OXFORD

Alexithymia and somatization in agenesis of the corpus callosum

Lynn K. Paul, [ID] [1,2,3] Shawneen R. Pazienza,[4] and Warren S. Brown [ID] [2,3]

[1]Division of Humanities and Social Sciences, California Institute of Technology, Pasadena, CA 91125, USA,
[2]Fuller Graduate School of Psychology, Travis Research Institute, Pasadena, CA 91101, USA, [3]International Research Consortium for the Corpus Callosum and Cerebral Connectivity (IRC5), Pasadena, CA 91106, USA, and [4]Austin Outpatient Clinic, Central Texas Veterans Health Care System, Austin, TX 78744, USA

Correspondence should be addressed to Lynn K. Paul, California Institute of Technology, Division of Humanities and Social Sciences, Baxter MC 228-77, Pasadena, CA 91125, USA.
E-mail: lkpaul@hss.caltech.edu.

Abstract

Deficient communication between the cerebral hemispheres is one of several prevailing neurobiological explanations for alexithymia and has been strongly supported by research on patients with commissurotomy. We examined self-reported symptoms of alexithymia in adults with agenesis of the corpus callosum (AgCC), a condition characterized by more subtle reductions in interhemispheric transfer than in commissurotomy. Sixteen adults with AgCC and full-scale intelligence quotient >80 were compared with 15 neurotypical controls group-matched for age and intelligence score. The AgCC group endorsed greater difficulty identifying and describing feelings and more vague physical symptoms than controls but similar levels of emotional experience and emotional coping. This finding of impaired emotional interpretation with intact emotional experience is consistent with findings in callosotomy patients, implicating the critical role of the corpus callosum in cognitive dimensions of emotion processing. Further study of alexithymia in AgCC using task-based measures may help clarify the nature of this relationship.

Key words: emotion; alexithymia; somatic complaints; corpus callosum; connectivity

Introduction

Alexithymia is a formal construct that describes deficient emotional expressiveness characterized by difficulty identifying and expressing feelings, a tendency toward somatic complaints, concrete and externally oriented thinking style, and a lack of imaginative thinking (Nemia *et al.*, 1976). Alexithymia is inversely related to emotional intelligence and to emotion-focused coping styles (Lumley *et al.*, 2005; Velasco *et al.*, 2006).

The variation of characteristics and symptom patterns in alexithymia may reflect a diversity of causes (Moriguchi *et al.*, 2006). Some argue that there are two basic forms or dimensions

of alexithymia: 'cognitive', characterized by deficiency in ability to identify and verbalize feelings, and 'affective', characterized by deficiencies in evaluating emotional experiences (Gazzaniga and LeDoux, 1978; Goerlich-Dobre *et al.*, 2015). For example, difficulty identifying and describing feelings may result from a general deficit in the cognitive processing of emotions (Lumley *et al.*, 2005). Whereas, difficulty identifying and describing feelings accompanied by a tendency toward somatic complaints (Sifneos, 1973; Lesser, 1981) may be caused by difficulty distinguishing bodily sensations related to emotional arousal, i.e. affective processing (Lumley *et al.*, 2005).

The current study examined the hypothesis that alexithymia and associated symptoms of somatization may result from disconnection between cognitive and affective processing systems—specifically disconnection of right hemisphere systems specialized for processing emotion, and left hemisphere systems specialized for processing language (TenHouten *et al.*, 1985, 1988).

Corpus callosum and verbal expression of emotion

Several lines of research suggest that interhemispheric transfer plays a critical role in emotion processing and expression, and, consequently, interhemispheric deficits contribute to alexithymia. For example, individuals with high alexithymia scores and no known brain abnormality reportedly have significantly slower reaction times than non-alexithymic individuals on tasks requiring interhemispheric transfer (Dewaraja and Sasaki, 1990; Parker *et al.*, 1999) and are significantly less accurate on a cross-hand finger localization task that requires interhemispheric transfer (Zeitlin *et al.*, 1989).

While these studies support an association between interhemispheric transfer deficits and alexithymia, studies of callosotomy patients (severed corpus callosum and intact anterior commissure) provide further clarity about the role of callosally mediated interhemispheric transfer in emotional expression. After callosotomy, information about an emotional stimulus presented to the left visual field did not transfer from the right hemisphere to the left, but the subjective emotional valuation did transfer (i.e. patients could provide an accurate emotional evaluation of an 'unseen' emotional stimulus; Gazzaniga and LeDoux, 1978). In daily life, individuals who had undergone commissurotomy had diminished ability to verbally express their emotions (alexithymia) and increased psychosomatic complaints consistent with the psychoanalytic understanding of somatization as a compensation for inability to express emotions (Hoppe and Bogen, 1977; TenHouten *et al.*, 1988). Together, these investigators argued that the corpus callosum was necessary for transferring emotional 'information' between the hemispheres, but emotional 'experience' (evaluations) may transfer via the anterior commissure or other pathways. The emergence of alexithymia following callosotomy suggests that eliminating interhemispheric transfer via the corpus callosum may be 'causally' related to alexithymia, but what if callosally mediated interhemispheric transfer is absent from birth?

In adults with agenesis of the corpus callosum (AgCC), a congenital abnormality where the axons that form the corpus callosum fail to develop or cross the midline (Rakic and Yakovlev, 1968), the absence of callosal connections does not limit interhemispheric transfer as markedly as callosotomy during adulthood (Lassonde *et al.*, 1991; Brown *et al.*, 1999). Could development of neural mechanisms that compensate for absence of callosally mediated interhemispheric transfer prevent alexithymia in these individuals?

