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Speech and language in bilateral perisylvian polymicrogyria: a systematic review

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ABBREVIATIONS

BPP	Bilateral perisylvian polymicrogyria
WDS	Worster-Drought syndrome

AIM We aimed to systematically review the speech production, language, and oral function phenotype of bilateral perisylvian polymicrogyria (BPP), and examine the correlation between the topography of polymicrogyria and the severity of speech, language, and oral functional impairment.

METHOD A systematic search of MEDLINE, EMBASE, and PubMed databases was completed on 26th October 2017 using Medical Subject Heading terms synonymous with BPP and speech, language, or oral motor impairment. In total, 2411 papers were identified and 48 met inclusion criteria.

RESULTS Expressive and receptive language impairment and oral structural and functional deficits are frequent in BPP. Expressive deficits are frequently more severe than receptive. Only one study used formal assessments to demonstrate the presence of speech disorder, namely dysarthria. Eight studies reported an association between diffuse BPP and more severe language impairment.

INTERPRETATION Findings confirmed that language deficits are common in BPP, though assessment of the specific speech phenotype is limited. The paucity of high quality studies detailing the specific communication phenotype of BPP highlights the need for further investigation. Improving understanding of this phenotype will inform the development of targeted therapies and lead to better long-term outcomes.

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What this paper adds:

- Speech, language, and oral functional impairments are common in individuals with bilateral perisylvian polymicrogyria.
- Posterior polymicrogyria is associated with a less severe language impairment than anterior polymicrogyria.
- Deeper investigation of speech is needed to understand implicated networks in this malformation.

[main text]

Polymicrogyria, an archetypal malformation of cortical development, has a range of well-recognized patterns.[1] Bilateral perisylvian polymicrogyria (BPP) is the most common pattern and affects regions of critical importance for speech and language function. Communication difficulties in this population have significant implications for patients' self-esteem and interaction with those around them. BPP involves excessive microscopic gyration and atypical cortical lamination of the Sylvian fissures and surrounding cerebral cortex. Here we describe the speech and language phenotype of BPP.

BPP is heterogeneous with regard to topography, symmetry, aetiology, and clinical phenotype. Given the perisylvian involvement, individuals with BPP often present with pseudobulbar palsy and praxis of the orofacial musculature, resulting in difficulties with salivary control and feeding or eating. Involuntary facial expressions are frequently preserved.[2,3] Epilepsy occurs in 43 to 87 per cent of patients and intellectual disability is frequent.[4,5] Both heritable and de novo genetic causes of BPP have been described.[6,7]

Between 1956 and 1973, Worster-Drought[8,9] described a clinical presentation of weakness and paralysis of the lips, tongue, soft palate, pharynx, and laryngeal muscles in 200 patients. An atypical jaw jerk, dysarthria, drooling, dysphagia, and preservation of emotive

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reflexes were also present. This collection of phenotypic features has historically been termed Worster-Drought syndrome (WDS). Some members of Worster-Drought's original cohort were later shown to have BPP.[1] Further studies have shown that some children with WDS have BPP,[10] whereas others have typical brain structure on magnetic resonance imaging (MRI).[11]

With advances in neuroimaging, confusion in terminology has arisen due to the multiplicity of terms used to describe what is now defined as BPP based on imaging findings. These include diagnoses based on imaging, such as bilateral opercular polymicrogyria[12] and bilateral perisylvian dysplasia,[13,14] and diagnosis based on a combination of clinical and imaging factors, such as congenital bilateral perisylvian syndrome.[15] While the term Foix–Chavany–Marie syndrome is typically associated with opercular infarcts, a developmental form has been described which is BPP.[2]

Given the overlap in clinical phenotype between imaging positive and imaging negative WDS and evidence for a genetic aetiology, consideration of WDS, congenital bilateral perisylvian syndrome, and BPP as a spectrum of perisylvian abnormalities has been proposed.[11,16] Indeed, it is proposed that patients with typical structural imaging may have subtle cortical disorganization undetectable on clinical imaging.[4,16] Support for such a spectrum is also drawn from families who are discordant for perisylvian abnormalities, for example where family members share a homogenous symptomatology but only some have MRI confirmed cortical malformation and others having no MRI findings.[4,11,16]

