural alteration of the brain's white matter connectivity, the impact of corpus callosum dysgenesis on cognition and behaviour has remained unclear. Here we build upon past clinical observations in the literature to define the clinical phenotype of corpus callosum dysgenesis better using unadjusted and adjusted group differences compared with a neurotypical sample on a range of social and cognitive measures that have been previously reported to be impacted by a corpus callosum dysgenesis diagnosis. Those with a diagnosis of corpus callosum dysgenesis ($n = 22$) demonstrated significantly higher persuadability, credulity, and insensitivity to social trickery than neurotypical ($n = 86$) participants, after controlling for age, sex, education, autistic-like traits, social intelligence, and general cognition. To explore this further, we examined the covariance structure of our psychometric variables using a machine learning algorithm trained on a neurotypical dataset. The algorithm was then used to test whether these dimensions possessed the capability to discriminate between a test-set of neurotypical and corpus callosum dysgenesis participants. After controlling for age and sex, and

Abbreviations: AQ, autism quotient; ASD, autism spectrum disorder; CCD, corpus callosum dysgenesis; ETQ, epistemic trust questionnaire; GS, Gullibility Scale; ICAR, international cognitive ability resource (progressive matrices); ICC, intraclass correlation coefficient; LOOCV, leave-one-out-cross-validation; McA-SL, MacArthur social ladder; NT, neurotypical; PC, principal component; R-GPTS, revised green paranoid thoughts scale; SIS, social intelligence scale.

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with Leave-One-Out-Cross-Validation across 250 training-set bootstrapped iterations, we found that participants with a diagnosis of corpus callosum dysgenesis were best classed within dimension space along the same axis as persuadability, credulity, and insensitivity to social trickery, with a mean accuracy of 71.7%. These results have implications for a) the characterisation of corpus callosum dysgenesis, and b) the role of the corpus callosum in social inference.

1. Introduction

Corpus callosum dysgenesis (CCD) is the collective term for congenital abnormalities of the corpus callosum. They include complete (agenesis) or partial absence, as well as a thick or thin (hypoplastic) corpus callosum (Edwards et al., 2014). The prevalence of CCD is estimated at 1–7 in 4000 live births, making CCD one of the most common congenital neurological malformations (Glass et al., 2008; Wang et al., 2004). While CCD can be detected via ultrasound or neuroradiological imaging from as early as 20 weeks' gestation (Pooh, 2009), there exist few behavioural phenotypes to qualify this diagnosis.

Individuals with CCD range in clinical presentation from being minimally impacted in cases of isolated CCD to severe cognitive impairment (Spencer-Smith et al., 2020), usually associated with syndromic forms of CCD (Brown & Paul, 2019; Edwards et al., 2014; Paul et al., 2007). Observational studies have noted difficulties in understanding second order meaning in language, such as proverbs (Brown et al., 2005; Rehmel et al., 2016), and deficits in executive function, such as difficulties in inhibition, cognitive flexibility, decision-making, and problem-solving (Brown et al., 2012; Brown & Paul, 2000; Marco et al., 2012). One particular class of difficulties reported within CCD are in the domain of social cognition. This includes poorer social insight, social logic, and self-perception (Brown & Paul, 2000; Kosky et al., 2021; Symington et al., 2010) as well as deficits in inference relating to first- and second order beliefs (Symington et al., 2010) and in the interpretation of social intentions (Brown & Paul, 2019). Indeed, difficulties in relationships and navigating the social world have been identified as a critical source of distress in those with a diagnosis of CCD (Maxfield et al., 2021).

Phenotypic features of CCD overlap substantially with those of autism spectrum disorders (ASD) (Demopoulos et al., 2015) – a diagnosis with a poorly defined structural neural correlate. This overlap includes over-adherence to social norms (Brown et al., 2021), the use of repetitive language, and communication difficulties (Paul et al., 2014). Children with CCD exhibit higher incidence rates of scoring above the clinical cut off using the Autism Quotient (Baron-Cohen et al., 2001, 2006) than the neurotypical (NT) population, with an estimated incidence rate of 44.6% (21/47) (Baron-Cohen et al., 2006) as rated by their parents, implying substantial comorbidity with CCD.

The social difficulties reported in CCD raise the question as to which variations in social functioning are most characteristic of CCD, and whether these variations can be explained as existing on a continuum with the NT population. Here, motivated by prior work on the social difficulties reported in CCD (Brown & Paul, 2000, 2019; Kosky et al., 2021; Maxfield et al., 2021; Symington et al., 2010) the focus of this work was on identifying any consistent psychometric differences that could not be explained by age, sex, education, poorer general cognitive ability, or autistic traits. In addition, we asked whether extremes within the psychological covariance of NT participants may explain phenotypic changes associated with CCD. This includes social traits such as persuadability and social intelligence, as well as general cognitive traits such as abstract non-verbal reasoning. This will provide additional instruments for understanding the role of defined anatomical deficits in CCD, alongside underpinnings of performance on refined cognitive tasks.

2. Materials and methods

We report how we determined our sample size, all data exclusions (if any), all inclusion/exclusion criteria, whether inclusion/exclusion criteria were established prior to data analysis, all manipulations, and all measures in the study.

2.1. Participants

Data was collected from two distinct participant cohorts (summarised in Table 1) – a NT group, acting as a control, and a set of participants with a CCD diagnosis, as confirmed via magnetic resonance imaging (Fig. 1). This study was not preregistered.

The CCD cohort consisted of 23 unique participants. These participants were recruited through convenience sampling from the Australian Corpus Callosum Dysgenesis Database (a database of individuals with disorders of the corpus callosum and immediate family members, created by the Brain Development and Disorders Laboratory) and through partnerships with the family support organisation Australian Disorders of the Corpus Callosum (AusDoCC; https://www.ausdocc.org.au). Data from the CCD group was collected between June and November 2021. Twelve of these participants had also completed the Autism Quotient, Social Intelligence Scale, and Gullibility Scale (see *Measures*) at a previous time point, collected between May and August 2020; this permitted a test–retest reliability analysis to be conducted on measures completed at both time periods by these CCD participants. Those from the CCD cohort who had participated in the 2020 survey were compensated with retail gift vouchers (valued at $15 AUD), with all CCD participants receiving retail gift vouchers (valued at $45 AUD) for their participation in the 2021 survey.

The NT cohort were recruited through the online research platform Prolific Academic. All respondents were between the

Table 1 – Descriptive statistics (mean [± SD]) for all measures completed by NT and CCD participants.