Agenesis of the corpus callosum

AgCC occurs in ~1 of every 4000 live births (Glass *et al.*, 2008). It can result from a variety of toxic, genetic or vascular causes, but only 30–45% of individuals have identifiable causes for their AgCC diagnosis (Paul *et al.*, 2007). Studying the sub-population of individuals for whom complete or partial AgCC is the primary neurological condition ('Primary AgCC'; Brown and Paul, 2019)—that is, those without other brain abnormalities and

who possess a full-scale intelligence quotient within the normal range [i.e. full-scale intelligence quotient (FSIQ) ≥80]—can help identify contributions of callosal interactions to higher cognitive and psychosocial capacities such as alexithymia.

According to Brown and Paul (2019), deficiency in interhemispheric transfer of complex sensory information and learning (e.g. Sauerwein and Lassonde, 1983; Brown *et al.*, 1999) is one of three core symptoms of Primary AgCC. Individuals with AgCC typically exhibit greater interhemispheric transfer than individuals with a commissurotomy, but far less than neurotypical individuals (Lassonde *et al.*, 1991; Brown *et al.*, 1999). For example, poor interhemispheric transfer is evident in mild-to-moderate difficulties on tasks necessitating bimanual coordination of motor movements (e.g. Mueller *et al.*, 2009) and on tasks that assess interhemispheric transfer of complex sensory information (e.g. Jeeves and Silver, 1988; Brown *et al.*, 1999). The other two core neuropsychological deficiencies posited by Brown and Paul (2019) involve cognitive processing speed (Marco *et al.*, 2012) and complex novel problem-solving (e.g. Fischer *et al.*, 1992; Schieffer *et al.*, 2000; Brown *et al.*, 2012). These three core deficits, in turn, produce a pattern of mild-to-moderate neuropsychological and psychosocial deficits in Primary AgCC (reviewed by Siffredi *et al.*, 2013; Brown and Paul, 2019). Among these secondary cognitive symptoms, individuals with Primary AgCC have impairments in response inhibition and switching (Marco *et al.*, 2012), sustained attention and vigilance (Brown *et al.*, 2020), encoding in list-learning (Erickson *et al.*, 2014; Paul *et al.*, 2016), and higher-order language skills (Paul *et al.*, 2003; Brown *et al.*, 2005a,b; Rehmel *et al.*, 2016).

Laboratory studies of adults with Primary AgCC have also revealed impairments in cognitive processing of emotions. Specifically, they have found exhibited deficits in strategic understanding and use of interpersonal emotions (Anderson *et al.*, 2017), poor identification of emotion in faces (Bridgman *et al.*, 2014), diminished ability to imagine the emotional implications and consequences of alternative behavioral decisions (Young *et al.*, 2019), and limitations imagining and inferring the mental, emotional and social states of others (Renteria-Vazquez *et al.*, under review; Brown and Paul, 2000; Paul *et al.*, 2004; Symington *et al.*, 2010; Turk *et al.*, 2010). Finally, when viewing emotionally arousing images, individuals with AgCC had significant skin-conductive responses that discriminated between emotions but provided unreliable ratings of emotional valence and arousal for each image (Paul *et al.*, 2006). This outcome is consistent with theories suggesting that information about emotion can be divided into cognitive and affective dimensions (Goerlich-Dobre *et al.*, 2015) and that the corpus callosum is necessary specifically for the cognitive processing of emotional information (Gazzaniga and LeDoux, 1978).

This pattern of emotion processing deficits suggests that despite developmental compensation and greater capacity for interhemispheric transfer, adults with AgCC are likely to exhibit alexithymia symptoms similar to those in adult callosotomy patients. Parent reports indicate alexithymia symptoms are common in children with AgCC—difficulty feeling or expressing their own emotions (O'Brien, 1994; Brown and Paul, 2000) and elevated rates of somatization (Badaruddin *et al.*, 2007)—but very little is known about how adults with AgCC experience the emotional processing deficits observed in laboratory experiments or if those deficits are associated with other symptoms of alexithymia such as increased somatization and externally oriented thinking.

Table 1. Summary statistics of participant demographic information

	AgCC, $n = 16$			Control, $n = 15$					
	M	s.d.	Range	M	s.d.	Range	t	P	95% CI
Age	30.50	10.74	16–52	31.07	9.48	21–45	0.155	0.88	−8.029, 6.896
FSIQ	99.88	12.88	81–129	101.13	10.11	84–116	0.301	0.77	−9.804, 7.287
VCI	102.50	15.28	82–131	104.33	10.30	89–126	0.389	0.70	−11.475, 7.808

Notes: M = mean; s.d. = standard deviation; FSIQ = full-scale intelligence quotient; VCI = verbal comprehension index; CI = confidence interval of difference between means.

Aims of this research

The purpose of this study was to further investigate the relationship between callosally mediated interhemispheric transfer and alexithymia in adults with Primary AgCC, by examining their individual experiences of emotions. In addition to the Toronto Alexithymia Scale-20 (TAS-20; Bagby *et al.*, 1994), participants completed questionnaires about current emotional experiences [Positive and Negative Affect Schedule (PANAS); Watson *et al.*, 1988], emotion processing and emotion expression for coping [Emotion Approach Coping Scale (EACS); Stanton *et al.*, 1994], experience of somatic symptoms and health problems [Symptom Checklist, SCL90-R; Derogatis, 1977, 1983: Rand 36-Item Health Survey 1.0 (RHS); Hays *et al.*, 1993] and interpretation of physical symptoms [Symptom Interpretation Questionnaire (SIQ); Robbins and Kirmayer, 1991].

