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REVIEW

Cognitive and Psychological Impacts of Congenital Corpus Callosum Disorders in Adults: A Scoping Review

Maree Maxfield[1] · Keith McVilly[2] · Alexandra Devine[1] · Helen Jordan[1]

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Abstract

Objectives Support for adults with congenital corpus callosum disorders (CCDs) is impeded by poor understanding of the impacts of a CCD on day-to-day functioning and quality of life. This scoping review examines existing literature to establish the evidence-based impacts of congenital CCDs in adults and identify gaps to inform future research, policy development, and service delivery.

Methods We conducted searches in Scopus, Medline Ovid, PsycInfo, Discovery, and ERIC. Studies meeting selection criteria were peer-reviewed, in English, published from 1980 to 2021, reported predominantly on participants 16 years or older who were diagnosed with a CCD by magnetic resonance imaging (MRI).

Results The thirty-eight included articles comprised 14 single/dual participant case studies and 24 group studies, comparing adults with a CCD with normative data or matched controls. Although most participants were of average IQ, CCDs affected day-to-day executive functioning, social interaction, and meeting expectations of adulthood. Cognitive impacts included difficulties with learning and memory, linguistic and emotional processing, and complex reasoning, with functional capacity typically decreasing as tasks and situations increased in complexity. Psychological impacts pertaining to feelings, emotions, and social awareness were reported in addition to associated mental health, psychiatric mood, and developmental and psychotic disorders including autism, anxiety, depression, and schizophrenia.

Conclusions Impacts were extremely heterogenous, presenting interwoven challenges to learning, executive functioning, social interaction, and mental health. Knowledge of these circumstances is vital for adults with CCDs, professionals, and family members to ensure appropriate services and support are available to promote good quality, inclusive lives for all adults with a CCD.

Keywords Corpus callosum · Impacts · Cognitive · Psychological · Psychiatric · Adults

The corpus callosum is the largest white matter tract in the brain. It connects the left and right hemispheres, enabling interhemispheric cognitive, sensory, and motor communication (Edwards et al., 2014; Hearne et al., 2019). A congenital corpus callosum disorder (CCD) is characterized by a completely or partially absent or misshapen corpus callosum, causing a heterogeneous array of cognitive, psychological, psychiatric, and physical impacts ranging from mild to severe (Brown & Paul, 2019; Edwards et al., 2014; Margari et al., 2016; Siffredi et al., 2018). One or more associated neurological developmental and psychiatric disorders including epilepsy, autism, intellectual disability, attention-deficit/hyperactivity disorder (ADHD), depression, anxiety, and schizophrenia are often present in individuals with a CCD (Bondade et al., 2018; Chinnasamy et al., 2006; Moes et al., 2009; Moreau et al., 2021; Popoola et al., 2019; Simon et al., 2008; Valenti et al., 2019).

Although a CCD is one of the most commonly detected brain abnormalities in newborns, an incidence of 1:4000 live births classifies it as a rare disease (Edwards et al., 2014; Glass et al., 2008). Children with a CCD are at increased risk of neurodevelopmental disorders and delays. For example, Lau et al. (2013) found that 45% of children and 35% of adolescents with a CCD met criteria for an autism diagnosis, and Siffredi et al. (2018) reported that while 20% of

✉ Maree Maxfield
m.maxfield@student.unimelb.edu.au

[1] Melbourne School of Population and Global Health, University of Melbourne, Victoria, Australia

[2] School of Social & Political Sciences, University of Melbourne, Victoria, Australia

children with a CCD indicated typical development, 50% experienced difficulties in intellectual, executive, behavioral, academic, and social function. However, CCDs in adults may be undiagnosed, with neurodevelopmental challenges attributed to associated diagnoses or even personal shortcomings (Maxfield et al., 2021; Paul et al., 2007). There are examples of undiagnosed adults presenting with incidental injuries or psychological/psychiatric symptoms warranting neuroimaging, which subsequently reveal a CCD (Bondade et al., 2018; Chinnasamy et al., 2006; Moreau et al., 2021; Popoola et al., 2019; Simon et al., 2008; Valenti et al., 2019). CCDs remain poorly understood within the health, social care, and education systems, and in the wider community (Edwards et al., 2014).

A CCD was once regarded as an "interesting anomaly occasionally and incidentally to be found at autopsy" (Goldensohn et al., 1941, p. 567). Until 1980, knowledge of the corpus callosum and its function was typically derived from autopsy or following surgical callosotomy (severing of the corpus callosum) and commissurotomy (severing of all brain hemispherical commissures) to treat epilepsy. Complete studies reporting cognitive and psychological impacts of congenital CCDs were scarce, with experiences of associated psychosocial disability receiving almost no attention (Brown & Paul, 2000). Congenital CCDs are now more accurately diagnosed by magnetic resonance imaging (MRI), computed tomography (CT), or prenatal ultrasound (Edwards et al., 2014; Mahallati et al., 2021).

Recent studies indicate a congenital CCD can be caused by exogenous insult, for example, infection or exposure to teratogens such as alcohol. However, most occurrences are understood to be of genetic etiology, with recent advances in genomics identifying more than 400 genetic causes (Alby et al., 2016; Edwards et al., 2016). Current corpus callosum research focuses on exogenous and genetic causes of CCDs, variations in anatomical presentation and pediatric developmental, and behavioral phenotypes (Ballardini et al., 2018; Barnby et al., 2022; Brown & Paul, 2019; Edwards et al., 2014; Siffredi et al., 2018). There are very few studies on the impacts of a congenital CCD on the day-to-day lives of adults, with no known studies examining the impact on quality of life (QoL). Such limited information creates barriers to diagnostic and prognostic knowledge and the design and provision of appropriate support.

Although pediatric CCD management is becoming better informed by early diagnosis and expanding biological research, failure to yet identify "a clear and unique neuropsychological phenotype" (Siffredi et al., 2018, p. 453) challenges consensus for support needs of children and adults. What is recognized, however, is that where individuals receive inadequate supports, a CCD can be disabling (Bogart & Irvin, 2017; Maxfield et al., 2021). Despite increased awareness of disability in society and legislated measures to promote educational and workplace inclusion, adults with disability are underrepresented in higher education and the workforce (Gray, 2020). They continue to experience discrimination and inadequate support from educators, employers, and colleagues (Bonaccio et al., 2020; Devine et al., 2019; Kavanagh et al., 2013; La Montagne et al. 2016). The subsequent discrimination and isolation experienced by individuals with disability can affect inclusion across other important life domains with negative impacts on socioeconomic, health, and QoL outcomes (Karahalios et al., 2020; Kavanagh et al., 2013). This is similar to the social disadvantage and reduced QoL experienced by individuals with other rare conditions (Anderson et al., 2013; Bogart & Irvin, 2017; Bryson & Bogart, 2020; Molster et al., 2016).

Research has captured identification and impact of congenital CCDs diagnosed in childhood in relation to cognitive (e.g., developmental delays and deficits in receptive and expressive language, learning, memory, and communication) (Bartha-Doering et al., 2021; Brown et al., 2005b; des Portes et al., 2018; Siffredi et al., 2017) and psychosocial functioning (e.g., emotional dysregulation and difficulties socializing with peers) (Badaruddin et al., 2007; Siffredi et al., 2018). Far less research has focused on the impact of congenital CCDs on the lives of adults. This scoping review, therefore, examines the existing literature to identify the evidence-based impacts of congenital CCDs in adults and identify gaps to inform future research, policy development, and service delivery.

Method

Review procedures were informed by Preferred Reporting Items for Systematic reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) (Page et al., 2021), Synthesis Without Meta-analysis (Campbell et al., 2020), and CAse REport (CARE) guidelines for screening of case studies (Riley et al., 2017). Using keywords, Boolean terms, and inclusion limiters, we established an iterative search strategy in peer-reviewed journals (see Fig. 1). The introduction of MRI in 1980 enabled gold standard confirmation of CCDs (Gooding et al., 1984), determining our time frame from 1980–2021. Thirty-eight articles met criteria for inclusion. The initial minimum age was 18 years. Most case control studies included a small number of participants aged 16–17 years; therefore, minimum participant age was reduced to 16 years. Three salient studies, each containing one 14–15 year old, were also included (Brown et al., 2005a; Farchione et al., 2002; Hinkley et al., 2016). Studies not clearly delineating between numbers of child and adult participants were excluded. Other excluded titles focused on physical impacts, which were not the focus of this review (e.g., Doherty et al., 2006; O'Brien, 1994).