Variable	NT (sample who completed measures previously)	NT	CCD (sample who completed measures previously)	CCD
n	110	86	12	22
Age	29.13 [7.89]	29.36 [7.60]	51.75 [18.38]	47 [17.26]
Sex	38.2% Female	40.2% Female	50% Female	59.10% Female
Education (*n*)				
Primary	0	1		0
Secondary (e.g., high school cert)	32	20		12
Undergrad (e.g., BSc, MBBS)	55	42		5
Postgrad (e.g., MSc, MA, PGc)	21	21		5
Doctorate (e.g., PhD, DClinPsy)	2	2		0
ICAR	6.66 [2.37]	6.56 [2.31]		4.73 [2.62]
Paranoia				
Persecutory ideation	13.2 [5.67]	12.2 [4.94]		15.1 [8.46]
Social reference	18.3 [7.15]	16.0 [6.08]		15.7 [6.21]
Gullibility				
Insensitive	18.2 [6.49]	17.9 [6.26]	23.9 [7.95]	22.8 [8.34]
Persuadable	14.6 [6.73]	13.1 [6.44]	22.3 [8.51]	20.2 [8.46]
Epistemic trust				
Trust		24.1 [4.85]		27.4 [4.71]
Mistrust		21.6 [4.29]		20.4 [5.39]
Credulity		12.9 [4.76]		18.6 [7.90]
MacArthur social ladder				
National	55.6 [20.16]	52.5 [21.02]		51.1 [24.15]
Community	48.1 [20.63]	49.0 [19.71]		50.5 [28.64]
Social intelligence		95.67 [23.46]	79.78 [32.99]	82.9 [21.08][a]
Autism				
Short scale		65.5 [9.96]	74.6 [14.10]	75.6 [12.13][a]
Revised scale		34.9 [4.92]	38.7 [7.54]	41.0 [6.45][a]

Education = highest level of education achieved as of the current date.

[a] These figures only include participants in group two who completed the Social Intelligence and Autism Quotient scales in CCD (n = 20). While the CCD and NT participants differed on characteristics such as Age and Sex, we aimed to control for these disparities by including Age, Sex, and General Cognitive Ability (ICAR) as confounders in all regression models that assessed group differences and regressed them against all psychometric variables during dimension reduction. This reduces the chance that our results may be explained by these demographic disparities.

ages of 18 and 60, had a minimum approval rate of 90% on Prolific Academic and reported no psychiatric or neurological diagnoses, that they resided in Australia, and that they spoke fluent English. All NT inclusion criteria were established prior to data analysis. During the month of April 2021, 110 NT participants took part in the first round of data collection. Of these 110 participants, 95 (86.3%) completed a second round of data collection during August to September of that same year. All NT participants were paid, through Prolific Academic, £3 for their participation at time point 1 and £5.13 for their participation at time point 2.

One NT participant failed over two checks included in the survey to ensure attentiveness (out of ten), while eight NT participants did not answer all required questions in the survey. These participants were consequently excluded from all analyses, leaving a final sample size of 86. All CCD participants passed all attention checks (out of ten) included in the survey. One CCD participant reported visual difficulties whilst completing the survey, and consequently their data was excluded from all analyses. This resulted in a final sample size of 22 CCD participants, with 12 CCD participants who had repeated measures data available for the test–retest analysis of the Gullibility Scale, and 10 CCD participants who had repeated measures data available for the test–retest analysis of the Social Intelligence Scale and Autism Quotient.

2.2. *Measures*

All experimental and control measures were administered to CCD and NT participants. We conducted independent analyses to assess the difference between groups on each measure, in addition to completing dimension reduction to assess whether covariance between measures differed within groups (see Fig. 1).

2.2.1. *Experimental measures*

2.2.1.1. GULLIBILITY. Participant gullibility was evaluated using the 12-item Gullibility Scale (GS) (Teunisse et al., 2020). This measure was included in this study due to clinical reports that CCD participants were more susceptible to social manipulation than their neurotypical contemporaries and prior qualitative work emphasising difficulties in understanding social cues as being integral to the experience of CCD participants (Maxfield et al., 2021). Furthermore, a pilot experiment (data not included) suggested that a more in-depth study was warranted. The GS is comprised of two subscales, each consisting of six questions. The first subscale, Persuadability, measures how readily a person thinks they can be fooled (e.g., ‘My friends think I'm easily fooled; My family thinks I'm a good target for scammers’). The second subscale, Insensitivity, measures the degree to which a participant believes they would be unable to