As seen in adult callosotomy patients and described in children with AgCC, we hypothesized that relative to controls, adults with AgCC would endorse greater alexithymia symptomology on the TAS-20, as well as increased reports of physical symptoms and psychological interpretation of physical symptoms. Although studies of adult callosotomy patients indicate that emotional evaluation is not dependent on callosal transfer, we hypothesized that in AgCC, callosal absence and associated cognitive symptoms of alexithymia experienced across the lifespan would interfere with processing affect and result in restricted emotional expression (i.e. reduced use of emotional coping and lower reported levels of positive affect and negative affect).

Methods

Participants

Participants included 16 individuals with AgCC (7 partial AgCC, 7 male, 7 right-handed) and 15 control participants (8 male, 12 right-handed). Groups were matched on age, FSIQ, verbal comprehension index (VCI) (see Table 1), as well as handedness, $\chi^2 = 2.9$, $P = 0.08$, and gender, $\chi^2 = 0.03$, $P = 0.09$ (with Yates correction).

Participants with AgCC were recruited through the National Organization for Disorders of the Corpus Callosum, referrals and participant-initiated contact. Control participants were recruited through online advertisements. To avoid confounding effects from limited general intellectual function, FSIQ ≥ 80 and 12+ years of education were required. Exclusionary criteria for all participants included English as a second language, intractable epilepsy, major central nervous system disorder other than AgCC and history of drug abuse, moderate-to-severe head injury or neurosurgery. AgCC diagnosis and presence of anterior commissure were confirmed through review of magnetic resonance imaging (MRI) scans. Three potential AgCC participants with other structural brain abnormalities (heterotopia) were excluded.

All participants were tested as a part of a larger research project, including determination of FSIQ and VCI using the Wechsler Adult Intelligence Scale-Third Edition (Wechsler, 1997). All participants read and signed an informed consent form prior to testing. This research was approved by the Human Subjects Review Committee at the Travis Research Institute, Fuller Graduate School of Psychology.

Instruments

TAS-20 (Bagby *et al.*, 1994) is a 20-item self-report questionnaire that provides a global measure of alexithymia and three sub-scale scores: (i) Difficulty Describing Feelings, ability to communicate emotions to other people, (ii) Externally-Oriented Thinking, degree to which the individual focuses on external rather than internal experiences and (iii) Difficulty Identifying Feeling, ability to identify and describe emotions and to distinguish them from bodily sensations.

PANAS (Watson *et al.*, 1988) measures self-ratings of how strongly an individual is experiencing 10 positive and 10 negative feelings at the time of assessment.

EACS (Stanton *et al.*, 1994) uses self-reported frequency of 16 behaviors to assesses the extent to which emotional expression (e.g. 'I let my emotions out') or emotional processing (e.g. 'I explore my emotions') are typically used to cope with highly stressful situations. The items focus on active attempts to display and examine one's emotions but do not ask about use of cognitive strategies to process emotion.

The somatization scale from SCL90-R (Derogatis, 1977, 1983) measures self-reported presence of 12 different physical symptoms during the past week.

SIQ (Robbins and Kirmayer, 1991) assesses self-reported presence of six somatic symptoms in the prior 3 months (prolonged headache, excessive sweating, sudden dizziness, dry mouth, heart pounding and fatigue), as well as likelihood of attributing these to psychological, environmental and physical causes.

RHS (Hays *et al.*, 1993) is a self-report measure of eight factors: general health perception, physical functioning, role limitations due to physical health, role limitations due to emotional problems, social functioning, emotional/mental health, bodily pain and energy/fatigue.

Procedure

All measures were administered remotely via a survey production website. At a previously determined time, the administrator called and assisted each participant in accessing the online survey. Instructions were presented online and also read aloud by the administrator. To demonstrate task comprehension, participants read the first two items aloud and responded online before independently completing the remainder of the session. The administrator was available by phone throughout testing and

Table 2. Summary statistics for all variables and group comparison of subscales

	AgCC, n = 16			Control, n = 15			t	df	P	CI
	M	s.d.	bsCI	M	s.d.	bsCI				
TAS-20										
Total**	49.5	13.74	42.69, 56.06	38.47	5.41	35.93, 40.87				
Describing+	14.00	5.01	11.88, 16.53	10.47	3.25	9.00, 12.07	2.31	29	0.028	0.41, 6.66
Identifying++	16.25	5.86	13.63, 19.13	10.73	3.28	9.17, 12.40	3.26	23.9	0.003	2.02, 9.01
Externally	19.25	5.40	16.69, 21.97	17.27	3.55	15.60, 19.13	1.20	29	0.24	−1.40, 5.37
EACS										
Expression	3.08	0.83	2.66, 3.48	3.20	0.55	2.88, 3.52	−0.08	27	0.94	−0.61, 0.56
Processing	2.82	0.82	2.53, 3.33	3.27	0.68	2.89, 3.64	−0.66	27	0.52	−0.83, 0.43
PANAS										
Positive	31.69	10.04	26.94, 36.56	30.57	10.36	25.25, 36.00	0.30	28	0.77	−6.52, 8.75
Negative	13.63	5.11	11.31, 16.03	13.93	7.65	10.46, 18.29	−0.13	28	0.90	−5.11, 4.51
SCL90-R**	23.06	6.13	20.31, 26.13	16.00	3.82	14.25, 18.14	3.84	25.5	0.001	3.18, 10.95
SIQ										
Psychological*	12.00	3.29	10.56, 13.56	9.87	2.17	8.87, 10.93	2.12	29	0.04	0.07, 4.19
Physical	8.50	2.03	7.59, 9.50	7.87	2.00	7.00, 8.97	0.88	29	0.39	−0.85, 2.11
Environmental	15.00	3.41	13.31, 16.59	14.60	3.27	13.07, 16.20	0.33	29	0.74	−2.05, 2.85
RHS										
Health percep.	58.00	9.60	53.33, 62.67	59.60	8.69	54.20, 64.40	0.13	27	0.90	−7.44, 8.44
Physical funct.	87.67	18.60	77.00, 95.33	85.00	29.91	64.75, 97.75	−0.20	27	0.85	−18.69, 15.45
Physical lim.	86.54	21.93	75.00, 96.15	87.50	24.30	71.25, 100.00	−0.55	25	0.59	−21.57, 12.50
Emotional lim.	89.74	21.01	76.94, 100.00	90.00	31.62	70.00, 100.00	−1.69	23	0.11	−22.83, 2.31
Social funct.	51.97	17.49	43.67, 61.10	88.75	19.94	75.63, 97.50	−0.76	27	0.46	−17.12, 7.91
Mental health	66.13	22.42	55.07, 76.80	74.40	14.14	65.00, 82.00	−1.31	27	0.20	−23.90, 5.31
Body pain	68.83	25.33	56.17, 81.42	81.25	13.76	72.63, 89.50	−2.06	22.6	0.052	−31.38, 0.12
Energy/fatigue	53.67	18.75	44.33, 63.17	56.00	18.07	45.5, 66.00	−0.52	27	0.61	−18.99, 11.32