The perisylvian region of the brain is the epicentre of language processing and production. Across this spectrum of perisylvian abnormalities, there is an association between extent and topography of cortical involvement and the severity of language impairment.[17,18] Significant language delays and differences between receptive and expressive language scores have been noted in the WDS and congenital bilateral perisylvian syndrome populations.[10,11,17] Receptive language abilities are within the typical to impaired range;[19,20] while expressive language is significantly impaired,[21] with many individuals non-verbal.[11] Speech production difficulties are also observed, linked to the oral praxis deficits.[21] Oral motor difficulties including restricted movement of the tongue and jaw are described, as well as feeding difficulties and aspiration. These significant speech production difficulties, coupled with oral motor praxis deficits, often give the impression of more profound cognitive impairment than is accurate.[19]

Given the historical overlap of several disorders with features of this disease, and now a MRI-based diagnosis, there is a need for a systematic review to clarify the speech,

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language, and oral function features of BPP. Our primary aim was to systematically review the speech production, language, and oral function phenotypes of BPP, with a secondary aim of examining the correlation between severity of speech, language, and oral functional impairment, and topography of polymicrogyria.

METHOD

This review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[22]

Eligibility

Participants with a diagnosis of BPP, bilateral perisylvian dysplasia, congenital bilateral perisylvian syndrome, bilateral anterior opercular syndrome, bilateral opercular polymicrogyria, WDS, and Foix–Chavany–Marie syndrome were included. Studies were included if any of their participants were diagnosed with BPP by MRI or autopsy; however results for any additional patients within these studies who were not diagnosed by MRI or autopsy were not reported. Studies were excluded if participants had acute, subacute, transient, progressive, or acquired forms of the above-mentioned conditions. For articles which included participants with multiple forms of cortical malformations or cortical regions affected by polymicrogyria, studies were excluded if they did not differentiate results according to (1) the type of cortical malformation (for example studies which reported on polymicrogyria but did not differentiate results according to the affected region, i.e. the perisylvian region), (2) unilateral versus bilateral pathology, or (3) acquired versus developmental aetiology.

Outcome measures

Studies were included if they reported qualitative, quantitative, or observational measures of speech and language. Studies were excluded in cases where an isolated difficulty or delay in speech and language was reported, without provision of a definition or detailed description of the observed communication subtype (e.g. dysarthria, apraxia, receptive language disorder) and how it was assessed. This criterion was introduced as many studies reported a child had ‘speech delay’, which could refer to a delay in acquiring language (including vocabulary, grammar, and morphology), or to delayed speech (as in articulation or motor production) errors.

Study type

All study types and levels of evidence were included so as to gain the widest sample available. Only studies published in English with full text available were included. Inclusion was not limited by age or sex of participants.

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Search strategy

A systematic search of MEDLINE, EMBASE, and PubMed databases was conducted by ROB and an external individual trained in database searching, using Medical Subject Headings and key words from 1946 to October 2017. Details of search strings are included in Table SI (online supporting information). Abstracts were identified and exported to Covidence.[23] Duplicates were identified and removed. Authors ROB and ATM read and screened the remaining titles and abstracts for inclusion based on the aforementioned criteria. All full text articles were assessed for eligibility by ROB. ATM, RL, and IES reviewed articles in cases where consensus was required.

Data extraction

Data from included studies was extracted and tabulated by ROB according to study type, number of participants, recruitment details, inclusion and exclusion criteria, age and sex of participants, and formal diagnosis. Features of speech, language, and oral motor function (e.g. praxis deficits, hypotonia) were documented. Speech features included dysarthria, nasality, delay, prosody, articulatory and phonological errors, and intelligibility. Language features included receptive, expressive, delay, and pragmatics. Cognitive scores relating to full scale, performance, and verbal IQ was extracted where available. Features of oral function included the presence or absence of pseudobulbar signs, jaw jerk, drooling and feeding difficulty, and mobility of the tongue and palate. Detail regarding the presence of epilepsy, a genetic diagnosis, or other relevant features was recorded. The form of measurement (quantitative, qualitative, or observational) was also documented for all features.

Given the lack of data available across studies where formalized assessment tools had been utilized, a binary rating of present/absent was given for each of the speech, language, and oral function subsections. A positive rating was given where any detail specific to speech or language difficulty could be established.

Data appraisal

The Scottish Intercollegiate Guidelines Network[24] was selected as the quality assessment tool for this review. The Scottish Intercollegiate Guidelines Network algorithm[24] was used to identify the level of evidence for each study. Level one was given to randomized controlled trials, two to case–control or cohort studies, and three to case series. Non-comparative studies were not given a numerical level, in accordance with the algorithm. A rating (++, +, –) was given to each study based on the risk of bias in accordance with checklist criteria. Studies which addressed more than half the criteria were assigned a '+' or '++' rating. Studies which

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did not address more than half of the Scottish Intercollegiate Guidelines Network checklist criteria were given a '–' rating.