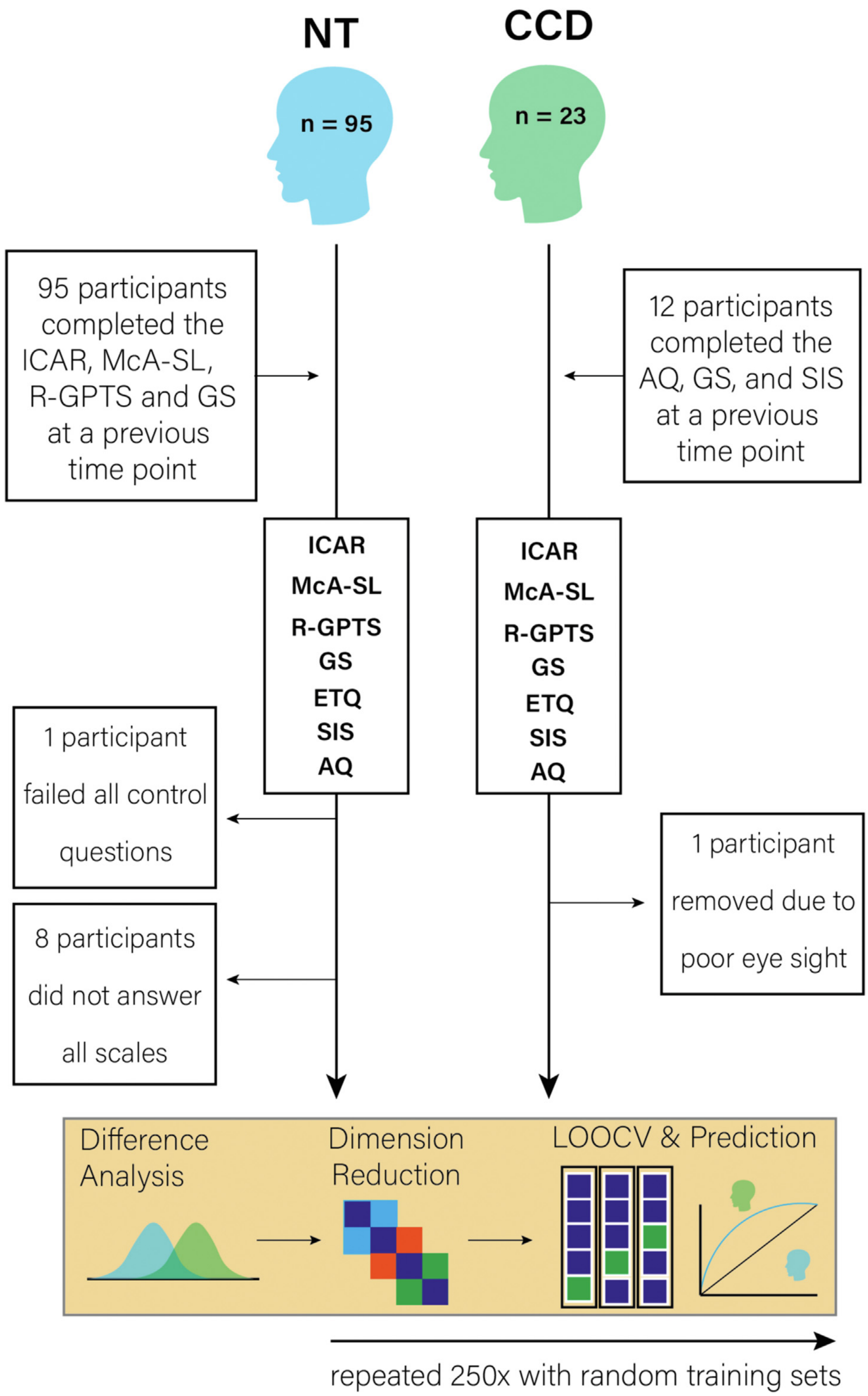

Fig. 1 – Study design. NT = neurotypical; CCD = participants with a diagnosis of corpus callosum dysgenesis; ICAR = matrix reasoning – international cognitive ability resource; R-GPTS = revised green paranoid thoughts scale; McA-SL = MacArthur social ladder; GS = gullibility scale; AQ = autism quotient; ETQ = epistemic trust questionnaire; SIS = social intelligence scale; LOOCV = leave-one-out-cross-validation.

detect social cues as to when they are being manipulated (e.g., ‘I'm pretty poor at working out if someone is tricking me’). Each item is measured on a 7-point scale, with participants rating how strongly they believe each statement from 1 (strongly disagree) to 7 (strongly agree). High scores are taken to be indicative that the participant is likely to be considered socially gullible. Due to the high correlation between these subscales, persuadability and insensitivity were also combined to create a single 'Gullibility' score, to facilitate later machine learning analyses (see Dimension Reduction & Prediction).

2.2.1.2. Epistemic trust. Motivated by qualitative work that suggests CCD participants may be overly trusting (Maxfield et al., 2021) and have difficulties understanding the mental state of others (Symington et al., 2010), we administered the Epistemic Trust, Mistrust and Credulity Questionnaire (ETQ) (Campbell et al., 2021) to assess whether those who were more readily persuadable were also generally more trusting and credulous. The ETQ includes three subscales: trust (e.g., 'I usually ask people for advice when I have a personal problem'), mistrust (e.g., 'I'd prefer to find things out for myself on the internet rather than asking people for information'), and credulity (e.g., 'I am often considered naïve because I'll believe almost anything'). Trust and mistrust have different statistical associations with scales of abuse and neglect (Teunisse et al., 2020), and therefore have been kept as separate subscales. Each item is rated on a scale of one (strongly disagree) to seven (strongly agree). Scores on the Trust, Mistrust, and Credulity subscale range from 6 to 42, with higher scores indicating higher Trust, Mistrust, and Credulity, respectively.

2.2.1.3. Paranoia. Since CCD and paranoia both may affect the ability of an individual to intuit the thoughts and intentions of others accurately (Fletcher & Frith, 2009; Symington et al., 2010) the Revised Green Paranoid Thoughts Scale (Freeman et al., 2021) was also included (R-GPTS). This questionnaire surveys the participant regarding their beliefs about the actions and motivations of others they have interacted with over the past month. This includes two, nine item subscales, one assessing social reference ('Reference'; e.g., 'I spent time thinking about friends gossiping about me') and a second assessing persecutory ideation ('Persecution'; e.g., 'People wanted me to feel threatened, so they stared at me'). Each item was scored from 0 (not at all) to four (totally). Previous use of the scale in clinical and non-clinical populations determined cut-off scores: average (Reference: 0–9; Persecution: 0–4), elevated (Reference: 10–15; Persecution: 5–10), moderately severe (Reference: 6–20; Persecution: 11–17), severe (Reference: 21–24; Persecution: 18–17), and very severe (Reference: 25+; Persecution: 28+). Persecutory ideation and social reference subscale scores were combined into a single 'Paranoia' score to reduce the effect of collinearity in later machine learning analyses (see Dimension Reduction & Prediction).

2.2.1.4. Relative social standing. CCD participants have reported that they commonly feel unable to find meaningful employment, are discriminated against, and often feel inferior to others (Maxfield et al., 2021). The MacArthur Scale of Subjective Social Status (McA-SL; hereafter known as the MacArthur Social Ladder) (Adler et al., 2000; Goodman et al., 2003) was used to assess how low or high in the social hierarchy participants view themselves relative to others. It consists of two sub-scales: one for their social ranking within their local community and another for their social ranking nationally. Each scale runs from 0 to 100, with participants being told that 0 means believing that they are ranked at the very bottom of their community/nationally, and 100 means believing that they are ranked at the very top of their community/nationally. The two MacArthur social ladder scales were averaged to generate a mean score for later machine learning analyses, due to their high correlation and identical scale resolution (see Dimension Reduction & Prediction).