Notes: *P < 0.05; **P < 0.01; +P$_{adj}$ < 0.05; ++P$_{adj}$ < 0.01; s.d. = standard deviation, bsCI = 95% confidence interval estimated from 1000 bootstrap samples with replacement; CI = 95% confidence interval of difference between means; TAS-20 = Toronto Alexithymia Scale; EACS = Emotion Approach Coping Scale; PANAS = Positive and Negative Affect Scale; SCL90-R = Symptom Checklist Somatization Scale; SIQ = Symptom Interpretation Questionnaire; RHS = Rand 36-Item Health Survey 1.0; percep. = perception; funct. = functioning; lim. = limitations.

Table 3. Means, standard deviations, and confidence intervals by AgCC subgroup for all variables

	cAgCC, $n = 10$			pAgCC, $n = 6$		
	M	s.d.	bsCI	M	s.d.	bsCI
TAS-20						
Total	52.67	11.67	45.44, 59.67	45.67	17.50	33.33, 58.00
Describing feelings	15	3.84	12.44, 17.22	12.67	6.89	7.67, 18.00
Identifying feelings	16.67	5.34	13.44, 20.33	16.00	7.48	10.83, 21.67
Externally oriented	21	5.68	17.33, 24.44	17.00	4.82	13.00, 20.00
EACS						
Expression	3.02	0.76	2.50, 3.50	3.02	1.00	2.30, 3.75
Processing	2.75	0.71	2.38, 3.25	3.00	0.89	2.33, 3.67
PANAS						
Positive	33.44	9.40	27.56, 39.44	30.5	11.78	22.25, 38.50
Negative	13.33	4.66	10.89, 16.39	12.00	3.10	10.33, 14.67
SCL90-R Health	24.44	6.17	20.67, 28.11	21.33	6.62	16.83, 26.33
SIQ						
Psychological	12.22	2.99	10.33, 14.00	10.67	2.94	8.67, 12.67
Physical	8.44	1.81	7.44, 9.56	8.00	2.10	6.83, 9.67
Environmental	15.11	3.18	13.22, 17.22	14.50	4.18	11.33, 17.17
RHS						
Health perception	55.63	9.43	49.38, 61.25	59.17	9.70	51.67, 65.83
Physical functioning	88.12	14.62	77.50, 96.25	85.00	25.10	65.00, 98.33
Physical limit.	84.38	22.90	68.75, 98.44	87.5	25.00	62.50, 100.0
Emotional limit.	87.71	26.23	66.66, 100.0	93.34	14.89	80.02, 100.0
Social functioning	58.13	19.75	45.75, 72.06	44.00	13.16	35.42, 54.33
Mental health	70.00	12.65	62.00, 77.50	62.00	33.63	37.00, 84.00
Body pain	63.44	21.21	50.94, 77.50	70.83	30.36	50.00, 91.67
Energy and fatigue	52.50	15.58	43.13, 64.38	53.33	24.83	34.17, 70.00

Notes: s.d. = standard deviation; bsCI = 95% confidence interval estimated from 1000 bootstrap samples with replacement; TAS-20 = Toronto Alexithymia Scale; EACS = Emotion Approach Coping Scale; PANAS = Positive and Negative Affect Scales; SCL90-R = Symptom Checklist Somatization Scale; SIQ = Symptom Interpretation Questionnaire; RHS = Rand 36-Item Health Survey 1.0; limit. = limitations.

called hourly to provide assistance. Participants called administrator upon completion.

Statistical comparisons were computed with SPSS. Mauchly's test of sphericity was conducted for each analysis of variance (ANOVA), and in cases where sphericity was violated at $P < 0.05$, the Huynh–Feldt correction was used if epsilon was ≥ 0.75 and Greenhouse–Geisser was used if epsilon was < 0.75. In exploratory analyses of subscales, adjustment for multiple comparisons was addressed with Bonferroni correction.

Results

Descriptive statistics for all measures are presented in Table 2.