RESULTS

Study selection

In total, 2411 were identified and exported to Covidence.[23] Of these, 680 duplicates were identified and removed. The remaining 1731 titles and abstracts were screened for inclusion. Eligibility was assessed with comprehensive review of 168 full text articles and 118 articles were excluded as they did not meet the criteria. An additional two articles were excluded as they reported isolated difficulty or delay in speech and language, in the absence of description or definition of the communication subtypes.[25,26]

Four studies were excluded during full text review as they reported on the same cohort and characteristics included in other studies.[3,18,27,28] In such cases, the study presenting the most detailed information relevant to our aims was included, and the other excluded. In cases where studies shared participants though reported different characteristics, both studies were included. Forty-eight studies met inclusion criteria for data extraction. Figure S1 (online supporting information) shows our process for study selection.

Characteristics of included studies

Of the 48 studies, 39 were non-comparative studies (level three) and one was a cross sectional study (Table SII, online supporting information). Retrospective (*n*=2) and prospective (*n*=4) cohort studies were identified, as well as two case–control studies. All had a quality level rating of '2+', indicating that the study fulfilled more than half of the Scottish Intercollegiate Guidelines Network checklist criteria relating to recruitment of participants, reliability and validity of assessment, identification of limitations, and analysis of data, though left some criteria undescribed, thus reducing reliability.[24] Four studies limited inclusion to participants with IQ/Performance IQ over 70[20,29] or 80,[30] or to individuals without cognitive impairment but did not define according to a specific IQ.[17] Four studies only included participants with a primary presenting problem of language delay[20,29,30] or diagnosis of specific language impairment,[31] now referred to as developmental language disorder.[32] Yasuda et al.[33] excluded participants with posterior polymicrogyria (parieto-occipital regions exclusively, without polymicrogyria on the anterior 2/3 of Sylvian fissure) and participants with additional visible abnormalities on MRI. Three retrospective studies excluded participants with insufficient available MR imaging.[1,6,11] Leventer et al.[1] also excluded participants with a diagnosis of schizencephaly. Two studies only included individuals with a diagnosis of arthrogyposis[34,35] and one with congenital hemiplegia.[36]

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Five studies included participants with genetic diagnoses, including 10q syndrome,[11] 22q11.2 deletion,[1,37] and variants in *BICD2*[35] and *PIK3R2*.[6] Kabuki syndrome was reported in individuals in two studies,[38,39] as well as one case of Peters anomaly.[39] Landau–Kleffner syndrome was reported in one single case study.[40] Three studies reported negative karyotype analyses.[41–43] Gropman et al.[44] reported that no genetic cause was identified; however, they did not detail the genetic investigations undertaken. Five studies reported on families with BPP.[4,16,17,29,45] Table SIII (online supporting information) provides further detail regarding cognition, genetics, and general health characteristics reported by each study.

Outcome measurements

Speech production phenotype

Thirty-six studies reported difficulty with speech production in at least one participant; however, often the nature of speech impairment was inadequately described to provide more than a binary rating of difficulty in speech production.

Dysarthria was the most common problem, usually identified during neurological examination (*n*=26). Only one study quantified the features of dysarthria in four participants with facial diplegia, using acoustic analysis of pitch and timing.[46] They found a loss of specific characteristics of consonants and vowels. Noise was observed in high frequency formants, voice onset time was prolonged in bilabial and alveolar stop consonants, and diadochokinetic rate was decreased. Monopitch and monoloudness were also identified. Jansen et al.[19] reported that patients with asymmetric BPP which spared one of the insular opercula had milder dysarthria than those with symmetric presentations in which both insulae were involved. Poor phonation was observed in some cases;[44,47] however it was not formally measured. Disprosody was reported in one patient.[48]

A wide variation in the severity of articulation and phonology errors was reported across 11 articles. One participant had only 10 per cent intelligibility[49] while, at the other end of the spectrum, another had only mildly impaired phonemic word generation.[48] Kim et al.[46] reported an atypical pattern of articulation of lingual, dental, and alveolar consonants in their four participants. Articulation praxis and buccofacial disorder were also described.[20] Graff-Radford et al. described a patient with BPP with poor speech clarity, where the ‘palate, tongue and lips played little role in articulation’.[2] Features consistent with a diagnosis of childhood apraxia of speech were observed in two patients.[21,45] Fluency difficulties were noted in two studies, with one patient developing a stutter in the context of evolving Landau–Kleffner syndrome.[40,44]

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Altered resonance was reported in four studies; three described patients with a nasal voice.[19,43,50] It was unclear from the information provided whether these observations related to instances of hypo-, hyper-, or mixed nasality, or other conditions known to affect resonance, such as structural abnormalities of the palate or dysarthria. Using data from spectrographic analysis, Kim et al.[46] reported increased nasalance in four patients.