2.2.2. *Control measures*

2.2.2.1. Autism. The phenotype of ASD is reported to overlap significantly with the phenotype of CCD (Demopoulos et al., 2015) – we sought to clarify this prior observation and assess whether ASD traits in CCD are distinguishable from the variance in the NT population. The prevalence of autistic-like traits in the participant cohorts was assessed using the Autism-Spectrum Quotient (AQ) (Baron-Cohen et al., 2001). The AQ is questionnaire consisting of 50 questions, rated on a 4-point scale, ranging from 'definitely disagree' to 'definitely agree'. The unadjusted and adjusted data analyses to examine differences between group, however, were based on the short version of the AQ (sAQ) (Hoekstra et al., 2011), which consists of 28 questions selected from the larger AQ; this was done because this sub-scoring method has been shown to be more reliable and internally consistent across clinical and non-clinical samples (Goodman et al., 2003). Possible scores on the sAQ range from 28 to 112, with higher scores indicating that participant has more autistic-like traits. A score of 72 is generally considered a useful cut-off for determining if individuals have a significant level of autistic-like traits (Baron-Cohen et al., 2001), although this does not in itself fulfil the requirements for a diagnosis of autism.

2.2.2.2. Social intelligence. Given the previously reported difficulties of CCD participants in understanding the emotional and social intentions of others (Kosky et al., 2021), Social intelligence was assessed using a 21-item questionnaire using the Tromsø Social Intelligence Scale (SIS) (Silvera et al., 2001) which was translated to English by Grieve and Mahar (Grieve & Mahar, 2013). This scale measures three aspects of social intelligence: social information processing (predictions of others' behaviour), social skills (the ability to interact with others), and social awareness (the detection of social cues). Responses were rated on a 7-point scale from 1 (describes me poorly) to 7 (describes me well). Higher scores indicated higher social intelligence, with scores ranging from 21 to 147.

2.2.2.3. Abstract non-verbal reasoning. It was necessary to control for any general cognitive variance that might otherwise explain differences between and within NT and CCD groups as it has been previously observed that CCD participants have difficulties completing complex, abstract tasks (Hearne et al., 2019). We assessed abstract non-verbal reasoning using the progressive matrices task within the Interactive Cognitive Ability Resource (ICAR) (Condon and Revelle, 2014). Participants are required to solve ten puzzles in addition to one practice puzzle. In each puzzle, participants are presented with nine shape configurations that follow a specific rule and asked to select a tenth configuration that fitted the rule from six possible answers. Scores on this test range from 1 to 10, with higher scores indicating better abstract non-verbal reasoning. Legal copyright restrictions prevent public archiving of the ICAR-Raven's Matrices which can be obtained from the copyright holders in the cited references, or can be retrieved from the ICAR project (https://icar-project.com/).

2.3. Procedure

All procedures relating to this study were approved by the University of Queensland human research ethics committee (approval ref: 2014/HE000535), and the design of the study itself was created with input from sitting members of the Executive Committee of the Australian Disorders of the Corpus Callosum (AusDoCC) support group. The Executive Committee includes members with a lived experience of CCD. All psychometric questionnaires were electronically administered remotely using the Gorilla Experiment Builder for the behavioural sciences (Anwyl-Irvine et al., 2020), except for the survey administered to the CCD group in 2020, which was electronically administered in the laboratory. The psychometric measures were presented to each participant in a random order, with the order of the questions within each measure similarly randomised. Numeric values and visual indicators were not rendered on a scale until the participant provided an input (via mouse click) to the computer, after which these indicators became visible.

2.4. Analysis

All analyses were conducted in *R* (4.0.0) (R Core Team, 2020) on a Mac OS (Big Sur, 11.5.2; 2.6 GHz 6-core Intel i7).

2.4.1. *Difference analysis*

For analytic clarity, we initially conducted unadjusted comparisons to quantify the raw differences in measures between NT and CCD samples prior to adjusting for confounders. Kruskal–Wallis tests were conducted to assess unadjusted group differences for each scale. The ‘psych’ (Revelle, 2020) package (2.0.9) was used for descriptive analytics, t-tests, and Kruskal–Wallis analyses.

We then progressed to adjusted analyses to assess differences between NT and CCD samples by additionally controlling for confounders using linear models. Given the relatively small CCD sample and wanting also to control for additional variables such as age and sex in our regression models, we further tested the stability of group differences further using Bayesian regression models which provide uncertainty estimates around each estimated coefficient. Bayesian regression models were fit using the ‘brms’ (Bürkner, 2017) package, which utilises the ‘Stan’ programming framework for hierarchical Bayesian estimates and employed a Markov-Chain Monte Carlo (MCMC) method based on a No U-Turn Sampler (NUTS) to draw from the posterior distribution. Each model used four MCMC chains, and each chain ran 2000 iterations (1000 warmup). All models were checked for adequate convergence ($\widehat{R} < 1.1$) and posterior predictive checks were conducted to ensure the model was able to simulate the true observations adequately.

2.4.2. *Dimension reduction and prediction*

We sought to test whether the psychological phenotype of CCD may be explained by exaggerations to natural psychological variation within NT populations. To do this we trained an unsupervised model on a subsampled set of NT data. This provided an estimate of the covariance structure latent within the psychological variation of NT participants.

We then asked the model to predict whether a test participant from test set NT or CCD samples could be distinguished along the pre-established psychological covariation approximated within the training NT group.

We included nine variables in the dimension reduction: the ICAR, revised Autism Quotient, Social Intelligence, Gullibility, Trust, Mistrust, Credulity, Paranoia, and the McA-SL. We chose to use dimension reduction (Principal Component Analysis) to understand better how the interrelationship between features may be characteristic of CCD, rather than their independent contribution in a large linear model. As the sAQ contains several items that overlapped with the Social Intelligence Scale, the decision was made to remove these items and create a Revised sAQ sub-scale to avoid collinearity in the analysis (R-sAQ; see Supplementary materials; Table S1). We then regressed out the influence of age and sex on each variable across both NT and CCD data sets using linear models. The resulting residuals of these regressions for each variable were then used for the dimension reduction and prediction.

We first conducted unsupervised exploratory dimension reduction on a random training set of NT data ($n = 60$, ~70%) using the ‘factoextra’ (Kassambra & Mundt, 2020) package. This uses the principal components of the data extracted using the ‘prcomp’ function to assess the latent structure that may explain variance between multiple measures. We retained dimensions explaining more than 10% of the variance. We used these top dimensions obtained from the training data to predict whether a participant was a member of either the CCD or NT group using the left-out test participants in the NT sample ($n = 26$) and all participants in the CCD ($n = 22$) group. Predictions were made by applying Leave-One-Out-Cross-Validation (LOOCV) to three different classifiers – Random Forest (RF), Support Vector Machine (SVM), and a Bayesian General Linear Model (Bayes GLM). From the winning model (Fig. S4) we assessed the distribution of accuracy and extracted the confusion matrix to assess the sensitivity and specificity of the model.