Toronto Alexithymia Scale-20

TAS-20 scores were higher in the AgCC group than the control group in a group-by-subscale repeated measures ANOVA, $\eta_p^2 = 0.225$, $F(1, 29) = 8.44$, $P = 0.007$. ANOVA also revealed a significant difference across subscales, $\eta_p^2 = 0.46$, $F(1.7, 48.54) = 25.07$, $P < 0.001$, but not a significant interaction of group-by-subscale, $\eta_p^2 = 0.06$, $F(1.7, 48.54) = 1.95$, $P = 0.16$. A significantly greater number of participants with AgCC exceeded the clinical cutoff score for alexithymia ($n = 5$) or possible alexithymia ($n = 1$) than control participants ($n = 0$), $X^2(1) = 5.59$, $P = 0.018$.

In exploratory group comparisons of sub-scores, the AgCC group endorsed significantly more difficulty on Difficulty Identifying Feelings, $d = 1.33$, and Difficulty Describing Feelings, $d = 0.86$, but did not differ from controls on Externally Oriented Thinking, $d = 0.45$.

Emotional experience and expression (PANAS/EACS)

Although the AgCC group endorsed difficulty on the TAS-20, they did not differ from the control group on endorsement of positive $d = 0.11$, or negative, $d = 0.05$, emotional experiences at the time of testing (PANAS), nor did the AgCC group differ from controls on use of emotion expression and/or emotion processing for coping (repeated measures ANOVA of two EACS subtests: group, $\eta_p^2 = 0.007$, $F(1, 27) = 0.199$, $P = 0.659$; subtest, $\eta_p^2 = 0.039$, $F(1, 27) = 1.10$, $P = 0.304$; group-by-subtest interaction $\eta_p^2 = 0.012$, $F(1, 27) = 0.339$, $P = 0.565$).

Expressions of somatic symptoms (SCL90-R/RHS)

The AgCC group endorsed more vague somatic symptoms than the control group on the SCL90-R Somatization scale, $d = 1.52$, but did not differ significantly from controls on any of the eight factors from RHS. Although not significant following false discovery rate correction, the AgCC group endorsed less bodily pain than the control group, $d = 0.87$.

Attribution style (SIQ)

Group-by-attribution style (psychological, environmental or physical) repeated measures ANOVA revealed a significant main effect of attribution style, $\eta_p^2 = 0.84$, $F(2, 28) = 70.71$, $P < 0.001$, but no significant effects related to group (group, $\eta_p^2 = 0.06$, $F(1, 29) = 1.87$, $P = 0.18$; group-by-attribution style, $\eta_p^2 = 0.09$, $F(2, 28) = 1.447$, $P = 0.25$). Exploratory group comparisons of attribution style suggested greater rates of psychological attributions in the AgCC than control group, $d = 0.79$ (large effect size but

not significant after Bonferroni correction), and no significant differences on physical and environmental attributions.

Discussion

The results of this study indicate that alexithymia is more common in adults with Primary AgCC than in controls matched on age, Intelligence Quotient (IQ) and handedness and provide further evidence that interhemispheric transfer deficits may result in a specific pattern of alexithymia. As hypothesized, participants with AgCC were more likely than controls to have difficulty identifying and describing their emotions and tended to report more vague physical symptoms in the absence of notable health problems and attribute psychological factors to their physical states more frequently than controls. However, in contrast to our hypothesis, they gave no indication of deficits in emotional experience. The AgCC and control groups endorsed similar levels of attention to emotions (i.e. balance of focus on external *vs* internal experiences), experience of positive and negative emotions at the time testing, and frequency of attempts to acknowledge, actively process and express emotions in response to stressful situations. As hypothesized, deficiencies in emotional expression and elevated use of somatization (i.e. 'cognitive' symptoms of alexithymia) continue from childhood (O'Brien, 1994; Badaruddin *et al.*, 2007) into adulthood, and these symptoms are recognized by the individuals with AgCC themselves.

In summary, our findings support conclusions drawn from studies of adult callosotomy and commissurotomy patients (Gazzaniga and LeDoux, 1978; Goerlich-Dobre *et al.*, 2015)—namely that the corpus callosum is necessary for transferring emotional 'information' between the hemispheres but not for processing emotional 'experience' (evaluations). Moreover, we offer evidence that neurodevelopmental mechanisms that compensate for absence of callosally mediated interhemispheric transfer do not facilitate transfer of emotional 'information' between the hemispheres and that, in contrast to our hypothesis, the presence of cognitive alexithymia during development does not interfere with recognition of emotional experience (i.e. 'affective' alexithymia).

Although dependence on self-report is a potential limitation of the current study, the pattern of emotional processing described by these participants with AgCC—impaired ability to describe emotions but intact capacity to experience them—is consistent with results from a study that directly measured physiological arousal. The prior study recorded typical skin-conductive responses in individuals with AgCC when viewing emotionally arousing images, but participants provided restricted/atypical verbal ratings of their emotional reaction to the images (Paul *et al.*, 2006). Thus, both self-reports and direct assessment of physiological arousal indicate that individuals with AgCC have typical physiological experiences of emotions and engage with emotions in a typical manner, despite disruption in the cognitive assessment and/or verbal description of their emotions.

In individuals with AgCC, as in callosotomy patients (Gazzaniga and LeDoux, 1978), this pattern of alexithymia is hypothesized to result from the disconnection between cognitive and affective processing systems—specifically disconnection of right hemisphere systems specialized for processing emotion and left hemisphere systems specialized for processing language (TenHouten *et al.*, 1985, 1988). Our findings are also consistent with the theory that left hemisphere serves as an 'interpreter' of one's own affective states and other ambiguous information (Gazzaniga, 2000), and as a result of deficient interhemispheric transfer in AgCC, the interpreter receives inadequate or inaccurate information from throughout the brain.