Speech delay was discussed in several studies; however in most cases it was difficult to determine whether the outcome was actually speech delay (defined as acquisition of speech sounds at a later developmental age than expected in age-matched peers) or language delay (a delay in language onset in the absence of diagnosed disability or developmental delay in other cognitive or motor domains).[51] Cases identified with language delay are discussed under language results below. Regression of speech was noted in a single case with Landau–Kleffner syndrome where it was difficult to distinguish from loss of language, consistent with the patient's presentation.[40] See Table SIV (online supporting information) for additional details of the speech characteristics reported in each study.

Language phenotype

Thirty-three studies reported language difficulty in one or more participants (Table I). Twenty studies reported participants with delayed language abilities and eight included individuals without verbal language. Of the 48 studies included, 30 reported informal and formal assessments of cognition and 26 identified cognitive impairment in one or more participant. Four studies identified a stronger performance IQ than verbal IQ.[19,29,30,33] A negative correlation between performance IQ and extent of BPP was also shown.[19]

Expressive language difficulties were reported in 18 studies. Five studies did not formally assess language, however they reported a clinical impression that expressive language difficulties were more severely impaired than receptive abilities.[5,35,38,43,52] Six studies included participants who met diagnostic criteria for developmental language disorder.[17,20,29–31,53] Eight studies used standardized assessments to measure expressive language deficits and identified syntactic difficulties in three.[20,29,53] Semantic deficits were reported to be within the typical range by Boscariol et al.[53] and impaired by Hage et al.[20] and Kilinc et al.[48] Three studies reported phonological awareness difficulties.[29,30,53] Pragmatic language impairment was found in one study[57] and was deemed typical in five.[20,29,30,41,53]

Receptive language difficulties were described in seven studies, with six using formal or systematic language assessment.[2,5,19,20,29,50] Oliveira et al.[29] analysed receptive language results according to BPP localization. No participants with BPP restricted to the posterior region of the sylvian fissure demonstrated receptive language difficulties (range of standard

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scores 92–109). However, in participants with diffuse BPP, standard scores ranged from 66 (impaired) to 107 (typical). Two studies reported that receptive language difficulties were more pronounced in sentences of increasing length and complexity.[2,5] Hage et al.[20] found that 5 out of 7 participants had impaired comprehension on short and long sentences, while 1 out of 7 had impaired comprehension on long sentences only.

In some instances, receptive language was a relative strength. Eckert et al.[54] and Kilinc et al.[48] found typical receptive language skills in their participants, which included cohorts with typical cognition and borderline intellect respectively. Clinical impression of typical receptive language was reported in three studies.[35,41,55] Nevo et al.[56] reported 'almost normal' receptive language abilities although no formal assessment of receptive language abilities was detailed in this study.

A range of communication modalities was used including augmentative and alternative methods of communication. Clark et al.[58] reported 2 out of 7 participants using a combination of vocalization and sign language, and 2 out of 7 others utilizing vocalization and alternative methods of communication. Participants in other studies used gestural communication[56,59] or communication aids.[35] Table SV (online supporting information) provides additional details of the language characteristics reported in each study.

Seven studies demonstrated an anatomical association between diffuse BPP and more severe language impairment, compared to cases in whom BPP was restricted to the posterior parietal region.[4,17,20,29,31,33,45] Conversely, two studies found no significant differences or correlations respectively between the severity of language delay and subtypes of polymicrogyria.[1,19] Two MRI studies used diffusion tensor imaging tractography to demonstrate bilateral absence of the arcuate fasciculus in participants with BPP and language impairment.[48,49] One study identified a unilateral arcuate fasciculus in three participants who had some language development and found bilateral absence in non-verbal individuals with BPP.[49] The non-verbal participants also had more severe cognitive and motor impairments.