To ensure our dimension reduction and prediction procedure were not biased to a particular training set, we repeated the above procedure 250 times for each model using random NT training and test data on each bootstrapped iteration (Training $n = 60$; ~70%; Test $n = 26$; ~30%). We then report the average variance explained and loading of variables on each of the top dimensions from the principal component analysis, the average accuracy of the winning LOOCV model, and averaged confusion matrices across all 250 bootstrapped iterations. A confusion matrix allows the estimate of the model's ability to distinguish between true- and false-positives, and true- and false-negatives, in this case averaged over all 250 bootstrapped iterations. Our iterative bootstrap procedure allows us to quantify the error inherent in the method and prevents overfitting to one training sample.

2.4.3. *Data availability*

All anonymised data and analysis code are freely available from https://github.com/Brain-Development-and-Disorders-Lab/Barnby_etal_2021.

3. Results

The NT participants were relatively young, mostly male, and mostly educated at the undergraduate level (see Table 1). The CCD participants were significantly older than NT participants (CCD mean[SD] age = 47 [17.26]; NT mean[SD] age = 29.4 [7.60]; t (25.01) = 5.14, 95% CI: 9.90, 23.13; $p < .001$), were mostly female (CCD = 59.1% female; NT = 40.2% female) and were mostly educated at the high school level (see Table 1). For a comparison with previously reported data see the Supplementary materials (Text S1).

3.1. *Group differences*

Simple unadjusted Wilcoxon-rank sum tests of difference between NT and CCD participants (Fig. 2) showed that CCD participants were on average lower in abstract non-verbal intelligence (ICAR; $\chi^2(1) = 10.06$, $p = .002$). CCD participants

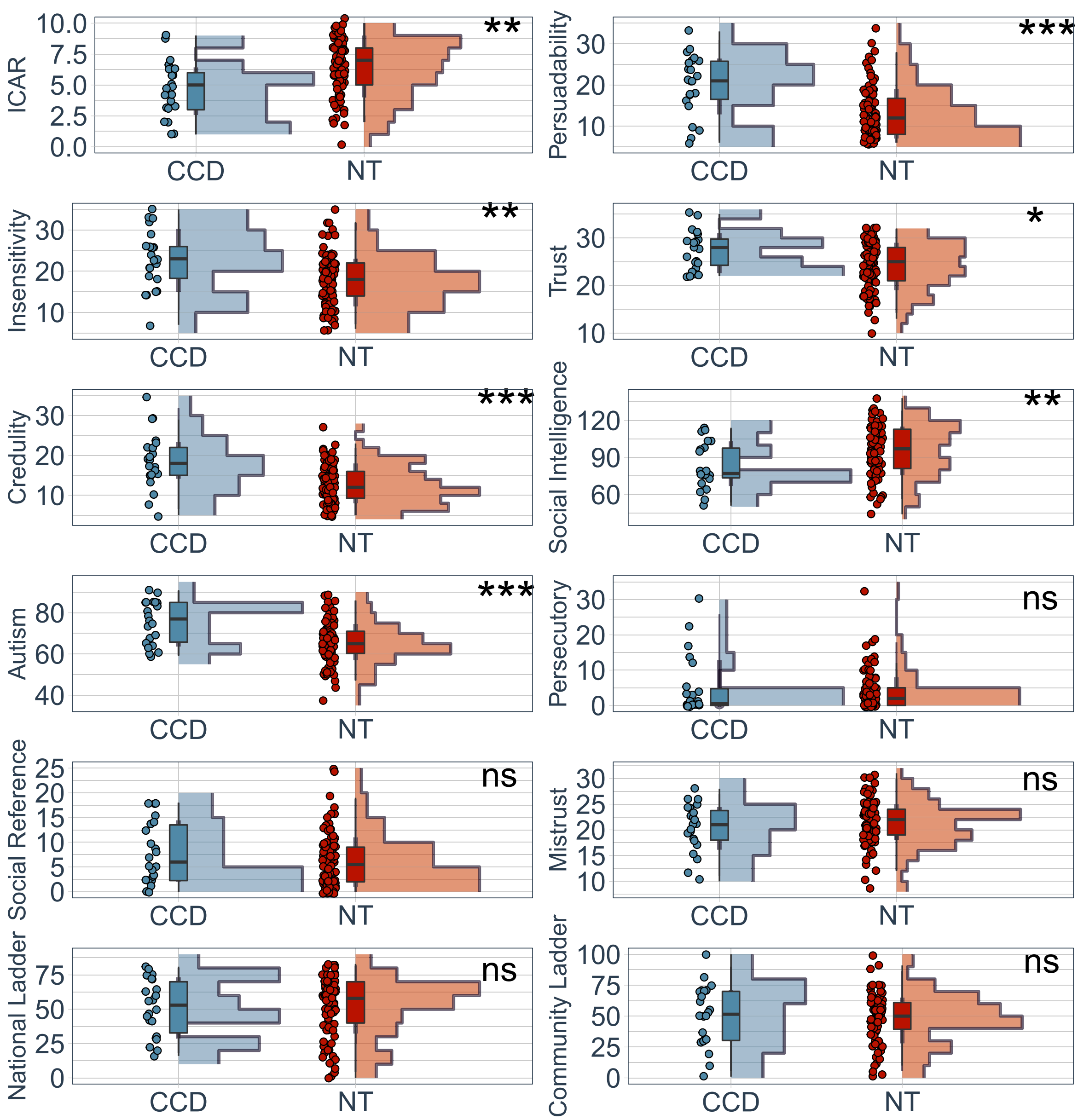

Fig. 2 – Unadjusted Kruskal–Wallis tests between CCD and NT participants for each psychometric measure. CCD participants were on average lower in general cognitive ability and social intelligence, and higher on persuadability, insensitivity to social trickery, trust, credulity, and autistic-like traits compared to neurotypical participants. Adjusting for age, sex, and education however removed the difference in general cognition, and adjusting for age, sex, education, and general cognition removed the difference in social intelligence. Points on each graph represent individual scores for each measure within each group. Boxplots represent the median and quartile range. Histograms represent the density of points for each group at each score on the scale as a function of sample size. ns = not significant; *$p < .05$; **$p < .01$; ***$p < .001$.

were more persuadable ($\chi^2(1) = 14.52$, $p < .001$), and more insensitive to social cues of trickery ($\chi^2(1) = 8.76$, $p = .003$), more trusting ($\chi^2(1) = 6.39$, $p = .011$), and scored higher on credulity ($\chi^2(1) = 13.41$, $p < .001$). CCD participants also scored higher in autistic traits ($\chi^2(1) = 12.36$, $p < .001$) and lower on social intelligence ($\chi^2(1) = -7.65$, $p = .006$) compared to NT participants. CCD participants did not perceive themselves to be any higher or lower than NTs on either of the MacArthur Social Ladders (National Ladder: $\chi^2(1) = .11$, $p = .75$; Community Ladder: $\chi^2(1) = .25$, $p = .62$), nor were any less mistrusting than NT participants ($\chi^2(1) = .92$, $p = .34$). There was no difference between groups for persecutory ideation ($\chi^2(1) = .30$, .58) or social reference ($\chi^2(1) = .69$, $p = .41$).