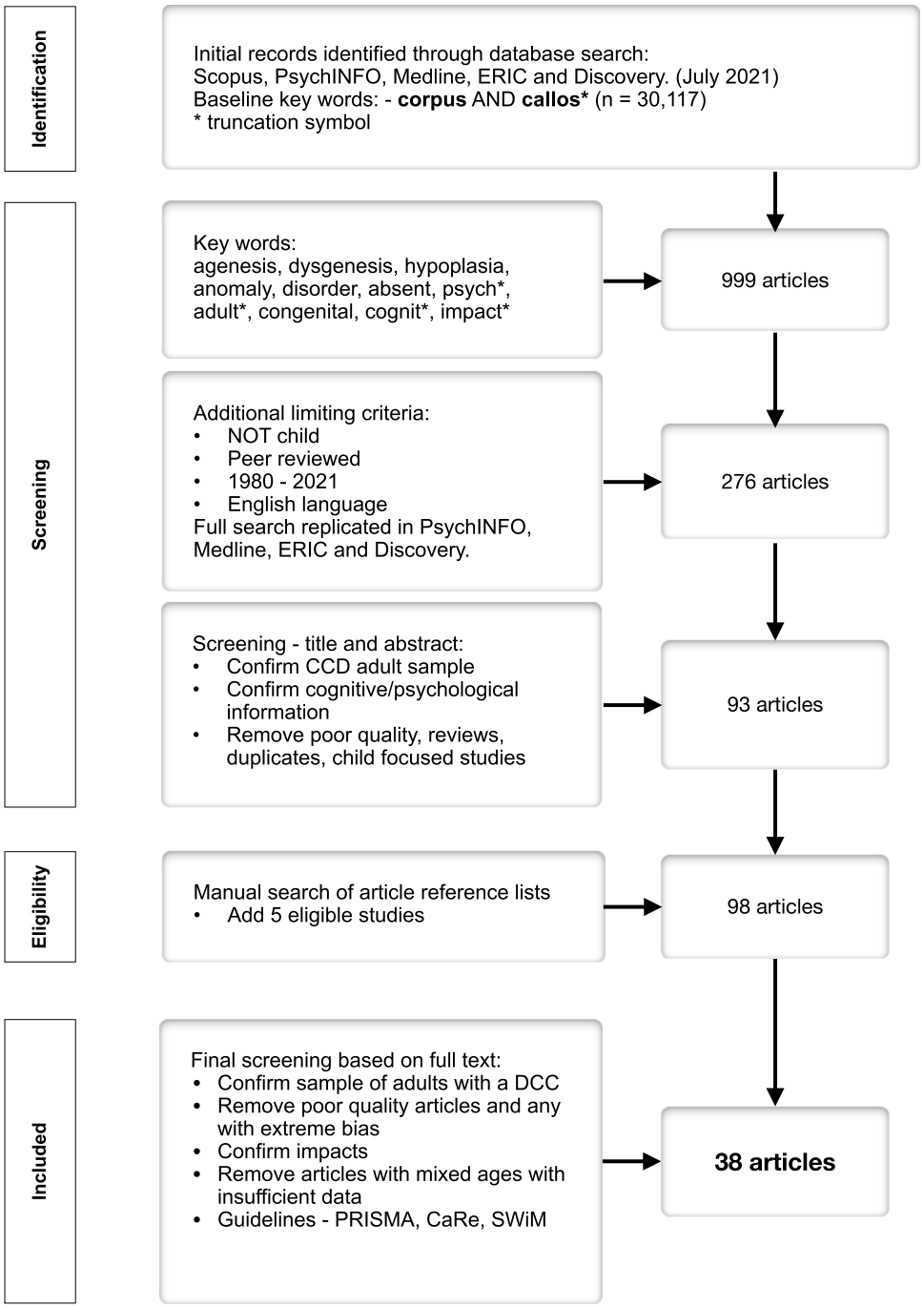

Fig. 1 Flow diagram of literature selection

Results

Study and participant characteristics

Cognitive and psychological impacts of congenital CCDs on adults were described in 38 articles (see Table 1). Twenty-four group studies compared adults with a CCD to population normative levels or matched controls. Fourteen were single- or dual-participant case studies. Most studies were conducted in the USA (27/38), with other locations including Australia (4), India (2), Switzerland (1), Germany (1), UK (2), and Canada (1).

Data indicated that some participants were recruited from preexisting US databases (e.g., California Institute of Technology and Travis Institute, California) and took part in multiple studies. Demographic details of some subgroups within

Table 1 Characteristics of included peer-reviewed studies arranged by author

Author, year, and country	Measuring	CCD: study type, age, gender, IQ, and recruitment	Controls: age, gender, IQ, and recruitment	Purpose	Key findings
Anderson et al. (2017) USA	Emotional intelligence	Group: standardized assessmentCCD: $n=16$, 18–57 y, $\mu=35.31$ y, (9 M, 7 F) IQ 83–129, $\mu=98.69$ Selected from Travis Institute database	General population normative evaluation data	Clarify the nature of emotional intelligence in adults with ACC	The cc is not essential for experiencing and thinking about basic emotions but necessary for more complex processes in the context of social interactions
Barker et al. (2021) Australia	Neuropsychological assessment	Single case control CCD: $n=1$ M 40 y IQ 123 QBI data base and AusDoCC	$n=10$ Age $\mu=36.4$ y (10 M) IQ $\mu=119.7$ University of Queensland research participation scheme, newsletters	Report case of a 40 y/o male with superior intellectual abilities in the context of corpus callosum dysgenesis (CCD), partial rhombencephalosynapsis, and verbal adynamia	Heterogeneity of CCD outcomes is reiterated in the first known profile of an adult with partial rhombencephalosynapsis, a superior IQ, and a CCD. Problems with selection and generation of ideas, verbal adynamia, and reduced spontaneous speech may be associated with CCDs, with inter- hemispheric transfer a key factor in spontaneous speech production
Bhattacharyya et al. (2016) India	Mental Status Examination	Case study CCD: $n=1$ M 25 y IQ "normal" Clinical presentation	Not applicable	Report a case of a 25 y/o male, clinical psychiatric presentation at tertiary care hospital	Recurrent brief depression can be a manifestation of ACC
Bondade et al. (2018) India	Clinical presentation for medical and neurological examination	Case study CCD: $n=1$ M 22 y IQ "average" untested Clinical presentation	Not applicable	Report a case of a 22 y/o male presenting with psychosis	Brain abnormalities are increasingly reported in psychiatric patients. Neuroimaging investigation is important for psychotic illness
Bridgman et al. (2014) USA	IQ Tracking eye movements to measure recognition of facial emotion and associated social gaze	Group: case control CCD: $n=9$ Age $\mu=28.22$ y (7 M, 2F) IQ $\mu=98.22$ NODCC conference attendees	$n=9$ Age $\mu=34$y (9 M) IQ $\mu=112$ Online advertisement	Examine recognition of facial emotion and its association with social gaze	Atypical face scanning with diminished attention to eyes and reduced colossal activity may contribute to emotional processing deficits
Brown and Paul (2000) USA	IQ Range of academic skills, abstract comprehension and reasoning, problem solving, interhemispheric information transfer, mood and thought disturbance symptoms, and social situations	Case study CCD: $n=2$ Age 16–18 y, (1 M) IQ 108 Age 21–23 y (1 M) IQ 87	Not applicable	Examine cognitive and psychosocial abilities to determine whether a DCC presents specific problems in complex cognitive operations and psychosocial deficits	Deficits in cognitive operations, including abstract reasoning, concept formation and problem solving, cause disability in social cognition due to diminished interhemispheric transfer of complex information

Table 1 (continued)

Author, year, and country	Measuring	CCD: study type, age, gender, IQ, and recruitment	Controls: age, gender, IQ, and recruitment	Purpose	Key findings
Brown et al., (2005a) USA	IQ Comprehension of narrative and visual humor Interpreting and understanding non-literal language—jokes and cartoons	Group: case control CCD: $n=16$ 14–55 y $\mu=25.6$ y (13 M, 3F) IQ 83–116 $\mu=94.9$ ACC Network and ACC Directory	$n=31$ Age$\mu=23.7$ y (30 M, 1 F) IQ $\mu=93.2$ Local employment agency	Study the comprehension of humor in individuals with ACC	Suggests a common origin for comprehension of jokes, non-literal language and proverbs with difficulties most likely related to reduced capacity to understand second order meanings
Brown et al. (2020) USA	Attention, vigilance and impulsivity	Group: standardized assessmentCCD: $n=18$ 16–52 y $\mu=28.06$ y (10 M, 8 F) IQ 80–113 $\mu=96.33$ NODCC conference attendees	Normative test data	Determine whether problems in attention, inhibitory control and vigilance are characteristic of ACC	Adults with a DCC have moderate levels of difficulty in sustained attention, particularly maintaining response to inhibition and vigilance (modulated by age and sex)
Brown et al. (2021) USA	Knowledge of social norms and appropriate behavior	Group: case control CCD: $n=17$ 19–55 y, $\mu=34.5$ y (9 M, 8 F) IQ 88–115 $\mu=108.67$ Travis Institute database	$n=21$ Age $\mu=35.81$ y (10 M, 11 F) IQ $\mu=108.67$ Online advertisement	Determine whether high functioning adults with ACC can accurately identify appropriate behaviors within social contexts	Deficits evident in understanding social norms, with adults with ACC showing a tendency to over-adhere significantly more than controls
Buchanan et al. (1980) USA	Key alexithymic traits	Case study CCD: $n=1$ M 37 y IQ 98 Family member diagnosed	Not applicable	Address the neurophysiological explanation of alexithymia	Hemispheric disconnection provides an environment for alexithymia, supporting a neurophysiological perspective regarding impacts of inadequate connections
Cavalari and Donovick (2015) USA	IQ Psychological symptomology, depression, suicide risk, daily functioning, academic skills, and neuropsychological assessment	Case study CCD: $n=1$ F 20 yIQ within normative range Binghampton University study	Not applicable	Review neuropsychological, behavioral and psychosocial assessment in relation to developmental delay	Heterogeneous DCC presentation necessitates unique individual symptom profiles for efficient and appropriate academic and habitative services
Chinnasamy et al., (2006) Australia	Clinical examination, neuropsychological testing and review of past testing	Case study CCD: $n=1$ F 24 y IQ "low average" Clinical presentation	Not applicable	Review presentation with schizophrenia with consequent discovery of DCC	Comprehensive neuropsychiatric assessment results must be specifically tailored to create individual unique clinical profiles
Erickson et al. (2014) USA	Verbal learning and memory, attention span, learning efficiency, delayed memory, and memory accuracy	Group: case control CCD: $n=26$. 16–52 y, $\mu=27.9$ y (14 M, 12 F) IQ 80–129, $\mu=97.35$ NODCC conference attendees	$n=24$ Age $\mu=28.29$ y (13 M, 11 F) IQ $\mu=101.7$ Online advertisement: Craigslist.com	Assess verbal learning and memory in ACC	Reduced performance in significant deficits in delayed and cued recall and new learning suggests that the cc facilitates interhemispheric elaboration and encoding of verbal information