However, in AgCC, we cannot rule out the potential contribution of extra-callosal structural abnormalities that commonly accompany callosal absence in AgCC (e.g. colpocephaly and the presence of Probst bundles) or microscopic brain abnormalities not visible in MRIs, e.g. low numbers of Von Economo neurons (Kaufman *et al.*, 2008). Thus, while alexithymia and somatization in AgCC is most likely associated with callosal absence, consistent presence of some other undetected brain abnormality cannot entirely be ruled out on the basis of currently available data.

Due to the small sample size, we were unable to examine possible differences between participants with complete AgCC and those with partial AgCC. It is noteworthy that these subgroups did not differ in percent of participants with clinically elevated TAS scores (partial = 33%; complete = 30%). Additionally, for all variables in this study, the complete and partial AgCC groups had overlapping bootstrapped confidence intervals of the means (Table 3), suggesting that the current findings are not impacted by the presence of residual callosal connections. However, this certainly merits further investigation. Because partial AgCC is characterized by considerable variability in the pattern of interhemispheric connectivity of the remaining callosal fibers (Wahl *et al.*, 2009), it may be informative to examine the relationship between alexithymia symptoms and connectivity patterns as assessed with diffusion and functional MRI.

The corpus callosum and reductions in interhemispheric connectivity have been linked to a variety of developmental diagnosis (Paul, 2011). In comparison to other clinical populations, the rate of clinically diagnosable alexithymia in our AgCC group (31.25%) is lower than rates seen in individuals with autism (40%, Tani *et al.*, 2004; 48.1%, Hill *et al.*, 2004), chronic pain (53%, Cox *et al.*, 1994) and eating disorder (61.3%, de Groot *et al.*, 1995; 68.8%, Taylor *et al.*, 1996) but comparable to rates of alexithymia reported in multiple sclerosis (30.6%, Chahraoui *et al.*, 2008) and major depressive disorder (26.9%, Leweke *et al.*, 2012). Thus, as seen on many other cognitive and psychosocial dimensions studied in AgCC, there is a clear and significant shift of the distribution toward disability, as well as notable overlap with the distribution of symptoms in other developmental, psychiatric and neurological populations.

The elevated likelihood of cognitive alexithymia in our sample of individuals with both complete and partial AgCC provides further evidence that the corpus callosum plays a critical role in cognitive processing of emotions. Future studies using direct assessment of alexithymia symptoms in AgCC examined over the lifespan and in comparison with individuals who have other developmental diagnoses may help clarify the role of interhemispheric connectivity in development of emotional processing and expression and generate new ideas for treating alexithymia.

Open practices statement

The data and materials for all experiments will be available at the International Research Consortium for the Corpus Callosum and Cerebral Connectivity (IRC[5]) and are currently available by contacting the corresponding author. None of the experiments was preregistered.

Conflict of interest

The authors declare no conflicts of interest.

References

Anderson, L.B., Paul, L.K., Brown, W.B. (2017). Emotional intelligence in agenesis of the corpus callosum. *Archives of Clinical Neuropsychology*, **32**(3), 267–79.

Badaruddin, D.H., Andrews, G.L., Bölte, S., *et al.* (2007). Social and behavioral problems of children with agenesis of the corpus callosum. *Child Psychiatry and Human Development*, **38**, 287–302.

Bagby, R.M., Parker, J.D., Taylor, G.J. (1994). The twenty-item Toronto Alexithymia Scale—I. Item selection and cross-validation of the factor structure. *Journal of Psychosomatic Research*, **38**(1), 23–32.

Bridgman, M.W., Brown, W.S., Spezio, M.L., Leonard, M.K., Adolphs, R., Paul, L.K. (2014). Facial emotion recognition in agenesis of the corpus callosum. *Journal of Neurodevelopmental Disorders*, **6**, 32.

Brown, W.S., Jeeves, M.A., Dietrich, R., Burnison, D.S. (1999). Bilateral field advantage and evoked potential interhemispheric transmission in commissurotomy and callosal agenesis. *Neuropsychologia*, **37**(10), 1165–80.

Brown, W.S., Paul, L.K., Symington, M., Dietrich, R. (2005a). Comprehension of humor in primary agenesis of the corpus callosum. *Neuropsychologia*, **43**(6), 906–16.

Brown, W.S., Symingtion, M., Van Lancker-Sidtis, D., Dietrich, R., Paul, L.K. (2005b). Paralinguistic processing in children with callosal agenesis: emergence of neurolinguistic deficits. *Brain and Language*, **93**(2), 135–9.

Brown, W.S., Anderson, L., Symington, M., Paul, L. (2012). Decision-making in individuals with agenesis of the corpus callosum: expectancy-valence in the Iowa Gambling Task. *Archives of Clinical Neuropsychology: The Official Journal of the National Academy of Neuropsychologists*, **27**, 532–44.

Brown, W.S., Panos, A., Paul, L.K. (2020). Attention, impulsivity, and vigilance in agenesis of the corpus callosum. *Neuropsychology*, **34**(7), 744–49.

Brown, W.S., Paul, L.K. (2000). Cognitive and psychosocial deficits in agenesis of the corpus callosum with normal intelligence. *Cognitive Neuropsychiatry*, **5**(2), 135–57.

Brown, W.S., Paul, L.K. (2019). The neuropsychological syndrome of agenesis of the corpus callosum. *Journal of the International Neuropsychological Society*, **25**, 324–30.

Chahraoui, K., Pinoit, J.M., Viegas, N., Adnet, J., Bonin, B., Moreau, T. (2008). Alexithymia and links with depression and anxiety in multiple sclerosis. *Revue Neurologique (Paris)*, **164**(3), 242–5.