Bayesian general linear models were employed to examine the unadjusted estimates further (and quantify estimate noise) by accounting for group-based differences in age, sex, and education. The results of this analysis indicate that the CCD participants were no longer lower in abstract non-verbal intelligence (median posterior estimate (*m*): −1.30, 95% Credible Interval (95% CI): −2.71, .10).

Delving further into individual items on the ICAR, mixed Bayesian regression modelling of reaction time between CCD and NT groups, with '(Question Number|ID)' as a random variable, demonstrated that NT participants were significantly quicker at answering questions (*m*: −15571.22, 95% CI: −30066.21, −1446.41; see Fig. S3) regardless of whether their answers were correct or incorrect. Correct answers were not slower overall (*m*: 2070.80, 95% CI: −7318.45, 11901.53) and there was no interaction between group and whether an answer was answered correctly or incorrectly on reaction time (*m*: −5782.85, 95% CI: −16794.47, 5604.07). Likewise, by regressing normative item difficulty (previously defined for the ICAR progressive matrices (Subotić et al., 2020)) and group (with ID as a random variable) against whether participants got an item correct or incorrect, we observed that increasing item difficulty led to fewer correct answers regardless of group identification (*m*: −1.76, 95% CI: −2.41, −1.12), and that there was an interaction between group and difficulty, such that CCD participants provided significantly fewer correct answers as difficulty increased compared to controls (*m*: −.78, 95% CI: −1.49, −.09). As a result of this finding, the participant's average ICAR score was included in all future models, alongside age, sex, and educational attainment, to assess whether psychometric effects may be explained by lower abstract non-verbal intelligence.

All significant effects from the simple group comparisons remained when controlling for the ICAR, age, sex, and education: CCD participants were more persuadable (*m*: 9.76, 95% CI: 5.67, 13.66), more insensitive to noticing social trickery (*m*: 7.39, 95% CI: 3.40, 11.47), more trusting (*m*: 4.52, 95% CI: 1.61, 7.46) and had higher credulity (*m*: 7.68, 95% CI: 4.61, 10.80). CCD participants also scored higher in autistic traits (*m*: 8.53, 95% CI: 2.15, 14.92), although were no longer lower on social intelligence (*m*: −9.59, 95% CI: −22.35, 2.86) compared to NT. Those with a diagnosis of CCD were still no different to NT participants in mistrust (*m*: −1.76, 95% CI: −4.49, .88), social reference (*m*: 3.22, 95% CI: −.15, 6.45), or persecutory ideation (m: .11, 95% CI: −3.79, 3.66), or on the MacArthur social ladders.

When additionally including autism and social intelligence alongside age, sex, education, and ICAR score in a Bayesian general linear model predicting gullibility subscales, CCD participants still scored higher in persuadability (*m*: 8.43, 95% CI: 4.47, 12.45) and insensitivity (*m*: 6.51, 95% CI: 2.95, 10.03). In other words, differences in age, sex, education, general cognition, autistic traits, and social intelligence accounted for less variability in the linear regression model than having a diagnosis of CCD.

3.2. *Dimension reduction and prediction*

Spearman correlation matrices for the scales were used during the dimension reduction in each group (R-GPTS, AQ, SIS, McA-SL, ETQ, GQ), in addition to calculating whether associations were significantly different between groups (Fig. S3). There was only one significant difference in the correlation matrices between groups; a significant positive association between Credulity and Mistrust (that existed for both the NT group, $r_{spearman} = .21$, $p = .047$, and the CCD group, $r_{spearman} = .68$, $p = .01$) which significantly differed from each other following permutation testing (10,000 sampled repetitions: $p = .021$).

To avoid overfitting on a single NT sample, dimension reduction and prediction modelling were conducted using 250 bootstrapped iterations, each drawing on randomly sampled training data per iteration ($n = 60$; ~70%) and reporting the average accuracy and 95% confidence intervals across all bootstrapped iterations. Three principal components were identified, which each explained more than 10% of the variance in the model, with the three components together explaining 62.2% of the variance in total ($PC1_{\%} = 34.5$, 95% CI: 34.2, 34.8; $PC2_{\%} = 15.6$, 95% CI: 15.5, 15.7; $PC3_{\%} = 12.1$, 95% CI: 12.0, 12.2). Upon reviewing the averaged absolute covariance matrices from all 250 training bootstrapped iterations over a threshold of .30 (Fig. S3A), and the contribution of variables within dimension space (Fig. 3D & E), absolute loading values above the threshold were generated for gullibility and credulity that loaded jointly on PC1 and PC2 (PC1: Gullibility = .410 95% CI: .407, .413; Credulity = .413, 95% CI: .409, .418; PC2: Gullibility = .332, 95% CI: .319, .346; Credulity = .407, 95% CI: .396, .419) and trust with PC2 and PC3 dimensions (PC2 = .594, 95% CI: .580, .608; PC3 = .380, 95% CI: .357, .404) while all other variables were only above the loading threshold with either PC1, PC2, or PC3 (see Fig. 3A).

The top three principal components extracted from dimension reduction were used in a bootstrapped LOOCV to predict group classification (CCD or NT) in the held-out NT data and CCD data for each bootstrapped iteration. We compared RF, SVM and Bayes GLM models for predictive accuracy. We found that the Bayes GLM was most accurate (mean accuracy = 71.7%. 95% CI: 71.1%, 72.4%; Fig. 3C), although was not significantly different than the SVM (Fig. S4; $W_{(249)} = 33,354$, $p = .19$). An averaged confusion matrix was extracted for predicted and observed classifications across all 250 LOOCV bootstrapped iterations (Fig. 3B).