Table 1 (continued)

Author, year, and country	Measuring	CCD: study type, age, gender, IQ, and recruitment	Controls: age, gender, IQ, and recruitment	Purpose	Key findings
Farchione et al. (2002) USA	Diagnostic clinical assessment for OCD	Case study CCD: $n=2$ M 29 y, F 14 y IQ unknown Parent contact: Uni of Maine Listserv	Not applicable	Parental contact requesting review of a DCC	Links between DCC and OCD are speculative but feasible. Adds to the knowledge base of dysfunction in OCD mediated by hypoplasia of the corpus callosum
Hearne et al. (2019) Australia	Investigating the functional networks underlying cognitive reasoning with a cognitive task, and brain network analyses	Group: investigative study CCD: $n=7$ 24–64 y, $\mu=38$ y (5 M, 2 F) IQ 88–124, $\mu=102$ QBI data base and AusDoCC	$n=30$ Age $\mu=23.6$ y (13 M, 17 F) Subsample from previous QBI study	Use high quality MRI to investigate the functional networks underlying cognitive reasoning in individuals with a DCC	Confirm hypotheses that low complexity demands in DCC produce similar results to neurotypical controls but connectivity and neural activity are reduced as task complexity is increased
Hinkley et al. (2012) USA	Coherence in the alpha (8–12 Hz), beta (12–30 Hz) and gamma (30–55 Hz) bands, hemispheric connectivity	Group: case control CCD: $n=18$ 17–57 y, $\mu=31$ y (6 F, 12 M) IQ 77–129, $\mu=100$. UCSF Comprehensive Centre for Brain Development	$n=18$ Age $\mu=29$ y (8 M, 10 F) IQ $\mu=105$ San Francisco Bay area	Demonstrate that lack of normal callosal development leads to deficits in functional connectivity in specific cognitive domains	DCCs produce selective functional connectivity disruptions correlating to cognitive impairment, also seen in neurodevelopmental and psychiatric disorders
Hinkley et al. (2016) USA	Cortical activity during language processing and speech preparation and execution	Group: case control CCD: $n=25$ 14–70 y, $\mu=32.5$ y (17 M, 8 F) IQ 73–129, $\mu=100.4$ UCSF Brain development research program (BDRP) database	$n=21$ Age unknownIQ $\mu=104.1$ San Francisco Bay area	Measure cortical activity during language processing, speech preparation and execution, testing the hypothesis that rather than language being assigned to the left hemisphere it is represented in both hemispheres and lateralized across the corpus callosum	Impairments in corpus callosum formation correlate with poor function in verbal performance. The cc assists with driving language lateralization
Jeeves and Temple (1987) Scotland	Visual recognition, oral fluency, sentence creation, using cues for item identification—semantics, rhyming words, grammatical sentence forms, and sentence-picture matching of different grammatical forms	Case study CCD: $n=2$ M 20 y, IQ 94, F 22 y, IQ 75 Clinical presentation (referral)	Not applicable	Compare the measurement results of 2 individuals with a DCC to a previous study	Data indicate the corpus callosum is not necessary to develop normal specific language function but do not refute the general theory that the cc is important for language lateralization
Lau et al. (2013) USA	Autism screening	Group: normative assessmentCCD: adult $n=39$ 16–74 y, $\mu=28.2$ y (25 M, 14 F) IQ$\geq$70 UCSF (BDRP) database Self and parent report	Published AQ validation studies	Directly measure the occurrence of autism traits in individuals with ACC and investigate the neural underpinnings of the association	Traits present in adults with DCC meet pre-screening criteria for ASD. Individuals with ASD should be screened for a DCC

Table 1 (continued)

Author, year, and country	Measuring	CCD: study type, age, gender, IQ, and recruitment	Controls: age, gender, IQ, and recruitment	Purpose	Key findings
Lombardo et al. (2012) UK	Judging accuracy of descriptions of self and others, explicit self-focused attention and emotional awareness, describing feelings, and measuring empathy	Case study CCD: $n=1$ M 29 y IQ 85 MRC AIMS Consortium study	$n=30$. Grp. 1, age μ 29.3y, IQ $\mu=117$. Grp. 2. (ASD group) $n=30$, age $\mu=29.1$, IQ $\mu=117$ Part of larger study	Compare one case of ACC autism within the domains of self-referential and social cognitive processing with 2 groups	Understanding mechanisms in cognitive and psychosocial difficulties may be facilitated with more exploration of co-occurring diagnoses of DCC and ASD
Mangum et al. (2021) USA	Executive function	Group: normative assessment, CCD: $n=36$ 18–72 y, $\mu=33.72$ y (18 M, 18 F). IQ 78–129, $\mu=100.14$ NODCC distribution, participant-initiated contact, proxies selected by DCC participants	Normative T scores	Explore problems in higher order executive functions and the lack of self-awareness in individuals with ACC	Adults with DCC experience problems in everyday executive function but lack insight and are not self-aware of the severity of impacts as reported by others
Marco et al. (2012) USA	Response inhibition and cognitive flexibility, executive function	Group: case control CCD: $n=19$ (adults $\geq$ 22 y) IQ 80–129, $\mu=97.44$ UCSF BDRP, Travis Institute, Caltech, AgCC Network and NODCC	$n=33$ Control data base	Examine the impact of ACC on cognitive inhibition, flexibility and processing speed with respect to inhibition control and cognitive flexibility	Indicates that executive functioning deficits in DCC appear to be primarily a consequence of slow cognitive processing
Ocklenburg et al., (2015) Germany	Handedness—left, right, ambidextrous, left or right ear advantage, interhemispheric integration	Group: case control CCD: $n=6$ 16–52 y, $\mu=28.5$ y (4 M, 2 F) IQ 89–104, $\mu=99$ Advertised on internet	$n=30$ Age $\mu=24.7$ y (20 M, 10 F) IQ $\mu=104.83$	Directly assess the impact of the presence or absence of the CC on the existence and the extent of functional hemispheric asymmetries	Reported slow reaction and reduced accuracy in interhemispheric information integration. Greater hemispheric autonomy in DCC may be the reason for reduced hemispheric specialization
Paul et al. (2021) USA	Alexiythymia symptomology, emotional experiences, emotional processing and expression for coping, experience of somatic symptoms, health problems, and interpretation of physical symptoms	Group: case control CCD: $n=16$ 16–52 y, $\mu=30.5$ y (7 M, 9 F) IQ 81–129, $\mu=99.88$. NODCC conference attendees, referrals, participant contact	$n=15$ Age $\mu=31.7$ y (8 M, 7 F) IQ $\mu=101.13$ Online advertisement	Further investigate the relationship between corpus callosal interhemispheric transfer and alexithymia in adults with a DCC and examine individual experiences of emotions	Adults with a DCC and alexithymia show intact emotional experience with impaired emotional interpretation. The corpus callosum is significant in emotional processing
Paul et al. (2003) USA	Non-literal language comprehension and interpreting meaning of proverbs	Group: case control CCD: $n=10$ 16–31 y, $\mu=22.2$ y (10 M) IQ 83–105, $\mu=93$ ACC network	$n=14$ Age $\mu=$ y 14 M IQ $\mu=93.4$ Community college psychology courses and employment agency	Examine the impact of callosal absence on the processing of pragmatic and paralinguistic (more than just words) information	Reported deficits in understanding non-literal language and language cues (essential for social communication) plus a lack of interhemispheric integration of vital language aspects processed in the right hemisphere.

Table 1 (continued)

Author, year, and country	Measuring	CCD: study type, age, gender, IQ, and recruitment	Controls: age, gender, IQ, and recruitment	Purpose	Key findings
Paul et al. (2004) USA	Assessing 3 elements of story-generation: logic, social understanding and content	Group: case control CCD: $n=6$ 17–28 y, $\mu=23$ y (6 M) IQ 87–105, $\mu=94.5$ Neurologist referral and ACC network (part of larger group)	$n=8$ Age $\mu=20.63$ y (8 M) IQ $\mu=96.3$ Community college psychology courses and employment agency	Assess social processing deficits through analysis of responses by individuals with ACC to pictures from the Thematic Apperception Test	Impairments evident in story logic, generating appropriate narratives, understanding socially complex scenes, and social understanding
Paul et al (2006) USA	Verbal ratings of arousal and valence, and skin-conductance response	Group: case control CCD: $n=9$ 19–37 y, $\mu=24$ y (7 M, 2 F) IQ 91–105, $\mu=106$ Part of a larger study, Travis Institute	$n=12$ Age $\mu=24$ y (8 M) IQ $\mu=96$ Source unknown	Explore how both brain hemispheres normally function together to generate emotional responses to stimuli	Emotional responses are supported by intact right hemisphere mechanisms, with dysfunction when impaired (in DCC). Impairments in normal verbal ratings of arousal are in line with alexithymia models
Paul et al. (2014) USA	Autism screening	Group: case control CCD: $n=26$, 16–54 y, $\mu=28.77$ y (16 M, 10 F) IQ 78–129 $\mu=95.46$ NODCC conference attendees, CalTech	Autistic adults: $n=28$ Age $\mu=29.6$ y (23 M, 5 F) IQ $\mu=109.5$ Existing research registry, Caltech	Test the hypothesis that behavioral and cognitive impairments in individuals with agenesis of the corpus callosum may overlap with ASD	Although DCCs are a major risk factor to develop autism, specific features distinguish them from autistic behaviors. Raises important questions for further research in genetic and environmental causes for DCC and ASD
Paul et al. (2016) USA	Verbal and visual memory processing	Group: case control CCD: $n=30$ 16–35 y, $\mu=28.47$ y (19 M, 11 F) IQ 78–129, $\mu=98.33$ NODCC conference attendees, Caltech	$n=30$ Age $\mu=29.47$ y (21 M, 7 F) IQ $\mu=100.97$ Online advertisement, employment agencies	Examine verbal and visual memory processing in individuals with ACC	Learning and memory impairments include immediate and delayed recall of words, delayed recognition and retention of faces and poor recall of story themes
Pelletier et al. (2011) Canada	Cerebral processing, expressive and receptive language	Group: case control CCD: $n=6$ 22–46 y, $\mu=36.67$ y (4 M, 2 F) IQ (65–110), $\mu=81.5$ Notre Dame Hospital	Grp. 1 (IQ matched) $n=6$Age $\mu=39.5$ y (4 M 2 F) IQ $\mu=95.2$Grp. 2 (high IQ) $n=5$ Age $\mu=27$ y (2 M 3 F) IQ $\mu=127$ Source unknown	Explore language lateralization in six individuals with ACC using an fMRI protocol	The corpus callosum is not essential to establish lateralized language functions
Popoola et al. (2019) USA	Clinical assessment and pathology	Case study CCD: $n=1$ M 45 y IQ "poor" Clinical presentation	Not applicable	Understand presentation and symptoms associated with neuropsychiatric manifestations	Further evidence required to support the correlation between DCCs and the onset of psychiatric presentations
Rehmel et al (2016) USA	Proverb interpretation and comprehension	Group: case control Experiment 1: CCD: $n=19$ 16–55 y, $\mu=25.89$ y (15 M, 4 F) IQ 83–131, $\mu=98.26$. Experiment 2: DCC: $n=19$ 16–52 y, $\mu=25.47$ y (10 M, 9 F) IQ 80–129, $\mu=95.68$ AgCC Network, NODCC	$n=33$ Age $\mu=24.48$ y (30 M 3 F) IQ $\mu=97.58$ Online advertisement: Craigslist.com	To better clarify the importance of callosal connections in supporting correct generation and recognition of meaning in proverb interpretation	Deficits occur in abstraction, accuracy and comprehension of second order meaning. Relevant to misunderstanding in daily communication and social interaction