Cox, B.J., Kuch, K., Parker, J.D., Shulman, I.D., Evans, R.J. (1994). Alexithymia in somatoform disorder patients with chronic pain. *Journal of Psychosomatic Research*, **38**(6), 523–7.

de Groot, J.M., Rodin, G., Olmsted, M.P. (1995). Alexithymia, depression, and treatment outcome in bulimia nervosa. *Comprehensive Psychiatry*, **36**(1), 53–60.

Derogatis, L.R. (1977). *SCL-90R (Revised) Version Manual*. Baltimore, MD: Johns Hopkins University School of Medicine.

Derogatis, L.R. (1983). *SCL-90-R: Administration, Scoring & Procedures Manual-11 for the Revised Version*. Towson, MD: Clinical Psychometric Research.

Dewaraja, R., Sasaki, Y. (1990). A left to right hemisphere callosal transfer deficit of nonlinguistic information in alexithymia. *Psychotherapy Psychosomatics*, **54**(4), 201–7.

Erickson, R.L., Paul, L.K., Brown, W.S. (2014). Verbal learning and memory in agenesis of the corpus callosum. *Neuropsychologia*, **60**, 121–30.

Fischer, M., Ryan, S.B., Dobyns, W.B. (1992). Mechanisms of interhemispheric transfer and patterns of cognitive function in acallosal patients of normal intelligence. *Archives of Neurology*, **49**(3), 271–7.

Gazzaniga, M.S. (2000). Cerebral specialization and interhemispheric communication: does the corpus callosum enable the human condition? *Brain*, **123**, 1293–326.

Gazzaniga, M.S., LeDoux, J.E. (1978). *The Integrated Mind*. New York, NY: Plenum.

Glass, H., Shaw, G., Ma, C., Sherr, E.H. (2008). Agenesis of the corpus callosum in California 1983–2003: a population-based study. *American Journal of Medical Genetics Par A*, **146A**(19), 2495–500.

Goerlich-Dobre, K.S., Votinov, M., Habel, U., Pripfl, J., Lamm, C. (2015). Neuroanatomical profiles of alexithymia dimensions and subtypes. *Human Brain Mapping*, **36**(10), 3805–18.

Hays, R.D., Sherbourne, C.D., Maxel, R.M. (1993). The RAND 36-item health survey 1.0. *Health Economics*, **2**, 217–27.

Hill, E., Berthoz, S., Frith, U. (2004). Brief report: cognitive processing of own emotions in individuals with autistic spectrum disorder and in their relatives. *Journal of Autism and Developmental Disorders*, **34**(2), 229–35.

Hoppe, K., Bogen, J. (1977). Alexithymia in twelve commissurotomized patients. *Psychotherapy and Psychosomatics*, **28**, 148–55.

Jeeves, M.A., Silver, P.H. (1988). Interhemispheric transfer of spatial tactile information in callosal agenesis and partial commissurotomy. *Cortex*, **24**, 601–4.

Kaufman, J.A., Paul, L.K., Manaye, K.F., *et al.* (2008). Selective reduction of Von Economo neuron number in agenesis of the corpus callosum. *Acta Neuropathoogical*, **116**(5), 479–89.

Lassonde, M., Sauerwein, H., Chicoine, A.J., Geoffroy, G. (1991). Absence of disconnexion syndrome in callosal agenesis and early callosotomy: brain reorganization or lack of structural specificity during ontogeny? *Neuropsychologia*, **29**(6), 481–95.

Lesser, I. (1981). A review of the alexithymia concept. *Psychosomatic Medicine*, **43**, 531–43.

Leweke, F., Leichsenring, F., Kruse, J., Hermes, S. (2012). Is alexithymia associated with specific mental disorders? *Psychopathology*, **45**(1), 22–8.

Lumley, M.A., Gustavson, B.J., Partridge, R.T., Labouvie-Vief, G. (2005). Assessing alexithymia and related emotional ability constructs using multiple methods: interrelationships among measures. *Emotion*, **5**(3), 329–42.

Marco, E.J., Harrell, K.M., Brown, W.S., *et al.* (2012). Processing speed delays contribute to executive function deficits in individuals with agenesis of the corpus callosum. *Journal of the International Neuropsychological Society*, **18**(3), 521–9.

Moriguchi, Y., Ohnishi, T., Lane, R., *et al.* (2006). Impaired self-awareness and theory of mind: an fMRI study of mentalizing in alexithymia. *NeuroImage*, **32**(3), 1472–82.

Mueller, K.L.O., Marion, S.D., Paul, L.K., Brown, W.S. (2009). Bimanual motor coordination in agenesis of the corpus callosum. *Behavioral Neuroscience*, **123**, 1000–11.

Nemia, J.C., Freyberger, H., Sifneos, P.E. (1976). *Alexithymia: A View of the Psychosomatic Process*. London, England: Butterworths.

O'Brien, G. (1994). The behavioral and developmental consequences of callosal agenesis. In: Lassonde, M., Jeeves, M.A., editors, *Callosal Agenesis: A Natural Split Brain?* New York, NY: Plenum Press, 235–46.

Parker, J., Neightley, M., Smith, C., Taylor, G. (1999). Interhemispheric transfer deficit in alexithymia: an experimental study. *Psychosomatic Medicine*, **61**, 464–8.

Paul, L.K., Van Lancker-Sidtis, D., Schieffer, B., Dietrich, R., Brown, W.S. (2003). Communicative deficits in agenesis of the corpus callosum: nonliteral language and affective prosody. *Brain and Language*, **85**(2), 313–24.