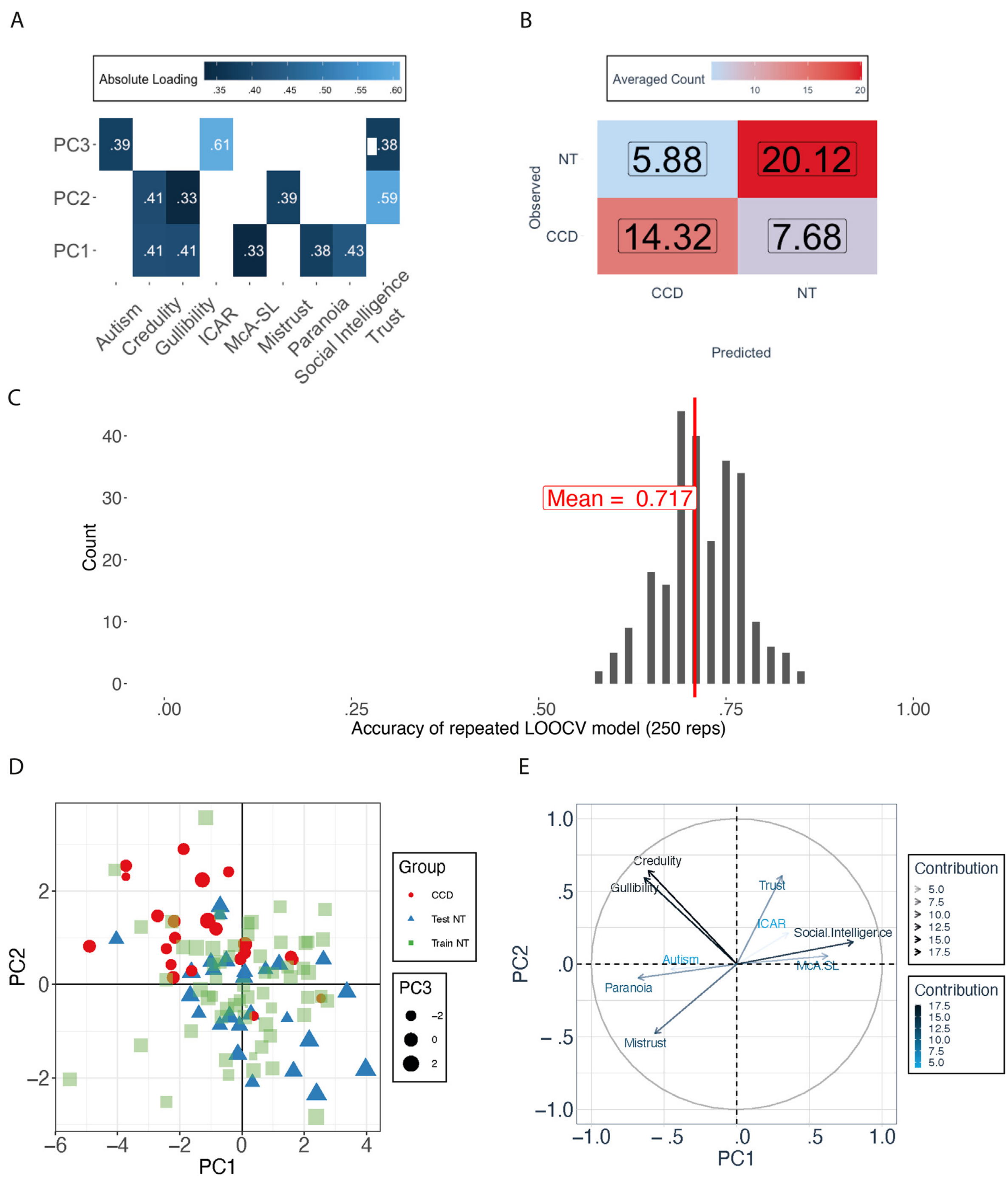

Fig. 3 – Dimension rotation and LOOCV results across 250 bootstrapped iterations (A) Averaged absolute loading between each variable and the top three principal components over all 250 repetitions. All values < .30 are filtered out. (B) Averaged bootstrapped confusion matrix (250 repetitions) for each Leave-one-out-cross-validation analysis using a Bayesian GLM classifier. X = non-significant association (alpha = .05). (C) Bootstrapped LOOCV model accuracy scores (250 repetitions) using a random 70:30 split of training and test NT data. We always used CCD data as held-out test data to determine whether natural psychological variation in the NT training data would be sensitive to CCD caseness. (D) Projected location in dimension space of test-set NT participants (blue triangles) and CCD participants (red dots) when considered within a random repetition from dimension space built on training set NT participants (green squares). (E) Loading and contribution of each variable to the top two dimensions from the same random repetition as (D).

4. Discussion

CCD is easily identified by structural imaging, but the corresponding behavioural phenotype is unclear and highly heterogenous. In this exploratory study we assessed the psychometric profile of CCD participants compared to NT participants. Motivated by prior work on the social difficulties reported in CCD (Brown & Paul, 2000, 2019; Kosky et al., 2021; Maxfield et al., 2021; Symington et al., 2010) and high comorbidity of ASD in this population (Brown et al., 2021), the focus of this work was on identifying any consistent psychometric differences that could not be explained by age, sex, education, poorer general cognitive ability, or autistic traits. It was determined that persuadability, insensitivity to noticing social trickery, credulity, trust, and autistic traits were significantly higher in CCD participants compared to NT populations following adjustment by Bayesian general linear models. Principal Component Analysis suggested that persuadability and insensitivity to social trickery formed separate dimensions in the NT population, and the resultant covariance structure was able to accurately predict whether test participants belonged to the CCD or NT group. The result of this analysis was that a normative model built from cognitive and social variables drawing on NT data is reasonably predictive of classifying the CCD phenotype, which is supportive of the theory that there is a consistent psychological phenotype associated with CCD.

Defining a clear psychological phenotype for CCD is a difficult challenge – cognitive and behavioural expressions in CCD are highly heterogenous, and previous works have typically used small samples to draw observations (Brown & Paul, 2019). The covariance structure extracted from the dimension reduction suggests that those diagnosed with CCD are primarily typified by exaggerations in persuadability, credulity, and insensitivity to social trickery. Those with lived experienced of CCD have anecdotally reported their difficulties in understanding the social intentions of others, and it may be that a predisposition to be overly trusting has led some of those with CCD into abusive relationships or finding themselves being the target of antisocial behaviours, such as bullying (Maxfield et al., 2021). More broadly, this highlights the necessity of having CCD recognised as a vulnerable group in healthcare policy so that adequate social and financial support can be arranged. While we do not have sufficient power in this study to form a fully realised, clinically validated model for diagnostic utility, this preliminary model may be useful to examine more nuanced functional changes to brain activity as a result of structural callosal differences (e.g., thickness), and the model's relationship with different dimensions of cognition (e.g., non-verbal reasoning and verbal knowledge (Danielsen et al., 2020)). It will be important to replicate these findings in a new CCD sample, as well as in those who have a clinical diagnosis of ASD without CCD, and individuals who have had their corpus callosum surgically severed as an adult (i.e., callosotomised, or split-brain individuals given their similar structural changes but different behavioural phenotype) (Siffredi et al., 2013) to assess the specificity of the findings reported here to those born with CCD, rather than acquiring a callosal disconnection later in life.