Table 1 (continued)

Author, year, and country	Measuring	CCD: study type, age, gender, IQ, and recruitment	Controls: age, gender, IQ, and recruitment	Purpose	Key findings
Renteria-Vazquez et al. (2021) USA	Capacity to make appropriate social and mental state inferences	Group: case control CCD: $n=14$ 21–51 y, $\mu=32$ y (6 M, 8 F) IQ $\mu=99.14$. Source unknown	Control grp.: $n=14$, 18–61 y, Age $\mu=35.79$ y (11 M, 3 F), IQ $\mu=107.29$ ASD grp.: $n=13$, age $\mu=28.85$ y. (10 M, 3 F) IQ $\mu=110.92$ Source unknown	Clarify the impairments in social imagination and of mental states in adults with ACC or ASD to assess similarities and differences in social processing deficits	Individuals with DCC or ASD displayed significantly less social imagination than controls. Understanding of complex and novel social interactions was limited
Roxanas et al. (2014) Australia	IQ Academic skills, memory, attention, abstract reasoning, language, response inhibition, and emotional state	Case study CCD: $n=1$ F 26 y IQ low 50 s, ID Clinical presentation	Not applicable	Describe the case of a person with ACC, intellectual disability, antisocial behavior and lying	There may be a stronger association between DCCs with antisocial behavior and lying than is realized
Simon et al. (2008) Switzerland	Attention, problem solving in executive function, interhemispheric processing, memory recall and working memory	Case study CCD: $n=1$ F 23 y IQ "normal" Clinical presentation	Not applicable	Present a case of alien hand syndrome and schizophrenia	Corpus callosum disconnection may have caused presentation of schizophrenia and alien hand syndrome
Swayze et al. (1990) USA	Neuroanatomical and neuropathologic abnormalities in patients with schizophrenia using MRI, identifying a disorder of the corpus callosum	Case study $N=140$ (adults for MRI) CCD: $n=2$ M 39 y borderline IDF 33 y average Clinical presentation	Not applicable	Search for corpus callosum anomalies in 140 patients with schizophrenia	Disruptions in the brain's wiring may lead to schizophrenia with greater prevalence than is known
Symington et al. (2010) USA	Social cognition, applying social knowledge to real-life situations, reading social cues, understanding thoughts of others and identifying social faux pas	Group: case control CCD: $n=11$ 15–55 y, $\mu=27.8$ y (8 M, 3 F) IQ 78–116, $\mu=96.8$ ACC network and NODCC conference attendees	$n=13$ Age $\mu=25.9$ y IQ $\mu=101.7$ Employment agencies, local service businesses	Compare adults with ACC and controls on measures of social cognition	Deficiencies evident in social cognition: poor paralinguistic emotional processing, understanding non-literal speech and difficulty integrating information from multiple sources
Young et al. (2019) USA	Awareness of consequences of behavioral decisions on the welfare of others in a social context	Group: case control CCD: $n=28$ 17–55 y, $\mu=29.89$ y (18 M, 10 F) IQ 80–129, $\mu=95.57$. ACC network and NODCC conference attendees	$n=32$ Age $\mu=26.59$ y (23 M 9 F) IQ $\mu=101.09$ Online advertisement: Craigslist.com	Clarify the nature of social and emotional cognition in ACC regarding imagining consequences of decisions	Deficiencies in the capacity to imagine emotional and cognitive consequences of an individual's actions on others in complex social situations

CCD, corpus callosum disorder/dysgenesis (or DCC, disorder of the corpus callosum); *IQ*, intelligence quotient; *M*, male; *F*, female; *μ*, mean; *y*, years; *ACC*, agenesis of the corpus callosum; *cc*, corpus callosum; *NODCC*, National Organisation for Disorders of the Corpus Callosum; *OCD*, obsessive compulsive disorder; *QBI*, Queensland Brain Institute; *AusDoCC*, Australian Disorders of the Corpus Callosum; *UCSF*, University of California San Francisco; *ASD*, autism spectrum disorder; *BDRP*, Brain Development Research Program; *CalTech*, California Institute of Technology; *MRC*, Medical Research Council

studies were not always accurately disaggregated, rendering it impossible to accurately aggregate statistics. Therefore, a mean age of 32.9 years was an estimation and calculated using data reported for a total of all included individuals with a CCD ($n = 465$), aged from 16 to 74 years, reported in 34/38 studies. Three additional, salient case–control studies (Brown et al., 2005a; Hinkley et al., 2016; Symington et al., 2010) each contained a participant aged 14–15 years, with whole of study population, mean ages of 25.6, 27, and 32.8 years, respectively. One case–control study without individual or mean-age data (Marco et al., 2012) identified a group of 19 adults aged 22 years or older.

Studies collected data using diverse instruments to measure cognitive and psychological function. For example, Behavior Rating Inventory of Executive Function—Adult Version (Roth et al, 2005) and Toronto Alexithymia Scale-20 (Bagby et al., 1994) were employed to identify and describe participants. Although cognitive and psychological deficits are known to affect QoL for individuals with rare conditions and disability, no studies examined QoL for adults with a CCD. Neuroimaging identified individuals with complete agenesis, partial agenesis, or hypoplasia of the corpus callosum. Impacts typically overlapped, and symptomology specific to each presentation was inconsistent. Therefore, in this review, all presentations will be referred to individually as a corpus callosum disorder (CCD) or collectively as corpus callosum disorders (CCDs). Other assessments included general intelligence, comprehension, communication, and more specific tests of achievement. Assessments of autism and personality traits were also reported in some studies. Intelligence quotient (IQ) data were supplied in 36/38 studies. Most IQ measures were drawn from Weschler instruments (Weiss et al., 2010). Thirty-three studies described participants with average intelligence levels at or above the accepted level for intellectual disability (i.e., FSIQ > 70). Two case studies (Farchione et al., 2002; Popoola et al., 2019) provided no measured intelligence data but noted developmental delays affecting schooling. Swayze et al. (1990), Pelletier et al. (2011), and Roxanas et al. (2014) included participants with intelligence scores below the level denoting intellectual disability (i.e., FSIQ ≤ 70).

Focus of studies

The following sections synthesize the key findings of the 38 included studies examining the cognitive and psychological impacts of CCDs on adults (see Table 2).

Cognitive domain

For the purpose of this review, the cognitive domain refers to the mental processes associated with acquiring, retaining, retrieving, and manipulating knowledge, generating understanding and problem solving, exercising judgment, imagining new possibilities, and the act of undertaking these processes in everyday contexts. Twenty-nine studies examined cognitive impairments and their impacts on adults with a congenital CCD, with twenty focusing on language. Adults with a CCD were reported to experience diverse impacts, with impairments in linguistic and emotional processing, learning and memory, attention, executive function, social cognition, and complex reasoning.

Language

Lateralization

The development of language is a key cognitive function in humans. Language lateralization is the understanding that language is essentially processed in the left hemisphere of the brain (Gazzaniga et al., 1962). Although advances in technology are ameliorating understanding, researchers have debated whether language processing is dependent upon interhemispheric transfer via the corpus callosum. Three studies (Jeeves & Temple, 1987; Ocklenburg et al., 2015; Pelletier et al., 2011) reported a degree of hemispheric autonomy, in contrast with four studies (Hearne et al., 2017; Hinkley et al., 2012, 2016; Paul et al., 2003) reporting that a CCD impairs hemispheric function required for language lateralization. However, each of these studies noted that further research is warranted.