Paul, L.K., Schieffer, B., Brown, W.S. (2004). Social processing deficits in agenesis of the corpus callosum: narratives from the Thematic Appreciation Test. *Archives of Clinical Neuropsychology*, **19**(2), 215–25.

Paul, L.K., Lautzenhiser, A., Brown, W.S., *et al.* (2006). Emotional arousal in agenesis of the corpus callosum. *International Journal of Psychophysiology*, **61**(1), 47–56.

Paul, L.K., Brown, W.S., Adolphs, R., *et al.* (2007). Agenesis of the corpus callosum: genetic, developmental and functional aspects of connectivity. *Nature Reviews Neuroscience*, **8**(4), 287–99.

Paul, L.K. (2011). Developmental malformation of the corpus callosum: a review of typical callosal development and examples of developmental disorders with callosal involvement. *Journal of Neurodevelopmental Disorders*, **3**, 3–27.

Paul, L.K., Erikson, R., Hartman, J., Brown, W. (2016). Memory functioning in individuals with agenesis of the corpus callosum. *Neuropsychologia*, **86**, 183–92.

Rakic, P., Yakovlev, P.I. (1968). Development of the corpus callosum and cavum septi in man. *Journal Comparative Neurology*, **132**(1), 45–72.

Rehmel, J.L., Brown, W.S., Paul, L.K. (2016). Proverb comprehension in individuals with agenesis of the corpus callosum. *Brain and Language*, **160**, 21–9.

Renteria-Vazquez, T., Brown, W.S., Kang, C., Graves, M., Castelli, F., Paul, L.K. (2021). *Social Inferences in Agenesis of the Corpus Callosum and Autism: Semantic Analysis and Topic Modeling. Journal of Autism and Developmental Disorders*.

Robbins, J.M., Kirmayer, L.J. (1991). Attributions of common somatic symptoms. *Psychological Medicine*, **21**(4), 1029–45.

Sauerwein, H.C., Lassonde, M. (1983). Intra- and interhemispheric processing of visual information in callosal agenesis. *Neuropsychologia*, **21**, 167–71.

Schieffer, B., Paul, L., Brown, W. (2000). Deficits in complex concept formation in agenesis of the corpus callosum [Abstract]. *Journal of the International Neuropsychological Society*, **6**, 164.

Siffredi, V., Anderson, V., Leventer, R.J., Spencer-Smith, M.M. (2013). Neuropsychological profile of agenesis of the corpus callosum: a systematic review. *Developmental Neuropsychology*, **38**, 36–57.

Sifneos, P.E. (1973). The prevalence of "alexithymic" characteristics in psychosomatic patients. *Psychotherapy and Psychsomatics*, **22**, 255–62.

Stanton, A.L., Danoff-Burg, S., Cameron, C.L., Ellis, A.P. (1994). Coping through emotional approach: problems of conceptualization and confounding. *Journal of Personality and Social Psychology*, **66**(2), 350–62.

Symington, S.H., Paul, L.K., Symington, M.F., Ono, M., Brown, W.S. (2010). Social cognition in individuals with agenesis of the corpus callosum. *Social Neuroscience*, **5**(3), 296–308.

Tani, P., Lindberg, N., Joukamaa, M., *et al.* (2004). Asperger syndrome, alexithymia and perception of sleep. *Neuropsychobiology*, **49**(2), 64–70.

Taylor, G.J., Parker, J.D., Bagby, R.M., Bourke, M.P. (1996). Relationships between alexithymia and psychological characteristics associated with eating disorders. *Journal of Psychosomatic Research*, **41**(6), 561–8.

TenHouten, W.D., Hoppe, K.D., Bogen, J.E., Walter, D.O. (1985). Alexithymia and the split brain. IV. Gottschalk-Gleser content analysis, an overview. *Psychotherapy and Psychosomatics*, **44**(3), 113–21.

TenHouten, W.D., Walter, D.O., Hoppe, K.D., Bogen, J.E. (1988). Alexithymia and the split brain: VI. Electroencephalographic correlates of alexithymia. *Psychiatric Clinics of North America*, **11**(3), 317–29.

Turk, A., Brown, W.S., Symingtion, M., Paul, L.K. (2010). Social narratives in agenesis of the corpus callosum: linguistic analysis of the Thematic Apperception Test. *Neuropsychologia*, **48**, 43–50.

Velasco, C., Fernandez, I., Paez, D., Campos, M. (2006). Perceived emotional intelligence, alexithymia, coping and emotional regulation. *Psicothema*, **18 Suppl**, 89–94.

Wahl, M., Strominger, Z., Jeremy, R.J., *et al.* (2009). Variability of homotopic and heterotopic callosal connectivity in partial agenesis of the corpus callosum: a 3T diffusion tensor imaging and Q-ball tractography study. *American Journal of Neuroradiology*, **30**(2), 282–9.

Watson, D., Clark, L.A., Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: the PANAS scales. *Journal of Personality and Social Psychology*, **54**(6), 1063–70.

Wechsler, D. (1997). *WAIS-III: Wechsler Adult Intelligence Scale*. 3rd edn, San Antonio, TX: The Psychological Corporation.

Young, C.M., Folsom, R.C., Paul, L.K., Su, J., Mangum, R.W., Brown, W.S. (2019). Awareness of consequences in agenesis of the corpus callosum: semantic analysis of responses. *Neuropsychology*, **33**, 275–84.

Zeitlin, S., Lane, R., O'Leary, D., Schrift, M. (1989). Interhemispheric transfer deficit and alexithymia. *American Journal of Psychiatry*, **146**, 1434–9.