Oral function phenotype

Forty-five studies reported oral function difficulties in at least one participant. Boscariol et al.[31] and Miller et al.[36] also reported participants (6/10 and 3/3 respectively) with typical oromotor abilities. Two studies[35,54] did not report on oromotor difficulties in their participants.

Seventeen studies described participants with pseudobulbar signs. Pseudobulbar signs were identified in all 12 patients in two series.[16,51] The largest cohort found that 28 out of 31 showed pseudobulbar signs,[11] while in a cohort of families including 13 individuals with

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BPP,[29] only two participants had pseudobulbar signs. The presence of pseudobulbar signs was associated with diffuse BPP and was not found in patients with BPP restricted to the posterior parietal regions.[17] Fourteen studies reported a reduction in tongue movement, including elevation, protrusion, and lateral movement, including all 31 participants in one study.[5]

Structural changes in the oropharynx were observed, including cleft palate (*n*=1)[11] and high arched palate (*n*=2).[37,60] Functional deficits of the palate were also seen such as lack of elevation during phonation,[2,44] reduced motion,[4,38,48] and delayed movement.[61]

Other structural and functional oromotor difficulties were reported in small numbers. There was one reported instance each of tongue tie[12] and irregular dentition,[60] and three of micrognathia.[5,44] Functional oromotor impairments predominated including participants with oral dyspraxia,[30,38] weakness of facial musculature,[52,57] facial asymmetry,[19] set facial expression,[46,52] spasticity of jaw muscles,[48] dissociation of voluntary and involuntary facial expressions,[2,60] facial diplegia,[49,62] and an open or gaping mouth posture.[50,52,60] Participants with limited ability to purse their lips[56,63] and a marked gag reflex leading to difficulty performing tongue movements and opening the mouth[63] were also reported. Drooling was reported in 24 studies.

Impact of oral function on feeding

Feeding and swallowing difficulties were reported in 29 studies, especially apparent during infancy and the early years of life (*n*=9). Seventeen studies reported the presence of dysphagia (including swallowing impairment and choking). A history of aspiration was reported in three studies,[44,58] including 17 out of 23 patients in one cohort.[11]

Impairment specific to the oral phase of swallow, including masticatory problems, was reported in eight studies.[6,41,42,48,50,56,62,64] Patients requiring dietary modifications or assistance were reported in three papers, including 24 out of 28 participants in Clark et al.[11] requiring a modified adult diet, and 3 out of 28 requiring tube feeding. It is likely that many of the feeding difficulties occur as a functional consequence of the oral structural and functional difficulties experienced by this population. Table SVI (online supporting information) provides additional details of the oral functional characteristics reported in each study.

Literacy

Specific literacy difficulties were reported in seven studies. Boscariol et al.[30] and Brandão-Almeida et al.[17] reported 7 out of 11 and 10 out of 29 patients respectively with a diagnosis of dyslexia. Agraphia and alexia were reported in two participants by Graff-Radford et al.[2]

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Other mixed findings were seen, including intact reading and spelling abilities,[29,38] and deficits.[19,29,53,54] Table SIII provides additional details of the literacy characteristics reported in each study.

DISCUSSION

We report the findings of a systematic review of the speech and language phenotype of BPP and explore the association between the topography and extent of BPP and the severity of speech and language impairment. Our review only included studies of patients with a MRI or autopsy diagnosis of BPP, distinguishing it from historical studies of cohorts with the characteristic clinical features but included both lesional and non-lesional cases.[11,21,29] Forty-eight studies were analysed, published between 1946 and October 2017. A large proportion of included studies were single case studies, reflecting the previous reliance on observational methodologies and small case studies. Nevertheless, our review paints a clear picture of the spectrum of speech and language phenotypes in individuals with BPP.

Expressive and receptive language impairment is common in BPP, and expressive language impairment is typically more severe than receptive language impairment. Indeed, a number of studies included participants with no verbal output. Conversely, 4 of the 48 studies restricted inclusion to individuals with no or mild cognitive impairment only. This makes interpretation and comparisons of results between studies challenging and limits the development of a balanced understanding of the overall spectrum of language abilities and communicative participation in this cohort. In a population with widely documented cognitive deficits, it is important that the full range of abilities is captured for prognostic counselling and treatment studies.