Jeeves and Temple (1987) hypothesized that callosal absence was not the cause of language impairment and that some individuals with a CCD would have no language deficits. They examined the function of the corpus callosum in processing language of two adults with a CCD, replicating a single participant case study of an adult with language deficits (Dennis, 1981). While two of the three total participants displayed a range of deficits, one performed well in almost all language tests. Jeeves and Temple (1987) surmised that their data suggested that the corpus callosum was not essential for normal development of certain functions of language. However, the authors acknowledged their findings did not definitively refute the hypothesis that the corpus callosum is integral in lateralization and regarded it as an unresolved issue requiring further investigation.

Pelletier et al. (2011) conducted a functional magnetic resonance imaging (fMRI) study of six adults with a CCD and two control groups. Control group 1 was matched on IQ, age, and education, with group 2 comprising younger participants with a high IQ, controlling for variables known to affect lateralization, including increasing age and limited cognitive abilities (Lebel & Beaulieu, 2009; Szaflarski et al., 2006). Receptive and expressive speech, syntactic

Table 2 Cognitive and psychological domains: summary of results and references for included studies

Domain	Area of impact	Summary	References
Cognitive domain	*Language:*	Cognitive challenges and barriers were encountered with language, in key areas of linguistic processing, comprehension, and learning and memory. Reduced levels of attention and impaired executive functioning, social cognition, emotional processing, and complex reasoning were evident as were deficits in grasping novel concepts or higher order reasoning	Barker et al., 2021, Brown & Paul, 2000, Brown et al., 2005a, Brown et al., 2020, Cavalari & Donovick, 2015, Erickson et al., 2014, Hearne et al., 2019, Hinkley et al., 2016, Hinkley et al., 2012, Jeeves & Temple, 1987, Mangum et al., 2021, Marco et al., 2012, Ocklenburg et al., 2015, Paul et al., 2003, Paul et al., 2016, Pelletier et al., 2011, Popoola et al., 2019, Rehmel et al., 2016, Renteria-Vazquez et al. 2021, Symington et al., 2010
	Lateralization	Debate continues about whether language processing is dependent upon interhemispheric transfer via the corpus callosum. Studies noted that further research is warranted	Hearne et al., 2017, Hinkley et al., 2016, Hinkley et al., 2012, Jeeves & Temple, 1987, Ocklenburg et al., 2015, Paul et al., 2003, Pelletier et al., 2011
	Linguistic processing and comprehension	Receptive linguistic processing is particularly affected when content is novel, non-literal or increases in complexity, necessitating second order reasoning	Barker et al., 2021, Brown & Paul, 2000, Brown et al., 2005a, Paul et al., 2003, Rehmel et al., 2016, Symington et al., 2010
	Learning and memory – auditory, visual, and verbal	Difficulties with encoding, retention, and retrieval of language, suggesting these results were reasons for impaired verbal performance and literacy weaknesses	Cavalari & Donovick, 2015, Erickson et al., 2014, Hinkley et al., 2016, Paul et al., 2016
	Attention	Reduced levels of sustained attention, particularly in the areas of vigilance and maintaining response inhibition	Brown et al., 2020
	Executive function	Deficits in adequate basic reasoning skills when applied to functional daily living tasks. Impaired by slow cognitive processing, complexity of tasks and difficulties with higher order reasoning	Cavalari & Donovick, 2015, Mangum et al., 2021, Marco et al., 2012
	Social cognition	Poor self-awareness and insight evident in reasoning, social insight, understanding humor, and paralinguistic language (body language and facial expressions). Increased credulity, persuadability, and risk of social trickery	Barker et al., 2021, Brown & Paul, 2000, Brown et al., 2005a, Brown et al., 2021, Mangum et al., 2021, Paul et al., 2004, Rehmel et al., 2016, Renteria-Vazquez et al., 2021, Young et al., 2019
	Emotional processing	Can identify basic emotions in self and others but difficulties arise as complexity increases. Reduced emotional intelligence identified	Anderson et al., 2017, Bridgman et al., 2014, Buchanan et al., 1980, Cavalari & Donovick, 2015, Lombardo et al., 2012, Paul et al., 2006, Paul et al., 2021, Symington et al., 2010
	Complex reasoning	Evidence of deficits and impairment increased significantly as cognitive tasks and processes became more complex	Brown & Paul, 2000, Brown and Paul et al. 2005a, Cavalari & Donovick, 2015, Erickson et al., 2014, Hearne et al., 2019, Hinkley et al., 2012, Mangum et al., 2021, Marco et al., 2012, Ocklenburg et al., 2015, Paul et al., 2016, Rehmel et al., 2016, Renteria-Vazquez et al., 2021

Table 2 (continued)

Domain	Area of impact	Summary	References
Psychological domain	Psychological/psychiatric	For the purposes of the current review, the psychological domain is understood to refer to the mental and emotional state of a person and its counterpart, and the psychiatric domain is understood to refer to mental, emotional, (neuro) developmental, and behavioural disorders (i.e., conditions that might be diagnosed in Diagnostic and Statistical Manual of Mental Disorder [DSM-5] or International Statistical Classification of Diseases and Related Health Problems [ICD-11])	Bhattacharyya et al., 2010, Bondade et al., 2018, Chinnasamy et al., 2006, Farchione et al., 2002, Lau et al., 2013, Lombardo et al., 2012, Paul et al., 2014, Popoola et al., 2019, Renteria-Vazquez et al., 2021, Roxanas et al., 2014, Simon et al., 2008, Swayze et al., 1990
	Psychiatric symptomology	Overlapping symptomology is evident between CCDs and some mood and behavioural diagnoses in the DSM-5. Individuals presenting with symptoms or diagnoses of mood disorders and other mental health issues may discover a congenital CCD following neuroimaging. Further research is needed to establish whether adults with a CCD are at increased risk of mood disorders and other psychiatric issues	Bhattacharyya et al. Bondade et al., 2018, Chinnasamy et al., 2006, Farchione et al., 2002, Popoola et al., 2019, Roxanas et al., 2014, Simon et al., 2008, Swayze et al., 1990,
	Developmental disorder: autism	Adults with a congenital CCD may present with autistic traits that meet the criteria for a diagnosis of autism spectrum disorder (ASD)	Lau et al., 2013, Lombardo et al., 2012, Paul et al., 2014, Renteria-Vazquez et al., 2021
	Psychosocial	Problems were identified with relationships and social functioning affected by difficulties with emotional processing and social cognition. The understanding and application of societal norms combined with the capacity to identify and process emotions are interwoven in day-to-day life, interpersonal engagement, and associated psychological conditions. In these results, we recognize that the domains of social cognition, emotional regulation and psychological impacts may be conflated, reflecting the extreme heterogeneity of impacts	Anderson et al., 2017, Barker et al., 2021, Bridgman et al., 2014, Brown & Paul, 2000, Brown et al., 2005a, Brown et al., 2021, Buchanan et al., 1980, Cavalari & Donovick, 2015, Chinnasamy et al., 2006, Farchione et al., 2002, Hearne et al., 2019, Lau et al., 2013, Lombardo et al., 2012, Mangum et al., 2021, Paul et al., 2004, Paul et al., 2006, Paul et al., 2014, Paul et al., 2016, Paul et al., 2021, Popoola et al., 2019, Rehmel et al., 2016, Renteria-Vazquez et al., 2021, Roxanas et al., 2014, Simon et al., 2008, Swayze et al., 1990, Symington et al., 2010, Young et al., 2019

decision-making, story-listening, and verbal fluency tasks were examined. Results indicated no difference in lateralization between the participants with a CCD and control groups in receptive speech. A minor difference was observed in expressive speech results between participants with a CCD and the high-IQ control group. The authors surmised that the corpus callosum is not essential to establish lateralized functions of language and that language develops bilaterally in the acallosal brain. Supporting Pelletier's hypothesis, Ocklenburg et al. (2015) applied a dichotic listening task to adults with a CCD and matched controls to assess differences between simple and complex interhemispheric integration. Communication between the brain hemispheres was found to be substantially altered and significantly reduced in adults with a CCD. The hemispheres in the acallosal brain appeared to operate more independently, suggesting a higher degree of hemispheric autonomy. However, due to the small sample, no correlation coefficients reached significance. Therefore, it was not conclusively determined that the corpus callosum is not essential to lateralization.

In contrast to the findings of Jeeves and Temple (1987), Pelletier et al. (2011), and Ocklenburg et al. (2015), four studies investigating communication deficits in groups of adults with average-range IQ indicated that corpus callosum disruption may affect hemispheric language processing (Hearne et al., 2017; Hinkley et al., 2012, 2016; Paul et al., 2003). In a case–control study with adult males with a CCD and matched controls, Paul et al. reported significant deficits in responding accurately to non-literal language, for example, proverbs or idioms. Additionally, difficulties were reported in tasks requiring interhemispheric linguistic processing, such as generating a meaningful explanation for proverbs, processing emotional prosody (indications of attitude), and recognizing meaning of non-literal expressions.

Two studies by Hinkley et al., (2012, 2016) employed functional neuroimaging to measure ipsilateral (same side) and contralateral (opposite side) hemispheric neural activity and connectivity in brains of participants engaged in language reasoning tasks including speech preparation, speech execution, and language processing. Using magnetoencephalography (MEG), Hinkley et al. (2012) assessed problem solving and verbal processing speed. Results comparing 18 adults with a CCD and 18 neurotypical matched controls reported compelling evidence that functional interactions are affected within and between brain hemispheres in the absence of a fully formed corpus callosum. Analyzing linguistic tests and high-resolution MEG results, Hinkley et al. (2016) compared adults with a CCD with neurotypical controls, reporting that participants with a CCD may have bilaterality or right hemisphere dominance. The authors found that the efficacy of specific brain regions, for example, language processing areas in the left hemisphere, is affected by poor functional connectivity in the absence of a corpus callosum. They concluded that a CCD impairs verbal performance, with the corpus callosum helping to drive language lateralization (p. 4522). Although definitive understanding of the relationship between corpus callosum anomalies and lateralization is not yet fully established, the studies indicated that left hemispheric lateralization is associated with normal corpus callosal development.