The results of this work also demonstrate that persuadability, credulity, and insensitivity to social trickery are statistically dissociable from the other general and social cognitive scales we included in this analysis within the general population. This is consistent with parallel work in field of hypnosis research, regarding the trait of ‘suggestibility’, a phenomenon consistent with gullibility, especially ‘secondary suggestibility’ (Eysenck & Furneaux, 1945). Suggestibility has been found to share little to no relationship with canonical personality dimensions defined in Big 5 or OCEAN, such as agreeableness and neuroticism (Gudjonsson, 1983; Liebman et al., 2002; Norris, 1973; Pires et al., 2013), but is considered an independent cognitive facet (Pires et al., 2013), and has demonstrated a high degree of stability, persisting over a period of 25 years in the same group of individuals (Piccione et al., 1989) Participant responsiveness to direct verbal suggestions (i.e., ‘Direct Verbal Suggestibility’, or DVS; Oakley et al., 2020; Oakley et al., 2021; Oakley & Halligan, 2017), with and without hypnosis, was outside the scope of this work and so it remains unclear whether exaggerated persuadability and insensitivity to social trickery in our CCD samples will translate into DVS. Rigorously exploring the possibility that CCD relates to both gullibility (second order suggestibility) and DVS in the future works may highlight an important role of the corpus callosum in this separable social trait, and work toward a clearer phenotype of the diagnosis.

Our finding that CCD participants are significantly more likely to score higher on autistic-like traits than the general population is consistent with previous work showing that a large minority of children diagnosed with CCD are also comorbid with ASD (Lau et al., 2013). It has been hypothesised that CCD may be a risk factor in the development of ASD and may explain many of the social difficulties observed in CCD (Paul et al., 2014). However, prior work has also found that after parent-rated assessments were included, many of the ASD scores in CCD participants were attenuated below the clinical threshold (Paul et al., 2014). As qualitative work has identified the preference for many individuals with CCD to be alone because of negative social experience, such as ostracism, abuse, and social anxiety (Maxfield et al., 2021), it may be that many of the autistic-like qualities that the sAQ aims to measure are confounded by these learnt social responses following social exclusion, rather than CCD sharing many biologically causal links with ASD. Indeed, we find that even after controlling for ASD-like traits and social intelligence, exaggerations in credulity, insensitivity to social trickery, and persuadability remain. Therefore, while phenomenologically CCD and ASD have multiple similarities, their biological, social, and psychological causes may be very different.

Finally, this study corroborates our previous work indicating that CCD impacts abstract non-verbal reasoning (Hearne et al., 2019). In a Latin Square Task, it was found that increasing task complexity led to more reasoning errors and increased reaction times (Hearne et al., 2019). Our sample of CCD individuals were no different from our NT sample in terms of their overall ICAR scores when age, sex, and education was controlled for; however, CCD participants were more prone to incorrectly answering more complex items on the ICAR (as defined by Subotic and colleagues) (Subotić et al., 2020) wrongly when compared to neurotypical individuals, even when considering item difficulty as an independent factor in whether a participant answered an item correctly or not. This supports the hypothesis that CCD participants are more prone to errors when faced with increasing complexity in abstract non-verbal reasoning. However, this hypothesis requires further testing with cognitive tasks that require the navigation of non-verbal environments, such as the assessment of model-free and model-based reasoning using symbolic stimuli (Keramati et al., 2016).

A limitation of the current study is that individuals with CCD may exhibit reductions in metacognitive efficiency (data not reported here) and therefore gathering data from self-reflective scales alone may not be accurate. In future work, it may prove useful to obtain family-rated and clinician-rated behaviours of the participants to confirm self-reported scores. It should be noted however that the same issue extends to the NT participants. Likewise, it has been noted that collecting data online using psychometric self-report measures can incur spurious results (Zorowitz et al., 2021). This was controlled for, in part, by having both the NT and CCD groups complete periodic attention and comprehension checks. However, the utilisation of online testing for CCD participants does offer certain advantages over lab-based observation. For example, those with CCD commonly experience high social anxiety and unease in unfamiliar environments (Maxfield et al., 2021), such as attending a laboratory session for in-person testing. Furthermore, online-testing permits geographically isolated individuals, either by their physical distance from the laboratory or public health restrictions, to participate and gather important cognitive and phenomenological data in a time and cost-efficient manner. It is imperative, however, that appropriate controls (reverse coded items, attention check questions, comprehension questions) are given alongside any surveys and tasks that are administered remotely to all participants to ensure self-report and online-tested cognitive tasks are reliable. Finally, while the CCD cohort was representative of a broad range of cognitive capabilities, this did not extend to those with severe intellectual disabilities. Therefore, the primary findings of this work may not readily generalise to those who are profoundly impaired. Finally, while dimension reduction allows examination of covariance changes across multiple measures simultaneously, it reduces interpretability of the relationship between specific variables and CCD. As demonstrated in our analysis pipeline, future work should always include individual-feature analysis alongside our model.

In summary, the psychometric dimensions of CCD participants were assessed in comparison with NT populations. It was identified that CCD participants demonstrate exaggerated vulnerabilities to social persuasion and are less aware of their possibly being deceived. Principle Component Analysis identified that persuadability and insensitivity to social trickery were dissociable elements in the NT population, and the resultant covariance structure was able to accurately predict whether test participants belonged to the CCD or NT group. It is our hope that these results can be used as a foundation on which to develop a more robust model to predict CCD phenomenology, as well as expound upon the contributions the corpus callosum makes to social inference.

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Open practices

The study in this article earned an Open Data – Protected Access badge for transparent practices. Materials and data for the study are available at https://github.com/Brain-Development-and-Disorders-Lab/Barnby_etal_2021

Declaration of competing interest

None to declare.

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Supplementary data

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