Six studies described participants who met diagnostic criteria for developmental language disorder (previously known as specific language impairment). These studies defined developmental language disorder as being a deficit in language, not in keeping with the child's mental age,[17] or to children with language delays in the absence of intellectual deficits,[29] pervasive developmental disorders, or severe environmental deprivation.[20,30,31,53] There is contention in the literature regarding the appropriateness of diagnosing developmental language disorder in the presence of more complex patterns of impairment, in this case, the presence of BPP.[32,67] We propose that language deficits in this population may be more appropriately described to as 'language impairment associated with BPP'.

Oral functional and structural impairments were documented in 45 of the 48 studies, indicating their high prevalence in BPP. Pseudobulbar signs were the most frequent feature, reflecting the original historical observations. Structural and functional palatal impairments

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were also described. A range of other oral deficits were reported to occur infrequently, highlighting the phenotypic heterogeneity of BPP. Feeding difficulties in infancy and adulthood were reported in 29 studies. Despite their frequent documentation, no studies used formal assessment tools to accurately measure oral structural or functional deficits.

This review highlights that while a handful of studies have used standardized assessment or validated scales to demonstrate language impairment in individuals with BPP, only one study[46] has formally assessed speech sound production or oral function in this population. Despite 26 studies reporting the presence of dysarthria, Kim et al.[46] was the only study to methodically assess the characteristics of dysarthria in a small case series. While there have been some preliminary reports of clinical speech deficits such as articulation errors, limited data is available regarding the functional implications of speech production deficits, such as intelligibility. This is critical in order to for clinicians to interpret and design appropriate therapy targets. The speech production and oral functional phenotypes in BPP are currently based on observational reports of impairment rather than a fine-grained quantitative approach. While the availability of validated assessment tools to measure such domains is limited, thorough description of speech characteristics across a large cohort would assist in gaining a more comprehensive understanding of this phenotype.

A critical question is whether the topography of BPP correlates with the severity of speech or language impairment. Seven studies found an association between diffuse BPP and more severe language impairment, compared with milder impairment in the setting of restricted BPP.[4,17,20,29,31,33,45] However, one study demonstrated no significant correlation between extent of BPP and severity of language impairment, the only study to use statistically substantiated evidence (Spearman's rank correlation coefficient with two-tailed *p*-values).[19] Two studies demonstrated unilateral and bilateral absence of the arcuate fasciculus, a tract critical for speech and language impairment, in participants with BPP and varying degrees of language impairment.[48,49] The presence of pseudobulbar signs was associated with diffuse BPP in comparison to BPP restricted to posterior parietal regions only.[17] As formal speech production assessments have not been performed, direct correlation of the topography and severity of BPP with the severity of speech sound impairment has not yet been examined.

The paucity of fine-grained studies detailing the speech and language phenotype of BPP highlights the need for further formal, systematic assessment, in order to better understand the communication profiles of individuals with BPP, a major malformation of cortical development. Such an investigation should include individuals across the full range

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of cognitive abilities, encompassing standardized assessment measures and validated scales of language and speech ability. Thorough prospective characterization and description of speech characteristics including dysarthria, articulation, and intelligibility, as well as oral structural and functional deficits must be included. Speech, language, and oromotor deficits are common in BPP. Improving their characterization will inform the development of targeted therapies and lead to better long-term outcomes.

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The authors have stated that they had no interests that might be perceived as posing a conflict or bias.

Supporting information

The following additional material may be found online:

Table SI: Details search strings

Table SII: Methodological characteristics of included studies

Table SII: Literacy, cognition and general health characteristics

Table SIV: Speech phenotype

Table SV: Language phenotype

Table SVI: Oral structural and functional phenotype

Figure S1: Flow chart outlining study selection process

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Table I: Number of studies reporting impairment in speech, language, oral structure and function, literacy, and cognitive domains

Phenotypic domain	Phenotypic feature	Number of studies reporting impairment in at least one participant (*n*=48)
Speech	Generalized difficulty	36
	Speech sound production (articulation and phonology)	11
	Altered resonance	4
	Disfluency	2
	Dysarthria	24
Language	General	33
	Delay	20
	Non-verbal	8
	Use of AAC	4
	Receptive	7
	Expressive	18
	Semantic	2
	Syntactic	3
	Phonological awareness	3
	Pragmatics	1
Oral structure and function	General	45
	Pseudobulbar signs	17
	Reduced mobility of tongue	14
	Palatal structural or functional impairment	10
	Feeding/swallowing	29
	Drooling	24
Literacy	General	7
	Reading	5
	Writing	4
Cognition	Cognitive impairment (>1 SD below the mean)	26

AAC, augmentative and alternative communication.

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