Linguistic Processing and Comprehension

Six studies examined expressive and receptive linguistic processing (Barker et al., 2021; Brown & Paul, 2000; Brown et al., 2005a; Paul et al., 2003; Rehmel et al., 2016; Symington et al., 2010). Adults of average intelligence and diagnosed with a CCD displayed little or no significant difference from normative levels or controls in comprehension of simple or literal language. However, when faced with novel aspects, increased linguistic complexity in non-literal interpretations, non-verbal language, and second-order reasoning (finding meaning where it is not immediately obvious), adults with a CCD typically exhibited significant impairment.

Results in two studies employing the Gorham Proverb Test (1956) and Delis–Kaplan Executive Function System (Delis et al., 2001) indicated deficits in complex linguistic reasoning (Brown & Paul, 2000; Rehmel et al., 2016). Participants were unable to generate appropriate answers or accurately identify meaning, and significant impairment was noted in non-literal elements. Deficits were evident in understanding and recognizing the elements that make up linguistic prosody (rhythm, pitch, intonation, and timing). Barker et al. (2021) compiled the first known profile of an adult with a CCD, a superior IQ and partial rhombencephalosynapsis (fusion of the cerebellar hemispheres). Problems were evident with selection and generation of ideas, presenting as verbal adynamia (reduced spontaneous speech), suggesting that interhemispheric transfer is a key factor for spontaneous speech production and dynamic aphasia may be associated with CCD.

Paul et al. (2003) utilized the Formulaic and Novel Language Comprehension Test (Kempler & Van Lancker Sidis, 1996) to measure the use of pragmatic (practical) and paralinguistic (nonverbal) language of 10 adult males of average intelligence. When compared with matched controls, results were similar for comprehension of literal aspects. However, for non-literal elements, adults with a CCD displayed significant impairment with deficits in understanding proverbs and recognizing linguistic prosody. Symington et al. (2010) further supported these findings in a study employing the Thames Awareness of Social Inference Test (McDonald et al., 2003). Adults with a CCD displayed deficits in comprehension of the more complex, second-order meanings of prosody and interpreting body language. Examining

non-literal figurative and metaphorical language interpretation and comprehension of humor, Brown et al. (2005a) reported that adults with CCD demonstrated significant deficits.

Learning and Memory-Auditory, Visual, and Verbal

Four studies reported difficulties with learning and memory involving encoding, retention, and retrieval of language. Results of the California Verbal Learning Test – Second Edition (Delis et al., 2000) for a group of 26 adults with a CCD (Erickson et al., 2014) and a single-participant case study (Cavalari & Donovick, 2015) indicated deficits in the amount of verbal information recalled and elaboration of verbal information (the capacity to draw inferences within the brain's knowledge base). Both studies noted deficits causing delayed recall of verbal information and difficulty learning new information. Cavalari and Donovick suggested this as a cause for weakness in spelling and reading. Employing the Wechsler Memory Scale (Weiss et al., 2010), Paul et al. (2016) compared adults with CCD with matched controls, identifying delays in auditory, visual, and verbal memory particularly in recalling verbal story content and faces. Using MEG technology, Hinkley et al. (2016) substantiated these findings, suggesting correlations between disrupted corpus callosum connections and impaired verbal performance in acallosal participants.

Attention

Brown et al. (2020) used the Conners' Continuous Performance Test II (Conners, 2000) to measure attention, impulsivity, and vigilance and assess whether related deficits were symptomatic of a CCD. Results for adults with a CCD noted reduced levels of sustained attention and difficulties maintaining response inhibition when compared with normative levels. Overall analysis concluded that adults with a CCD experience moderate difficulties in sustaining attention, particularly in the areas of vigilance and maintaining response inhibition and more notably in young males.

Executive function

Executive function is the skill set used to effectively perform everyday activities. It involves working memory, flexible thinking, and self-control, combining multiple, high-level, cognitive skills to manage learning, work, and life (Anderson, 2008). Two case–control studies (Mangum et al., 2021; Marco et al., 2012) and a single case study (Cavalari & Donovick, 2015) reported deficits in executive functioning in adults with a CCD. Impairments were attributed to slow cognitive processing, increased complexity of tasks, difficulties with higher-order reasoning, poor self-awareness and insight, and deficits in adequate basic reasoning skills when applied to functional daily living tasks.

Social cognition

A total of 26 articles reported a range of cognitive difficulties in communication, social cognition, and emotional processing, causing psychosocial impacts affecting social functioning in adults with a CCD. Impacts indicated poor self-awareness and insight, in addition to difficulties with reasoning and understanding humor, prosody, and paralinguistic language (body language and facial expressions). Such challenges contributing to reduced social functioning and mental health are reported in the psychological/psychiatric domain below.

Emotional processing

Anderson et al. (2017), Bridgman et al. (2014), and Symington et al. (2010) examined emotions in adults with CCDs, concluding that adults with CCDs showed reduced emotional intelligence, defined as "the ability to perceive and express emotion, assimilate emotion in thought, understand and reason with emotion, and regulate emotion in the self and others" (Salovey & Mayer, 1990, p189). Adults with CCDs exhibited impairments in facial recognition and a lack of attention to the eye region when scanning faces (Bridgman et al., 2014) and problems interpreting paralinguistic cues (Symington et al., 2010). Anderson et al. found that while adults with CCDs were able to identify basic emotions in themselves and others, impairments became apparent with more complex applications in social interactions.

Problems identifying more complex emotions in themselves and others suggested an association between CCDs and alexithymia, the inability to recognize and describe one's own emotions. Two case studies identified alexithymia and reduced social function occurring with CCDs (Buchanan et al., 1980; Lombardo et al., 2012). Paul et al. (2006) examined emotional arousal, with results suggesting associations between corpus callosal disruptions and alexithymia. Paul et al. (2021) employed the Toronto Alexithymia Scale-20 (Bagby et al., 1994) to measure alexithymia through identification, description, and expression of feelings. Results showed that deficits in identifying and describing feelings were more prevalent in adults with a CCD than matched controls, indicating that the corpus callosum may play a critical role. The authors suggested that additional task-based measures may further clarify the relationship.

In one of the few studies involving participants with intellectual disability, Roxanas et al. (2014) described a

26-year-old female (FSIQ 67) whose neurological assessment results indicated mild intellectual disability with impaired processing speed, poor working memory, and difficulties understanding deception in social stories. Antisocial and risky behaviors including chronic lying were evident. Although anecdotal reports of chronic lying or confabulation (relating untrue information without deceitful intent or knowledge) have been described in individuals with a CCD, they are yet to be quantified (Wright, 2017).

Complex reasoning

Overall, studies consistently reported that adults with a CCD, within the range of average intelligence, did not differ significantly from matched controls without CCD within simple language, learning, memory, and problem-solving tasks. However, evidence of deficits and impairment was more pronounced as cognitive tasks and processes became more complex (Brown & Paul, 2000; Brown et al., 2005a; Cavalari & Donovick, 2015; Erickson et al., 2014; Hearne et al., 2019; Hinkley et al., 2012; Mangum et al., 2021; Marco et al., 2012; Ocklenburg et al., 2015; Paul et al., 2016; Rehmel et al., 2016; Renteria-Vazquez et al., 2021). In simple language reasoning tasks, several studies reported that participants with a CCD showed little or no difference when compared with controls. However, with novel concepts, increased numbers of tasks, and higher degrees of difficulty, reports consistently indicated that deficits became more evident as task complexity increased. Hearne et al. (2019) employed fMRI to measure brain activity of adult participants with and without CCDs while engaged in nonverbal reasoning puzzles. In adults with CCDs, processing speed slowed as the puzzles became more difficult, with a measurable reduction in neural activity and connectivity. Although both groups returned similar results in noncomplex tasks, as task complexity was parametrically increased, performance of adults with a CCD decreased.

In summary, the literature identified diverse cognitive impacts, with findings reported in group studies typically supporting measurement and observation in case studies. Deficits were reported in complex problem solving, reasoning and concept formation, processing speed in expressive and receptive language, academic performance, attention and memory, repetitive behaviors, identifying and verbalizing emotions, understanding and applying social cues, confabulation, and processing information about others. Studies identified difficulties with emotional processing, for example identifying emotions and using language to understand and express emotion. Some conflation between cognitive issues and psychological/psychiatric functioning and well-being was evident and will be addressed in the following section.

Psychological/Psychiatric Domain

For the purpose of this review, the psychological domain refers to patterns of thoughts, feelings, and emotions. The psychiatric domain refers to mental, emotional, (neuro) developmental, and behavioral disorders included in diagnostic manuals such as the American Psychiatric Association's (2022) *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; text rev. *DSM-5-TR*) or the World Health Organization's (2019) *International Statistical Classification of Diseases and Related Health Problems* (11th Ed.; ICD-11). Thirteen articles examined adults diagnosed with a congenital CCD and at least one additional condition including obsessive compulsive disorder (OCD), ADHD, depression, anxiety, autism spectrum disorder (ASD), and schizophrenia. During revision of the previous edition, (DSM-4) the DSM-5 Task Force and Work Groups noted that the classifications within and between many disorders can be fluid over the life course in congruence with the overlapping symptomology apparent in adults with CCD (Parker, 2014).

Psychiatric Presentations

Eight case-studies described individuals presenting to clinical practices with psychiatric diagnoses including schizophrenia (Chinnasamy et al., 2006; Simon et al., 2008; Swayze et al., 1990), alien hand syndrome (Simon et al., 2008), OCD (Farchione et al., 2002), psychosis (Bondade et al., 2018), ADHD (Roxanas et al., 2014), and depression (Bhattacharyya et al., 2010; Popoola et al., 2019; Swayze et al., 1990). Following exploratory neuroimaging, all were found to have a congenital CCD.

In three studies conducting neuropsychological assessments of adults diagnosed with schizophrenia, Chinnasamy et al. (2006), Simon et al. (2008), and Swayze et al. (1990) reported weaknesses in cognitive, behavioral, and social domains, prompting follow-up neuroimaging to investigate possible neurological anomalies. They were subsequently found to have undiagnosed congenital CCDs. Swayze suggested that although research in this area was inconclusive, a subset of individuals diagnosed with schizophrenia may have congenital corpus callosum anomalies, warranting further research. All authors emphasized the importance of neuroimaging for accurate diagnoses, while Chinnasamy et al., supported by Cavalari and Donovick (2015), emphasized that the heterogeneity of impacts rendered individual profiles essential for appropriate management.

Developmental Disorder: Autism

Four studies examined autistic traits in adults with a congenital CCD (Lau et al., 2013; Lombardo et al., 2012; Paul et al., 2014; Renteria-Vazquez et al., 2021). Employing the

self-reporting Autism Spectrum Quotient (Baron-Cohen et al., 2006), Lau et al. identified autistic traits exceeding the ASD screening cut-off in 18% of adults with a CCD compared to 2.3% of adult controls. They stated the importance of seeking autism screening for adults with a CCD who displayed repetitive behaviors and deficits in social skills and communication. Conversely, for adults diagnosed as autistic, neuroimaging exploring structural etiology is important to identify possible corpus callosum structural alterations. The prevalence of congenital corpus callosum anomalies in adults diagnosed with ASD is unknown (Lau et al., 2013).

A study by Paul et al. (2014) involving adults with a CCD and autistic adults found that assessment of autistic criteria, reported by adults with a CCD, differed from proxy reports by their parents. Results indicated that 8/26 adults with a CCD met the criteria for autism when assessed by the self-reported Autism Diagnostic Observation Schedule (Lord et al., 2000) and clinical presentations. Subsequent addition of recollective parental reports available for 22/26 adults with a CCD reduced the number who formally met the ASD criteria to 3/22 (four were unavailable). The authors asserted that the discrepancy in information that reduced the number of adults meeting an ASD diagnosis potentially denied them access to support that such a diagnosis can offer.

Lombardo et al. (2012) compared one male diagnosed with a CCD and ASD with adults with ASD (without CCD) and 30 neurotypical controls. Across a range of self-referential cognition and empathy measures, social difficulties were typically more pronounced in the individual and the ASD group when compared with controls. However, overall results for the adult with a CCD indicated more significant deficits in memory sensitivity and processing social-cognitive information about other people when compared with both groups. Results of measuring social inferences and imagination in groups of adults with a CCD, adults with ASD, and controls by Renteria-Vazquez et al. (2021) supported these findings. Adults with ASD and CCDs displayed "impoverished social imagination and attribution of mental states" (p. 577).

Psychosocial Impacts

The APA dictionary of psychology (2022) defines *psychosocial* as "the intersection and interaction of social, cultural, and environmental influences on the mind and behavior." Psychosocial issues associated with deficits in emotional and cognitive processing might underpin emergent psychological/psychiatric problems affecting physical and mental well-being and effective interpersonal engagement. Twenty-six studies identified problems with relationships and social functioning caused by difficulties with emotional processing and social cognition, contributing to associated conditions such as anxiety and depression. In these results, we acknowledge that the domains of social cognition and emotional regulation may be conflated, reflecting the heterogeneity of CCD impacts.

Communication deficits caused by reduced interhemispheric processing of complex information were found to result in misunderstandings and inappropriate social interactions. Brown and Paul (2000) reported psychosocial impacts evident during interpretation and generation of social narratives requiring decoding (making sense of information) and encoding (converting thoughts to communication). Young et al. (2019) reported reduced interpretation of meaning and use of fewer social and emotional insight words. Impairments in social functioning were attributed to deficits in skills requiring second-order reasoning, for example interpreting body language or other figurative language where meaning is not immediately obvious.

Brown et al. (2000, 2005a, 2021), Mangum et al. (2021), Paul et al., (2003, 2004), Rehmel et al. (2016), Renteria-Vazquez et al. (2021), Symington et al. (2010), and Young et al. (2019) examined a number of parameters directly affecting social interaction. Adults with a CCD demonstrated impoverished social norm perception and a greater rigidity in adherence to learnt social norms (Brown et al., 2021; Renteria-Vazquez). Difficulties were apparent in understanding subtleties of social nuances. Adults with a CCD applied significantly less imagination than neurotypical controls when drawing inferences from nuances and paralinguistic cues to interpret social norms. Additionally, adults with a CCD experienced difficulties generating appropriate narratives demonstrating understanding of complex social scenes and deficiency in capacity to imagine the emotional and cognitive consequences of their actions on others (Paul et al., 2004; Renteria-Vazquez et al.). Comparing social perceptions of adults with CCDs with matched controls, Symington et al. assessed capacity for judging the thoughts, feelings, and intentions of others, providing insights into problems with interpreting complex social situations. Again, capacity for adults with CCDs was significantly reduced with authors concluding that performance was affected by difficulties with second-order linguistic processing, interpreting non-literal cues, and problems processing information from multiple sources.

Reduced coherence of non-literal language cues, poor recognition and inference of second-order meaning, and lack of awareness of self and others compromise social engagement. Compared with controls, adults with a CCD were significantly less discerning of the thoughts and intentions of others, with poor elaboration of complex and novel social interactions (Renteria-Vazquez et al., 2021). Parents described their adult children as missing the point of subtle language in stories and jokes and having poor social judgment (Brown & Paul, 2000). Barnby et al (2022) have reported significantly increased credulity, persuadability,

and susceptibility to social trickery in adults ($n = 22$) with a CCD when compared with neurotypical controls ($n = 86$), increasing the risk of social exploitation. Consistent with results in the cognitive domain, studies indicated that psychosocial difficulties increased as social skills and interactions became more complex, affecting relationships and social capacity. A diversity of psychological/psychiatric impacts is compounded by the heterogeneity of presentations affecting adults with a CCD.

Discussion

This scoping review synthesizes the evidence of the cognitive and psychological impacts of CCDs among diagnosed adults. Thirty-eight quantitative, peer-reviewed articles from 1980 to 2021 employed a range of psychometric measures to examine how adults with congenital CCDs compared with matched controls or normative levels. The introduction of MR neuroimaging in 1980, combined with expanding sample sizes in the decades that followed, ensured more precise interrogation of earlier hypotheses. Gazzaniga et al. (1962) examined impacts of surgical disconnection of the hemispheres (split brain), concluding that although they did affect interhemispheric communication it did not cause disability. David (1992) compared interhemispheric transmission of "acallosals" ($n = 3$) with "normals" (n = 46), concluding that caution was required when interpreting the acallosals' performance. Brown and Paul (2000) documented a range of impacts found in two adults with a CCD, establishing a foundational springboard for much of the ensuing CCD research. As such, knowledge of the causes, presentation, and impacts of CCDs has continued to expand, with extreme heterogeneity presenting challenges to accurate prognosis and expedient intervention.

The absence of a synthesis of literature specific to impacts on adults with congenital CCDs motivated this review. Examination of the 24 group studies and 14 single- or dual-participant case studies revealed diverse impacts of congenital CCDs on cognitive and psychological/psychiatric functioning for adults. Challenges were compounded by heterogeneity, difficulties gaining a definitive diagnosis, and diagnostic overshadowing. More evidence is nonetheless required to inform policy and practice to better support adults with CCDs.

Cognitive and Psychological Function

Researchers have debated on the role of the corpus callosum in language processing, with some studies surmising that the corpus callosum was not essential to develop lateralization and other language function. However, studies with larger samples, employing functional imaging techniques, produced more substantive results. They surmised that although language is processed within and between the hemispheres, corpus callosum disruption affects language processing and language lateralization, reporting greater deficits in interhemispheric communication identified in tasks requiring processing of complex language and problem-solving.

Processing delays were identified with encoding, retention, and retrieval of language. Although most participants were of average intelligence, academic performance was often inconsistent, indicating significant weakness in one or more key academic areas. Across the studies, adults with CCDs were consistently reported to successfully complete simple tasks but experienced greater difficulty as complexity increased. Adults with a CCD understood literal meanings but displayed deficits in more complex language containing expressive and receptive non-literal or second-order meanings. Impairments were apparent in linguistic processing, novel problem-solving, learning, memory, attention, executive function, and social interaction, with deficits evident in tasks involving understanding and interpreting proverbs, humor, metaphors, social vignettes, idioms, and paralinguistics.

Social communication difficulties were evident with linguistic processing of elaborative language, non-literal language, and prosodic emotional cues; all of which are important elements for effective social communication (Blasko & Kazmerski, 2006; Thoma & Daum, 2006). Delayed and inaccurate processing of receptive and expressive language inhibited successful learning and relationships. Despite individuals having adequate basic language skills, results indicated a range of deficits in the interpretation of language of others and the capacity for participants to express their own thoughts and emotions, creating psychosocial challenges. Similar findings have been reported in children with a CCD (Moes et al., 2009; Siffredi et al., 2018). Although subtle symptoms in children may be overlooked when cognitive and psychosocial demands are less complex, such deficits create barriers for adults to appropriately meet the demands of executive functioning, personal independence, and societal expectations (Dunkel & Harbke, 2017; Mithen et al., 2015).

Processing complex narratives is a predictor of children's future academic achievement and cognitive gains (Fivush et al., 2006; Plotka & Wang, 2019). In this review, adult participants with a CCD reported a history of delays in childhood and adolescence, including language, educational misunderstanding, and inadequate recognition of CCDs. During adolescence, the corpus callosum is instrumental in meeting the growing demands of increasingly complex cerebral processing required in educational and social environments. This is typically a time when individuals with a CCD noticeably fall behind their peers (Brown & Paul, 2019; Chavarria et al., 2014; Genc et al., 2018). Inadequate formal support in childhood significantly impairs language, memory, literacy,

and social interaction, with failure to intervene often driven by the unfounded assumption that language, literacy, and other educational and social needs would simply resolve themselves in adulthood (Clegg et al., 2005). Lack of intervention and support contributes to inadequate preparation for the complex demands of adulthood, causing significant social difficulties in independent living and maintaining relationships and employment, in addition to developing mental health and psychiatric issues (Clegg et al.). Impacts of complex cognitive and psychosocial challenges become more pronounced for adults with a CCD as expectations of functioning with greater independence increase (Australian Disorders of the Corpus Callosum 2020; Brown and Paul; Maxfield et al., 2021). As suggested by Roxanas et al. (2014) and Renteria-Vazquez et al. (2021), proficiency in performing simple social tasks does not always translate to the more complex inferential social skills required for the development of socially inclusive relationships. Companionship is noted as an important factor in alleviating stress and enhancing well-being for people with rare conditions, and compromised social functioning presents risk factors for exclusion and isolation (Bryson & Bogart, 2020).Therefore, psychosocial impairments in adults with a CCD that affect engagement in socialization and relationships are of concern.

Heterogeneity and Misdiagnosis

At a functional level, the consequences of misinterpreted heterogeneity produced anxiety, fatigue, poor self-esteem, and social isolation for adults who presented in the average intelligence range but were often misunderstood. Self or proxy descriptions of one or more of these problems were mentioned in 16 studies. As such, in addition to the aforementioned functional impacts, adults with a CCD contend with diagnostic delays, misdiagnosis, and dismissive attitudes from professionals informed by inadequate resources and confounded by complex, heterogeneous CCD symptomology (Jeeves, 1965; Maxfield et al., 2021; Paul et al., 2007; Schilmoeller & Schilmoeller, 2000). For individuals with rare conditions, experiences of professional consultations with inaccurate resources and practices create stigma, mental and physical harm, and exclusion (Anderson et al., 2013; Bryson & Bogart, 2020; Molster et al., 2016; Zurynski et al., 2017). Drawing from Jeeves (1965), some medical professionals perpetuate a persistent myth, advising individuals and their families that "there are thousands of perfectly normal people walking around with no corpus callosum" (Schilmoeller & Schilmoeller, 2000 p. 225), despite evidence to the contrary (O'Brien, 1994; Schilmoeller & Schilmoeller, 2000).

Subsequent delays, lack of intervention, and inconsistent guidelines compound issues for adults with CCDs and their families, clinicians, educators, and researchers. Although posing a wicked public health problem, the most significant problems are experienced by the adults themselves. If heterogeneity is not recognized and understood by policy, procedural, and professional support, adults with a CCD face the risk of chronic mismanagement. Consequently, this potentially affects personal independence, safety, employment, and social inclusion, risking mental health and well-being and creating barriers to acceptable QoL.

Overlapping Symptomology and Psychiatric Diagnoses

Individuals with mental illness have greater levels of unmet physical and mental health needs compared to the general population. It is well established that people with mental health diagnoses have significantly higher medical comorbidity and reduced life expectancy (Jones et al., 2008; Walker et al., 2015). Adults with CCDs who experience psychological/psychiatric impacts such as depression, anxiety, schizophrenia, poor mental health, and autistic traits are at risk of additional complications (Compton et al., 2008; Yamamoto et al., 2014; Zhao et al., 2017). Opportunities for independence and embodied social connections are diminished, exacerbating isolation (Pellicano et al., 2021).

Neuroimaging has revealed microstructural alterations in corpus callosum morphology, associated with schizophrenia in individuals who do not have a congenital CCD (Kelly et al., 2018; Walterfang & Velakoulis, 2014). The world's first large-scale meta-analysis by the Enhancing Neuro Imaging Genetics through Meta Analysis (ENIGMA) consortium confirmed white matter alterations in individuals with schizophrenia (Kelly et al., 2018). Additionally, evidence indicates links between impoverished corpus callosal connections with alterations in shape and volume of the corpus callosum, and diagnoses including autism, ADHD, anxiety and depression, and schizophrenia (Kelly et al., 2018; Koshiyama et al., 2020; Moreau et al., 2020, 2021; Valenti et al., 2019; Walterfang & Velakoulis, 2014; Walterfang et al., 2009a; Walterfang et al., 2009b). Reasons suggested to explain overlapping symptomology among associated psychiatric diagnoses are altered morphology specifically in the corpus callosum of individuals without a CCD or shared genetic etiology for CCDs, autism, ADHD, and schizophrenia (Koshiyama et al., 2020; Moreau et al., 2020, 2021; Paul et al., 2014; Sherr, 2003).

Regarding corpus callosum disconnection specifically, the broad and complex areas of psychiatry include a body of earlier research around surgical disconnection in addition to more current investigations of surgical and congenital disconnection (David, 1994; Gazzaniga et al., 1962; Kelly et al., 2018; Koshiyama et al., 2020). David (1994) suggested that brain maturation may cause the emergence of

a structural corpus callosum abnormality that has lain dormant. Taylor and David (1998) examined 56 children and adults with agenesis of the corpus callosum, half of whom were diagnosed with intellectual disability (ID). One-third of adults with a CCD presented with psychiatric disorders, including psychosis ($n=3$), depression/anxiety ($n=5$), and lack of impulse control ($n=4$), suggesting a potential causal association. However, these data were drawn from psychiatric patients presenting to the British Neurological Surveillance Unit (BSNU) neuropsychiatric and neurological clinics, posing limitations in this study (which was not included for review).

Although neurodevelopmental disorders, mood disorders, anxiety, depression, and schizophrenia are reported in adults with congenital CCDs, further research is needed to conclusively explain their comorbidity. There is limited evidence as to whether a congenital CCD poses an increased risk for adults to develop psychotic disorders such as schizophrenia. There are no known cross-disorder, large-scale meta-analyses within the CCD population (Koshiyama et al., 2020; Lee et al., 2020). Walterfang and Velakoulis (2014) suggest that more comprehensive whole-of-brain/illness studies may determine whether the corpus callosum is "the 'seat' of the illness or merely its reflector" (p. 11). However, all psychiatric diagnoses can present similar outcomes such as social stigma and unmet support needs.

Diagnostic Overshadowing

Experiences of societal discrimination and unsupportive attitudes from professionals typically cause individuals to avoid disability and healthcare interventions (Thornicroft, 2003). For adults with a CCD, one cause may be a type of diagnostic overshadowing, occurring when professionals restrict their considerations during the assessment process and consequently attribute symptoms (and behaviors) to a more commonly observed associated diagnosis such as autism, intellectual disability, anxiety, depression, and schizophrenia, (Booth et al., 2011; Levitan & Reiss, 1983). When adults with a CCD present with few discernible impacts and a scant documented history, CCD symptoms and needs may be misinterpreted or disregarded in favor of a focus on more familiar diagnoses such as autism, ADHD, and alexithymia. While an autism diagnosis currently gains better access to systemic disability support, it can overshadow recognition of broader, heterogeneous CCD impacts (Booth et al., 2011; Valenti et al., 2019). Clinicians adopting a multidimensional approach that considers heterogeneity and cognitive complexity would improve management and support for adults with a CCD. With a more holistic approach, the medical odyssey of accurate CCD diagnosis that can take months or even years could be minimized to elicit more appropriate management outcomes. The heterogeneity of CCDs and paucity of knowledge highlight the need for research to further examine comorbid psychopathologies in a diverse CCD cohort.

Although some psychological symptoms may emerge in childhood, challenges typically escalate for adults, with demands of independence such as sustaining relationships and employment. Complex hidden disabilities and rare conditions hinder functional capacity, leading to exhaustion, isolation, and exclusion (Arnold et al., 2019; Bogart & Irvin, 2017; Pellicano et al., 2021). When undiagnosed individuals present with mood, developmental, and behavioral disorders, neuroimaging is warranted to identify or eliminate undiagnosed CCDs. This review highlights the importance of recognizing and supporting adults with CCDs who are at risk of developing psychiatric and other mental health disorders.

Limitations and Implications for Future Research

This review included literature spanning 4 decades, during which technological advances have enabled significant improvements in diagnostic accuracy. Most studies were conducted in the USA (27/38), with several recruiting from intersecting participant databases, presenting possible recruitment bias. All studies were in English and quantitative. The self-reported experience of those with CCD was not considered. Participants were generally drawn from homogenous populations with minimally identifiable ethnic diversity. Diversity in future research may be strengthened by such collaborative global consortia as ENIGMA, The Cognitive Genetics Collaborative Research Organization (COCORO), and the International Research Consortium for the Corpus Callosum and Cerebral Connectivity (IRC^5).

Most studies (33/38) specified participants within an average intelligence range, spanning FSIQ of 80 or above, specifying avoidance of possible confounding effects of ID as their rationale. Increased representation of adults with ID is vital to accurately represent the diversity of the community of adults with CCD. Although numbers indicated an over-representation of male participants, some individuals were represented in multiple studies with insufficient quantifying data available for gender analysis.

No studies specifically examined QoL. Nonetheless, with reduced cognitive and psychosocial functioning and the effect of heterogeneity of CCDs on definitive diagnosis and appropriate supports, it is reasonable to expect that CCDs also affect QoL, warranting further investigation. Future CCD research would also benefit from qualitative methodology incorporating phenomenological and participatory paradigms. The most effective means to learn more about the lives of people is to involve and ask those who are actually living them.

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Declarations

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